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DOI:

[10.4103/jdep.jdep_42_21](https://doi.org/10.4103/jdep.jdep_42_21)

Document Version

Publisher's PDF, also known as Version of record

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Citation for published version (APA):

Hussain, S., Hussain, S., Ghouri, N., & Meeran, K. (2021). Management of adrenal insufficiency. *Journal of Diabetes and Endocrine Practice*, 4(3), 90-92. https://doi.org/10.4103/jdep.jdep_42_21

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Volume 4 • Issue 3 • July-September 2021

Journal of Diabetes and Endocrine Practice

An Official Publication of the Gulf Association of Endocrinology and Diabetes

Management of Adrenal Insufficiency

Patients with adrenal insufficiency (AI), irrespective of whether the cause is primary, secondary, or tertiary, require glucocorticoid replacement, without which they can suffer life-threatening consequences from an adrenal crisis. There have been a number of reported preventable cases of adrenal crises due to various reasons including inappropriate omission of glucocorticoids and failure to increase doses during acute illnesses.^[1] The role of the patient in recognizing when an increase in glucocorticoid doses is required is central to minimize the risk to themselves; thus, the importance of patient education is repeatedly emphasized.^[2,3] Published existing literature has identified deficiencies in the patients' understanding of steroid sick day rules,^[2,4] how to administer parenteral hydrocortisone,^[2,4,5] and when to seek medical attention.^[2]

However, reports highlight gaps in clinician knowledge, particularly on the recognition, and the management of AI.^[4,6-8] Given that healthcare professionals have a central role in patient education, it is essential that clinicians, irrespective of grade are familiar with steroid sick day rules and pharmacokinetics to avoid preventable adverse patient outcomes. Furthermore, the increasing use of drugs such as immune checkpoint inhibitors and the endocrinopathy side effects associated with these further supports the need for all physicians, not just endocrinologists, to recognize, and promptly initiate treatment AI.^[9,10]

In the current issue of the Journal of Diabetes and Endocrine Practice, Beshyah and Ali have clearly highlighted the need for urgent clinician education on the management of patients with AI within multiple disciplines including endocrinology, in the Middle Eastern/Northern African (MENA) countries.^[11]

Options for Glucocorticoid Replacement

Glucocorticoid replacement therapy is the cornerstone of AI management. Most commonly, this is administered as 15–25 mg hydrocortisone in divided doses, with the largest dose given upon waking, aiming to mimic the body's natural circadian rhythm.^[12] In some patients, once-daily modified-release hydrocortisone preparations such as Plenadren are an alternative,^[13] but this is not currently widely used.

Prednisolone is increasingly used as an alternative to multidose hydrocortisone^[14] due to its once-daily administration and smoother action.^[15] The availability of prednisolone assays means that, unlike previously, patients can now have their doses adjusted according to the steroid profiles. Although more research on optimal prednisolone dosing in AI is required, evidence suggests replacement doses of 3–5 mg is sufficient.^[16]

While in the United Kingdom (UK), 1 mg prednisolone tablets are available, this is not the case in many MENA countries. Consequently, 5 mg prednisolone tablets would need to be administered instead, which may have accompanying undesirable side effects from supraphysiological glucocorticoid replacement.

Case reports and trials describe continuous subcutaneous hydrocortisone infusions in patients with AI;^[17,18] however, this is not common practice, and more research is currently underway.

Clinicians should be aware of the signs and symptoms of glucocorticoid under- and over-replacement to adjust doses accordingly. Close and long-term patient follow-up is required with regular assessment and optimization of cardiovascular risk, a major cause of increased morbidity and mortality in patients with AI.^[19]

Glucocorticoid Replacement during Acute Illnesses

General steroid sick day rule advice given to adult patients is to double glucocorticoid replacement doses when unwell (e.g., when febrile, on antibiotics for an infection or after minor surgery) and to administer high-dose (100 mg) intramuscular hydrocortisone if they are severely unwell, unable to tolerate oral steroids, or there are concerns surrounding steroid absorption.^[1] Up-to-date UK guidance released during the recent COVID-19 pandemic recommends higher oral glucocorticoid doses for those with coronavirus who can self-manage their illness without hospital admission.^[20] For those requiring parenteral hydrocortisone, there is evidence suggesting a continuous infusion is better than intermittent bolus injections during times of major stress.^[21]

Glucocorticoid Replacement in Special Circumstances

There are several circumstances when glucocorticoid replacement doses may need to be adjusted. Two examples of this include pregnancy and Ramadan. Patients with AI who are pregnant must be aware of the need to increase glucocorticoid replacement doses (usually by 20%–40%) during the third trimester. Unlike dexamethasone and betamethasone, hydrocortisone does not cross the placenta due to the action of placental 11-beta hydroxysteroid dehydrogenase, which converts cortisol to inactive cortisone.^[22] Once in active labor, patients should be managed as per the major illness

guidelines with parenteral hydrocortisone. While further research is required on how to optimally manage patients who partake in religious fasting during the month of Ramadan, it is vital that patients on long-term steroids undergo an assessment by their endocrinologist several months beforehand to establish if fasting is indeed a viable option. For those in whom fasting is deemed safe, potential options could include continuing once daily hydrocortisone, administering the second dose of hydrocortisone at dusk when breaking the fast, or temporarily switching to equivalent doses of once-daily prednisolone.^[23] It is essential that patients are reminded of sick day rules, carry a steroid warning card, and have a valid intramuscular hydrocortisone pack that they are trained in using in the event of an adrenal crisis.

CONCLUSIONS

Despite the small number of participants, Beshyah and Ali's study^[11] is important and as referenced in their work, supports the findings of many others in different parts of the world.^[1,6] An improved understanding of adrenal crisis recognition and management is imperative to eliminate avoidable harm, ensure ideal patient outcomes, and improve the patient experience.

A repeat evaluation of clinician understanding, following a well-structured education program addressing the deficiencies identified by Beshyah and Ali, would be advisable and should help the authors to reach their ultimate aim of delivering high-quality emergency care to patients with AI in their region.^[11]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Received: 26-08-21 **Accepted:** 26-08-21 **Web Published:** 22-09-21

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Access this article online	
Quick Response Code:	Website: www.jdeponline.com
	DOI: 10.4103/jdep.jdep_42_21

How to cite this article: Hussain S, Hussain S, Ghouri N, Meeran K. Management of adrenal insufficiency. J Diabetes Endocr Pract 2021;4:90-2.