

# Glucocorticoid-induced adrenal insufficiency

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, torsdagen den 23 november 2023, klockan 09:00

av Margrét Jóna Einarsdóttir

Fakultetsopponent:

Marianne Klose MD, PhD

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## Avhandlingen baseras på följande delarbeten

- I. Einarsdóttir MJ, Ekman P, Trimou P, Olsson DS, Johannsson G, Ragnarsson O. **High prescription rate of oral glucocorticoids in children and adults: a retrospective cohort study from Western Sweden.** *Clin Endocrinol (Oxf)*. 2020;92(1):21-28.
- II. Einarsdóttir MJ, Ekman P, Molin M, Trimou P, Olsson DS, Johannsson G, Ragnarsson O. **High mortality rate in oral glucocorticoid users: a population-based matched cohort study.** *Front Endocrinol (Lausanne)*. 2022;13:918356.
- III. Einarsdóttir MJ, Trimou P, Johannsson G, Ragnarsson O. **Undertreated and undiagnosed adrenal insufficiency as a premature cause of death in glucocorticoid users.** *Manuscript*
- IV. Einarsdóttir MJ, Bankvall M, Robledo-Sierra J, Rödröm PO, Bergthorsdóttir R, Trimou P, Hasséus B, Ragnarsson O. **Topical clobetasol treatment for oral lichen planus can cause adrenal insufficiency.** *Oral Dis*. 2023. *Epub ahead of print*.
- V. Einarsdóttir MJ, Kristjansdóttir HL, Bergthorsdóttir R, Johannsson G, Trimou P, Lewerina C, Ragnarsson O. **Intermittent high-dose glucocorticoid treatment does not cause adrenal insufficiency in patients with diffuse large B-cell lymphoma - a prospective study.** *Acta Haematol*. 2023. *Epub ahead of print*.

**SAHLGRENKA AKADEMIN  
INSTITUTIONEN FÖR MEDICIN**



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## Abstract

*Background:* Glucocorticoids (GCs) are effective in treating many diseases and are widely used. However, glucocorticoid treatment can down-regulate the hypothalamic-pituitary-adrenal axis and lead to glucocorticoid-induced adrenal insufficiency. This thesis aimed to investigate the prevalence of oral GC prescriptions, related mortality, and the prevalence of GC-induced adrenal insufficiency during topical GC treatment and during intermittent high-dose GC therapy.

*Methods:* Individuals, living in Västra Götaland county, with prescriptions of prednisolone  $\geq 5$  mg/day (or equivalent dose of other GCs) for  $\geq 21$  days during 2007–2014 were identified in The Swedish Prescribed Drug Register. By using a personal identification number, patients were cross-linked with four other Swedish registries to collect information on indication for GC treatment, comorbidities, and cause-of death. To study if death was related to GC-induced adrenal insufficiency, medical records from 300 patients who died from sepsis were investigated. Twenty-seven patients with oral lichen planus receiving topical GC were studied and in a prospective study 10 adults with lymphoma receiving intermittent, high-dose GC were included.

*Results:* During 2007–2014, 14.1% of inhabitants ( $n=223\ 211$ ) in Western Sweden received prescriptions for oral GCs at doses associated with risk of developing GC-induced adrenal insufficiency. GC users had a 2-fold overall risk of dying compared to controls (adjusted hazard ratio 2.1, 95% confidence interval 2.0–2.1). Under- and undiagnosed GC-induced adrenal insufficiency possibly contributed to the death in 47 of 300 (16%) patients considered to have died from sepsis. Approximately 20% of patients receiving chronic topical GCs in the oral cavity had GC-induced adrenal insufficiency. None of the patients receiving intermittent high-dose GC therapy had GC-induced adrenal insufficiency.

*Conclusion:* Oral GC treatment is common and can lead to GC-induced adrenal insufficiency and increased mortality. GC-induced adrenal insufficiency is underdiagnosed and awareness is essential for the diagnosis and treatment.

**Keywords:** glucocorticoid, adrenal insufficiency, mortality