TREATMENT MODALITIES FOR PELVIC GIRDLE PAIN IN PREGNANT WOMEN

Helen Elden

UNIVERSITY OF GOTHENBURG

Perinatal Center
Department of Obstetrics & Gynecology
Institute of Clinical Sciences
Sahlgrenska Academy

Göteborg, Sweden
2008

To
Ingegerd, Vera, Karin,
Viran, Elsa, Olga, Inga and
Sofie the most significant
women in my life.

and Peder the most
significant man in my life

CONTENTS

ABSTRACT

TREATMENT MODALITIES FOR PELVIC GIRDLE PAIN IN PREGNANT WOMEN

Helen Elden

Department of Obstetrics and Gynaecology. The Institute for Clinical Sciences, Sahlgrenska Academy, Göteborg University, Göteborg, Sweden

BACKGROUND: Pelvic girdle pain (PGP) affects about 20% of pregnant women. It causes great suffering for the individual and high costs for society. Persisting PGP have been reported in 10 to 75% three months after pregnancy and some women have also stated that PGP has been the beginning of a chronic condition. Risk factors for PGP are history of low back pain, history of PGP or trauma to the pelvis. Available evidence of research of treatment for the condition is insufficient to recommend any particular treatment modality for PGP. Also, the use of acupuncture for PGP is sparse due to insufficient documentation of adverse effects of this treatment in this specific condition. The main purpose of this thesis was to study efficacy, safety and post pregnancy effects of standard treatment, acupuncture and stabilising exercises given to pregnant women with PGP. Based on this knowledge, our ultimate aim is to increase our knowledge about treatment of PGP. **METHODS:** Paper I reports on a randomised single-blind trial comparing efficacy of standard treatment plus acupuncture, standard treatment plus stabilising exercises and standard treatment alone in 386 pregnant women with diagnosed PGP. Paper II is a follow up study of the original randomised trial in which adverse effects during pregnancy and delivery, influence on the mother, fetus, pregnancy and the pregnancy outcome are reported. Paper III describes regression of PGP during 12 weeks after pregnancy among these women. Paper IV reports on a double-blind randomised trial in which effects of penetrating acupuncture and non-penetrating sham acupuncture as adjunct to standard treatment are compared in 115 pregnant women with diagnosed PGP. The aim with this study was to investigate if specific treatment effects of penetrating acupuncture go beyond effects of non-specific effects and individual attention. **RESULTS: A**cupuncture as well as stabilising exercises as adjunct to standard treatment constituted efficient complements to standard treatment for the management of PGP during pregnancy. Acupuncture administered with a stimulation that may be considered strong lead to minor adverse complaints on the mothers but had no observable severe adverse influences on the pregnancy, mother, delivery or the fetus/ neonate. Regression of PGP after delivery was excellent with no differences in recovery between the three treatment groups. Both penetrating acupuncture and non-penetrating sham acupuncture lead to clinically relevant decrease of median pain after treatment but there were no significant difference between groups. Those who had received penetrating acupuncture were in regular work to a higher extent than those women that received non-penetrating sham acupuncture. The penetrating acupuncture group had superior ability in 7 of 13 daily activities (dressing; outdoor walks; climbing stairs, standing bent over a sink; running; heavy work and lifting heavy objects) than the non-penetrating sham acupuncture group. **CONCLUSION:** We have shown that acupuncture and stabilizing exercises as adjunct to standard treatment are effective for PGP during pregnancy. Even if our study was of insufficient size to exclude negative effects on delivery, perinatal morbidity and mortality as well as on CTG the study result adds support to the view that acupuncture even with stimulation that may be considered as strong is not accompanied by any severe adverse influences on the pregnant women or the fetus/neonate. Even if more studies are required, our data provides the most comprehensive data reported to date. Our data suggest that irrespective of treatment modality, regression of PGP occurs in the great majority of women within 12 weeks after delivery. Penetrating acupuncture had no additional effect on PGP reduction compared to non-penetrating sham acupuncture but it improved the ability to perform daily activities keeping more women in regular work. Thus, the data imply that needle penetration contributes to the previously reported beneficial effects of acupuncture.

KEY WORDS: Pelvic girdle pain**,** pregnancy, acupuncture, non-penetrating sham acupuncture, stabilising exercises, randomised controlled trial.

POPULÄRVETENSKAPLIG SAMMANFATTNING PÅ SVENSKA

Var femte gravid kvinna drabbas av bäckensmärta (BS). Tillståndet innebär stora obehag för individen och leder ofta till sjukskrivning och därmed till höga kostnader för samhället. Det har rapporterats att en stor del andel har kvar besvären tre månader efter förlossningen. Risken för att utveckla BS under graviditet ökar om kvinnan haft besvär från ländryggen eller bäckenet tidigare och om hon utsatts för trauma mot bäckenet. Effektiv behandling saknas. Akupunktur har använts sparsamt eftersom dokumentation saknas av eventuella skadliga bieffekter. Syftet med den här avhandlingen var att jämföra de kliniska effekterna av standardbehandling, akupunktur och stabiliseringsträning för behandling av BS under graviditet samt jämföra akupunktur med placebo akupunktur.

I studie ett inkluderades 386 gravida kvinnor. De lottades slumpmässigt till standardbehandling, standardbehandling plus akupunktur eller standardbehandling plus stabiliserande sjukgymnastik under sex veckor. Standardbehandlingen innebar individuell information om tillståndet, ergonomiska råd, ett mjukt bäckenbälte samt ett hemträningsprogram med övningar med syfte att stärka musklerna som stabiliserar bäckenet. Syftet med akupunkturen var att ta bort smärtan och på så vis förhindra utveckling av muskeldysfunktion. Akupunkturstimuleringen var stark jämfört med tidigare studier på gravida. Syftet med den stabiliserande sjukgymnastiken var att få en god hållning och en optimal muskelstabilisering av bäckenet och på så vis bibehålla muskelfunktion. En mer effektiv smärtlindring erhölls efter både akupunktur och stabiliseringsträning jämfört med standardbehandling och förbättringen kunde bekräftas av en oberoende undersökare.
I en uppföljningsstudie, studie två, studerades påverkan av ovanstående behandlingsregimer på mor, graviditet, foster, förlossning och det nyfödda barnet. Resultaten visade att mindre allvarliga biverkningar i samband med akupunktur var vanliga hos modern men däremot noterades ingen allvarlig påverkan på modern, graviditeten, fostret, förlossningen eller det nyfödda barnet. Allvarliga komplikationer under graviditet och förlossning är ovanliga vilket innebär att den aktuella studien saknade statistisk styrka att helt kunna utesluta allvarlig påverkan.
I en tredje studie studerades effekterna av behandlingen efter förlossningen. Resultaten visade på en utmärkt prognos oberoende av vilken behandling kvinnorna fått under graviditeten. Tre av fyra kvinnor var smärtfria tre veckor efter förlossningen och endast fyra kvinnor hade kvarvarande BS 12 veckor efter förlossningen.
I en fjärde studie randomiserades 115 kvinnor till standardbehandling plus akupunktur med penetrerande nålar (”vanlig” akupunktur) respektive till standardbehandling plus akupunktur med icke-penetrerande nålar (”ytlig stimulering”) under åtta veckor. Kvinnorna var ovetande om vilken behandling de hade fått. Lika god smärtlindrig erhölls i de båda behandlinggrupperna. Hos kvinnorna som fått ”vanlig” akupunktur ökade förmågan att utföra dagliga aktiviteter (påklädning; promenera; gå i trappor; stå framåtböjd; springa; tungt arbete och tunga lyft) och en större andel var i arbete jämfört med kvinnorna som fått den ytliga formen av akupunktur.

Sammanfattningsvis visade våra studier att akupunktur och stabiliseringsträning är effektiva för behandling av BS under graviditet. Trots att studien saknade styrka för att helt kunna utesluta en ökad risk för förtidsbörd och andra ovanliga komplikationer så kan resultaten bidra till att minska rädslan för att behandla gravida kvinnor med BS med akupunktur. Vi kunde också visa att gravida kvinnor med BS tillfrisknar snabbt efter förlossningen. Den ökade möjligheten att kunna utföra dagliga aktiviteter efter penetrerande akupunktur indikerar att djupet av nålstimuleringen spelar roll för den tidigare rapporterade positiva behandlingseffekten av akupunktur.

This thesis is based on the following original papers, which will be referred to in the text by their Roman numerals:

I **Elden H, Ladfors L, Olsen MF, Ostgaard HC, Hagberg H**. Effects of acupuncture and stabilising exercises as adjunct to standard treatment in pregnant women with pelvic girdle pain: randomised single blind controlled trial. *BMJ* 2005;330 (7494):761-764.

II **Elden H, Ostgaard HC, Olsen MF, Ladfors L, Hagberg H.** Treatment of pelvic girdle pain with acupuncture: adverse effects during pregnancy and delivery. *Submitted.*

III **Elden H, Hagberg H, Olsen MF, Ladfors L, Ostgaard HC**. Regression of pelvic girdle pain after delivery: follow- up of a randomized single blind controlled trial with different treatment modalities. *Acta Obstet Gyn Scand.* 2008; 87: 201-208.

IV **Elden H, Olsen MF, Ostgaard HC, Stener-Victorin E, Hagberg H.** Acupuncture as an adjunct to standard treatment for pelvic girdle pain in pregnant women: randomised double blind controlled trial comparing acupuncture with non-penetrating sham acupuncture. *Submitted.*

ABBREVIATIONS

ACU	Acupuncture treatment
Ah shi points	tender points
AS	Apgar Score
ASLR-test	Active Straight Leg Raising test
BMI	Body mass index
BL	Bladder channel
CES-D	The Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
CNS	Central Nervous System
CTG	Cardiotocography
CGRP	Calcitonin Gene-Related Peptide
De-qi	A special sensation after insertion of the acupuncture needle described as: tension, numbness, heaviness, muscle fatigue, light pain, soreness, tingling and/or warmth in the region of the needle penetration, and often a radiating sensation from the point of insertion.
DNIC	Diffuse Noxious Inhibitory Control system
DRI	Disability Rating Index (function)
DPQ	The Dutch personality Questionnaire (Psycho social factors)
EA	Electro-Acupuncture
EDA	Epidural analgesia
ES-D	Emotional and sexual relation ship with the partner
EQ-5D	European Quality of life 5 dimensions Questionnaire (Quality of Life)
EQ-5D VAS	European Quality of life health thermometer (Quality of Life)
GB	Gall Bladder channel
GV	Governor Vessel channel
g.w.	Gestational weeks
HRQL	Health-related quality of life (Quality of Life)
IASP	International Association for the Study of Pain
KEBK	Questionnaire (Pain).
KI	Kidney channel
LI	Large Intestine channel
MBHI	Million behavioural health inventorial manual (Function)
MMQ	The Maudsley Marital Questionnaire (Marital and sexual adjustment)
MRI	Magnetic resonance imaging
NA	Noradrenaline
NRM	Nucleus Raphe Magnus
NRS	Numerical Rating Scale
NHP	Nottingham Health profile (Quality of Life)
LBP	Low Back Pain
NS	Not significant
ODI	Oswestery Disability Index (Function)
PAG	Peri Aqueductal Greyr
PGP	Pelvic Girdle Pain
PGR	Symptom-giving Pelvic Girdle Relaxation
P4	Posterior Pelvic Pain Provocation test
PI	Pelvic Instability
PJS	Pelvic Joint Syndrome
PMI	Pregnancy Mobility Index (Function

pp	Postpartum
pp-test	Pain provocation tests
PPP	Posterior Pelvic Pain
QBPDS	Quebec Back Pain Disability Scale (Pain and function)
QUALY	Quality Adjusted Life Years
RCT	Randomised Controlled Trial
RDQ	Roland Disability Questionnaire (Function)
RPT	Registered Physiotherapist
S	Standard treatment
SI	Sacroiliac
SD	Standard Deviation
SE	Stabilizing Exercises
SP	Substance P
ST	Stomach channel
TCM	Traditional Chinese Medicine
TENS	Transcutaneous Electrical Nerve Stimulation
yrs	Years
VAS	Visual Analogue Scale
VIP	Vasoactive Intestinal Polypeptide
VRS	Verbal Rating Scale
VS	Versus
wks	Weeks
5-HT	5-hydroxytryptamine (serotonin)
WHO	World Health Organization

BACKGROUND

Pelvic girdle pain (PGP) during pregnancy is a common complaint for women all over the world [1-16], irrespectively of the socio-economy of the countries. PGP has been frequently dismissed as trivial and inevitable although it significantly affects quality of life [17 18] and causes considerable disabilities in daily activities such as walking, lifting, climbing stairs, lying flat on the back, turning in bed, housekeeping, exercising, working, during leisure, hobbies and sexual life [18-25]. PGP increases with advancing pregnancy and in one of three women the pain gets severe [23 26]. Fear of development of this pain can be reason to avoid a new pregnancy [27 28] and some women have stated that PGP was the beginning of a chronic condition [29 30]. The syndrome also has a considerable social impact because of the high cost for society since it is one of most common causes to sick-listening among pregnant women [31-33]. A number of possible risk factors for PGP during pregnancy are mentioned in the literature: high fetal weight, maternal weight[34] multiparty, age, oral contraceptives, smoking behaviour, pelvic pain during earlier pregnancies, previous episodes of low back pain (LBP), sex of child [28], oral contraceptives [35], in-vitro fertilization [36] and strenuous work [23]. Evidence remains for previous LBP, previous PGP and previous trauma to the pelvis [37].

A historical perspective of PGP

Back pain during pregnancy was first described by Hippocrates (c.460- c.377 BC).who had a hypothesis that an irreversible relaxation and widening of the pelvis occurred during the first pregnancy, which led to instability of the sacroiliac joints, and subsequently a symptomatic inflammation [38]. In Sweden, observations reporting of such pain were described in 1839 by the physician Cedersjöld, who postulated that softening of joints and ligaments of the pelvis was due to the pregnancy and that it caused an instability of the pelvic joints which led to pain in the pelvic region. Other well-known symptoms recognized today as pain when turning in bed and difficulty in walking was also observed. Cedersjöld described that the pain could be eased after application of a girdle, which should be placed around the pelvis and narrowed as tight as the women could tolerate. This application of the girdle was also used as a diagnostic tool. Thus, if the girdle did not ease the pain, the diagnosis could be excluded[39].

Back pain during pregnancy has been called*: low back pain, backache, symptom-giving pelvic girdle relaxation, symphysiolysis, back pain, peripartum pelvic pain, pelvic pain, pelvic joint instability, posterior pelvic pain, pelvic instability, pregnancy-related pelvic pain, sacroiliac pain and SI-joint dysfunction.*

Scientific knowledge of PGP has increased over the past 20 years. Data support the concept that pelvic pain during pregnancy is a specific form of back pain that differs from back pain in non-pregnant women and men. A guideline working group, the World Group 4, European Cost Commission, consisting of experts in the field was founded with the aim of formulating grounds to support the proposition that this condition is a specific form of back pain. This work resulted in the newly published guidelines, The European Guidelines for the diagnosis and treatment for PGP [37], which declare that there is a need for a term that describes the pelvic musculoskeletal pain and excludes gynaecological and/or urological disorder. The new term is Pelvic girdle pain (PGP) and it is defined as follows:

"Pelvic girdle pain generally arises in relation to pregnancy, trauma or reactive arthritis. Pain is experienced between the posterior iliac crest and the gluteal fold, particularly in the vicinity of the sacroiliac joints. The pain may radiate in the posterior thigh and can occur in conjunction with/or separately in the symphysis. The endurance capacity for standing, walking and sitting is diminished. The diagnosis of PGP can be reached after exclusion of lumbar cases. The pain or functional disturbances in relation to PGP must be reproducible by specific clinical tests".

This definition is comparable to Ostgaards earlier classification of pregnancy-related posterior pelvic pain [40] used in this thesis except for isolated symphyseal pain included in the guidelines, as PGP. This thesis describes treatment effects for the specific back pain seen in pregnant women classified according to Ostgaards criteria.

The pelvic structures and stabilization of the sacroiliac (SI) joints

Knowledge of the regional anatomy of the pelvis is important for understanding PGP. The pelvis consists of two iliac or "hip" bones joined to a wedge shaped bone, called the sacrum. The two hip bones are connected at the front by the symphysis pubic. The joints between the sacrum and the hip bones at the back are the sacroiliac joints. These joints are stabilised by a dense network of ligaments, which means that under normal conditions, very little movement occurs. Normally, when we are lying or standing the pelvis is in a locked or stable position but during walking, mobility as well as stability in the pelvis must be optimal, i.e. there is a need for an intermittent stability of the SI- joints that makes the pelvic stable when loaded and moving when un-loaded. The stabilization of the sacroiliac joints is improved by a 'selfbracing and self-locking mechanism' of the SI joints also described as the "form closure" [24 41] and the "force closure" [24 41-43] (Fig. 1). The locking ability of the SI-joints is accomplished by the irregular joint lines. The force closure consists of several mechanisms. Firstly, nutation (forward rotation) of the sacrum occurring during loading situations such as moving from laying supine to sitting and standing increase tension of the posterior ligaments leading to more compression of the joint surfaces and thus more stability of the SI joints [44]. Secondly, compression of the SI-joints is increased by the thoraco-lumbar fascias and muscles [8] Two muscles that are strongly connected to the ligaments around the SI- joint are the multifidus muscle and the transversus abdominis muscle. It has been found that contraction of the transversus abdominis muscle stiffens the SI-joints [45] and that co-contraction of the multifidus muscle and the transversus abdominis muscle even improves lumbar stability [42]. These muscles are both lumbar stabilizers and pelvis stabilizers and the pelvic floor is most likely also involved in the dynamic stability of the lumbar-pelvic region [42 46].

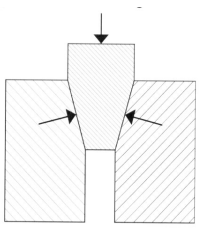


Fig. 1. Form and Force closure

Etiology

PGP can begin as early as 8-12 weeks of pregnancy or within three weeks after delivery [37].The condition is a complex disorder and underlying mechanisms remain unclear. Different hypotheses of patophysiology have emerged indicating that etiology is multifactorial and poorly understood. In order to prepare for the fetal passage through the pelvis there is an increase of the hormone relaxin in the blood [36]. Secretion starts early in pregnancy and affects the laxity of ligaments in the pelvic girdle [44], that will lead to a less stable pelvis. Also, as the pregnancy advances, the abdominal diameter will increase and in some women the elongated weakened abdominal muscles will lead to insufficient muscle force in dynamic stabilization of the SI-joints. This concept is supported by studies showing a dysfunction of back muscles among back pain patients [47] and among pregnant women with PGP [8 48 49]. On the other hand, conflicting results regarding changes in relaxin hormone levels exist [50-53] and there is no absolute relationship between PGP and increased motion in the pelvic joints [44 54] . Some women

appear to be capable to handle this increased range of motion by an improved muscle function whilst other women cannot. In conclusion, the increase of joint motion is small and not a problem per se. There is strong evidence that pain is derived from insufficient tense muscles. There is some evidence that pain is derived from ligaments. However, there is no evidence that pain is derived from the bony parts of the SI-joints. It has been suggested that regain of muscle control is important for reduction of development of muscle weakness and thereby reducing PGP [37].

Prevalence

Previous research has found that every other women experience LBP and/or PGP during some time of their pregnancies. However, great variation (range from 4% to 90% median 50%) in prevalence has been reported [3 40 55-57 2 9 22 58-64]. In four studies (4.724 participants in total) in which specific tests were used to confirm the diagnosis [22 40 65] a point prevalence of 20,1% of PGP was reported. Most women recover from PGP within 3 months post partum (Table 1). However, follow-up studies have shown that 10-75% of the women had persisting pain 1-3 months after delivery [6 18 21 29 55 56 66-70] and that 5-75% experience pain and reduced daily activities one year or more after delivery [21 71]. About 7% has persisting serious PGP and/or LBP at 2 years as well as 6 years postpartum[72]. Only a minority of women improve after the first 6 months [72]. The reason for the discrepant results related to PGP during pregnancy as well as postpartum probably reflect that some of the studies are prospective and some are retrospective and that different diagnostic tools and criteria have been used and also that woman with lumbar pain have been included as well. In addition, the diagnosis in most of the studies is mostly based on self-reports through questionnaires or interviews which is insufficient when differentiating between LBP and PGP [24].

Table 1. Summary of published studies reporting of regression of LBP and/or PGP after pregnancy

Author	Criteria used	Original design and number of participants	Follow-up time and measuring instrument	Results
Berg et al [59]	All pregnant women attending antenatal clinics	Prospective cohort study (n=862)	***6-12 months pp.*** self reported pain. pp-tests	9% had severe back pain at 6-12 months pp.
Ostgaard et al. Noren et al [20 26 72-74]	All pregnant women attending antenatal clinics	RCT study (n=855) 362 received treatment	***18 months, and 6 yrs pp*** Pain (VAS) Pain drawing **3 years pp:** Physical examination; Pain-drawing, Pain (VAS) during 3 daily activities	37 % had back pain and 7 % of them had serious back pain 18 months pp.. 20% had back pain. 13% of them had PGP or combined PGP /LBP 3 yrs pp. 16 % had back pain 6 yrs pp.
Kristiansson [58]	All pregnant women attending antenatal clinics	Prospective cohort study (n=200). 15-20% got pain-relieving treatment during pregnancy	***12 wks pp***: Back status including pp-tests. Pain-drawing, Pain (VAS), DRI	9,4% had back pain 12 wks pp.
Larsen et al. [22]	All pregnant women attending antenatal clinics with PGR and pain in 2/5 daily activities	Prospective cohort study (n=227)	***2, 6, 12 months pp*** Interview, clinical examination, pp-tests	5%, 4 % and 2 % had pain 2, 6 and 12 months pp respectively.

Table 1 continued				
Turgut et al. [16]	Women with back pain during index pregnancy	Prospective cohort study (n=88)	***0, 1, 3 6 months pp*** Pain (VAS) Location of pain	59 %, 55%, 46 % and 43% had back pain at 0, 1, 3 and 6 months pp respectively.
Brynhildsen et al. [27]	LBP during pregnancy that required sick leave	Prospective cohort study of women with LBP during pregnancy (n=62) compared to. controls (n=84) without LBP	***12 yr pp*** Pain drawing	85% of the women with LBP during pregnancy had recurrent LBP when not pregnant compared to 64% of controls.
To and Wong [15]	Consecutive patients with singleton pregnancies	Prospective observational cohort study (n=326)	***24 months pp*** Pain-drawing, VAS, need for sick-leave	40/189 (21 %) women had persistent unspecific back pain 24 months pp..
Lindal et al. [55]	Consecutive patients	Prospective observational study (n=111)	***3 months pp*** Self reported pain (VAS), Smoking Birthweight	54 % had persistent LBP. Smokers had more LBP. Birthweight did not affect the risk of LBP.
Albert et al. [75],	Pain in one or more of the pelvic joints confirmed with unspecified objective findings	Prospective observational study (n=341)	***1,3,6,12,18 and 24 months pp*** Physical examination including pp-tests	63% were pain free 1 month pp and 8,6 % had symptoms and objective findings 2 yrs pp.
Nilson –Wkmar et al. [21]	PGP < 35 g.w. ≥ 3 pp-tests positive	Intervention study A: information (n=40) B: A +Home exercises (n=41) C: A + in clinic exercises (n=37).	***3, 6 and 12 months pp***. VAS DRI	43 % (A),65% (B) and 66% (C) had back pain 3 months pp. 25 % (A), 29% (B) and 68 % (C) had back pain 6 months pp. 52 % (A), 58 % (B) and 57 % (C) had back pain 12 months pp.
Padua et al. [76]	Women in their 8th and 9th months of pregnancy with unspecific back pain	Observational study (n=76)	***1 yr pp***. RDQ, age, weight gain during pregnancy LBP before pregnancy, sex of fetus	41/57 (71%) had unspecific back pain 1 yr pp. Male fetus was related to back pain.
Van de Pol et al. [56]	All women attending antenatal ward with singleton low risk pregnancy	Longitudinal cohort study 672 /1244 (54%) women participated in the study	***3 months plus 1 year pp*** Self reported pain, sick-leave, Pain drawing, PMI, DPQ, ES-D, MMQ, Sick-leave	4.4% and 2.4 % of women with PI had persisting pain 3 months and 1 year pp respectively.

Table 1 continued				
Hansen et Al. [29]	Pain in the lower back when performing at least two of five daily activities and a positive Patrick's Faber test	Observational study n=58 of 227 women with PGR during pregnancy compared to 20 controls. Women with PGR were examined regularly until recovery or 12 months pp	***2, 6 and 12 months pp*** Physical examination including Patrick's Faber test at 6 & 12 months pp MBHI, X-rays of pelvis and lower spine. MRI of the pelvis. Gynecologic examination, test of hypermobility, blood analysis, urine dipsticks	25% had PGR > 4 months pp. MBHI showed an overrepresentation of pain-related traits in the PGR group
Gutke et al. [77]	Typical pain drawing ≥2 positive pp-tests Women with isolated symphyseal pain were not classified as having PGP	Prospective cohort study (n=262) 46/262 of the women received some sort of treatment	***3 months pp*** Physical examination pp-tests. Pain drawing, Pain (VAS). 5Q-5D, 5Q-5D-VAS, ODI, Trunk muscle endurance, hip extension and gait speed.	17 % had PGP, 10% had LBP and 6% had combined PGP and LBP 3 months pp. The combination had the worst prognosis
Rost et al. [69]	Women with back pain during index pregnancy	Cohort study (n=430) of exercises and postural advice	***18 months pp*** Pain and disability	10% had back pain 18 months pp.
Bastianenen et al. [6].	Women >18 years that wanted treatment for back pain 2 weeks after delivery.	869 women from a prospective observational study	***3 wks pp***. Pain, limitations in activities, clinical examination to exclude specific pathology	126/ 869 (14,5%) complained of back pain 3 wks pp
Mogren [78]	Pain in the lower back > 1 week and a typical pain drawing	Prospective observational study (n=464 /639, 77 %)	***6 months pp*** Pain drawing, sick leave	43 % had persistent LBP and 20 % had been on sick-leave 6 months pp.
Morkved et al .[4]	Nulliparous ≥ 20 g.w. Typical paindrawing Self reported pain	Intervention study (n=301)	***3 months pp*** Self reported pain, sick-leave, Pain drawing, and functional status.	26 % of the women that received training had unspecific back pain vs. 37% of controls 3 months pp.

Pain

Pain is defined by the International Association for the Study of Pain (IASP), as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described with such damage [79]. It is a warning signal essential for survival and intimately related to homeostasis [80]. Pain could be classified into different categories with specific characteristics: nociceptive pain: transient pain in response to noxious stimulus; inflammatory pain: spontaneous pain and hypersensitivity to pain in response to tissue damage and inflammation; neuropatic pain: spontaneous pain and hypersensitivity to pain in association with damage to or a lesion of the nervous system; and functional pain, which is hypersensitivity to pain resulting from abnormal central processing of normal input[81]. Pain can be acute or chronic; the latter defined as pain lasting more than three months. It is important to consider that pain does not only originate from the syndrome it is a subjective experience affected of a combination of emotional, physiological, cognitive, environmental and social factors [82].

Symptoms of PGP

PGP may be concentrated in the buttock area and it may shift localization from side to side and can also be accompanied by pain in the symphysis. PGP may be stabbing and/or dull and sometimes sending shooting pains down the back of the legs but not down to the foot. It is usually made worse by prolonged standing and/or sitting and when turning in bed. PGP is often worse in the evenings and at night and the degree of evening pain is often related to amount of activity during the day. In some women the legs may feel very weak and a typical sudden difficulty (locking) in moving one or the other leg forwards when walking can be experienced. This symptom has been found to be specific for PGP and is named “Catching of the leg” [49].

Diagnosis

Diagnosis can only be reached after exclusion of lumbar causes, which should be based on both reports from the women and the physical standardised examination including specific clinical tests which reproduce pain in the pelvic girdle (Fig.3) [3 23 37 40 83-85]. The European Guidelines for the diagnosis and treatment for PGP does not recommend palpation tests, x-ray, CT, scintigraphy, diagnostic injections and diagnostic external pelvic fixation for the diagnosis of PGP [37]. The posterior pelvic pain provocation test [85 86] and Patrick’s Faber test [85] have superior sensitivity if pain is evident in the SI-joints. Modified Trendelenburg’s test [85] and palpation of the symphysis [85] are superior with regard to sensitivity if the pain is evident in the symphysis. The tests have high intertester reliability [85 86]. Straight leg test or Lasegue test can be used to exclude nerve root syndrome. As a functional test, the Active Straight Raising leg (ASLR) test is recommended. This test has been reported to be an appropriate diagnostic test to discriminate between patients who are disabled by PGP and healthy subjects. The test is easy to perform and reliability, sensitivity and specificity are high [8]. PGP can be divided into subgroups depending on the number of affected joints in the pelvic girdle [65]. Women with pelvic girdle syndrome i.e. bilateral SI pain plus symphysiolysial pain have been found to have the worst prognosis; those with isolated symphysiolysial pain the best [75].

Treatments

Several treatments have been evaluated for treatment of LBP and/or PGP during pregnancy (Table 2-3). The guidelines [37](searching until 2004) recommend exercises and individualized treatment program focusing on specific stabilising exercises and state that information, massage and pelvic belt can be used as a part of multifactorial individualized treatment program and also that acupuncture during pregnancy may reduce PGP although higher quality studies are needed. A more recent updated systematic Cochrane review [87] (searching until 2006) including eight studies (1305 patients) agree that pregnant specific exercise programs, physiotherapy and acupuncture added to usual care can be helpful to reduce back or pelvic pain during pregnancy. Only two studies on interventions in women

with PGP and or LBP post partum have been performed [88 89]. The study by Mens et al. showed no effect of a stabilising program while the stabilising program used by Stuge [88] et al. showed favourable effects that lasted 2 years after delivery [89].

Table 2. Previous studies with reference to treatments (other than acupuncture) for lumbo-pelvic pain during pregnancy. Studies on solely symphysiolysis are excluded and studies of acupuncture for lumbo-pelvic pain are presented separately in Table 3.

Author	Intervention	Inclusion criteria	Design and number of participants	Measuring instrument	Results
Mantle et al. [90]	A: Information , ergonomic advice, abdominal muscles and pelvic floor contractions and, pelvic tilting vs. B: No treatment	All women attending antenatal care > 16 g.w.	Prospective controlled study A: (n=85), 8 sessions B: (n=90)	Pain. infant weight	Both interventions relieved pain equally well
Berg et al. [59]	A: Pelvic belt vs. B: Mobilisation	Unspecific back pain	One-group design study A: (n=79) B: (n=10)	Pain	Both interventions relieved pain equally well
Thomas et al. [91]	A: Ozzlo pillow vs. B: Standard pillow	Low-risk pregnancy ≥36 g.w.	RCT Cross-over trial (n=109) One wk each with A and B	Pain (VAS) Sleep (VAS)	A relieved pain better than B. No difference with regard to insomnia
Ostgaard et al. [32]	A: = Controls: Classes with information, ergonomic advise and exercises vs. B: Individual lessons or C: No treatment	All women attending two antenatal clinics	Quasi-RCT A: 5 x 30 min (n=139) B: 2 x 45 min (n=123) C: (n=145)	Pain (VAS) Pain drawing Sick-leave	Pain-related problems were reduced in groups B and C, and sick-leave was reduced in C. A non-elastic SI- belt offered some pain relief in 82% of the women with PPP.
Ostgaard et al. [31]	Classes with information, ergonomic advise and exercises vs. controls	Women with back pain and controls without back pain	Prospectie coort study A: (n=54) B (n=81)	Sick-leave	Sick leave for lumbar back and PPP in the intervention group was significantly reduced with the program.
Dumas et al. [12]	A: Aerobic exercises vs. B: No treatment	Non smoking > 12 g.w.	Prospective consecutive study A: (n=27) B: (n=38)	Posture Knee laxity Pain (NRS) Functional limitations during pregnancy and pp	No difference between groups during pregnancy or pp

Table 2 continued					
Noren et al. [20]	A: Individual advice and physiotherapy vs. B: No treatment	LBP or PPP verified with clinical examination	Prospective consecutive study A:5 visits to the RPT (n=54) B: (n=81)	Pain (VAS) Pain drawing Sick leave	Fewer women in A were on sick leave
Field et al. [92]	A :Massage therapy vs. B: Relaxation therapy	Unspecific back pain	RCT A: (n=14) B: (n=12)	Pain (VAS), Anxiety, attitude, depression, and sleep. Urine samples assayed for cortisol, catecholamine's and serotonin Delivery outcomes	A reduced anxiety, improved mood, sleep and reduced pain better than B
Kihlstrand et al. [93]	A. Water-gymnastics & relaxation Vs. B: No treatment for prevention of back pain/LBP	Unspecific back pain at 17 - 22 g.w.	RCT A: 30 min plus 30 min 3t/wk. (17-20 times) (n=129) B: No treatment (n=129)	Pain intensity (VAS) Sick-leave Weight gain; Pregnancy outcome, infant weight	Decreased sick-leave in A compared to B. No other difference in pregnancy outcomes between groups
Suputtitada et al. [94]	A. Sitting pelvic tilt exercises vs. B: No treatment	Primigravida healthy women at 26-30 g.w.	RCT A: 30 min exercises plus 30 min relaxation 3 t/week until delivery (n=42) B: (n=42)	Pain (VAS) Pregnancy length, AS at 1, 5 minutes Safety	Decreased back pain in A compared to B No negative effects on mother, delivery or fetus/neonate in both groups
Nilson –Wkmar et al.e t al. [21]	A: Information + nonelastic SI belt vs. B: Same as A+ home exercises or C: Same as A+ In clinic exercises	< 35 g.w. ≥ 3 positive pp-tests confirming PGP	RCT A: (n=40) B: (n=41) C: (n=37).	Pain (VAS) DRI Pain drawing	No significant difference in pain or function during pregnancy or pp between the groups

Table 2 continued					
Garshabi et al [13]	A. Exercise vs B: No treatment	Primigravida, 20-28 years with unspecific back pain at 17 to 22 g.w.	RCT A: 3 t /wk (n=161) B: (n=105)	KEBK . Degree of lordosis and flexibility of the spine, weight gain; pregnancy length. infant weight	Decreased pain in A compared to B. No difference between groups in increased lordosis Weight gain., pregnancy length or infant weight
Martins et al. [95]	A. Specific stretching exercise in groups vs. B: Usual care	LBP and/or PPP	RCT A: (n=33) B: (n=36) Both for 8 wks	Pain (VAS)	61% in A reported total relieve of pain compared to 11% in B
Haugland et al. [71]	A: Education programme plus pelvic belt vs. B: No treatment	Pelvic pain at 18-32 g.w. Pos p4 test and/ or symphysis pressure test; absence of nerve-root syndrome.	RCT A: (n= 275) B (n=285)	Pain (VAS) at daily functions and pp- tests at 6 and 12 months pp	11 % and 7 % had much pain at 6 months and 12 months with no differences between groups.
Granath et al. [96]	A: Land-based physical exercises vs. B: Water aerobics for prevention of LBP and PGP	≥11 g.w. wks PGP according to Ostgaards criteria [31]	Quasi-RCT A: (n=198) B: (n=192) Both 1/wk during pregnancy	Number of women getting LBP or PGP, Days on sick-leave	Reduced LBP and days at sick-leave in B compared to A
Morkved et al. [4]	A: Exercises in groups vs. B: No treatment for prevention of lumbo-pelvic pain	Nulliparous ≥ 20 g.w. typical pain-drawing	RCT A: 1 hour/wk for 12 wks (n=148)- B: (n=153)	Selfreported lumbo-pelvic pain DRI Sick-leave	A reduced pain more than B during pregnancy No difference between groups 3months pp. Equal numbers on sick-leave
Kalus et al. [97]	A: Belly Bra vs. B: Tubigrip	Unspecific back pain 20-36 g.w.	RCT A (n=55) B: (n=60) Both interventions for 3 wks.	Pain severity (VAS), physical activity and satisfaction with life	Both interventions decreased pain equally well but A was better in alleviating the impact of pain on physical activities and reduced the use of analgesic medication better than B.

Acupuncture

Acupuncture (Latin Acus, needle an punctura, puncture) is a method of treatment that is an integral part of Traditional Chinese Medicine (TCM). Acupuncture has thousands years of history for pain relieve and treatment of diseases. The pain relieving effect has been studied from a Western scientific perspective during the last decades. It has been shown that activation of afferent nerve fibres with low frequency EA can cause an increase of opioid peptides (ß-endorphin) in cerebrospinal fluid in human subjects [98] and evidence for the involvement of the ß-endorphin system is that the pain relieving effect can be blocked by the opioid antagonist, naloxone [99]. Moreover, experiments have shown that when a nerve is blocked by local anaesthesia or cut off, acupuncture is ineffective in the parts supplied by that nerve, showing that acupuncture effects are mediated via afferent nerve fibres [100 101]. Results from anatomical and neurophysiological research together with reported beneficial result from randomized controlled studies lead to a decision by the authorities in Sweden to allow acupuncture for pain relief in 1984. Acupuncture has been reported to affect different components of perceived pain, i.e., to alleviate the sensory discriminative aspect (intensity) and to lessen the affective component (unpleasantness) of pain[102]. Acupuncture has been found helpful for a various of conditions such as nausea and vomiting in early pregnancy [103], pain during delivery [104], pain relief during oocyte aspiration [105-108] chronic neck pain [109], shoulder pain [110] osteoarthritis of the knee [111 112], chronic low back pain [113 114 115] tension-type headache [116], acute dental pain [117] migraine [118], dysmenorre [119], vasomotor symptoms in postmenopausal women [120-122] and that acupuncture given with embryo transfer improves rates of pregnancy and live birth among women undergoing in vitro fertilization [123].

Acupuncture involves penetration of the skin with thin needles at acupuncture points or trigger points "Ah Shi points". The standard acupuncture nomenclature published by the WHO listed about 400 acupuncture points and 20 meridians connecting most of the points [124]. The needles are placed in local points in the area of the pain in combination with segmental and extra-segmental distal points in the arms and legs. Both local and distal points could be manually and/or electrically stimulated. The afferent stimulation activates ergo-receptors transmitting information in A-beta or type II or III afferents into the spinal cord, and then to the sensory cortex, resulting in the perceived sensation of De qi. This sensation is described as tension, numbness, heaviness, warmth in the region of needle penetration and often a radiating sensation from the point of insertion.

It has been suggested that De-qi is essential for beneficial effects, that the needle placement is of importance and that six or more treatments with stimulation of six or more acupuncture points for about 20-40 minutes is important in achieving a positive result [100 125]. Because there is probably need for some duration of the stimulation to release opioid peptides or other transmitters [99]. However, there is no scientific evidence concerning how the needling should be administered and the most optimal doses the effects of acupuncture may be far less point-specific as has been previously suggested from available clinical evidence [115 126]. Physiological and psychological explanation of the effect of acupuncture is complex. There are several suggested mechanisms of action of acupuncture, which can be summarized as follows:

Periphery level

Insertion of the acupuncture needle induces release of a number of neuropeptides such as Substance P (SP), vasoactive intestinal polypeptide (VIP), and calcitonin gene-related peptide (CGRP), which results in vasodilatation and increased nutritional blood flow [127-129]. It has also been reported that the increased blood flow in the muscles caused by acupuncture may flush out the algesic or sensitizing substances and induce pain relief [130].

Segmental level

Pain inhibition at the segmental level is induced by the evoked De-qi sensation that activates A-delta and possibly C-fibres in the muscle [131]. This leads to an inhibition of nociceptive transmission in the spinal cord via pre- and postsynaptic inhibitory mechanisms, e.g. the gate control mechanism [132 133].

According to this theory, there is a physiological gate mechanism in the dorsal horn of the spinal cord in which sensory signals only can pass when the gate is open. Stimulation of muscle afferents in the area of pain arouses inhibitory interneurons in the dorsal horn and subsequently blocks the gate. An optimal effect is obtained by stimulating the somatic segments related to the pain, i.e. clinically effective local acupuncture points adjacent to the painful area; which will elicit the gate-control mechanism [134 135].

Generalized neurohormonal mechanism
Activation of A-delta and possibly C-fibres results in production and release of endogenous opioids, particularly ß-endorphin from the hypothalamic nucleus, the nucleus arcuatus, and the nucleus tractus solitarius in the brainstem [100 102 136 137].

Descending pain inhibitory systems
Activation of A-delta and possibly C-fibres stimulates the midbrain periaqueductal grey matter (PAG) to produce ß-endorphin and neurotensin and stimulates brainstem nuclei nucleus raphe magnus (NRM) to produce serotonin (5-HT) and noradrenalin, which in turn activate two pain-alleviating, descending neuronal pathways: the serotoninergic (5-HT) and the noradrenergic (NA) systems. These descending systems inhibit the nociceptive transmission at the spinal level in the dorsal horn by activation of inhibitory interneurons that release enkephalin and dynorphin at the spinal level. In addition ß -endorphin also affects a variety of extra-hypothalamic functions such as mood and immune function.

Diffuse Noxious Inhibitory Control system (DNIC)
Another possible mechanism in the pain relieving effect of acupuncture is that acupuncture activates the so called DNIC. This is a physiological system based on the theory that pain can be alleviated by painful stimulation at other areas then those where the pain was elicited. It has been reported that the endorphin system is involved in DNIC and that it is not necessary to apply the pain stimuli in the affected area as the pain modulating effect is unspecific and not related to the site of stimulation [138 139]. However, it is not clear whether this system is involved in the mechanism of acupuncture analgesia.

Oxytocinergic system
It has been suggested that the oxytocinergic system may be involved in the pain modulation activated by non-painful sensory stimulation such as acupuncture, massage, vibration, and thermal stimulation [140]. Oxytocin is produced and released from the hypothalamic paraventricular nucleus and projects to areas within the brain involved in regulation of pain, autonomic functions, and behaviour [141]. Central administration of oxytocin (intraventricular injection or intrathecal injection) has shown to enhance acupuncture analgesia in the rat, while central administration of anti-oxytocin serum weaken acupuncture analgesia in a dose-dependent manner [142] . However this has still not been shown in humans.

Unspecific treatment effect i.e. physiological effects
Acupuncture can also work in a vary of ways to reduce stress, by altering autonomic tone and psychoneuroimmunological state [101]. These findings are consistent with the results of mechanistic studies demonstrating that acupuncture analgesia occurs centrally through the release of endorphins and monoamines [143 144]. At present, there are some studies supporting the efficacy of acupuncture for LBP and or PGP. The results of these studies are encouraging, both in terms of pain relief and improved function (Table 3).

Table 3 .Summary of RCT's of acupuncture for PGP and/or LBP during pregnancy.

Author	Objective	Inclusion criteria	Intervention	Measuring instrument	Results
Wedenberg et al. [145]	A: ACU vs. B: individual-ized physical therapy	Unspecific back pain <32. g.w.	A (n=30) -10 needles during 10 sessions, mostly auricular acupuncture B: (n=30)	Pain (VAS) Function (DRI)	Significant improvement in pain and function in A. No significant changes in pain or function in B. Differences between groups not presented.
Guerreiro da Silva et al. [7]	A: ACU vs. B: Paracetamol and anti-spasmodic drug	Unspecific back pain at 15-30 g.w.	A: (n=27) = 8-12 sessions with 12 needles for 25 minutes B. (n=34)=	Pain (NRS) Function (NRS) Dosage of medication, Infant weight; AS	Significant decrease in pain and use of analgesic as well as increased function in A compared to B.
Kvorning et al. [146]	A. ACU vs. B: No treatment	Unspecific back pain in the 3:rd trimester of pregnancy	A: 10 x 30 minutes with 4-8 needles (n=44) B. (n=44)	Min - Max pain (VAS) Pain during 8 daily activities on a 3-point scale: G.w. at delivery; Infant weight; AS	Pain decreased significantly in A compared to B.
Lund et al. [147]	A. ACU vs. B: Superficial ACU	PGP diagnosis with pp-test 22-36 g.w.	A (n=35) B: (n=35) Both groups: 10 x 30 minutes with 10 needles	Pain (VAS) at rest and during three daily activities three times a day. NHP (pain)	Decreased pain intensity at rest and in daily activities, improvement in quality of life was reported in both groups with no differences between groups

Safety

Serious adverse events of acupuncture are rare in the hands of a competent practitioner [148-153] and it has been suggested that acupuncture is safe as a treatment option for women in early pregnancy [103]. However, the use of acupuncture in the second and third trimester of pregnancy is sparse due to several reasons. Firstly, it has been considered contraindicated to puncture points in the lumbosacral region, i.e. somatic segments according to the innervation of the uterus, (Th 10-L2, S2-S4) [154], or to stimulate strongly in pregnancy, as it may induce preterm labor [155-157]. Secondly, information about long-term safety of acupuncture for PGP is lacking [146 148]. Most studies are limited only to immediate adverse events [158]. Only two studies [7 146] of insufficient size to draw firm conclusions, have reported no negative influences on infant weight and Apgar score. Thus, additional information on the safety of acupuncture during pregnancy is warranted.

AIMS OF THIS THESIS

The main purpose of this thesis was to study efficacy, safety and post pregnancy effects of standard treatment, acupuncture and stabilising exercises given to pregnant women with well defined, isolated PGP during pregnancy. Based on this knowledge, our ultimate aim is to increase our knowledge about treatment of PGP.

The specific aims were to:

- present data of influence of acupuncture on the fetus measured with Cardiotocography
- report potential adverse effects of acupuncture on the pregnancy, mother, delivery and the fetus/ neonate and compare the results with adverse effects of standard treatment alone and stabilising exercises.
- describe regression of PGP after delivery in women that received standard treatment, acupuncture and stabilising exercises.
- investigate whether specific treatment effects of acupuncture go beyond effects of non-specific effects and individual attention.
- evaluate if deep acupunctural stimulation has a greater treatment effect than validated non-penetrating sham acupuncture on pain intensity, sick-leave, function and quality of life in patients with PGP during pregnancy.

PATIENTS AND METHODS

This section is a brief description of the methods used in the studies that comprise this thesis. Comprehensive descriptions can be found in the individual papers.

Ethics

The women received written and verbal information about the studies from their doctor and/or midwife. Thereby, the women had time to consider their participation. It was explained that their participation was voluntary and that they could discontinue their participation at any time without explanation and without consequences for their management. In RCT I, Women gave their oral consent at inclusion visit before start of the baseline assessment. In RCT II, written informed consent was obtained at screening before performance of baseline assessment. The Ethics Committee at Göteborg University approved both studies, ref: 452-99 and 059-06

Subjects and design

Figure 1 summarizes patients flow, withdrawals and analysed variables in paper I –III. Figure 1 in paper IV summarizes patients flow, withdrawals and analysed variables in paper IV. Table 5 summarizes the information about number of subjects, design, variables and outcome instruments used in the different papers. This information is also specified below.

Paper I

In this randomized single-blind controlled study, 386 women (mean age 30.5; SD 4.3 years) with PGP according to Ostgaard's criteria[40] were enrolled and randomised into treatments with standard treatment, standard treatment plus acupuncture or standard treatment plus stabilising exercises during 6 weeks. Patients were asked to avoid other treatments during the intervention period. All possible adverse events were recorded. Women who did not complete their participation were considered lost to follow-up. (Fig. 1) The women included in the analysis of the pain scores (VAS) one week after end of treatment were, standard treatment, n= 108 (mean age 30.8; SD 4.8 years), standard treatment plus acupuncture, n= 107 (mean age 30.6; SD 4.0 years), standard treatment plus stabilising exercise group, n= 106 (mean age 30.0; SD 4.0 years). An equal number of women (n= 108, n= 110 and n= 112 respectively) were included in the analysis of assessments by the independent examiner. For the evaluation of change in rated pain intensity in the mornings and evenings, the VAS was used. Recovery from severity of PGP after end of treatment was assessed by the independent examiner who was blinded to group assignment. In addition, data were coded and entered by personnel from an independent institution and the statistician who did the analysis was blinded to group and treatment.

Paper II

In this study data of adverse effects of acupuncture compared to stabilising exercises and standard treatment alone on the pregnancy, mother, delivery and the fetus/ neonate were recorded in 383/386 of the women who participated in study I (paper I). To assess the cardiovascular effect of acupuncture, fetal heart rate, maternal heart rate and blood pressure were monitored before and after all acupuncture sessions in order to measure the influence of acupuncture on the fetal heart rate. Cardiotocography (CTG) was measured before-during and after acupuncture sessions in 43 women. The CTG traces were assessed both by a computerized system for interpretation of tracings (Oxford 8000 computerised CTG analyser) and visually by an experienced obstetrician. To evaluate adverse effects, patients rated their opinions about the treatments at follow-up after treatment and the women's records were searched to assess the influence of treatments on pregnancy and delivery. Data were coded and entered by personnel from an independent institution and the statistician who did the analysis was blinded to group and treatment.

Paper III

In this follow-up study regression of PGP after delivery was evaluated in the women who participated in RCT 1 (paper I). Post treatment effects after delivery were evaluated. After drop outs, the number of women included in the analysis of pain scores (VAS) were – standard treatment, (n=99), (mean age 31.0; SD 0.5 years), standard treatment plus acupuncture, (n=125), (mean age 30.0; SD 4.2 years), and standard treatment plus stabilising exercises, (n=107), (mean age 30.0; SD 0.4 years).The women that stated that they did not continue with their diaries, standard treatment, (n=33), standard treatment plus acupuncture, (n=30) and standard treatment plus stabilising exercises, (n=25) were considered pain-free from week one after delivery. The number of women assessed by the independent examiners 12 weeks after delivery were – standard treatment, (n=105), standard treatment plus acupuncture, (n=109) and standard treatment plus stabilising exercises, (n=114). The women's reports of pain (VAS) and the results from the physical examination 12 wks after delivery were used as measures of regression of PGP after pregnancy. For the evaluation of change in rated pain intensity in the mornings and evenings, the VAS was used. The women were instructed not to continue with their diaries if the pain disappeared and to restart the registration again if the pain would return.. The diaries were collected at follow-up. Recovery from severity of PGP after end of treatment was assessed by the independent examiner who was blinded to group and treatment. In addition data were coded and entered by personnel from an independent institution and the statistician who did the analysis was blinded to group and treatment.

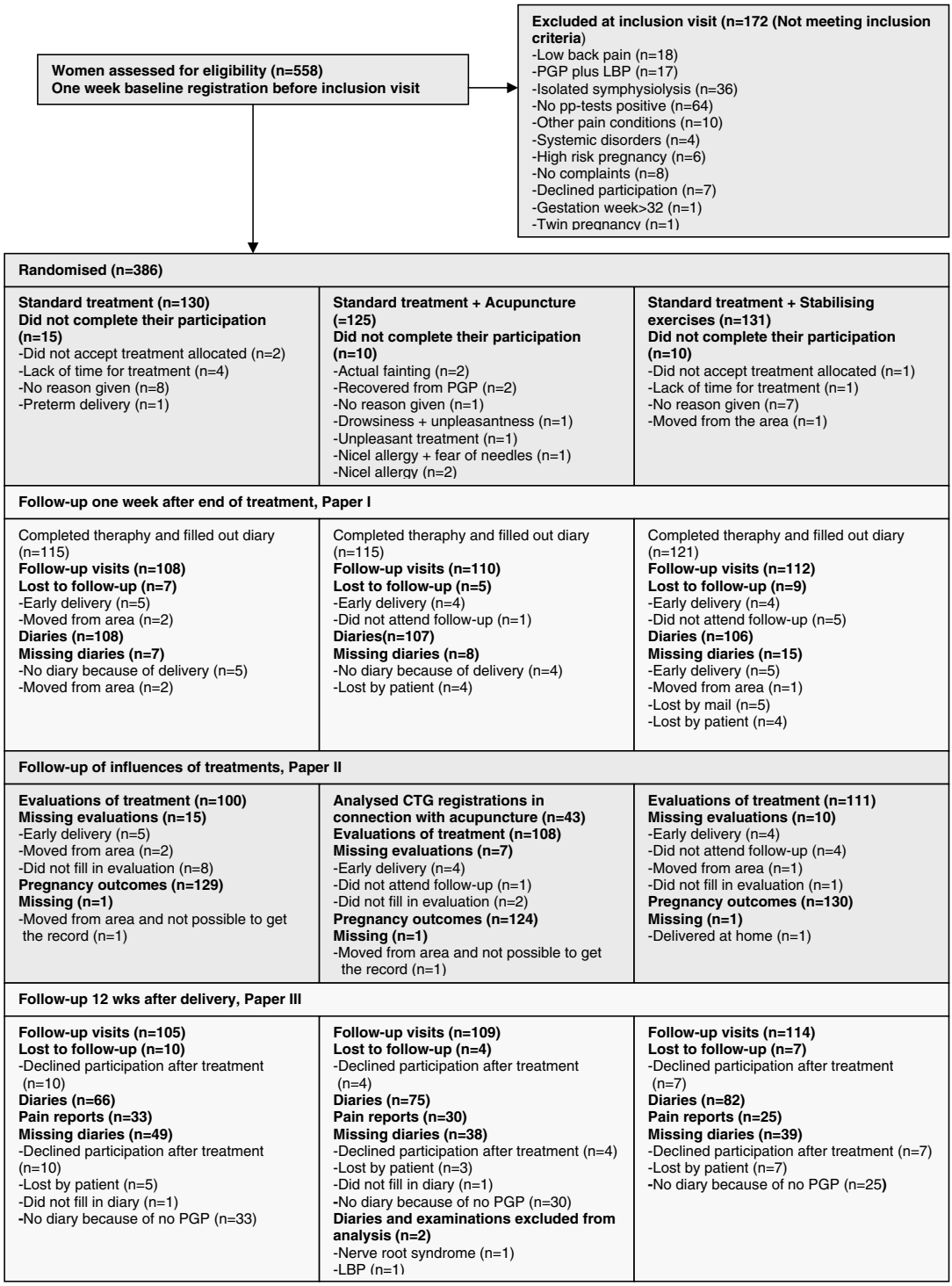
Paper IV

In this randomized double-blind clinical controlled study, 115 women (mean age 30.7; SD 4.4 years) with PGP according to Ostgaard's criteria[40] were enrolled and randomised to standard treatment plus acupuncture or standard treatment plus non-penetrating sham acupuncture during 8 weeks. Patients were asked to avoid other treatments during the intervention period. All possible adverse events were recorded. Of 115 participants, 108 participants completed therapy (Fig.1, paper IV). Analysis was done according to intention-to-treat, i.e. all randomized participants were included in the analysis. For the evaluation of change in rated pain intensity in the mornings and evenings, the VAS was used. Intervention credibility was evaluated after 3 treatments Pain unpleasantness was measured on a VAS. Health-related quality of life was measured using the EuroQol health instrument score (EQ-5D) and, the EuroQol health instrument thermometer (EQ-5D VAS). Function was measured with back-specific measures of self-reported functioning, the Oswestery Disability Index scale (ODI) and on the Disability Rating Index (DRI). Frequency of sick-listing and regular work was registered the last treatment week. Recovery from severity of PGP after end of treatment was assessed by the independent examiner who was blinded to group and treatment. Moreover, participants were blinded to whether they were receiving sham or active treatment. The therapist maintained "neutral" communications with participants and avoided providing cues that might reveal whether she was performing real or non-penetrating sham acupuncture and, the doctors that handled the decisions about sick-listing were blinded to treatment allocation. In addition, the person who did the analysis was blinded to group and treatment.

Table 5. Number of subjects, design, variables and outcome instruments used in the different papers

Paper	Design	Variable	Instruments
I	Single-blind RCT Difference between groups	Self reported intensity of pain related to motion Severity of PGP	VAS Assessment by independent examiner: pain provocation tests; pain-drawing; pain when turning in bed
II	Follow-up of adverse events of treatments	Adverse events Cardiovascular effect of acupuncture Influence of acupuncture on the fetus Pregnancy complications Opinion of treatment Influence on delivery Influence on neonate	Patients records Fetal heart rate, maternal heart rate and blood pressure CTG Patients records VRS, questionnaire Patient's records; Analgesia and oxytocin augmentation; duration of labour, frequency of preterm birth; operative delivery Patients records Apgar score, cord-blood gas/ acid base balance; infant weight
III	Follow-up of regression of PGP	Current PGP intensity related to motion Recovery of severity of PGP	VAS, patients reports Assessment by independent examiner -Pain provocation tests (Figure 3) - Pain-drawing - Pain when turning in bed - number fulfilling all criteria for PGP
IV	Double-blind RCT Difference between groups	Current PGP intensity related to motion Pain unpleasantness, Sick-leave Regular work Function Health-related quality of life Credibility of treatment Recovery of severity of PGP Adverse events Opinion of treatment	VAS VAS VRS, Percentages VRS DRI, ODI, EQ-5D VRS Assessment by independent examiner: pain provocation tests; functional test; pain-drawing; pain when turning in bed; number fulfilling all criteria for PGP VRS

Fig. 2. Summary of patients flow in paper I-III



Outcome variables, assessment and assessment instrument

Cardiovascular effect of acupuncture (Paper I and IV)

Fetal heart rate, maternal heart rate and blood pressure were monitored before and after all acupuncture sessions to assess the cardiovascular effect of acupuncture.

CTG (Paper II)

Influence of acupuncture on the fetal heart rate was measured with computerised CTG analyser before-during and after acupuncture sessions in 43 women. The CTG traces were assessed both by Oxford 8000 computerised CTG analyser (Oxford Sonicaid Ltd, Oxford, England) and visually by an experienced obstetrician [159]. CTG was recorded prior, during and after treatment (30 minutes each time or until the trace was approved as being normal).

Visual Analogue Scale (VAS) (Paper I, III and IV)

Primary outcome in papers I, III and IV was current PGP intensity related to motion in the mornings and in the evenings. The continuous, horizontal, Visual Analogue Scale, VAS (0-100mm) [160] with the anchor points, "no pain" and "worst considerable pain" was used for this purpose. The women scored their present pelvic pain intensity related to motion every morning and every evening in the diaries. In study IV the VAS was used for ratings of current perceived discomfort of PGP once a week. The anchor points were "no discomfort" and "worst considerable discomfort." VAS <10 mm was chosen as a definition of no pain according to the literature [77 161]. It has been reported that >30% or 13 mm reduction on a VAS represents, on average, the minimum change in acute pain that is clinically relevant [162 163].

The Disability Rating Index scale, DRI (Paper IV)

Once a week, the women scored their ability to do 13 daily activities on DRI, a VAS 0-100, in which 0 represents "ability to do the activity without difficulty" and 100 represents "not capable at all to perform the activity "[164]. The scored daily activities are dressing; outdoor walks; climbing stairs, sitting for a longer time; standing bent over a sink; carrying a bag; making a bed; running; light work; heavy work; lifting heavy objects and participating in exercise and sports. The minimum clinically significant change on the DRI is not known.

The Oswestery Low Back Pain Disability Questionnaire (ODI) (Paper IV)

The ODI[165] was used for measurement of back-specific functioning, i.e. daily activities that might be affected by PGP. The women rated their perceived disability on 10 different items: pain intensity, personal care, and lifting, walking, sitting, standing, sleeping, sexual life, social life and travelling. The items are scored from 0 to 5. The scores of all items are summarized, giving a possible maximum score of 50. The total score is then doubled and expressed as percentages where 0% represents no disability; 0 to 20% no or minimal disability; 20 to 40% moderate disability; 40 to 60% severe disability; 60-80% crippled and 80 to 100% bed bound.

The Euro-qol health instrument (EQ-5D) (Paper IV)

The EQ-5D [166 167] was used to measure health-related quality of life, HRQL. This instrument is developed for assessment of HRQL within population surveys and it provides a simple descriptive profile and a single index value for health status. The EQ-5D aims to create a health state classification through, which an overall index can be derived using preferences from the general population, and thereby enabling a calculation of Quality Adjusted Life Years (QUALYs). QUALYs are quantitative estimates reflecting how individual value health states, and are typically scored from 0 to 1. The EQ-5D self-report questionnaire (EQ-5D) essentially consists of two pages comprising the EQ-5D descriptive system and the EQ VAS. The first part consists of five items that measures health state in terms of mobility, self care, usual activities, pain and/or discomfort and anxiety. The women can select one of the following response alternatives 1 = no problems, 2 = moderate problems and 3 =

severe problems. The instrument has the possibility of defining 243 health states. Each health state has a linked value and possible health states range from -0.43 to 1 in which -0.43 is the lowest health state and 1 the optimal health state. The second part of the instrument (EQ-5D VAS) is a vertical VAS (0-100, in which 0 is the lowest thinkable health state and 100 the optimal health state). The minimal important difference for the EQ-5D VAS has been reported to range between 0.09-0.22 for improvement on the EQ-5D VAS, and from 3.82 to 8.43 on the EQ-5D VAS [168].

Severity of PGP (Paper I, III and IV)

Severity of PGP was assessed by an independent skilled physiotherapist within one week after intervention and at follow up 12 weeks after delivery in study I and within one week after intervention in study II. To assure that the standardized assessment was performed in an identical manner, the independent examiners met before the study was started. The same assessment was done for diagnosis of PGP before enrolment in both studies. All tests used are recommended by the European guidelines for diagnosis and treatment of PGP [37] and have all been used in studies of PGP during pregnancy and/or postpartum [89]. The test procedure is shown in fig. 3.

The posterior, pelvic pain provocation test, the P4 test (Paper I, III and IV)

The woman is supine with 90 degrees of flexion of the hip and knee on the tested side (Fig. 3). The examiner stabilizes the contralateral side of the pelvis over the superior anterior iliac spine. A light manual pressure is applied on the patients flexed knee, along the longitudinal axis of the femur. The test is performed bilaterally. The test is considered as "positive" if the woman reports a familiar, well-localized pain on the provoked side deep in the gluteal area [83-85].

Patrick's Faber test (Paper I, III and I)

The woman is supine. One leg is flexed, abducted, and rotated out so that the heel rests on the opposite kneecap. The test is performed bilaterally. The test is considered as "positive" if the woman reports a familiar, well-localized pain on the provoked side deep in the gluteal area (The hip joint is affected if the test results in pain on the medial side of the knee and femur or in the inguinal region) [85].

Modified Trendelenburg test (Paper I, III and IV)

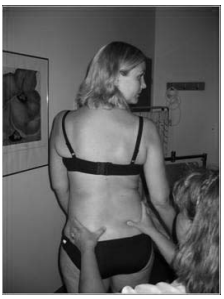
The woman is standing. She turns her back to the examiner and, standing on one leg, she flexes the other leg 90^{o} (hip and knee). The test is considered as positive if the test provokes pain in the pelvic joints PGP[85].

Palpation of the pubic symphysis (Paper I, III and IV)

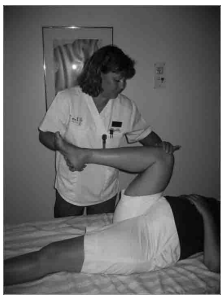
The woman is supine. The entire front side of the pubic symphysis is gently palpated during 5 seconds. If the palpation causes pain persisting more than 5 s after removal of the examiners hand, the test is recoded as positive [85].

The Active Straight Leg Raising test (ASLR test) (Paper IV).

The woman is supine with the legs straight and the feet 20 cm apart. The woman is then instructed to try to raise one leg above the examining table 20 cm without bending the knee, and then to rate the difficulty in performing the task from no difficulties at all (=0); minimal difficulties (=1), somewhat difficult (=2); fairly difficult (=3); very difficult (=4); unable to do (=5). After this, the same procedure is done with the other leg. The scores of both sides are added. A total score of =0 is considered negative, scores of 1-10 as positive [169].

Free movements in the spine

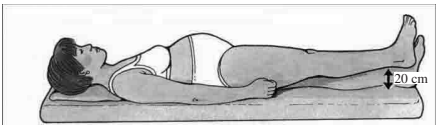
Free movements in the hips

The Straight Leg test

The p4 test.

The Patrick's Faber test.

A modified Trendelenburg test.

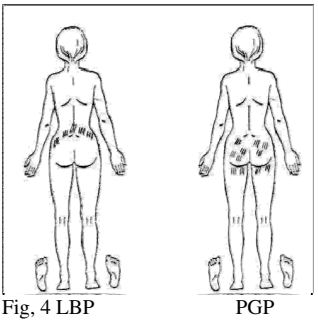


The ASLR test

Fig.3. The independent examiner performed the standardized clinical examination to exclude LBP and nerve root syndrome and confirm the diagnosis of PGP.The functional test, The ASLR test was added in paper IV

Pain location (Paper I, III and IV)

Pain location together with the women's report of location of the pain was investigated by a pain drawing before enrolment, at follow ups after treatment and 12 weeks after delivery. Figure 4 shows the difference in location of PGP and LBP. Pain drawings have been used in most studies of prevalence and treatments for women with PGP and/or LBP.



Fig, 4 LBP PGP

Pain when turning in bed (Paper I, III and IV)

Before enrolment and at follow-up the women answered if they had pain when turning in bed. It was one of the inclusion criteria as well as a measurement of severity of PGP.

Intervention credibility (Paper IV)

Credibility of the intervention was evaluated after three treatments using a validated item adapted from previous literature [170]. Credibility was scored on a 5-point scale (from 0 = maximum credibility to 5 = no credibility). The items were:

- Confident that treatment can help problem?
- Recommend treatment to friend with similar PGP?
- Does treatment make sense to you?
- Do you think treatment would be successful in treating other problems?

In addition, at follow-up after end of intervention the patients answered a question: "Which treatment do you believe you received?" The possible responses were (1) "penetrating acupuncture", (2) "non-penetrating acupuncture" and (3) "uncertain".

Sick-listing and regular work (Paper IV)

Numbers of women on sick-leave were registered before study start and at the last treatment week and numbers of women in regular work were registered the last treatment week.

Treatments

Standard treatment (paper I & IV)

Standard treatment consisted of patient education, specific exercises, a semi-plastic pelvic belt and a traditional home training programme designed to increase strength in the abdominal and gluteal muscles. The patients were told to be active but not to overload the pelvis, e.g. by keeping the pelvis symmetric during daily activities and informed about the importance of necessary rest. The aim of this information was to reduce fear, and to enable patients to become active in their own treatment. Information and advice were given at inclusion and follow up. Patients were told that they were free to call the physiotherapist at any time during pregnancy.

The semi- plastic belt (paper I & IV)

Application of a pelvic belt has been shown to decrease mobility of the SI-joints [171] and reduce pain and decrease the effects of PGP on daily functions [10 31]. Thus the aim with the semi- plastic belt (Puff Igång AB, Sweden, Figure 4) was to improve the stability of the pelvic girdle and thereby relieve symptoms of pain and disability.

Fig. 4. A semi-plastic belt

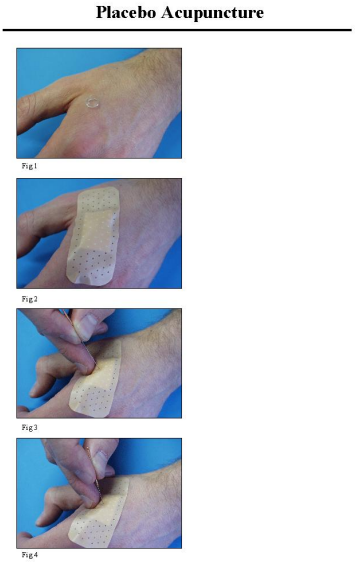
Acupuncture (paper I & IV)

Selection of points
The selection of acupuncture points for treatment in both studies was based on clinical experience and expert knowledge of acupuncture in pregnant women with PGP. Ten classical acupuncture points were selected individually in the same segments as the location of PGP after diagnostic palpation to identify sensitive spots. Two acupuncture points on the medial side of the leg and foot were selected in the same segment as the PGP (Table 6). The aim with the stimulation was to activate both segmental and central control systems. In addition, two points on the hands and head were chosen, extra-segmentally to the PGP, to strengthen and lengthen the effect on the central control systems. The location of stimulation was the same in both studies.

Needles
Three types of sterilized steel acupuncture needles were used for acupunctural stimulation: 30-70 mm length and Ø 0.30 mm (HEGU, Hegu AB, Landsbro, Sweden), and (Streitberger placebo-/sham-needles (0.30 x 30 mm), Asia-med GmbH & Co, Pullach, Germany).

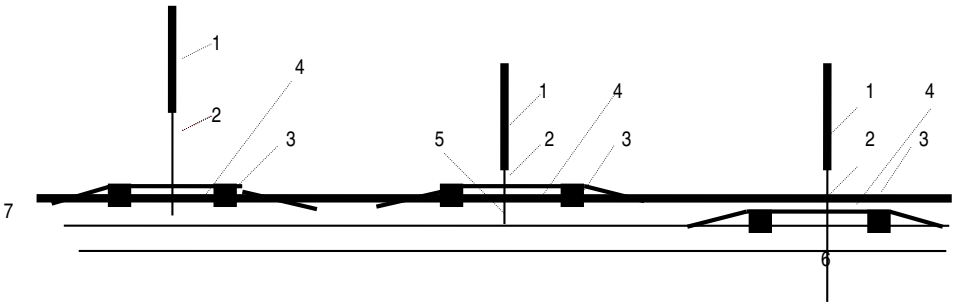
Non-penetrating sham acupuncture (paper IV)
In Paper IV, a validated sham acupuncture device was used to evaluate specific needle effects of acupuncture (Fig. 5-6). The aim with the placebo acupuncture was to reassure that the non-specific effects were equal between groups. Possible explanations of acupuncture effects suggested by previous trials such as the intensity of provider contact or the physiological effects of needling were thus excluded.

Administration techniques for acupuncture and non-penetrating sham acupuncture (paper IV)
The sham acupuncture device looks exactly like a real acupuncture needle but the tip of the needle is blunted. When the non-penetrating sham needle is “inserted into the skin” participants see and feel the needle penetration. Both the genuine and the sham needles were delivered through a handle, but the shaft of the sham needle does not penetrate the skin, instead it collapses into the handle and creates an illusion of penetration (Fig. 5-6).



- Placebo needle and acupuncture needle have to be applied in the same manner:
    1. Locate and disinfect the acupoint
    2. Apply the ring at the acupoint (fig. 5 1)
    3. Cover and fix the ring with the plaster (fig. 5. 2)
    4. Stick the needle through the plaster inside the ring (fig 5. 3)
- The acupuncture needle will penetrate the skin and has to be moved into deeper tissues until the patient reaction will indicate De Qi.
- As soon as the placebo needle touches the skin, the handle of the needle has to be pushed over the needle (fig. 5. 4). After treatment time the placebo needle has to be removed quickly gripping it at the needle, not at the handle. The picture is published with permission from Asia-med GmbH & Co.

Fig. 5. Description of needle placement in Paper IV



1 needle handle, 2 needle, 3 plastic ring, 4 plaster, 5 blunt tip of the needle, 6 sharp tip of the needle, 7 cutis

Figure 6.Diagram: Placebo-needle when touching the skin (left) and after retraction of the needle into the handle (middle), real acupuncture needle (right). With permission from Asia-med GmbH & Co.

Stimulation, intensity and duration
In papers I & IV the needles were manually stimulated every tenth minute although no attempt was made to evoke De-qi in the non-penetrating sham group. Treatments was repeated 12 times and lasted for 30 minutes. In paper I treatment was given twice a week for 6 weeks. In paper IV, treatment was given twice a week for four weeks and once a week for four weeks.

Table 6 Acupuncture points used for the treatment of PGP in pregnant women together with anatomical position and innervation of acupuncture points

Points	Segmental innervation	Muscle localisation
GV 20 ***Baihui***	Nn. trigeminus (V). Occipitalis minor (C2), Occipitalis major (C2-3)	Aponeurosis epicrani tissue
LI 4***Hegu*** bilateral	Nn, ulnaris. medianus (C8, Th 1)	Mm.interosseus.dorsalis.I lumbricalis II, adduktor pollicis
BL 26 ***Guanyuanshu"*** bilateral	Nn. thoracodorsalis (C6-8) toracicus (Th 9-12), lumbalis (L1-3)	Nn. thoracolumbalis, m.erector spinae
BL 32 ***Ciliago*** bilateral	Nn. thoracodorsalis (C6-8) toracicus (Th 9-12), lumbalis (L1-3)	Fascia thoracolumbalis, m. erector spinae
BL 33 ***Zongliao*** bilateral	Nn. thoracodorsalis (C6-8) toracicus (Th 9-12), lumbalis (L1-3)	Fascia thoracolumbalis, m. erector spinae
BL 54 ***Zhi Bian*** bilateral l	N. gluteus inferior (L5, S1-2)	M. gluteus maximus
KI 11 ***Heng Gu*** bilateral	N. thoracius (Th 6-12), subcostalis	Vagina m. recti abdominis
BL 60 ***Kunlun*** bilateral	N. suralis (S2)	Fibrotic tissue
EX 21 ***Yaoyen*** bilateral l	Nn. lumbalis, sacralis (L4-5, S1-2)	Fascia thoracolumbalis, m. erector spinae
GB 30 ***Huantiao*** bilateral	N gluteus inferior (L5, S1), obturatorius internus (L4-5, S1)	Mm. gluteus maximus, gemellus superior, piriformis
SP 12 ***Chong Men*** bilateral	Nn. thoracicus, lumbalis (Th 7-12, L1)	Aponeurosis mm. obliquus externus, abdominus internus
ST 36 ***Zuzanli*** bilateral	N. peroneus profundus (L4-5)	M. tibialis anterior

Stabilising exercises

Selection and mode of exercises
The aim of the stabilising exercises was to regain motor control by retraining a co-contraction pattern of the deep trunk muscles i.e. form and force closure (Fig. 7-8). Attempt was made to correct posture and patients were instructed to avoid overloading of the pelvic structures in daily life to correct posture and avoid overloading of the pelvic structures in daily life [42 45 172]. Essential for the intervention, was to make the women aware of how different positions of the lumbo-sacral configuration and the amount of activity affects the pain and to experience how muscle control affects the posture as well as the pain. Initially, the women received additional information about anatomy and PGP and the genesis of pelvic pain and discussion about how the basic written regimen could be integrated at home and at work. Thereafter, exercises were given according to Richardson and Jull [172] but modified because of the pregnancy.

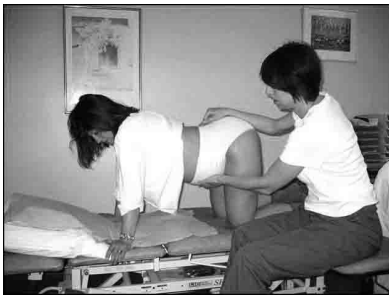


Fig. 7. Co-contractions in M Transversus Abdominis and Mm Multifidii in static postures

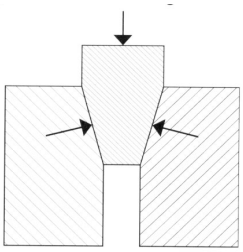


Fig 8. Activation of the Form and Force closure

Exercises

Exercises started with isolated low force co-contractions in M Transversus Abdominis and Mm Multifidii in static postures. With the patient standing in four point kneeling, with scapulae stabilizers activated and a normal lordosis, the women were asked to relax the abdomen and slowly contract the pelvic floor during relaxed breathing. The patient was thereafter taught to observe how the lower abdomen lifted during and relaxed again after the contraction of the pelvic floor. The physiotherapist held one hand on the stomach over the transversus abdominis to expose the movement, give feed-back and control that other abdominal muscles were relaxed. The other hand palpated the paraspinal muscles. The activation of the pelvic floor started a co-contraction in the M Transversus Abdominis and the women were thereafter told to keep this activation for ten seconds during relaxed breathing. These exercises were, when a correct contraction could be made, followed by increasingly more difficult challenges as the patient's skills improved, until more complex movements could be performed with optimal muscle control. Patients with severe pain in global muscles, as external hip-rotators also received exercises for increasing blood-circulation. These were performed using many repetitions with low force in a restricted range of motion in a side-lying position with a pillow between the legs or sitting without foot support.

Intensity and duration

The patients were offered treatments individually for a total of 6 hours during 6 weeks.
All exercises were carefully instructed individually, and supervised at each visit, but performed as home-exercises on a daily basis. The women were required to integrate the exercises in daily activities and to exercise in short sessions on several occasions during the day.

Massage

The aim with the massage was to increase blood-flow in the gluteal muscles and hip extensors, which to our clinical experience is often overloaded. Massage was given once or a few times by the physiotherapist the patient and partner was thereafter instructed how to perform the massage at home. The massage treatment consisted of standardized massage techniques, i.e. stroking (effleurage) and kneading (petrissage).

STATISTICS

The SAS software package (SAS Institute, Cary, N.C), version V8 or the SPSS, version 13.0 were used for statistical analysis. P<0.05 was considered significant in all studies. The statistical methods used for the 4 papers are described in Table 7. This information is also specified below.

Power calculations

The sample size calculation in RCT I (paper I-III) was based on a supposed mean pain score related to motion at baseline of 60 mm (VAS) in all three groups. We did not expect any treatment effect in the standard group. After treatment, we assumed that the mean pain score (VAS) in the standard group would be 60 mm and that the mean pain score would be 50 mm in one treatment group and 40 mm in another. To achieve a 90% power of detecting a significance (at the two sided 5% level), with an assumed standard deviation of 40, 103 patients were required for each study group. To compensate for a loss to follow-up of 20 %, 386 patients were required. When analysing the study we decided to apply the Mann-Whitney U test for comparisons with respect to changes of VAS with Bonferroni's correction. The power achieved with that method was 86% for comparison of the two most extreme groups. The sample size calculation in RCT II (paper IV) was based on the ability to detect an improvement of 15 mm on the VAS the last treatment week. A minimum of 100 participants with data the last treatment week would be sufficient to detect this effect with 80% power at the two sided 5% level. To compensate for drop-outs we included 115 participants.

Statistic methods

In *Paper I* analyses of variance (ANOVA) were used to analyse baseline data. The Mann–Whitney U test was used to compare differences between the groups concerning continuous and χ^2 was used for analysis of categorical variables. A subgroup analysis of treatment effects in patients divided in *four sub groups;* one-sided SI pain, double-sided SI pain, one-sided SI pain plus symphysis pubic pain; and pelvic girdle syndrome (double-sided SI pain plus pubis symphysis pain) was done. Data was presented as mean±standard deviation, median, [25^{th}, 75^{th} centiles], *n* and percent. Median differences and 95 % confidence intervals for the differences between medians were calculated on the basis of the Mann-Whitney test. Adjustments (multiplication by three) of the p-values due to multiple comparisons were performed by the Bonferroni's method. Analyses were performed by intention to treat i.e. all patients were analysed according to allocation but pain relieving effect was only analysed in those completing treatments.

In *Paper II* data were presented as mean± SD, *n* and percent. Continuous data were tested for significance with Kruskal-Wallis test. If a significant difference was found between any of the three groups, Mann Whitney U test was used to compare one group against one another. Dichotomous data were tested for significance with Fischer's exact test. Adjustments (multiplication by three) of the p-values due to multiple comparisons were performed by Bonferroni's method when appropriate. An adjusted p-value < 0.05 was considered statistically significant. Calculation of statistical tests and descriptive evaluations were carried out using SAS software package, version V8. Side effects were recorded in all the cases randomised except for one woman that delivered at home and two women moving out of town.

In *Paper III* the Mann–Whitney U test was used to compare differences between the groups concerning continuous variables and χ^2 was used for analysis of categorical variables. Data were presented as median, [25^{th}, 75^{th} centiles], *n* and percent. Adjustments (multiplication by three) of the p-values due to multiple comparisons were performed by Bonferroni's method. Analyses were

performed by intention to treat, i.e. if values were missing or the women had stopped registration due to disappearance of pain, the last value was carried forward [173].

In *Paper IV* a pre test analysis was performed without affecting the significance level but increasing the power to determine the best kind of comparison. In treatment studies, where baseline values of the efficiency variables are determined and no differences between the treatment groups at baseline are present, we have two possibilities to perform the comparisons. In order to assess efficiency the groups can be compared with respect to the difference between the value at the end of follow up and the baseline value or with respect to the value at the end of follow up. Derivations yield that the last type of comparison is more powerful if the correlation coefficient between the baseline and the end of follow up values is less than 0.5. The pre test analysis (Spearman's nonparametric correlation coefficient) showed that the correlation coefficient between the baseline and the end of follow up values was less than 0.5 for all outcome variables except the zero-one variable 'being on the sick-list'. For the last mentioned variable there was a substantial coincidence between the baseline and the post-treatment state. Thus with the mentioned exception the efficacy comparisons were performed with respect to the values at the end of the follow-up.

The t-test was used for parametric data. The Mann–Whitney U test or Kruskal Wallis test was used to compare differences between the groups concerning continuous variables and, χ^2, Fisher's exact test or test for trend in contingency table for categorical variables [174]. A subgroup analysis of treatment effects in patients divided in *five* sub *groups;* one-sided SI pain, double-sided SI pain, one-sided SI pain plus symphysis pubic pain; pelvic girdle syndrome (double-sided SI pain plus symphysis pubic pain), and isolated symphyseal pain was done. Number of patients fulfilling criteria for PGP was also calculated. Data was presented as mean±SD, median, [25th, 75th centiles] *n* and percent. Median differences and 95 % confidence intervals for the differences between medians were calculated on the basis of the Mann-Whitney test. For missing data and for participants who withdrew, intention-to-treat analysis was applied to outcome data using the last recorded data.

Table 7. Statistical methods used in the different papers in the thesis.

Statistical methods	Paper I	Paper II	Paper III	Paper IV
t-test				x
Mann Whitney U test	x	x	x	x
Chi-Squared test	x		x	x
Kruskal Wallis test		x		
Fisher's exact test		x		x
ANOVA	x			
Spearman's nonparametric correlation coefficient				x
Test for trend in contingency table for categorical variables				x

RESULTS AND DISCUSSION

Paper I

This study showed that acupuncture as well as stabilizing exercises as adjunct to standard treatment relieved PGP in pregnant women. Evening pain (VAS) decreased 34 mm (52%) in the acupuncture group, 15 mm (25 %) in the stabilising exercises group and 5 mm (8%) in the standard group. The independent examiners confirmed that attenuation of severity of PGP was greatest in the acupuncture group. No serious adverse events were reported in either of the groups.

Comments

The main finding in this study was that acupuncture as well as stabilising exercises constituted efficient complements to standard treatment for pregnant women with PGP. In the standard group, pain remained constant during the treatment period. This is in line with earlier findings that PGP will normally increase with advancing pregnancy [175] and that solely standard treatment for PGP gives unsatisfactory pain relief [37 175]. Standard treatment included use of a pelvic belt, which has been reported to decrease SI joint laxity [176]. However, it has been found useful in some studies [31 97] and ineffective in others [11 21] Nevertheless it would seem beneficial in the long term for women to use their muscles to provide stability to the pelvis rather than rely on an external device.

It has been suggested that regain of muscle control is important for reducing development of muscle weakness and PGP [37]. There are only three RCTs of stabilising exercises for PGP. The first one reported beneficial effects in women with persisting PGP after delivery [89]. The second study by Nilsson-Wikmar et al. studied a group of women with PGP during pregnancy using stabilising exercises of the global muscles. This trial showed no pain reliving effect of information and home training exercises and pain increased after in clinic exercises. In addition, ability to perform daily activities decreased in all groups. However, the authors discussed that exercises may be more specified to really achieve stability than the ones used in the study [21]. The third study of women with PGP postpartum focused on only global muscles and showed no effect. The results indicated that the exercises used aggravated the symptoms instead of relieving them. These exercises were not individualized and they were instructed by videotape. The training in our study aimed at having an effect on dysfunction of the muscle-tendon-fascia system that controls force closure of the pelvis[42]. It is not exactly known how the exercises influence this system but research has showed that contraction of the transversus abdominis decreases the laxity of the SI joint [45] and that co-contraction of the multifidus muscle and the transversus abdominis muscle improves lumbar stability [42]. In our trial, exercises for local muscles were used, because they are believed to be primary stabilisers [89], but we do not known whether an addition of global stabilizing muscles could have been even more effective for some women. It is also possible that they might have aggravated the pain. This needs to be evaluated in future trials. The stretch exercises and massage given in the stabilising group may have had some contributory effect in the women but the main training; however, was the stabilisation exercises that were performed at several occasions during the day in contrast to the stretch exercises or massage that was performed at the visits or occasionally by the woman's partner at home.

An updated systematic review found that acupuncture is more effective than no treatment or sham treatment for chronic LBP but that there are no differences in effectiveness compared with other conventional therapies. However, the review suggests that acupuncture and dry-needling are promising adjuncts to other therapies for chronic low back pain. But that there is a clear need for higher quality trials in this area as most studies are of lower methodological quality [177]. The acupuncture treatment in our studies succeeded to establish control of the pain and this may have been important in preventing dysfunction of muscles. Our results are supported by previous [145 146 178]and recently published studies of acupuncture for PGP [147] and/or LBP [7]. For women with severe pain, we think that acupuncture can

be combined with other treatments. A combination with stabilising exercises is an interesting alternative, which of course also needs further evaluation.

Paper II

This study showed no negative influence of acupuncture, stabilising exercises or standard treatment on the pregnancy, mother, delivery or the fetus or neonate. Minor adverse events (Needle pain, local haematoma, tiredness, nausea, actual fainting, and aggravation of symptoms) were common after acupuncture. However, the women in our study rated their experience with acupuncture favourably and a majority of them were willing to use the same treatment in the future if needed, suggesting that the adverse events of the treatment did not negatively impact their overall experience of the treatment.

Comments

This is the first large clinical trial of acupuncture, which may be considered strong, given during the second and third trimester of pregnancy to report on influences on CTG, the pregnancy, mother, delivery and the fetus. We found no evidence that acupuncture lead to an increased rate of preterm delivery or to servere influences on the pregnancy, mother, delivery or the fetus or neonate but the study was not powered to fully exclude such influences.

Large surveys have considerable strengthen the evidence for the safety in routine practice [149 179] but evidence on acupuncture during pregnancy is lacking. We think that fear of immediate and long-term serious adverse events of acupuncture in pregnant women have resulted in both a restricted use of acupuncture and a delayed start of the treatment in pregnant women. The underlying mechanisms of the therapeutic effects of an early start of treatment with acupuncture as well as with active physical therapy regime for PGP should therefore be addressed. Women affected with PGP typically adopt abnormal patterns of muscle activity, to relieve and avoid pain. The longer this pattern persists, the more pain will arise from the unphysiological burden on muscles and joints and the pain in turn will aggravate the dysfunction of muscles resulting in a vicious cycle. To reduce development of abnormal patterns of muscle activity [24], we decided to begin treatment as soon as possible after the first symptoms of PGP. Pregnant women at least 12 gestational weeks were invited to participate in the trial and 50 % of them started treatment in gestational week 14 to 25.

There is also a debate about which points and stimulation are appropriate to use in pregnancy For example, Smith et al. [103] recommend not more than four to six needles with gentle stimulation for 15-20 minutes when treating women with nausea and vomiting and Kvorning et al. started treatment with only two segmental points, stimulated to achieve De-qi twice during the session which only lasted for about three minutes. The needles were than withdrawn and the patient was allowed to rest for ten minutes [146] . We believe that an adequate dose of acupuncture probably is essential for the outcome of treatment and, as no scientific evidence of harm of acupuncture during pregnancy exists. We decided not to reduce the stimulation because of the pregnancy. We used 17 needles and stimulated them to de qi three times during 30 minutes and acupuncture points forbidden by others (LI 4, BL 31 and 33)[103 155-157] were used, therefore we believe that the acupuncture used in our study may be considered to be strong compared to earlier studies. Fortunately, this strategy resulted in significant pain relieving effects without serious adverse events.

Our data of no serious adverse events in pregnant women *during* the treatment course of acupuncture are in agreement with the other studies of PGP and/or LBP during pregnancy [7 145-147 178]
Our results of no serious effects on the pregnancy outcome is supported by Smith et al. who treated 583 pregnant women with acupuncture for hyperemesis during the first trimester [103]. But as in our study the sample size in that study was only able to detect large differences in pregnancy outcomes. Smith et al. declared that a sample size of 19,476 women would have been required to detect an increased from 6 to 7 %in spontaneous abortions. There is only two other studies of acupuncture for PGP that have reported pregnancy outcomes (infant weight and AS) and those studies had smaller sample sizes, used weaker stimulation and acupuncture was given mainly in late pregnancy [7 146].

The result indicates that minor adverse events are relatively common after acupuncture. This finding is concordant with earlier research in which a frequency of 7-11% of non-serious adverse events were reported [137 149 150]. Previous studies of physiotherapy for PGP and/or LBP in pregnant women supports that physiotherapy is safe for this condition [4 11-14 31 88 93 94 145 146 180 181].

Pregnancy outcomes were analysed in all women randomized except for one of the women in each group. Thus, we believe that the data provide some reassurance that acupuncture is not associated with any severe adverse influences on the pregnant women or the fetus or neonate. But to further determine if acupuncture is safe to use in pregnancy it is important that future clinical studies include pregnancy outcome information.

Paper III

The main finding in this follow up study was that irrespective of treatment modality, regression of PGP occurs in the great majority of women within 12 weeks after delivery. Approximately ¾ of all the women were free of pain three weeks after delivery. According to assessment by the independent examiner PGP had resolved in 99% of the women 12 weeks after delivery

Comments

This is the first study that has evaluated post pregnancy effects of acupuncture and stabilising exercises. Recovery after delivery was excellent with no significant differences between intervention groups. In the literature most data suggest a favourable prognosis after delivery but not to the same extent as in our study. The reason for the discrepancy of the results could be that that stricter criteria for PGP were applied presently than in other studies [75 70]. In addition, we could investigate regression of PGP in more detail as the women showed the progressive resolution of pain using daily recordings of VAS and these results were combined with a physical examination 12 wks after delivery.

Our data confirm previous results of almost total recovery of symphyseal pain [75] but it differs from other studies that have shown a correlation between severity of PGP (number of affected pelvic joints) and recovery [18 75]. There are some possible explanations for this finding; firstly all women in our study were offered some treatment which may not have been the case for women in the other studies, secondly, the treatments offered in our study may have been more effective, i.e. all women received individual information, which is superior to group information [182] and 2/3 of the woman were given additional acupuncture or specific stabilising exercises which was effective during pregnancy [183]. We believe that our definition chosen of no pain (VAS <10 mm) is appropriate for most women although we are aware that pain is essentially subjective and that 10 mm on a VAS may correspond to significant pain for some women. The findings of almost complete recovery of PGP 12 weeks after delivery is promising but needs to be confirmed in future RCTs with follow-up as well as in epidemiological studies which investigate the natural regression of PGP after pregnancy.

Paper IV

This study showed that acupuncture and non-penetrating sham acupuncture relieved PGP equally well. The acupuncture group showed better ability to take part in daily activities than women receiving sham and fewer women were sick-listed in the acupuncture group the last treatment week, although no statistical differences were found between the groups. Additionally, significantly more women in the deep acupunctural group were kept in regular work than women receiving sham. Health-related quality of life improved similarly in both treatment groups. No difference in function as measured by the ODI, decreasing pain unpleasantness as measured by VAS and, recovery from severity of PGP as assessed by the independent examiner was detected between treatment groups. No serious adverse events were reported in either of the groups.

Comments

This study showed that acupuncture did not reduce PGP more efficiently than non-penetrating sham acupuncture. However, decrease in pain was clinically relevant in both treatment groups as evening pain decreased 30 mm (45%) in the acupuncture group and 28 mm (41%) in the sham group. Also, acupuncture improved clinically relevant outcomes over non-penetrating sham i.e. better ability to take part in daily activities, fewer women on the sick list and consequently more women kept in regular work during and after end of treatment. Earlier studies of acupuncture for pelvic girdle pain have compared acupuncture with physiotherapy [145 146 183], analgesic drug and spasmodic drug [7], minimal acupuncture [184] or conventional treatment [7 183]. Our procedures differed in several important ways from those in previous trials. We included participants with a clinical diagnosis of PGP, used a credible validated non-penetrating sham acupuncture device, higher number of women completed therapy and we used more treatment sessions combined with more acupuncture needles than in the earlier studies. Our result that acupuncture decreases pain is supported by others [7 145 184]. Better capacity to perform general activities after acupuncture has been shown in one previous study [145].

The present study could not verify that deep acupunctural stimulation relieved PGP better than superficial stimulation However, the reported de qi sensation, needle pain, slight bleeding, fainting and sleepiness in the sham group suggest that the treatment was not totally inert. Thus it is possible that a needle touching the skin can be considered a form of sensory stimulation that activates afferent nerve fibers. It has recently been demonstrated that light touching the skin stimulates mechanoreceptors coupled to slow conducting unmyelinated (C) afferents. This modulates activity in the central nervous system [185]. It is likely that the non-penetrating acupuncture needles, which are meant to be inert, in fact activate C tactile afferents and consequently elicit physiological responses [186]. Thus, it is also possible that the pressure of the blunted tip may inadvertently replicate forms of true Japanese and Korean acupuncture [125]. This could partly explain why non-penetrating acupuncture and minimal acupuncture have been shown as effective as acupuncture in reducing pain[115 187-190]. On the other hand one could argue that the marked difference in the intensity of afferent stimulation between the groups would be expected to result in more pronounced difference in outcome than was actually seen.

It seems possible that acupuncture can work in a varity of ways by reducing stress, by altering autonomic tone and psychoneuroimmunological state [101]. These findings are also consistent with the results of mechanistic studies demonstrating that acupuncture analgesia occurs centrally through the release of endorphins and monoamines [143 144] , which is also true for the placebo effect. It is probably true that acupuncture has power-full non-specific effects. It has an aura of Eastern mystique and it is performed in a ritualistic manner. In addition, it is associated with long consultations that are in themselves prone to be therapeutic.

Another factor that could bias the result was that a higher proportion of participants in the sham group were sick-listed which allowed them to rest, which itself could have relieved the pain. It is well known that rest can relieve symptoms and that increased activity aggravates symptoms of PGP [12]. Hence, in our previous study we found that acupuncture reduced pain compared to controls under conditions of equal sick listing. Speculatively, pain may have decreased more in the acupuncture group if an equal number of participants in that group would have had the opportunity to be on sick leave. On the other hand, the improved ability to perform daily activities and possibility to maintain in regular work in the acupuncture group may actually represent an equally important outcome for these women as pain relief. The problem with the unequal numbers on sick-leave could have been solved if we had stratified for this factor at randomisation but unfortunately we did not consider that it this could be a problem.

This study suggests that the beneficial effect of acupuncture at least to some extent is due to effects of needle penetration, manual stimulation throughout treatment and elicitation of the de qi sensation by manipulation of the needles. Treatment response in the current study for genuine acupuncture was similar to the previous study [183] in that showed favourable results. Thus, it is clear that the course of

12 sessions of acupuncture, adjusted according to individual patients' needs delivered alongside advices, a semi plastic belt and home-training exercises must be considered to be an effective treatment modality. The data imply that needle penetration contributes to the previously reported beneficial effects of acupuncture. We believe that the data are important as it provides evidence of higher methodological quality of effectiveness of acupuncture for the treatment of PGP in pregnant women.

Methodological considerations

The RCT is considered the gold standard design when assessing the effects of treatments. Randomised controlled studies produce study groups comparable with respect to known as well as unknown risk factors, i.e. remove confounding factors. This procedure assures that groups are comparable at baseline which is important. If imbalance in group allocation results in more severely patients in the control group, selection bias can led to an artificially high response rate in the treatment group. Concealment of allocation, blinding and lack of patients' attrition to the study protocol are considered the most important methodological factors to ensure a high validity of a RCT. The allocation procedure in our RCTs was correct, assessors and the persons entering and analysing the data was blinded to treatment allocation and the drop-out was small in both studies. To assure blinding of the assessors women were asked not to reveal any information about their treatment during assessment. Because it is not possible to blind the women to standard treatment, acupuncture or stabilising exercises, the first RCT was single blinded. In RCT 2, it was not possible to blind the acupuncturist, but patients, the doctors that handled the decisions about sick-listing and the assessor were blinded, i.e. the study was double-blinded.

In RCT 1 the original power calculation was done using parametric tests but the final analysis was subsequently performed with Mann-Whitney U test with Bonferroni's correction after request from BMJ. In this calculation a power of 86% for comparison of the two most extreme groups was archived. We are aware of the loss of power in using non-parametric methods but we believe that the 20% increase in recruitment numbers over that required adequately compensated for this and the attrition rate. In addition, given the statistically significant findings and the relatively narrow confidence intervals we believe that the power of the study was appropriate.

The fact that the same criteria and treatments were used in both studies makes the studies homogenous and the results comparable. The relative large sample sizes in the studies and low drop out rates suggest that primary outcomes can be generalized. The most common observation made in systematic reviews of trials conducted for PGP and LBP in pregnant women is that with few exceptions, the numbers of patients were notable small [87]. Small trials are problematic because insufficient number of observations may miss a treatment effect.

The main outcome measure in both studies was pain related to motion on a VAS and, clinically relevant [162 163] effects were found in both studies. To measure improvement in function in paper IV, the DRI was used. Both the VAS and the DRI have been shown to have high reliability and validity [164] and they have been used in previous studies of interventions for PGP and/or LBP. The ODI [165 191] was used for measurement of back-specific functioning, i.e. daily activities that might be disturbed by PGP. We used the revised version (2.0) since we thought it was important to measure items concerning sexual life and pain intensity rather than pain medication[192]. Also, this version has been used in other studies of PGP during pregnancy[18] as well as postpartum[89]. HRQL was measured with the The EQ-5D [166 167] which also has been used in other studies of PGP during pregnancy [18] .
In RCT 1, pain relieving effect was only evaluated in cases fulfilling treatment. However, drop-out rate was equally distributed between the treatment groups and the pain reliving effect in the acupuncture group as well as in the stabilising exercise group was large compared to the standard

treatment group. Thus, we do not think that the method last value carrying forward would have changed the level of significance.

Protocols for acupuncture and the stabilising exercises used in the studies were based on expert knowledge about the treatments, i.e. midwifes, obstetricians, physiotherapists and orthopedist took part in planning the studies. Moreover, modification of the treatment was allowed, which have been stated to be necessary for optimal efficacy. Control for co interventions during the treatment period was done in both studies, i.e., women were asked to refrain from using co interventions during the study period. The women receiving acupuncture and stabilising exercises as adjunct to standard treatment received treatments individually for the same duration. Thus criteria for control of non-specific effect were included (same contact time and interaction between therapist and patient, manual contact during search for acupuncture points in the acupuncture group and manual contact during palpation of muscles and massage in the stabilising exercise group. The women receiving solely standard treatment received less attention but they were not given a placebo treatment; they received the best "usual care" known at that time, given individually by an experienced physiotherapist. Probably, the women were given more careful attention than in usual practice because they were participating in the study but we are aware of the fact that these women received only two treatment sessions, thus there was a difference in attention effect compared to the other two interventions. We also think that the women's preference and disappointments were equally distributed, as least for the women allocated to acupuncture and stabilising exercises, as we know that some women favoured acupuncture and some favoured the stabilising exercises. We believe that the therapists giving acupuncture and stabilising exercises were equally enthusiastic about their treatment program. They were experienced and they were treating the way they assumed was the best, based on clinical skill and theoretical knowledge. In paper IV, acupuncture and non-penetrating sham treatments were performed by the same registered midwife to ensure equal participant blinding in both groups and consistency of treatment. In this study there was no group receiving solely standard treatment. We decided not to include a group receiving solely standard treatment as this would be difficult to justify as our previous trial showed that PGP aggravated in that group. In addition, our primary aim with this study was to investigate if specific treatment effects of acupuncture go beyond effects of non-specific effects and individual attention.

A potential bias in the studies was that only a small number of all presumable patients were included, 558 women out of approximately 13 300 pregnancies (4.2%) wanted to participate in the first study and 165 women out of approximately 9000 pregnancies (1.4%) in the second RCT. However, all antenatal care units in the region were invited. Thus, we have no explanation for this but we believe that some midwifes and doctors were more active when recruiting patients than their colleges at other antenatal units. However, there were no differences in baseline characteristics between the study groups in either of the studies. Another consideration in RCT 2 is the possible selection effect arising from the fact that women that were recruited had an interest in acupuncture, which may limit the external validity of the trial to a population of patients who are willing to receive acupuncture treatment. On the other hand, this may be of minor clinical relevance because in clinical praxis only patients who consider acupuncture as a treatment option for themselves will be treated with acupuncture, which makes the results from this trial valid for this population.

A limitation of the follow up study after delivery is that about 29 % of the women did not fill in a complete diary because of the instruction that they were not obliged to continue their recording after disappearance of the pain. Nevertheless, the number of women who did not return diaries was similar in the different treatment group and the evaluation of the blinded observer 12 weeks after delivery confirmed that a majority of these women did not fulfil any of the criteria for PGP, which confirms the assumption that these women did not complete their diaries because of resolution of pain rather than because of neglect or other reasons.

The methodological problems in acupuncture studies need to be highlighted. Randomized, double-blind, placebo-controlled trials are generally considered as the best tool to separate the "specific" and

the “unspecific” or “placebo” effects of a therapy. However, it is difficult to design an appropriate control group in acupuncture trials because it is a painful invasive physical modality [170]. The two categories of control interventions for acupuncture thus far are sham acupuncture and placebo acupuncture. The type of sham acupuncture is critical in determining what question the trial can be designed to answer. Acupuncture at non-acupuncture points can be used as a test of specificity and placebo acupuncture, i.e. a non-penetrating acupuncture needles can be used to test efficacy. Sham acupuncture is invasive acupuncture that can vary in technique by puncturing nonacupoint sites or by inserting needled at various depths. However, it has been suggested that inserting needles at distant sites can still activate noxious inhibitory control, and therefore placebo acupuncture might me more appropriate because it minimizes the physiological response [193]. Placebo acupuncture is considered non-invasive acupuncture, in which there is no needle penetration at all, and methods can range from using blunted needles, fingernails, toothpicks, or retractable needles [194 195]. The Streitberger needle used in this study is a validated non-penetrating sham acupuncture needle, which gives a pricking sensations and creates the impression that acupuncture is performed without penetrating the skin [195] .

The use of a comparison group that received non-penetrating sham acupuncture provides reassurance that all features of the sham treatment were identical to the real treatment except for the feature under investigation, the specific needle effects .Thus, blinding in both groups was enhanced because the two treatments were comparable in appearance. Patient-blinding in acupuncture trials is crucial not least because patients beliefs regarding the receipt of acupuncture have shown to bear a stronger relationship to pain perception than the specific effects of acupuncture [196]. Moreover, it reassures that possible explanations of acupuncture effects suggested by previous trials, such as the intensity of provider contact or the physiological effects of needling are excluded. However, intervention credibility evaluated after three treatments showed that women receiving acupuncture were more confident in one of four items than women receiving non-penetrating sham acupuncture. But, blinding of the patients seems to have been maintained, as 66% percent of the patients who had been randomly assigned to the non-penetrating sham acupuncture group believed that had actually received real acupuncture, 30 % were unsure which treatment they had received and two patients believed that they had got non-penetrating needles. Of the 57 women in the acupuncture group, one woman believed that she had actually received non-penetrating sham acupuncture; 66 % was correct in believes and 33% were unsure which treatment they had received. Additionally, only acupuncture naive women were included which have been stated to be important to assure that expectations of the acupuncture procedure are not influenced by previous experience. Although it was not possible to blind acupuncturists to the form of acupuncture, the therapist maintained “neutral” communications with the patients and she avoided providing cues that could have revealed whether real or non-penetrating sham acupuncture was performed, which has been stated to be important [137].

More research is needed on this widespread problem of pregnancy. Further studies need to be performed to determine of mechanisms of PGP as well as of methods for prevention and treatment for PGP.

CONCLUSIONS

From the results of this thesis it can be concluded that stabilising exercises and acupuncture added to usual care can be helpful to reduce PGP during pregnancy.

Paper I

Acupuncture and stabilising exercises were efficient complements to standard treatment for the management of pelvic girdle pain during pregnancy. Acupuncture was superior to stabilising exercises in relieving evening pain.

Paper II

Findings from our trials suggest acupuncture was safe as a treatment option for women during the second and third trimester of pregnancy.

Paper III

Irrespective of treatment modality, regression of pelvic girdle pain when diagnosed according to the criteria of Ostgaard occurs in the great majority of women within 12 weeks after delivery.

Paper IV

Acupuncture had no additional effect on pelvic girdle pain reduction compared to non-penetrating sham acupuncture as assessed by VAS but is was superior to non-penetrating sham acupuncture in improving ability to do daily activities which may lead to more women kept in regular work. The data imply that needle penetration contributes to the previously reported beneficial effects of acupuncture and we think that the data provides evidence of higher methodological quality of effectiveness of acupuncture for the treatment of pelvic girdle pain in pregnant women.

AKNOWLEDGEMENTS

I wish to express my appreciation to all the women for their contributions to this study but also to all of those who have otherwise encouraged and supported the completion of this thesis. My hearty gratitude goes to the following persons:

Henrik Hagberg, my supervisor who let me into the field of research. I want to thank you for your invaluable support, for constructive scientific discussions and for always answering my e-mails right away.

Hans-Christian Östgaard, my co-supervisor, for being an enthusiastic teacher in the field of pelvic girdle pain, for fruitful discussions, great support and for always being available.

Lars Ladfors, my second co-supervisor for excellent help with planning of the study, statistical analysis and in commenting the papers.

Monika Fagevik-Olse'n has not only been of invaluable help in her work with the study patients, the statistical analysis, and in co-author ship, but has also become a dear friend. I want to thank you for your invaluable support during these years. You have always been there and encouraged me when I needed it the most.

Karin Frygner for introducing me into the field of acupuncture and for professional performance of the acupuncture treatment. If we had not met, this thesis would not have been done.

Eva Roos-Hansson and *Gunilla Zetherström* for invaluable help with the assessments of the patients and *Tina Larsson,* and *Karin Wettergren* for excellent help in treatments of the patients. I want to thank you for sharing your extensive knowledge about physical therapy with me and for being such good friends.

All midwifes and doctors in the region of Västra Götaland for enrolling and caring for study patients. *Birgitta Melander, Ann-Charlotte Linner, Ami Molin, Pia Marciniak, Agneta Ellstrom, Thokild Nielsen, Margareta Hellgren, Jan Söderlund, Katarina Kylebäck* and *Elisabeth Almström* are specially acknowledged for critically reviewing the study design.

Ian Milsom for his interest in the thesis and for valuable advices and support during this time.

Björn Andersch for encouragement and for showing sincere interest in my research and for his always cheerful face. Laughter is the best medicine?

Elisabeth Stener-Victorin for sharing your great knowledge in the field of sensory stimulation, for inspiring discussions**,** critically reviewing of the study design and for co-author ship.

Margareta Wennergren, Ulla-Britt Wennerholm, Kerstin Torgeby , *Håkan Lilja, Margareta Hellgren* and *Gunilla Sundell* for being supportive and for having expressed sincere interest in my research.

The staff at Chalmers University and *AnneGrete Löve* for entering results from the studies into the databases.

Björn Areskoug, Anders Oden and *Martin Gellerstedt* for excellent help with statistical analysis.

My workmates in the research unit *Gunilla Kaplan, Anja Andersson, Agneta Cederfors-Blom, Helene' Nielsen, Ellen Samuelsson* and *Annika Bolinder* for great friendship and many good laughs.

Sofie, the joy of my life, who had to share so much of my time with this work and for always reminding me of what is most important in life.

Peder, for putting up with me for so long in this seemingly endless task, for love and understanding, good cocking, and for always being by my side.

My workmates at "Spec BB/ Förl" at Sahlgrenska University Hospital/ Östra for their support.

All my friends, for still being there.

And lastly, *my parents* for all their love and support.

This work was financially supported by grants from The Vårdal Foundation, The Dagmar Foundation, The Trygg-Hansa Insurance Company, The Organon Foundation, The Sahlgrenska University Foundation, the Foundation of the Health and Medical care committee of the Region of Västra Götaland (Sweden), and Swedish governmental grants to researchers in the public health service (ALFGBG2863).

Finally time to rest

REFERENCES

1. Stendal H, Robinson A, Eskild A, Heiberg E, Eberhard-Gran M. pelvic girdle pain in pregnancy: The impact on function. *Acta Obstet Gyn Scand* 2006;85(2):160-164.
2. Fast A, Shapiro D, Ducommun EJ, Friedmann LW, Bouklas T, Floman Y. Low-back pain in pregnancy. *Spine* 1987;12(4):368-371.
3. Mousavi SJ, Parnianpour M, Vleeming A. Pregnancy related pelvic girdle pain and low back pain in an Iranian population. *Spine* 2007;32(3):100-104.
4. Morkved S, Asmund Salvesen K, Shcei B, Lydersen S, Bo K. Does group training during pregnancy prevent lumbopelvic pain? A randomized clinical trial. *Acta Obstet Gyn Scand* 2007(86):276-282.
5. Bjorklund K, Bergstrom S. Is pelvic pain in pregnancy a welfare complaint? *Acta Obstet Gynecol Scand* 2000;79(1):24-30.
6. Bastiaenen CH, de Bie RA, Wolters PM, Vlaeyen JW, Leffers P, Stelma F, et al. Effectiveness of a tailor-made intervention for pregnancy-related pelvic girdle and/or low back pain after delivery: short-term results of a randomized clinical trial [ISRCTN08477490]. *BMC Musculoskelet Disord* 2006;7:19.
7. Guerreiro da Silva JB, Nakamura MU, Cordeiro JA, Kulay L, Jr. Acupuncture for low back pain in pregnancy--a prospective, quasi-randomised, controlled study. *Acupunct Med* 2004;22(2):60-67.
8. Mens JM, Vleeming A, Snijders CJ, Koes BW, Stam HJ. Reliability and validity of the active straight leg raise test in posterior pelvic pain since pregnancy. *Spine* 2001;26(10):1167-1171.
9. Bullock J, Jull G, Bullock M. The relationship of low back pain to postural changes during pregnancy. *Austr J Physiotherapy* 1987:10-17.
10. Carr CA. Use of a maternity support binder for relief of pregnancy-related back pain. *J Obstet Gynecol Neonatal Nurs* 2003;32(4):495-502.
11. Depledge J, McNair PJ, Keal-Smith C, Williams M. Management of symphysis pubis dysfunction during pregnancy using exercise and pelvic support belts. *Phys Ther* 2005;85(12):1290-1300.
12. Dumas GA, Reid JG, Wolfe LA, Griffin MP, McGrath MJ. Exercise, posture, and back pain during pregnancy. *Clin Biomech* 1995;10(2):104-109.
13. Garshasbi A, Faghih Zadeh S. The effect of exercise on the intensity of low back pain in pregnant women. *Int J Gynaecol Obstet* 2005;88(3):271-275.
14. Rost CC, Jacqueline J, Kaiser A, Verhagen AP, Koes BW. Pelvic pain during pregnancy: a descriptive study of signs and symptoms of 870 patients in primary care. *Spine* 2004;29(22):2567-2572.
15. To WW, Wong MW. Factors associated with back pain symptoms in pregnancy and the persistence of pain 2 years after pregnancy. *Acta Obstet Gynecol Scand* 2003;82(12):1086-1091.
16. Turgut F, Turgut M, Cetinsahin M. A prospective study of persistent back pain after pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1998;80(1):45-48.
17. Olsson C, Nilsson-Wikmar L. Health-related quality of life and physical ability among pregnant women with and without back pain in late pregnancy. *Acta Obstet Gynecol Scand* 2004;83(4):351-357.
18. Gutke A, Ostgaard HC, Oberg B. Pelvic girdle pain and lumbar pain in pregnancy: a cohort study of the consequences in terms of health and functioning. *Spine* 2006;31(5):149-155.

19. Hansen A, Jensen DV, Wormslev M, Minck H, Johansen S, Larsen EC, et al. Symptom-giving pelvic girdle relaxation in pregnancy. II: Symptoms and clinical signs. *Acta Obstet Gynecol Scand* 1999;78(2):111-115.
20. Noren L, Ostgaard S, Johansson G, Ostgaard HC. Lumbar back and posterior pelvic pain during pregnancy: a 3-year follow-up. *Eur Spine J* 2002;11(3):267-271.
21. Nilsson-Wikmar L, Holm K, Oijerstedt R, Harms-Ringdahl K. Effect of three different physical therapy treatments on pain and activity in pregnant women with pelvic girdle pain: a randomized clinical trial with 3, 6, and 12 months follow-up postpartum. *Spine* 2005;30(8):850-856.
22. Larsen EC, Wilken-Jensen C, Hansen A, Jensen DV, Johansen S, Minck H, et al. Symptom-giving pelvic girdle relaxation in pregnancy. I: Prevalence and risk factors. *Acta Obstet Gynecol Scand* 1999;78(2):105-110.
23. Wu WH, Meijer OG, Uegaki K, Mens JM, Van Dieen JH, Wuisman PI, et al. Pregnancy-related pelvic girdle pain (PPP), I: Terminology, clinical presentation, and prevalence. *Eur Spine J* 2004;13(7):575-589.
24. Vleeming A, Stoeckart R, Volkers ACW, Snijders C. Relation between form and function in the sacroilaic joint. Part I: Clinical anatomical aspects. . *Spine* 1990a;15(2):130-132.
25. Mens JM, Vleeming A, Stoeckart R, Stam HJ, Snijders CJ. Understanding peripartum pelvic pain. Implications of a patient survey. *Spine* 1996;21(11):1363-1369; discussion 1369-1370.
26. Ostgaard HC, Roos-Hansson E, Zetherstrom G. Regression of back and posterior pelvic pain after pregnancy. *Spine* 1996;21(23):2777-2780.
27. Brynhildsen J, Hansson A, Persson A, Hammar M. Follow-up of patients with low back pain during pregnancy. *Obstet Gynecol* 1998;91(2):182-186.
28. Padua L, Padua R, Bondi R, Ceccarelli E, Caliandro P, D'Amico P, et al. Patient-oriented assessment of back pain in pregnancy. *Eur Spine J* 2002;11(3):272-275.
29. Hansen A, Jensen DV, Larsen EC, Wilken-Jensen C, Kaae BE, Frolich S, et al. Postpartum pelvic pain--the "pelvic joint syndrome": a follow-up study with special reference to diagnostic methods. *Acta Obstet Gynecol Scand* 2005;84(2):170-176.
30. Svensson HO, Andersson GB, Hagstad A, Jansson PO. The relationship of low-back pain to pregnancy and gynecologic factors. *Spine* 1990;15(5):371-375.
31. Ostgaard HC, Zetherstrom G, Roos-Hansson E, Svanberg B. Reduction of back and posterior pelvic pain in pregnancy. *Spine* 1994;19(8):894-900.
32. Noren L, Ostgaard S, Nielsen TF, Ostgaard HC. Reduction of sick leave for lumbar back and posterior pelvic pain in pregnancy. *Spine* 1997;22(18):2157-2160.
33. Sydsjo A, Sydsjo G, Wijma B. Increase in sick leave rates caused by back pain among pregnant Swedish women after amelioration of social benefits. A paradox. *Spine* 1998;23(18):1986-1990.
34. Mogren IM, Pohjanen AI. Low back pain and pelvic pain during pregnancy: prevalence and risk factors. *Spine* 2005;30(8):983-991.
35. Saugstad LF. Is persistent pelvic pain and pelvic joint instability associated with early menarche and with oral contraceptives? *Eur J Obstet Gynecol Reprod Biol* 1991;41(3):203-206.
36. Kristiansson P, Nilsson-Wikmar L, von Schoultz B, Svardsudd K, Wramsby H. Back pain in in-vitro fertilized and spontaneous pregnancies. *Hum Reprod* 1998;13(11):3233-3238.
37. Vleeming A, Albert HB, Ostgaard HC, Sturesson B, Stuge B. European guidelines for the diagnosis and treatment of pelvic girdle pain. *Eur Spine J* 2008;[E pub ahead of print].

38. Wu WH. Pregnancy-related Pelvic girdle Pain (PPP), An emphasis on transverse pelvis-thorax coordination during walking. Thesis. Vrije, 2003.
39. Genell S. Studies on Insufficienta pelvis (graviarum et puerperarum). *Acta Obstet Gyn Scand* 1949;28:1-37.
40. Ostgaard HC, Andersson GB, Karlsson K. Prevalence of back pain in pregnancy. *Spine* 1991;16(5):549-552.
41. Vleeming A, Volkers ACW, Snijders C, Stoeckart R. Relation between form and function in the sacroiliac joint. Part 2.Biomechanical spects. *Spine* 1990b;15(2):133-136.
42. Pool-Goudzwaard AL, Vleeming A, Stoeckart R, Snijders CJ, Mens JM. Insufficient lumbopelvic stability: a clinical, anatomical and biomechanical approach to 'a-specific' low back pain. *Man Ther* 1998;3(1):12-20.
43. Snijders C, Vleeming;A, Stoeckary R, Mens J, Koepsell T. *Biomechanics of the interface between spine and pelvis in different poistures. In: Vleeming A, Mooney V, Dorman T, Snijders CH, Stoeckart R eds. Movement, Stability &Low Back Pain. The essential role of the pelvis.*: Churchill Livingstone, 1997.
44. Sturesson B, Selvik G, Uden A. Movement of the sacroiliac joints, A roentgen stereophotogrammetric analysis. *Spine* 1989;14(2):162-165.
45. Richardson CA, Snijders CJ, Hides JA, Damen L, Pas MS, Storm J. The relation between the transversus abdominis muscles, sacroiliac joint mechanics, and low back pain. *Spine* 2002;27(4):399-405.
46. Pool-Goudzwaard A, van Dijke GH, van Gurp M, Mulder P, Snijders C, Stoeckart R. Contribution of pelvic floor muscles to stiffness of the pelvic ring. *Clin Biomech* 2004;19(6):564-571.
47. Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994;19(2):165-172.
48. Sihvonen T, Huttunen M, Makkonen M, Airaksinen O. Functional changes in back muscle activity correlate with pain intensity and prediction of low back pain during pregnancy. *Arch Phys Med Rehabil* 1998;79(10):1210-1212.
49. Sturesson B, Uden G, Uden A. Pain pattern in pregnancy and "catching" of the leg in pregnant women with posterior pelvic pain. *Spine* 1997;22(16):1880-83; discussion 1884.
50. Petersen LK, Hvidman L, Uldbjerg N. Normal serum relaxin in women with disabling pelvic pain during pregnancy. *Gynecol Obstet Invest* 1994;38(1):21-23.
51. Albert H, Godskesen M, Westergaard JG, Chard T, Gunn L. Circulating levels of relaxin are normal in pregnant women with pelvic pain. *Eur J Obstet Gynecol Reprod Biol* 1997;74(1):19-22.
52. Bjorklund K, Bergstrom S, Nordstrom ML, Ulmsten U. Symphyseal distention in relation to serum relaxin levels and pelvic pain in pregnancy. *Acta Obstet Gynecol Scand* 2000;79(4):269-275.
53. MacLennan AH, MacLennan SC. Symptom-giving pelvic girdle relaxation of pregnancy, postnatal pelvic joint syndrome and developmental dysplasia of the hip. The Norwegian Association for Women with Pelvic Girdle Relaxation (Landforeningen for Kvinner Med Bekkenlosningsplager). *Acta Obstet Gynecol Scand* 1997;76(8):760-764.
54. Damen L, Buyruk HM, Guler-Uysal F, Lotgering FK, Snijders CJ, Stam HJ. The prognostic value of asymmetric laxity of the sacroiliac joints in pregnancy-related pelvic pain. *Spine* 2002;27(24):2820-2824.

55. Lindal E, Hauksson A, Arnardottir S, Hallgrimsson JP. Low back pain, smoking and employment during pregnancy and after delivery - a 3-month follow-up study. *J Obstet Gynaecol* 2000;20(3):263-266.
56. Van De Pol G, Van Brummen HJ, Bruinse HW, Heintz AP, Van Der Vaart CH. Pregnancy-related pelvic girdle pain in the Netherlands. *Acta Obstet Gynecol Scand* 2007;86(4):416-422.
57. Orvieto R, Achiron A, Ben-Rafael Z, Gelernter I, Achiron R. Low-back pain of pregnancy. *Acta Obstet Gynecol Scand* 1994;73(3):209-214.
58. Kristiansson P, Svardsudd K, von Schoultz B. Back pain during pregnancy: a prospective study. *Spine* 1996;21(6):702-709.
59. Berg G, Hammar M, Moller-Nielsen J, Linden U, Thorblad J. Low back pain during pregnancy. *Obstet Gynecol* 1988;71(1):71-75.
60. Diakow PR, Gadsby TA, Gadsby JB, Gleddie JG, Leprich DJ, Scales AM. Back pain during pregnancy and labor. *J Manipulative Physiol Ther* 1991;14(2):116-118.
61. Endresen EH. Pelvic pain and low back pain in pregnant women--an epidemiological study. *Scand J Rheumatol* 1995;24(3):135-141.
62. Fast A, Weiss L, Ducommun EJ, Medina E, Butler JG. Low-back pain in pregnancy. Abdominal muscles, sit-up performance, and back pain. *Spine* 1990;15(1):28-30.
63. Golighty R. Pelvic arthropathy in pregnancy and the puerperium. *Physiotherapy* 1982;68(7):216-220.
64. Mantle MJ, Greenwood RM, Currey HL. Backache in pregnancy. *Rheumatol Rehabil* 1977;16(2):95-101.
65. Albert HB, Godskesen M, Westergaard JG. Incidence of four syndromes of pregnancy-related pelvic joint pain. *Spine* 2002;27(24):2831-2834.
66. Ostgaard HC, Andersson GB, Wennergren M. The impact of low back and pelvic pain in pregnancy on the pregnancy outcome. *Acta Obstet Gynecol Scand* 1991;70(1):21-24.
67. Ostgaard HC, Andersson GB. Previous back pain and risk of developing back pain in a future pregnancy. *Spine* 1991;16(4):432-436.
68. Kristiansson P, Svardsudd K, von Schoultz B. Back pain during pregnancy: a prospective study. *Spine* 1996;21(6):702-709.
69. Rost CC, Jacqueline J, Kaiser A, Verhagen AP, Koes BW. Prognosis of women with pelvic pain during pregnancy: a long-term follow-up study. *Acta Obstet Gynecol Scand* 2006;85(7):771-777.
70. Larsen EC, Wilken-Jensen C, Hansen A, Jensen DV, Johansen S, Minck H, et al. Symptom-giving pelvic girdle relaxation in pregnancy. I: Prevalence and risk factors. *Acta Obstet Gynecol Scand* 1999;78(2):105-110.
71. Haugland KS, Rasmussen S, Daltveit AK. Group intervention for women with pelvic girdle pain in pregnancy. A randomized controlled trial. *Acta Obstet Gynecol Scand* 2006;85(11):1320-1326.
72. Ostgaard HC, Zetherstrom G, Roos-Hansson E. Back pain in relation to pregnancy: a 6-year follow-up. *Spine* 1997;22(24):2945-2950.
73. Ostgaard HC, Andersson GB. Previous back pain and risk of developing back pain in a future pregnancy. *Spine* 1991;16(4):432-436.
74. Ostgaard HC, Andersson GB. Postpartum low-back pain. *Spine* 1992;17(1):53-55.
75. Albert H, Godskesen M, Westergaard J. Prognosis in four syndromes of pregnancy-related pelvic pain. *Acta Obstet Gynecol Scand* 2001;80(6):505-510.
76. Padua L, Caliandro P, Aprile I, Pazzaglia C, Padua R, Calistri A, et al. Back pain in pregnancy: 1-year follow-up of untreated cases. *Eur Spine J* 2005;14(2):151-154.

77. Gutke A, Josefsson A, Oberg B. Pelvic girdle pain and lumbar pain in relation to postpartum depressive symptoms. *Spine* 2007;32(13):1430-1436.
78. Mogren IM. BMI, pain and hyper-mobility are determinants of long-term outcome for women with low back pain and pelvic pain during pregnancy. *Eur Spine J* 2006;15(7):1093-1102.
79. IASP. A list with definations and notes on usage. *Pain* 1979;6:249-52.
80. Craig A. A new view of pain as a homeostatic emotion. *Trends Neurosci* 2003;26(6):303-307.
81. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med* 2004;140(6):441-451.
82. Holdcroft A, Power I. Recent developments: management of pain. *BMJ* 2003;326(7390):635-639.
83. Ostgaard HC, Zetherstrom G, Roos-Hansson E. The posterior pelvic pain provocation test in pregnant women. *Eur Spine J* 1994;3(5):258-260.
84. Kristiansson P, Svardsudd K. Discriminatory power of tests applied in back pain during pregnancy. *Spine* 1996;21(20):2337-43; discussion 2343-2344.
85. Albert H, Godskesen M, Westergaard J. Evaluation of clinical tests used in classification procedures in pregnancy-related pelvic joint pain. *Eur Spine J* 2000;9(2):161-166.
86. Ostgaard HC, Zetherstrom G, Roos-Hansson E. The posterior pelvic pain provocation test in pregnant women. *Eur Spine J* 1994;3(5):258-60.
87. Pennick VE, Young G. Interventions for preventing and treating pelvic and back pain in pregnancy. *Cochrane Database Syst Rev* 2007(2):CD001139.
88. Mens JM, Snijders CJ, Stam HJ. Diagonal trunk muscle exercises in peripartum pelvic pain: a randomized clinical trial. *Phys Ther* 2000;80(12):1164-1173.
89. Stuge B, Veierod MB, Laerum E, Vollestad N. The efficacy of a treatment program focusing on specific stabilizing exercises for pelvic girdle pain after pregnancy: a two-year follow-up of a randomized clinical trial. *Spine* 2004;29(10):197-203.
90. Mantle MJ, Holmes J, Currey HL. Backache in pregnancy II: prophylactic influence of back care classes. *Rheumatol Rehabil* 1981;20(4):227-232.
91. Thomas I, Nicklin J, Pollock H, Faulkner K. Evaluation of a matermity cusion (Ozzlo pillow) for back ache and insomnia inlate pregnancy. *Australian and New Zealand Journal Obstetrics and Gynecology* 1989;29(2):133-138.
92. Field T, Hernandez-Reif M, Hart S, Theakston H, Schanberg S, Kuhn C. Pregnant women benefit from massage therapy. *J Psychosom Obstet Gynaecol* 1999;20(1):31-38.
93. Kihlstrand M, Stenman B, Nilsson S, Axelsson O. Water-gymnastics reduced the intensity of back/low back pain in pregnant women. *Acta Obstet Gynecol Scand* 1999;78(3):180-185.
94. Suputtitada A, Wacharapreechanont T, Chaisayan P. Effect of the "sitting pelvic tilt exercise" during the third trimester in primigravidas on back pain. *J Med Assoc Thai* 2002;85 Suppl 1:170-179.
95. Martins R, Pinto e Silvia J. An exercise method for the treatment of lumbar and posterior pelvic pain in pregnancy [Tratmento da lumbalgia 3 dor pelvica. Posterior he gestacao por um metodo de exercisios]. *Revista Brasileira de Ginecologia Y Obstetricia* 2005;27(5):275-282.
96. Granath AB, Hellgren MS, Gunnarsson RK. Water aerobics reduces sick leave due to low back pain during pregnancy. *J Obstet Gynecol Neonatal Nurs* 2006;35(4):465-471.

97. Kalus SM, Kornman LH, Quinlivan JA. Managing back pain in pregnancy using a support garment: a randomised trial. *BJOG* 2008;115(1):68-75.
98. Sjolund B, Terenius L, Eriksson M. Increased cerebrospinal fluid levels of endorphins after electro-acupuncture. *Acta Physiol Scand* 1977;100(3):382-384.
99. Han JS. Acupuncture and endorphins. *Neurosci Lett* 2004;361(1-3):258-261.
100. Wang SM, Kain ZN, White P. Acupuncture analgesia: I. The scientific basis. *Anesth Analg* 2008;106(2):602-610.
101. Stux G, Hammerschlag R. *Clinical Acupuncture*. Berlin Heidelberg New York: Springer-Verlag, 2001.
102. Andersson S, Lundeberg T. Acupuncture--from empiricism to science: functional background to acupuncture effects in pain and disease. *Med Hypotheses* 1995;45(3):271-281.
103. Smith C, Crowther C, Beilby J. Pregnancy outcome following women's participation in a randomised controlled trial of acupuncture to treat nausea and vomiting in early pregnancy. *Complement Ther Med* 2002;10(2):78-83.
104. Ramnero A, Hanson U, Kihlgren M. Acupuncture treatment during labour--a randomised controlled trial. *BJOG* 2002;109(6):637-644.
105. Gejervall A, Stener-Victorin E, Molle rA, Janson P, Werner C, Bergh C. Electro-acupuncture versus conventional analgesia: a comparison of pain levels during oocyte aspiration and patients' experiences of well-being after surgery. *Hum Reprod* 2005;20(3):728-735.
106. Stener-Victorin E, Waldenstrom U, Nilsson L, Wikland M, Janson P. A prospective randomized study of electro-acupuncture versus alfentanil as anaesthesia during oocyte aspiration in in-vitro fertilization. *Hum Reprod* 1999;14(10):2480-2484.
107. Stener-Victorin E, Waldenstrom U, Wikland M, Nilsson L, Hagglund L, Lundeberg T, et al. Electro-acupuncture as a peroperative analgesic method and its effects on implantation rate and neuropeptide Y concentrations in follicular fluid. *Hum Reprod* 2003;18(7):1454-1460.
108. Humaidan P S-VE. Pain relief during oocyte retrieval with a new short duration electro-acupuncture technique--an alternative to conventional analgesic methods. *Hum Reprod* 2004;19(6):1367-1372.
109. Witt CM, Jena S, Brinkhaus B, Liecker B, Wegscheider K, Willich SN. Acupuncture for patients with chronic neck pain. *Pain* 2006;125(1-2):98-106.
110. Guerreiro de Hoyos JA, Andres MArtin MdC, Martin A, Baena de Leon EBy, Vigara Lopez M, Lopez TM, et al. Randomised trial of long term effect of acupuncture for shoulder pain. *Pain* 2004;112:289-298.
111. Vas J, Mendez C, Perea-Milla E, Vega E, Panadero MD, Leon JM, et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *BMJ* 2004;329(7476):1216.
112. Witt C, Brinkhaus B, Jena S, Linde K, Streng A, Wagenpfeil S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet* 2005;366(9480):136-143.
113. Furlan AD, van Tulder M, Cherkin D, Tsukayama H, Lao L, Koes B, et al. Acupuncture and dry-needling for low back pain: an updated systematic review within the framework of the cochrane collaboration. *Spine* 2005;30(8):944-963.
114. Manheimer E, White A, Berman B, Forys K, Ernst E. Meta-analysis: acupuncture for low back pain. *Ann Intern Med* 2005;142(8):651-663.
115. Brinkhaus B, Witt CM, Jena S, Linde K, Streng A, Wagenpfeil S, et al. Acupuncture in patients with chronic low back pain: a randomized controlled trial. *Arch Intern Med* 2006;166(4):450-457.

116. Melchart D, Streng A, Hoppe A, Brinkhaus B, Witt C, Wagenpfeil S, et al. Acupuncture in patients with tension-type headache: randomised controlled trial. *BMJ* 2005;331(7513):376-382.
117. Ernst E, Pittler MH. The effectiveness of acupuncture in treating acute dental pain: a systematic review. *Br Dent J* 1998;184(9):443-447.
118. Linde K, Streng A, Jurgens S, Hoppe A, Brinkhaus B, Witt C, et al. Acupuncture for patients with migraine: a randomized controlled trial. *JAMA* 2005;293(17):2118-2125.
119. Witt CM, Reinhold T, Brinkhaus B, Roll S, Jena S, Willich SN. Acupuncture in patients with dysmenorrhea: a randomized study on clinical effectiveness and cost-effectiveness in usual care. *Am J Obstet Gynecol* 2008;198(2):166 e1-8.
120. Wyon Y, Wijma K, Nedstrand E, Hammar M. A comparison of acupuncture and oral estradiol treatment of vasomotor symptoms in postmenopausal women. *Climacteric* 2004;7(2):153-164.
121. Nedstrand E, Wyon Y, Hammar M, Wijma K. Psychological well-being improves in women with breast cancer after treatment with applied relaxation or electro-acupuncture for vasomotor symptom. *J Psychosom Obstet Gynaecol* 2006;27(4):193-199.
122. Zaborowska E, Brynhildsen J, Damberg S, Fredriksson M, Lindh-Astrand L, Nedstrand E, et al. Effects of acupuncture, applied relaxation, estrogens and placebo on hot flushes in postmenopausal women: an analysis of two prospective, parallel, randomized studies. *Climacteric* 2007;10(1):38-45.
123. Manheimer E, Zhang G, Udoff L, Haramati A, Langenberg P, Berman BM, et al. Effects of acupuncture on rates of pregnancy and live birth among women undergoing in vitro fertilisation: systematic review and meta-analysis. *BMJ* 2008;[Epub ahead of print].
124. A Proposed Standard International Acupuncture Nomenclature: Report of a WHO Scientific Group Geneva:, 1991.
125. Ezzo J, Berman B, Hadhazy VA, Jadad AR, Lao L, Singh BB. Is acupuncture effective for the treatment of chronic pain? A systematic review. *Pain* 2000;86(3):217-225.
126. Lewith G, Vincent C. The evaluation of the clinical effects of acupuncture. A problem reassessed and a framework for future research. *Pain Forum* 1995;4:29-39.
127. Dawidson I, Blom M, Lundeberg T, Angmar-Mansson B. The influence of acupuncture on salivary flow rates in healthy subjects. *J Oral Rehabil* 1997;24(3):204-208.
128. Lundeberg T. Electrical stimulation techniques. *Lancet* 1996;348(9043):1672-1673.
129. Sato A, Sato Y, Schmidt R. *The impact of Somatosenory Input on Autonomic Functions*. Heidelberg: Springer-Verlag, 1997.
130. Kawakita K, Shinbara H, Imai K, Fukuda F, Yano T, Kuriyama K. How do acupuncture and moxibustion act? - Focusing on the progress in Japanese acupuncture research. *J Pharmacol Sci* 2006;100(5):443-459.
131. Kagitani F, Uchida S, Hotta H, Aikawa Y. Manual acupuncture needle stimulation of the rat hindlimb activates groups I, II, III and IV single afferent nerve fibers in the dorsal spinal roots. *Jpn J Physiol* 2005;55(3):149-155.
132. Sandkuehler J, Chen J, Cheng G, Randic M. Low frequency stimulation of afferent Að-fibers induces long-term depression of primary afferent synapses with substantia gelatinosa neurons in the rat. . *J Neurosci* 1997;17(16):6483-6491.
133. Melzack R, . Wall, PD. Pain mechanism: A new theory. *Science* 1965;150:971-979.
134. Wang SM, Kain ZN, White PF. Acupuncture analgesia: II. Clinical considerations. *Anesth Analg* 2008;106(2):611-621.

135. Sandkühler J. The organization and function of endogenous antinociceptive systems. *Prog Neurobiol* 1996;50(1):49-81.
136. Han J. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *TRENDS in Neurosciences* 2003;26(1):17-22.
137. Ernst E. Acupuncture--a critical analysis. *J Intern Med* 2006;259(2):125-137.
138. Morgan MM, Whitney PK. Behavioral analysis of diffuse noxious inhibitory controls (DNIC): antinociception and escape reactions. *Pain* 1996;66(2-3):307-312.
139. Le Bars D, Dickenson A, Besson J. Diffuse noxious inhibitiry controls (DNIC). I. effects on dorsal horn convergent neurones in the rat. *Pain* 1979;6(3):283-304.
140. Lund I GY, Yu LC, Uvnas-Moberg K, Wang J, Yu C, Kurosawa M, Agren G, Rosén A, Lekman M, Lundeberg T. Repeated massage-like stimulaton induces long-term effects on nociception: contribution of oxytocinergic mechanisms. *Eur J Neurosci* 2002;16(2):330-338.
141. Uvnas-Moberg K, Bruzelius G, Alster P, Lundeberg T. The antinociceptive effect of non-noxious sensory stimulation is mediated partly through oxytocinergic mechanisms. *Acta Physiol Scand* 1993;149(2):199-204.
142. Yang J, Yang y, Chen J, Liu W, Wang C, Lin B. Effect of oxytocin on acupuncture analgesia in the rat. *Neuropeptides* 2007;41(5):285-292.
143. Sims J. The mechanism of acupuncture analgesia: a review *Complement Ther Med* 1997;5:102-111.
144. Huang L, Ren M, Lu J, Han J. Mutual potentiation of the analgesic effects of [met5] enkephalin, dynorphin A-(1-13) and morphine in the spinal cord of the rat. *Acta Physiol Sin* 1987;39:454-461.
145. Wedenberg K, Moen B, Norling A. A prospective randomized study comparing acupuncture with physiotherapy for low-back and pelvic pain in pregnancy. *Acta Obstet Gynecol Scand* 2000;79(5):331-335.
146. Kvorning N, Holmberg C, Grennert L, Aberg A, Akeson J. Acupuncture relieves pelvic and low-back pain in late pregnancy. *Acta Obstet Gynecol Scand* 2004;83(3):246-250.
147. Lund I, Lundeberg T, Lonnberg L, Svensson E. Decrease of pregnant women's pelvic pain after acupuncture: a randomized controlled single-blind study. *Acta Obstet Gynecol Scand* 2006;85(1):12-19.
148. Vincent C. The safety of acupuncture. *BMJ* 2001;323(7311):467-468.
149. MacPherson H, Thomas K, Walters S, Fitter M. The York acupuncture safety study: prospective survey of 34 000 treatments by traditional acupuncturists. *BMJ* 2001;323(7311):486-487.
150. Macpherson H, Scullion A, Thomas KJ, Walters S. Patient reports of adverse events associated with acupuncture treatment: a prospective national survey. *Qual Saf Health Care* 2004;13(5):349-355.
151. Melchart D, Weidenhammer W, Streng A, Reitmyr S, Hoppe A. Prospective investigation of adverse effect of acupuncture in 97 733 patients. *Arch Intern Med* 2004;164(1):104-105.
152. White A, Hayhoe S, Hart A, Ernst E. Adverse events following acupuncture: prospective survey of 32 000 consultations with doctors and physiotherapists. *BMJ* 2001;323(7311):485-486.
153. Yamashita H, Tsukayama H, Tanno Y, Nishijo K. Adverse events in acupuncture and moxibustion treatment: a six-year survey at a national clinic in Japan. *J Altern Complement Med* 1999;5(3):229-236.
154. Netter FH. *Atlas of Human Anatomy*. Basle, Switzerland: CIBA-Geigy Limited, 1994.

155. Xinnong C. Chinese Acupuncture and Moxibustion. *Chinese Acupuncture and Moxibustion*. Beijing: Foreign Languages Press, 1987:330.
156. Zharkin N. Acupuncture in obstetrics. *Journal of Chinese Medicine* 1990(33):10-13.
157. Jayasuriya A. Clinical Acupuncture. New Delhi: B. Jain Publishers (p) Ltd., 1997:74-75.
158. Filshie FWA. *Medical Acupuncture*. Hong Kong: Churchill Livingstone, 1998.
159. Dawes GS, Moulden M, Redman CW. The advantages of computerized fetal heart rate analysis. *J Perinat Med* 1991(19):39-45.
160. Huskinsson EC. 'Measurement of pain'. *Lancet* 1974;9:1127-1131.
161. Enthoven P, Skargren E, Kjellman G, Oberg B. Course of back pain in primary care: a prospective study of physical measures. *J Rehabil Med* 2003;35(4):168-173.
162. Vas J, Perea-Milla E, Mendez C, Sanchez Navarro C, Leon Rubio JM, Brioso M, et al. Efficacy and safety of acupuncture for chronic uncomplicated neck pain: a randomised controlled study. *Pain* 2006;126(1-3):245-255.
163. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Ann Emerg Med* 2001;38(6):633-638.
164. Sahlen B, Sprangfort E, Nygren Å. The Disability Raiting Index: an instrument for the assessment of disability in clinical settings. *J Clin Epidemiol* 1994(47):1423-1434.
165. Fairbank JC, Couper J, Davies JB, O'Brien JP. The Oswestry low back pain disability questionnaire. *Physiotherapy* 1980;66(8):271-273.
166. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;33(5):337-343.
167. EuroQol G. EuroQol -a new facility for the measurement of health related quality of life. In: Policy H, editor, 1990:199-208.
168. Shikiar R, Willian MK, Okun MM, Thompson CS, Revicki DA. The validity and responsiveness of three quality of life measures in the assessment of psoriasis patients: results of a phase II study. *Health Qual Life Outcomes* 2006;4:71.
169. Mens JM, Vleeming A, Snijders CJ, Stam HJ, Ginai AZ. The active straight leg raising test and mobility of the pelvic joints. *Eur Spine J* 1999;8(6):468-473.
170. Vincent C, Lewith G. Placebo controls for acupuncture studies. *J R Soc Med* 1995;88(4):199-202.
171. Mens JM, Damen L, Snijders CJ, Stam HJ. The mechanical effect of a pelvic belt in patients with pregnancy-related pelvic pain. *Clin Biomech* 2006;21(2):122-127.
172. Richardson CA, Jull GA. Muscle control-pain control. What exercises would you prescribe? *Man Ther* 2000;1(1):2-10.
173. Gould AL. A new approach to the analysis of clinical drug trials with withdrawals. *Biometrics* 1980;36(4):721-727.
174. Maxwell AE. *Analyzing Qualitative Data*. London: Methuen, 1961.
175. Stuge B, Hilde G, Vollestad N. Physical therapy for pregnancy-related low back and pelvic pain: a systematic review. *Acta Obstet Gynecol Scand* 2003;82(11):983-990.
176. Damen L, Spoor CW, Snijders CJ, Stam HJ. Does a pelvic belt influence sacroiliac joint laxity? *Clin Biomech* 2002;17(7):495-498.
177. Furlan AD, Van Tulder M, Cherkin D, Tsukayama H, Lao L, Koes B, et al. Acupuncture and dry-needling for low back pain: an updated systematic review within the framework of the cochrane collaboration. *Spine* 2005;30(8):944-963.
178. Kvorning Ternov N, Grennert L, Åberg A, Algotsson L, Åkeson J. Acupuncture for low-back pain in late pregnancy. *Pain Medicine* 2001;2(3):204-207.

179. White A, Hayhoe S, Hart A, Ernst E. Adverse events following acupuncture: prospective survey of 32 000 consultations with doctors and physiotherapists. *BMJ* 2001;323(7311):485-486.
180. Nilsson-Wikmar L, Holm K, Oijerstedt R, Harms-Ringdahl K. Effect of three different physical therapy treatments on pain and activity in pregnant women with pelvic girdle pain: a randomized clinical trial with 3, 6, and 12 months follow-up postpartum. *Spine* 2005;30(8):850-856.
181. Noren L, Ostgaard S, Nielsen TF, Ostgaard HC. Reduction of sick leave for lumbar back and posterior pelvic pain in pregnancy. *Spine* 1997;22(18):2157-60.
182. Ostgaard HC, Andersson GB, Karlsson K. Prevalence of back pain in pregnancy. *Spine* 1991;16(5):549-552.
183. Elden H, Ladfors L, Olsen MF, Ostgaard HC, Hagberg H. Effects of acupuncture and stabilising exercises as adjunct to standard treatment in pregnant women with pelvic girdle pain: randomised single blind controlled trial. *BMJ* 2005;330(7494):761-764.
184. Lund I, Lundeberg T, Lonnberg L, Svensson E. Decrease of pregnant women's pelvic pain after acupuncture: a randomized controlled single-blind study. *Acta Obstet Gynecol Scand* 2006;85(1):12-19.
185. Olausson H, Lamarre Y, Backlund H, Morin C, Wallin BG, Starck G, et al. Unmyelinated tactile afferents signal touch and project to insular cortex. *Nat Neurosci* 2002;5(9):900-904.
186. Lund I, Lundeberg T. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? *Acupunct Med* 2006;24(1):13-15.
187. Streitberger K, Diefenbacher M, Bauer A, Conradi R, Bardenheuer H, Martin E, et al. Acupuncture compared to placebo-acupuncture for postoperative nausea and vomiting prophylaxis: a randomised placebo-controlled patient and observer blind trial. *Anaesthesia* 2004;59(2):142-149.
188. Park J, White AR, James MA, Hemsley AG, Johnson P, Chambers J, et al. Acupuncture for subacute stroke rehabilitation: a Sham-controlled, subject- and assessor-blind, randomized trial. *Arch Intern Med* 2005;165(17):2026-2031.
189. Karst M, Rollnik JD, Fink M, Reinhard M, Piepenbrock S. Pressure pain threshold and needle acupuncture in chronic tension-type headache--a double-blind placebo-controlled study. *Pain* 2000;88(2):199-203.
190. Foster NE, Thomas E, Barlas P, Hill JC, Young J, Mason E, et al. Acupuncture as an adjunct to exercise based physiotherapy for osteoarthritis of the knee: randomised controlled trial. *BMJ* 2007;335(7617):436-440.
191. Fairbank JC, Pynsent PB. The Oswestery Disability Index. *Spine* 2000;25:2940-2952; discussion 2952.
192. Meade TW, Dyer S, Browne W, Frank AO. Randomised comparison of chiropractic and hospital outpatient management for low back pain: results from extended follow up. *BMJ* 1995;311(7001):349-351.
193. Lao L, Bergman S, Hamilton GR, Langenberg P, Berman B. Evaluation of acupuncture for pain control after oral surgery: a placebo-controlled trial. *Arch Otolaryngol Head Neck Surg* 1999;125(5):567-572.
194. Hesse J, Mogelvang B, Simonsen H. Acupuncture versus metoprolol in migraine prophylaxis: a randomized trial of trigger point inactivation. *J Intern Med* 1994;235(5):451-456.
195. Streitberger K, Kleinhenz J. Introducing a placebo needle into acupuncture research. *Lancet* 1998;352(9125):364-365.

196. Bausell RB, Lao L, Bergman S, Lee WL, Berman BM. Is acupuncture analgesia an expectancy effect? Preliminary evidence based on participants' perceived assignments in two placebo-controlled trials. *Eval Health Prof* 2005;28(1):9-26.