CLINICAL MANAGEMENT OF ADRENAL INSUFFICIENCY (AI) SHOWS NOTABLE HETEROGENEITY – DATA FROM THE EUROPEAN AI REGISTRY (EU-AIR)

Robert D Murray,1 Bertil Ekman,2 Beverly A Jones,3 Claudio Marelli,4 Marcus Quinkler,5 Pierre MJ Zelisien,6 on behalf of the EU-AIR Investigators

1. Department of Endocrinology, Leeds Teaching Hospitals NHS Trust, St James’s University Hospital, Leeds, UK; 2. Department of Medicine and Health Sciences, Linköping University, Linköping, Sweden; 3. Shire PLC, Wayne, PA, USA; 4. Shire International GmbH, Zug, Switzerland; 5. Endocrinology in Charlottenburg, Berlin, Germany; 6. Department of Internal Medicine and Endocrinology, University Medical Centre Utrecht, Utrecht, Netherlands

INTRODUCTION

- Adrenal insufficiency (AI) is a life-threatening, rare disease resulting from failure of corticosteroid hormone secretion. Characteristic signs and symptoms of AI include fatigue, anorexia, weight loss, nausea and vomiting.
- Over the past 50 years, the mainstay of treatment for patients with AI has consisted of conventional glucocorticoid (GC) replacement therapy given orally two or three times daily; however, there are no consensus guidelines regarding the optimal GC regimen to AI.
- Discrepancy in GC replacement therapy, AI is associated with unfavourable metabolic effects, some of which are dose-dependent, but life expectancy remains reduced compared with the general population.
- Patients with AI who are receiving conventional GC replacement therapy also report impaired quality of life and the condition impacts on physical activity, and family, social and work life (including absenteeism from work).

AIMS

- The aim of this analysis was to describe the current management of AI in patients receiving conventional GC therapy who are enrolled in the European Adrenal Insufficiency Registry (EU-AIR).

METHODS

- EU-AIR is a prospective, multinational, multicentre, observational study that was initiated in August 2012 to monitor the daily care and modified-released hydrocortisone in AI and conventional GC replacement therapy during routine clinical practice in patients with chronic AI (ClinicalTrials.gov identifier: NCT01661387). The registry is sponsored by Shire.
- Written informed consent/assent is provided by each patient and their parent(s)/legal guardian(s) before enrolment in EU-AIR.
- All patients with a diagnosis of AI (primary AI, secondary AI or congenital adrenal hyperplasia) who are receiving modified-release hydrocortisone or other GC replacement therapies are eligible for inclusion in the study. All treatment decisions are made by the treating physician and/or patient.
- Routine visits occur every 6–12 months. Patient diaries are used to record intercurrent illnesses and illness-related dose changes between visits; this information is entered in the database in subsequent clinic visits.
- Data collection and entry are conducted as described previously.
- This descriptive analysis included data collected between 8 August 2012 and 5 November 2014 from patients with primary or secondary AI receiving conventional GC replacement therapy for 28 days or longer. Individuals may have received more than one GC replacement therapy and/or received a single GC therapy at different doses during this time period. Patients with congenital adrenal hyperplasia and those receiving dual-release hydrocortisone were not included in the analysis. Exposure records with a duration of less than 28 days were excluded, as were data on dosage and dose frequency that appeared to be temporary (for emergencies).

RESULTS

- In total, 964 patients with AI who were enrolled in EU-AIR had received conventional GC replacement therapy for a duration of 28 days or more between 8 August 2012 and 5 November 2014 (310 [31.9%] female; 310 [32.8%] with primary AI, 634 [65.4%] with secondary AI and 2 [0.2%] with unknown AI etiology). Mean ± standard deviation (SD) age at the time of analysis was 54.6 ± 16.4 years. Mean body mass index was 28.0 ± 5.5 kg/m². Patients came from 18 centres in four countries.

- Hydrocortisone was the most frequently used GC replacement therapy (91.8% of all patients with AI, and 68.6% had received prednisolone, 1.6% cortisone acetate, 0.1% dexamethasone and 0.3% had received another treatment).
- Patients with primary and secondary AI received mean (± SD) daily hydrocortisone doses of 23.3 (± 10.0) and 19.3 (± 5.9) mg/day, respectively. Overall, median daily doses of hydrocortisone differed depending on the frequency of dosing: 10 mg for once daily (n = 59), 20 mg for twice daily (n = 476), 20 mg for three times daily (n = 411) and 25 mg for four times daily (n = 21). However, care should be taken in the interpretation of conclusions and decisions made regarding data from small numbers of patients (i.e. < 30 patients).

Predisolone-treated patients

- Based on records of prednisolone use, the daily doses ranged from < 2 to > 7.5 mg. The dose range received by the most patients during the study period was 5 to < 6 mg/day, and was used at some time by 65.6% of patients (Figure 3).
- Prednisolone had been taken once daily by 47 patients (73.4%), twice daily by 19 patients (29.7%) and three times daily by 1 patient (1.5%).
- Overall, median daily doses of prednisolone did not vary depending on the frequency of daily dosing: 5 mg for once daily (n = 54) and twice daily (n = 20) dosing. However, care should be taken in the interpretation of conclusions and decisions made regarding data from small numbers of patients (i.e. < 30 patients).

CONCLUSIONS

- The results of this analysis demonstrate that there is considerable heterogeneity in the current management of AI in terms of the type of GC used, and the dosage and frequency of administration.
- These findings probably reflect the real-world practice of dose individualization in the absence of robust data supporting an optimal treatment regimen for long-term outcomes.
- Variability in GC dosing may have clinical consequences for patients. It is already known that some of the adverse effects of GC therapies are dose-dependent. Furthermore, GC over-replacement may lead to iatrogenic Cushinng’s syndrome, while under-replacement carries the risk of adrenal crisis.
- This descriptive analysis highlights the need for clinical treatment guidelines for GC use and monitoring in patients with AI.

REFERENCES