

Long-term effects of growth hormone replacement in hypopituitary adults on body composition, bone mass and cardiovascular risk factors

Akademisk avhandling

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Av

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Avhandlingen baseras på följande delarbeten:

- I. Götherström G, Elbornsson M, Stibrant-Sunnerhagen K, Bengtsson B-Å, Johannsson G, Svensson J. 2009 Ten years of growth hormone (GH) replacement normalizes muscle strength in GH-deficient adults. *Journal of Clinical Endocrinology and Metabolism* **94** 809-816.
- II. Elbornsson M, Götherström G, Bosæus I, Bengtsson B-Å, Johannsson G, Svensson J. 2012. Fifteen years of growth hormone (GH) replacement improves body composition and cardiovascular risk factors *Submitted*
- III. Elbornsson M, Götherström G, Bengtsson B-Å, Johannsson G, Svensson J. 2012 Fifteen years of growth hormone (GH) replacement increases bone mineral density in hypopituitary patients with adult onset GH deficiency. *European Journal of Endocrinology* **166** 787-795
- IV. Elbornsson M, Götherström G, Franco C, Bengtsson B-Å, Johannsson G & Svensson J. 2012 Effects of 3-year growth hormone (GH) replacement therapy on bone mineral density in younger and elderly adults with adult onset GH deficiency. *European Journal of Endocrinology* **166** 181-189
- V. Elbornsson M, Götherström G, Bengtsson B-Å, Johannsson G, Svensson J. 2012 Baseline characteristics and effects of ten years of growth hormone (GH) replacement therapy in adults previously treated with pituitary irradiation therapy *Submitted*

Abstract

Growth hormone (GH) deficient (GHD) adults have decreased bone mass and muscle strength, impaired body composition, disturbed serum lipid pattern and increased morbidity and mortality in cardiovascular and cerebrovascular diseases. GH replacement normalizes most of these aberrations within the first year of treatment.

This thesis aimed to investigate the effects of 10-15 years of GH replacement on muscle strength, bone mass and density, body composition, and cardiovascular risk factors. It also aimed to determine the effects of GH replacement in elderly patients and the importance of previous irradiation therapy for baseline characteristics and the treatment effects of GH.

All patients had adult onset GHD resulting from pituitary disease, most commonly a pituitary tumour. Upper leg muscle strength was measured using a Kin-Com dynamometer and hand grip strength was measured with Grippit®, an electronic grip force instrument. Body composition and bone data were mainly assessed using dual-energy X-ray absorptiometry (DXA). Laboratory measurements were performed using conventional methods.

After correcting for the age related decline in muscle strength, 10 years of GH replacement induced a sustained increase in knee flexor and extensor strength and hand grip strength. Fifteen years of GH replacement induced a transient decrease in body fat and sustained improvements of lean soft tissue and serum lipid profile. Fasting plasma glucose increased whereas HbA1c decreased. Sustained increases in total body and lumbar (L2-L4) spine BMC (bone mineral content) and BMD (bone mineral density) were seen. In the femur neck, BMC and BMD peaked at 7 years and then decreased toward baseline values. Men had a better treatment response in terms of bone parameters, but no major gender differences were seen in the other variables measured. Three years of GH replacement increased BMD and BMC in the lumbar (L2-L4) spine and femur neck in younger as well as elderly GHD patients, without differences in the treatment effect between the groups. Compared to non-irradiated patients, GHD patients previously treated with pituitary irradiation therapy displayed a more severely impaired cardiovascular risk profile at baseline. Both groups responded to GH replacement with improved body composition, bone mass and serum lipid pattern. However, more cardiovascular events were observed in the irradiated group.

In conclusion, 10-15 years of GH replacement in hypopituitary adults induced sustained improvements in muscle strength, body composition, bone mass and serum lipid pattern. Elderly and younger patients showed a similar treatment response in terms of bone mass and density. Previous pituitary irradiation is associated with a more severely impaired cardiovascular risk profile, which is partly reversed by GH treatment. Men had a better treatment response in bone parameters than women.

Key words: growth hormone deficiency, growth hormone replacement, bone mineral density, body composition, muscle strength, elderly, cardiovascular risk factors, pituitary irradiation.

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