Göteborg, 2022

Non-functioning pituitary adenomas

Studies on morbidity and mortality

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg, fredagen den 2 september, klockan 09.00

av **Casper Hammarstrand**

Fakultetsopponent:

Camilla Schalin-Jäntti, Associate Professor, Helsinki University Hospital

Avhandlingen baseras på följande delarbeten

I. Hammarstrand C, Ragnarsson O, Hallén T, Andersson E, Skoglund T, Nilsson A G, Johannsson G, Olsson D S.
Higher glucocorticoid replacement doses are associated with increased mortality in patients with pituitary adenoma.
European Journal of Endocrinology. 2017 Sep;177 (3):251-256.

II. Olsson D S, Hammarstrand C, Bryngelsson IL, Nilsson A G, Andersson E, Johannsson G, Ragnarsson O.
Incidence of malignant tumours in patients with a non-functioning pituitary adenoma.
Endocrine-Related Cancer. 2017 May;24 (5):227-235

III. Hammarstrand C, Ragnarsson O, Bengtsson O, Bryngelsson IL, Johannsson G, Olsson D S.
Comorbidities in patients with non-functioning pituitary adenoma: influence of long-term growth hormone replacement.
European Journal of Endocrinology. 2018 Oct 1;179(4):229-237.

IV. Hammarstrand C, Olsson D S, Koranyi J, Trimpou P, Landin-Wilhelmsen K, Johannsson G.
Growth hormone replacement therapy in adults with hypopituitarism: A longitudinal case-control study on lipid metabolism.
Manuscript.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

GÖTEBORGS UNIVERSITET

Göteborg, 2022

Non-functioning pituitary adenomas

Studies on morbidity and mortality

Casper Hammarstrand

Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Sweden

Abstract

Background and aims: Hypopituitarism is most commonly caused by benign pituitary tumors, often resulting in insidious symptoms that develop over a long time. Due to either a mass effect exerted by the tumor, or due to the surgical treatment, hormonal deficiencies may arise, requiring hormone replacement. Based on four studies, this dissertation aimed to investigate the influence of glucocorticoid and growth hormone replacement on mortality, morbidity and surrogate markers for cardiovascular disease.

Methods: In *paper I*, the influence of glucocorticoid replacement on mortality was studied in patients with NFPA with standardized mortality ratio, using the general population as reference, and hazard ratio calculated. In *paper II*, standardized incidence ratio (SIR) for malignant tumors was calculated for patients with NFPA using the general population as reference. In *paper III*, the influence of growth hormone replacement therapy on comorbidities was studied. Finally, in *paper IV*, changes in the concentration of LDL-cholesterol were compared between patients with growth hormone replacement and a random population sample of men and women.

Results: *Paper I* showed that glucocorticoid replacement doses of more than 20 mg per day were associated with excess mortality. In *paper II*, the overall incidence of malignant tumours was increased in NFPA patients. *Paper III* showed that the risk of type 2 diabetes mellitus and cancer was not increased for growth hormone replaced patients. Finally, in *paper IV*, LDL-cholesterol in growth hormone replaced patients was decreased above the secular trends seen in the general population.

Conclusions: Glucocorticoid replacement doses higher than 20 mg per day are associated with increased mortality. Patients with NFPA have an increased risk of developing cancer. However, growth hormone replacement seems to be safe concerning the risk of developing comorbidities, including cancer. Furthermore, growth hormone replacement can be considered beneficial for the lipid profile.

Keywords: Non-functioning pituitary adenomas, hypopituitarism, glucocorticoid replacement, growth hormone replacement, morbidity, mortality, cancer, LDL-cholesterol

ISBN: 978-91-8009-869-4 (TRYCK) http://hdl.handle.net/2077/71516
ISBN: 978-91-8009-870-0 (PDF)