Akademisk avhandling

Aspects of diagnosis and treatment of hypopituitarism in adult life

av

Helena Filipsson

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs universitet kommer att offentligen försvaras i Förmaket, Blå stråket 5, Sahlgrenska Universitetssjukhuset, Göteborg fredagen 20 mars 2009 kl 09.00

Huvudhandledare: Docent Gudmundur Johannsson
Sektionen för Endokrinologi, Sahlgrenska Universitetssjukhuset Göteborg

Fakultetsopponent: Professor Ulla Feldt-Rasmussen
Department of EndocrinologyRigshospitalet, Copenhagen Denmark

Avhandlingen baseras på följande delarbeten:

I. Detection of genetic hypopituitarism in an adult population of idiopathic pituitary insufficiency patients with growth hormone deficiency
Manuscript

II. Exploring the use of recombinant human thyrotropin in the diagnosis of central hypothyroidism
Filipsson H, Nyström E, Johannsson G

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

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, Norman L, Ragnarsson O, Johannsson G
Manuscript

UNIVERSITY OF GOTHENBURG
Abstract

Aspects of diagnosis and treatment of hypopituitarism in adult life

Helena Filipsson
Institutionen för internmedicin, Sahlgrenska Akademin vid Göteborgs universitet, och Sektionen för endokrinologi, Sahlgrenska Universitetssjukhuset, Göteborg

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 allele constellation in a compound PROP1 mutation was revealed in two siblings, with a phenotype of very late onset 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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