Akademisk avhandling

Aspects of diagnosis and treatment of hypopituitarism in adult life

av

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Avhandlingen baseras på följande delarbeten:

I. Detection of genetic hypopituitarism in an adult population of idiopathic pituitary insufficiency patients with growth hormone deficiency
Filipsson H, Savaneau A, Barbosa E L J, Barlier A, Enjalber A, Glad C, Palming J, Johannsson G, Thierry B
Manuscript

II. Exploring the use of recombinant human thyrotropin in the diagnosis of central hypothyroidism
Filipsson H, Nyström E, Johannsson G
European Journal of Endocrinology 2008 Aug;159(2):153-60

III. The impact of glucocorticoid replacement regimens on metabolic outcome and comorbidity in hypopituitary patients
Filipsson H, Monson JP, Koltowska-Häggström M, Mattsson A, Johannsson G
Journal of Clinical Endocrinology and Metabolism 2006 Oct;91(10):3954-61

IV. Discontinuation of long-term GH replacement therapy – a randomised, placebo controlled trial in adult GH deficiency
Filipsson H, Barbosa E L J, Nilsson AG, Norrman L, Ragnarsson O, Johannsson G
Manuscript

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Abstract

Aspects of diagnosis and treatment of hypopituitarism in adult life

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Management of adult patients with hypopituitarism can improve with better characterisation of idiopathic pituitary insufficiency (IPI) and clearer diagnosis of central hypothyroidism (CH). Moreover, optimised treatment strategies for glucocorticoid (GC) replacement therapy and of long-term growth hormone (GH) in GH deficiency (GHD) are needed.

This thesis contains four studies addressing these issues. By evaluating patients with IPI, mutations generating hypopituitarism were identified in an unselected adult IPI population. A new allel constellation in a compound *PROP1* mutation was revealed in two siblings, with a phenotype of very late inset ACTH-insufficiency. Those cases were only detected in patients with documented childhood-onset disease. A pilot study investigated the response of the thyroid gland after stimulation with 0.9 mg recombinant human thyreotropin (rhTSH) in patients with newly diagnosed CH and healthy controls. The untreated CH patients had lower free thyroxine response than controls. A database study containing 2424 hypopituitary patients, divided into ACTH insufficient and ACTH-sufficient (AS) patients, demonstrated a clear GC dose-response relation with metabolic outcome. Patients with hydrocortisone equivalent doses of <20 mg/day had a similar metabolic profile as AS patients. In a large study on GHD patients on long-term GH treatment quality of life (QoL), body composition, and metabolic outcome were evaluated during 4-month-GH-discontinuation in a double blind, placebo controlled design. QoL deteriorated, body composition moved towards a GHD state and metabolic parameters were impaired during placebo treatment.

These studies infer that genetic hypopituitarism should be searched for in IPI cases, especially in childhood onset disease and where there is a family history. The diagnosis of CH can be improved by an rhTSH test. In many cases, doses of GC can be reduced in ACTH-insufficient patients in order to improve their metabolic outcome and continuous long-term GH replacement is needed to maintain beneficial effects on QoL, body composition and metabolism.

Keywords: hypopituitarism, pituitary, diagnosis, treatment, GHD, central hypothyroidism, genetic, idiopathic, ACTH insufficiency, discontinuation

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