CORRESPONDENCE

Adrenal Cortical Insufficiency—a Life threatening Illness With Multiple Etiologies

by Prof. Dr. med. Marcus Quinkler, Prof. Dr. med. Felix Beuschlein, Dr. med. Stefanie Hahner, Dr. med. Gesine Meyer, Prof. Dr. med. Christof Schöfl, Prof. Dr. med. Günter K. Stalla in Volume 51–52/2013

Quality of Life Rated Too Negatively

The authors rate the quality of life of persons with adrenal cortical insufficiency, who are receiving glucocorticoid replacement, in rather too negative a way and explain the deficits with the timing of the glucocorticoid administration compared with the physiological secretion profile of cortisol in healthy persons (1). The physiological and pharmacodynamic effects of cortisol follow blood concentrations with a substantial delay. The authors emphasized the beneficial effects of a slow-release hydrocortisone preparation distributed by Viropharma, which needs to be taken once a day only, whereas the conventional basic substitution of adrenal insufficiency (AI) patients with hydrocortisone (HC) is given as two, rarely three, daily doses. At least four of the authors have received moneys from Viropharma, and all are participating in a register study sponsored by the company. Mention should have been made of the fact that the preparation distributed by Viropharma is about 20 times the price of hydrocortisone. If in the most important study of slow-release hydrocortisone (2) the latter had not been compared with three times daily unretarded HC but with prednisolone, which is effective for a longer duration, then it can be assumed that no advantage for the new preparation would have been found. Replacement therapy for AI patients, using 3–5 mg prednisolone in a single dose, is not a problem. In patients with primary AI the dose of 9- α -fluorocortisol as a mineralocorticoid (MC) has to be slightly higher than in those substituted with HC (3). In the study by Johannsson et al. (2) the advantage of the slow-release single dose of HC compared with 3 times daily HC (the mean daily dose of 30 mg in both groups was too high anyway) is hardly detectable. 15–25 mg HC is the regular dosage (4). Johannsson and one additional author hold equity interests in the manufacturing company, and further authors act as consultants to that company.

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Conflict of interest statement

The author declares that no conflict of interest exists.

In Reply

Since 2007 studies have been conducted in several European countries (Norway, the UK, Germany) of the quality of life in AI patients compared with the age-matched and sex-matched normal population. All studies showed in the statistical comparison that the quality of life of AI patients was notably lower than in the normal population. The clinical relevance seems to manifest itself in the fact that, correspondingly, a higher proportion of patients are able to work only within restricted limitations or are unfit for work. However, variability between individuals is high, and, similarly, there are patients whose quality of life is relatively high. The causes of the impairments are not known. After excluding comorbidities, the clinical picture is comparable for primary and secondary AI, and the assumption is that the non-physiological cortisol profile that is achieved by modern replacement therapy is relevantly associated with this. Data from relevant interventional studies are scarce, but support this hypothesis. All the authors' competing interests were reported in the study. None of us has equity interests. We mentioned the preparation in addition to others (prednisolone, prednisone [Lodotra], hydrocortisone [Chronocort]) and cited results from the registration trial. The authors did not provide a rating of "beneficial effect."

We would very much welcome a study comparing prednisolone and Viropharma's hydrocortisone preparation. At first glance, prednisolone seems sensible and has been tried and tested in clinical practice. But it has a much longer and possible very different effect on the glucocorticoid receptor. Female patients with primary AI who took 5 mg prednisolone had a notably lower bone density after several years' replacement therapy than female patients taking 20 mg hydrocortisone (1).

The registration trial for Viropharma's hydrocortisone preparation was conducted in Sweden, where the current average daily substitution dosage is 30 mg hydrocortisone. We agree with our correspondents that this dosage is too high. In Germany, as mentioned in our article, substitution treatment is given at a dosage of 15–25 mg hydrocortisone/day.

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Prof. Quinkler works as a consultant for Viropharma Inc. He received reimbursement of conference participation fees, travel and accommodation costs, as well as fees for the preparation of scientific continuing education events from Viropharma.