

Management of Adrenal Insufficiency: A Survey of Perceptions and Practices of Physicians from the Middle East and North Africa

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Abstract

Introduction: Treatment of adrenal insufficiency (AI) requires correct lifelong use of glucocorticoids (GCs) with early dose adjustments to cover the increased demand in stress to avoid life-threatening emergencies. **Objectives:** We determine the current specific knowledge of physicians in a convenience sample on the pathophysiological and clinical aspects of AI in the two regions of North Africa and the Middle East. **Materials and Methods:** Participants ($n = 96$) were invited to complete an electronic questionnaire with various possible answers on the subject of multiple-choice questions covering physiology, pharmacology, and clinical management and define respondents' professional profiles. **Results:** The present study suggests that in the investigated settings, physicians' knowledge of physiology and pharmacology GCs, medical replacement strategies in AI, and prevention of adrenal crisis may be insufficient. Great knowledge gaps were demonstrated. **Conclusions:** There is a need for continuous structured education and training on AI in both general medical and endocrine forums.

Keywords: Adrenal crisis, adrenal insufficiency, glucocorticoid replacement therapy, hydrocortisone, prednisolone

INTRODUCTION

Adrenal insufficiency (AI) comprises a group of rare diseases, including primary AI, secondary AI, and congenital adrenal hyperplasia.^[1,2] Glucocorticoid (GC) replacement is the cornerstone therapy in the management of AI, intended to prevent life-threatening complications related to AI and improve the well-being and quality of life in patients with AI.

Adrenal crisis is a grave complication of AI, occurring even in subjects on regular GC replacement. The incidence of adrenal crisis is estimated at 5–10 per 100 patient-years, with a mortality of 0.5 per 100 patient-years.^[3] The primary trigger identified for the development of adrenal crisis is a delay in increased GC dose in cases of infection.^[4,5] Patient education is essential to gain the skills needed to prevent acute impairment of their AI disorder.^[6,7]

Furthermore, previous findings suggest that the treating physicians are the patients' primary source of information regarding AI (89%). Professional healthcare workers are essential for sharing knowledge and advice regarding the

various aspects of managing the disease.^[8] However, a debate exists on whether physicians' knowledge regarding AI is sufficient, in part due to the rareness of this endocrine disorder.^[9-12] Significant barriers to diagnosis and management of AI were identified in some developing regions of the world with indicators of tiered healthcare that may expose deficiencies in management.^[13,14] Therefore, we aimed to examine AI management's current knowledge and perceptions among a sample of physicians from the Middle East and North Africa (MENA) region and in various specialties. Our long-term goal is to identify critical deficiencies in AI

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management by physicians in our region for better guidance of future educational efforts in the realm of AI.

MATERIALS AND METHODS

We aimed to determine the level of practical and clinically relevant knowledge of physicians in the MENA region. A convenience sample of physicians from a wide range of professional grades and experiences was surveyed. There is no single MEA regional endocrine society with a unified membership list that can define a study population. Therefore, the target population was identified from a list of electronic mails pooled from continuous professional development delegates, speakers, authors, or members of several medical groups in various parts of the MEA region. Consequently, six questions were added to the survey to help define the profiles of the respondents and their practices.^[15-20] Participants were asked to complete an electronic questionnaire sent via a commercial survey software (Survey Monkey, USA) with various possible answers on the subject of AI. The questions are analogous to a previously published study with similar objectives.^[9] In brief, questions covered the daily cortisol production rate in healthy individuals, various GC preparations used to treat AI, half-life time of hydrocortisone (HC), clinical signs of GC under- and over-replacement, and potential

therapeutic approaches with AI [Table 1]. Data are presented in descriptive statistics.

RESULTS

Respondents' profiles

A total of 96 physicians from various medical disciplines in the MENA regions completed the questionnaire [Table 2]. The majority (62.8%) were male. Half of the participants (50.0%) were consultant/attending physicians, while 36.5% were senior specialists, and the remainder (13.5%) were junior residents or interns. The predominantly represented single-specialty was adult endocrinology (44.2%). This was followed by general internal medicine with a particular interest in endocrinology (15.8%) and general internal medicine alone (11.6%). The majority reported working in clinical, public health services (67.7%), followed by the clinical, private sector services (20.8%). Nearly half of the respondents (49.0%) have treated ten or fewer patients with AI. Only 17.7% reported treating over 50 AI patients thus far.

Glucocorticoid physiology and pharmacology

Respondents' knowledge of physiology and pharmacology of GC hormones were assessed via two questions [Table 3]. Assessment of knowledge regarding normal daily rates of

Table 1: The survey questions and potential multiple-choice options

I. The demographic and professional profiles of participants	
Q1	Sex: (Male, female)
Q2	The following best describes my professional specialty? (Adult endocrinologist, GENERAL internal physician with interest in endocrinology, physician in general internal medicine, pediatric Endocrinologist, general pediatrician, surgeon in general, obstetrician/gynecologist, primary care doctor (GP or family physician), other (please specify))
Q3	Current professional grade (consultant/attending physician, specialist/fellow/senior registrar/intern/resident/senior house officer/junior registrar)
Q4	Current type of practice: (Academic: Mainly teaching and research with limited clinical activities, Clinical: Public health services, Clinical: Private sector)
Q5	How many patients with adrenal insufficiency have you been treating so far? (None, 1-10, 11-50, >50)
Q6	How would/do/did you educate your patients with adrenal insufficiency? (Personal dialogue, written information, via the internet)
II. "Adrenal insufficiency challenges" questionnaire*	
Q7	Which is the normal "daily cortisol production rate" in healthy individuals? (5-10 mg, 10-20 mg, 20-30 mg, > 30 mg)
Q8	What is the half-life of the hydrocortisone? (1 h, 8 h, 12 h, 16 h)
Q9	Which glucocorticoid preparations can be used for replacement therapy? (Hydrocortisone, prednisone/prednisolone, long-acting prednisolone, dexamethasone)
Q10	How would you adjust the glucocorticoid substitution regimen in the presence of acute severe disease? (Omission of 1-2 days, dose reduction by 50 percentage, no dose adjustment, increase by 2-5 fold, increase by ten fold)
Q11	Glucocorticoids dose adjustment is necessary for the following situations (please check all that applies) (fever > 38 C, physical exercise >30 min, Mental stress, e.g., during the exam, headache, rheumatic pain without fever, acute severe disease)
Q12	Please indicate signs of glucocorticoid "under-replacement" (Please check all that applies): (Headache, weight gain, weight loss, nausea, constipation, sleep disturbance)
Q13	Please indicate signs of glucocorticoid "over-replacement" (please check all that applies): (Weight loss, weight gain, low blood pressure, high blood pressure, increased blood glucose)
Q14	Please name three essential goals in "patients' education on adrenal insufficiency" (1, 2, 3)
Q15	Please indicate all of the following measures you think are required in patients with adrenal insufficiency (please check all that applies): (Issuing an emergency card, prescription of glucagon, information of the patients' relatives and friends, regular ultrasound monitoring of the kidneys and adrenal glands, no specific measures are necessary)
Q16	Do patients with adrenal insufficiency need a standby emergency medication? (Yes. No' if yes, please specify)
Q17	Which of the following measures should be taken by a patient with adrenal insufficiency before a trip for vacation (holiday): (Please check all that applies) (packing an emergency card, packing glucocorticoid preparation, packing the emergency medications, none of the above)

* adopted from Harbeck *et al.*^[9]

Table 2: Demographic and professional profiles of participants, and workload and style of communication for management of adrenal insufficiency

Questions and potential response option	Results* (%)
Sex (94)	
Male	59 (62.8)
Female	35 (37.2)
The professional specialty (95)	
Adult endocrinologist	42 (44.2)
General Physician with endocrine interest	15 (15.8)
General internal medicine physician	11 (11.6)
Pediatric endocrinologist and general pediatrician	11 (11.6)
Primary care doctors and others	16 (16.9)
Current professional-grade (96)	
Senior: Consultant/attending physician	48 (50.0)
Midgrade: Specialist/fellow/senior registrar	35 (36.5)
Junior: Intern/resident/senior house officer/junior registrar	13 (13.5)
Type of practice (96)	
Academic**	11 (11.5)
Clinical: Public health services	65 (67.7)
Clinical: Private sector	20 (20.8)
How many patients with adrenal insufficiency have you been treating so far? (96)	
None	17 (17.7)
1-10	47 (49.0)
11-50	15 (15.6)
>50	17 (17.7)
How would/do/did you educate your patients with adrenal insufficiency? (96)	
Personal dialogue	87 (90.6)
Written information	28 (29.2)
Via the internet	6 (6.3)

*n (%), **Mainly teaching and research with limited clinical activities

cortisol production in healthy individuals revealed split responses. While the dominant answer given was “10–20 mg” in 39.6% of respondents, near-equal responses were given for “5–10 mg” (29.2%) and “20–30 mg” (30.2%). The majority (58.8%) listed “8 h” as the half-life of HC, while only 22.3% identified “1 h” as the correct answer.

Patterns in clinical practices

Physicians' patterns in prescribing and monitoring the adequacy of GC replacement therapy were assessed via five questions [Table 1]. Results are presented in Tables 3. The majority (81.3%) identified HC preparations for use in GC replacement therapy. This was followed by prednisone/prednisolone reported by 46.9%, longer-acting formulations of prednisolone in 13.5%, and Dexamethasone also reported in 13.5%.

The most frequent sign reported for GC under-replacement was “nausea” (84.4%), followed by “weight loss” (81.3%), “headaches” (44.8%), and “sleep disturbances” (36.5%). Only 8.3% of respondents identified “weight gain” as a sign of GC under-replacement. The most frequent sign reported

for GC over-replacement was “high blood pressure” (91.6%), followed closely by “weight gain” (90.5%) and “increased blood glucose” (86.3%). Only 6.3% and 3.2% of respondents identified “weight loss” and “low blood pressure” as symptoms of GC over-replacement, respectively.

The situations most frequently identified as necessary for adjustments of GC dosages were “acute severe disease” (92.7%) and “fever more than 38°C” (79.2%). The most-reported adjustment in the GC regimen needed in the presence of acute severe disease was “increase dose by 2–5-fold” by 77.1% of respondents. 6.3% of respondents reported “GC dose reduction by 50%,” and similarly, 6.3% reported “omission of GC for 1–2 days” in response to necessary GC adjustments in severe illness.

Prevention of adrenal crisis

Assessments of perceptions and practices for the prevention of adrenal crisis are summarized in Tables 3 and 4. The majority of respondents (80.9%) identified the need for emergency, standby medications for patients with AI. In addition, 94.7% reported the need to issue an emergency card, and 80.9% reported the need for relative and friends' education regarding AI. Only 1.1% stated that no specific measures were necessary for the prevention of adrenal-related complications.

When traveling on holiday, the majority instructed patients to pack their GC preparations (90.5%), pack an emergency card (89.5%), and pack their emergency medications (70.5%). Finally, most physicians (90.6%) would educate their patients on all the above via direct, personal dialogues. Fewer physicians would utilize written information (29.2%) or Internet resources (6.3%).

DISCUSSION

Lifesaving GC therapy was introduced over 60 years ago, but several advances in treatment have taken place since then. For instance, little is known about short- and long-term treatment effects and morbidity and mortality.^[21] Data from systematic cohort and registry studies have demonstrated potential disadvantages of unphysiological GC replacement. Hence, new modes of replacement that aim to mimic normal GC physiology.^[21] Furthermore, how best whatever limited information is used clinically is not clear. A recent, single-institution study in Germany evaluated the knowledge and competence of a group of physicians from various specialties regarding the management of AI.^[9] The study identified significant deficiencies and knowledge gaps concerning AI management amongst physicians despite the institution's specialized status.^[9] Similar results of a needs assessment exercise showed that primary care physicians both needed and desired professional development targeting AI diagnosis and management.^[10] The study suggested a strong need to improve physicians' education on GC replacement treatment in AI.^[22] This is particularly relevant to clinical practice in developing regions of the world, where more challenges have been observed.^[13,14] The German study

Table 3: The adrenal survey

Questions and potential response option	Responses (%)
Which is the normal “daily cortisol production rate” in healthy individuals? (96) (mg)	
5-10	28 (29.2)
10-20	38 (39.6)
20-30	29 (30.2)
>30	1 (1.0)
What is the half-life of the hydrocortisone? (94) (h)	
1	21 (22.3)
8	55 (58.5)
12	18 (19.1)
16	0 (0.0)
Which glucocorticoid preparations can be used for replacement therapy? (96)	
Hydrocortisone	78 (81.3)
Prednisone/prednisolone	45 (46.9)
Long-acting prednisolone	13 (13.5)
Dexamethasone	13 (13.5)
How would you adjust the glucocorticoid substitution regimen in the presence of acute severe disease? (96)	
Omission of 1-2 days	6 (6.3)
Dose reduction by 50 percentage	6 (6.3)
No dose adjustment	9 (0.0)
Increase by 2-5-fold	74 (77.1)
Increase by 10-fold	10 (10.4)
Glucocorticoid dose-adjustment is necessary for the following situations (please check all that applies) (96)	
Fever >38 C	76 (79.2)
Physical exercise more than 30 min	19 (19.8)
Mental stress e.g., during examinations	29 (30.2)
Headache	4 (4.2)
Rheumatic pain without fever	17 (17.7)
Acute severe disease	89 (92.7)
Please indicate signs of glucocorticoid “under-replacement” (Please check all that applies) (96)	
Headache	43 (44.8)
Weight gain	8 (8.3)
Weight loss	78 (81.3)
Nausea	81 (84.4)
Constipation	13 (13.5)
Sleep disturbance	35 (36.5)
Please indicate signs of glucocorticoid “over-replacement” (please check all that applies): (95)	
Weight loss	6 (6.3)
Weight gain	86 (91.6)
Low blood pressure	3 (3.2)
High blood pressure	87 (91.6)
Increased blood glucose	82 (86.3)
Please indicate all of the following measures you think are required in patients with adrenal insufficiency (please check all that applies)	
Issuing an emergency card	89 (94.7)
Prescription of glucagon	19 (20.2)
Information of the patients’ relatives and friends	76 (80.9)
Regular ultrasound monitoring of the kidneys and adrenal glands	9 (9.6)
No specific measures are necessary	1 (1.1)
Do patients with adrenal insufficiency need a standby emergency medication? (94)	
Yes	76 (80.9)
No	18 (19.1)
Which is a patient should take the following measures with adrenal insufficiency before a trip for vacation (holiday): (Please check all that applies) (95)	
Packing an emergency card	85 (89.5)
Packing glucocorticoid preparation	86 (90.5)
Packing the emergency medications	67 (70.5)
None of the above	1 (1.1)

came from a specialized endocrine department which limits the generalizability. In contrast, our study included both endocrinologists and nonendocrinologists, giving a more representative sample of doctors whom AI patients may face at the time of stress. We refrained from making any subgroup analysis due to the small sample size. Indeed, previous studies demonstrated that 45% of patients were diagnosed only after hospitalization due to an adrenal crisis despite prior evident signs of AI.^[23] Furthermore, it has been demonstrated that 68% of patients with AI had an incorrect diagnosis at first.^[24] However, in none of the studies, information was available on the physicians' education, knowledge on GC replacement, or medical specialty. The findings of the present study and the two previous studies^[9,10] fill this gap in various professional groups and support the idea to provide ongoing education to physicians on AI, a rare but essential disorder since patients rely in large parts on the information provided by their physicians.^[19]

Besides, special attention is needed in several special situations in clinical practice where the possibility of AI. Adrenal suppression may occur despite following recommended GC tapering regimens and suspicion of GC-induced AI requires careful diagnostic workup and quick introduction of a GC replacement treatment.^[11] HIV-associated AI is commonly seen in Africa.^[13] Deliberate manipulation of replacement therapy while observing Ramadan fasting in people with AI may induce a state of under replacement and possibly precipitate an adrenal crisis. Professional guidance and continuous monitoring of the management of AI during Ramadan fasting are needed.^[25,26]

CONCLUSIONS

The present data demonstrate a suboptimal knowledge of the practical aspects of the management of AI. The present study confirms the observations from the German study in a larger sample and more realistically representative participants in a setting with a potentially higher risk. The study supports the notion that there might be a need for additional structured education and training on AI in local, national, and regional conferences to improve physicians' knowledge and enhance their clinical skills and confidence on the disease and thereby foster timely and optimal treatment.

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Authors' contribution

Both authors contributed to the conception of the study. SAB adopted and managed the survey. Both authors jointly drafted and revised the manuscript and approved its final version.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The study was approved by the Institutional Renew Board of the Dheikh Khalifa Medical City, Abu Dhabi, UAE. All participants provided an informed consent prior to accessing the survey.

Availability of data

The raw data will be available by reasonable requests to the corresponding author.

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