Glucocorticoids – outcome in patients with glucocorticoid deficiency and Cushing's syndrome

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av
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Avhandlingen baseras på följande delarbeten:

I. Oskar Ragnarsson, Helena Filipsson-Nyström, Gudmundur Johannsson. **Glucocorticoid replacement therapy is independently associated with reduced bone mineral density in women with hypopituitarism**. *Clin Endo 2012; 76: 246-52.*

II. Oskar Ragnarsson, Charlotte Höybye, Peter J Jönsson, Ulla Feldt-Rasmussen, Gudmundur Johannsson, Beverly MK Biller, Maria Kołtowska-Häggström. **Co-morbidity and cardiovascular risk factors in adult growth hormone deficiency following treatment for Cushing's disease or non-functioning pituitary adenomas during childhood**. *Eur J Endocrinol 2012; 166: 593-600.*

III. Oskar Ragnarsson, Peter Berglund, Derek N. Eder, Gudmundur Johannsson. **Long-term cognitive impairments and attentional deficits in patients with Cushing's disease and cortisol producing adrenal adenoma in remission**. *Submitted manuscript.*

IV. Oskar Ragnarsson, Morton G. Burt, Ken K. Y. Ho, Gudmundur Johannsson. **Effect of short-term growth hormone and testosterone treatment on body composition and glucose homeostasis in men receiving chronic glucocorticoid therapy**. *Manuscript.*

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GLUCOCORTICOIDS – OUTCOME IN PATIENTS WITH GLUCOCORTICOID DEFICIENCY AND CUSHING'S SYNDROME

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ABSTRACT

Glucocorticoids (GCs) are steroid hormones that have a major impact on human metabolism and are essential for life. Chronic GC overexposure, called Cushing's syndrome, is characterized by central obesity, muscle atrophy, osteoporosis, hypertension, impaired glucose tolerance and neurocognitive impairment. Cushing's syndrome can be caused by increased endogenous GC production or arise due to pharmacological GC treatment.

This thesis is based on four studies, including four different patient populations, aimed at investigating outcomes in patients with Cushing's syndrome and patients receiving current standard GC replacement therapy for adrenal insufficiency. In a large study of patients with hypopituitarism it was demonstrated that GC replacement therapy was independently associated with reduced bone mineral density in women with adrenal insufficiency receiving an average daily hydrocortisone dose of approximately 20 mg. In another study of adult patients, treated for Cushing's disease during childhood, final adult height was compromised in the majority of the patients and the prevalence of hypertension was high. In a study of patients in long-term remission after successful treatment for Cushing's syndrome, numerous domains of cognitive function were impaired at long-term follow-up in comparison to healthy individuals. Finally it was demonstrated that short-term treatment with growth hormone and testosterone increases skeletal muscle mass in men on chronic low dose GC treatment.

In conclusion, this thesis demonstrates that long-term GC exposure has various long-term adverse health related consequences for patients receiving GC replacement therapy and in patients in long-term remission from Cushing's syndrome. Furthermore, anabolic treatment with growth hormone and testosterone has the potential to improve GC induced muscle wasting.

Key words: Cardiovascular risk, bone mineral density, paediatric, final height, cognitive function, fatigue, attentional network test, body composition, sarcopaenia, growth hormone

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