

Management of Thyroid Diseases and Steroid Replacement in Ramadan: A Review Study

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ABSTRACT

Most Muslims fast during the holy month of Ramadan. Patients with thyroid diseases do not normally need medication adjustment and are able to fast safely. On the other hand, hypothyroid patients are prescribed with thyroxine tablets, which should be taken on an empty stomach at bedtime or half an hour before Sohur. Hyperthyroid patients receiving treatment with methimazole or carbimazole have to adjust to 1-2 daily doses, while patients using propylthiouracil need to change their drug regimen. Severely symptomatic hyperthyroid patients require immediate treatment and must avoid fasting for a few days. Since adrenal insufficiency might be life-threatening, proper education is essential for these patients if they are willing to fast in Ramadan. In this regard, the educational content should be focused on the disease, proper medication, alarming signs and symptoms, sick day rules, dietary regimen, and physical activity.

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Introduction

During the holy month of Ramadan, Muslims across the world abstain from eating and drinking from dawn (Sohur) to sunset (Iftar) for one month. Prolonged fasting is associated with metabolic and hormonal changes in the body (1), which could be well tolerated by healthy individuals. However, these changes may lead to health problems in patients with certain chronic diseases. Although patients are commonly exempt from fasting, many of them wish to fast during Ramadan. To respect their decision, they should be offered proper advice in order to be able to fast.

Patients with thyroid diseases require no major treatment adjustments in Ramadan. On the other hand, patients with adrenal insufficiency need proper advice regarding drug compliance, dietary habits, and alarming signs and symptoms since they are more vulnerable to adrenal crisis in Ramadan. Adrenal crisis occurs due to several factors, such as prolonged fasting duration (up to 15-20 hours in some

countries) and changes of the dietary pattern (excess consumption of fats, sugar and spicy food). Moreover, food and water contamination are potential risk factors in Iftar parties during Ramadan due to the mass production of food and unhygienic food practices.

This study aimed to review the current evidence so as to provide guidelines for patients with thyroid diseases and adrenal insufficiency who are willing to fast in Ramadan.

Hypothyroidism

During Ramadan, minimal changes are observed in the levels of thyroid hormones in a normal person (2). A few studies have suggested that thyroxine (T4) level significantly drops in male and female fasting individuals during Ramadan, while the level of thyroid-stimulating hormone (TSH) increases significantly in men (TSH and T4 levels remain within the normal range). In women, there is a positive correlation

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between T4 changes and duration of fasting (days). However, these changes revert to pre-Ramadan levels after the month of Ramadan (3, 4).

Thyroid hormone replacement and influential factors in its absorption

Treatment of primary and secondary hypothyroidism involves thyroid replacement with thyroxine and its levo-isomer, known as levothyroxine. In this treatment, it is recommended that thyroxine be taken orally (on an empty stomach) since its absorption is affected by food and medication intake (e.g., iron and calcium preparations, vitamins, aluminum antacids, cholestyramine resin, sucralfate, activated charcoal, soy products, raloxifene, and food and herbal remedies) (5-8). Moreover, absorption of levothyroxine is remarkably influenced by a fibre-enriched diet and caffeine consumption (9, 10). On the other hand, levothyroxine absorption reduces from 80% with empty stomach to 60% in the fed state, resulting in variably higher TSH levels (11).

In this regard, the standard recommendation dictates that levothyroxine be administered half an hour before breakfast on an empty stomach in order to prevent food or medication interference (12). While consumption of thyroxine with food is not advised (12), it could be taken at bedtime since it exerts the same effects as when it is taken on an empty stomach (13, 14).

Optimal timing of thyroid medication use during Ramadan

Metabolism of thyroxine is altered in Ramadan due to several factors, including the changes in gastrointestinal motility due to prolonged fasting, effect of heavy meals, changes in the circadian rhythm, and effect of deiodinase activity. Therefore, it is postulated that in Ramadan, thyroxine/levothyroxine should be taken half an hour before Sohur. However, it might be difficult for many patients to wake up early; as such, they are likely to miss the dose or take the medication with the Sohur meal. To overcome this problem, it is recommended that patients use levothyroxine at bedtime, which exerts identical lowering effects on TSH levels (15-18).

Optimal timing for thyroid medication use after Ramadan

After Ramadan, thyroid patients must revert

back to their routine regimen of thyroxine ingestion.

Hyperthyroidism

Data is scarce on the management of hyperthyroid patients during Ramadan. Newly diagnosed or untreated thyrotoxic patients may present with alarming signs and symptoms, such as diarrhoea, dehydration, polydipsia and tachycardia, which are likely to deteriorate with prolonged fasting. On the other hand, mildly thyrotoxic patients are usually able to fast safely, whereas dehydration and diarrhoea could occur in severely thyrotoxic patients. As such, these patients are advised to avoid fasting for a few days until symptomatic relief. This is supported by the teachings of the Holy Quran, which clearly exempt ill individuals from fasting, allowing them to compensate for the missed fasting days later. Such issues must be addressed by a local religious scholar.

Thyrotoxicosis is an emergency condition requiring early diagnosis and treatment. Thioamides, such as methimazole, carbimazole, and propylthiouracil, are effective in the management of these patients. Thioamides inhibit the organification of iodine into tyrosine residues in thyroglobulin in the thyroid, as well as the coupling of iodotyrosines.

Management of thyrotoxicosis during Ramadan

Thyroid uptake scan should be performed to differentiate hyperthyroidism (excessive thyroid hormone production, 90% of cases) from thyroiditis (thyroid gland inflammation, 5-10% of cases), which are considered the main causes of thyrotoxicosis. Treatment of the aforementioned conditions largely differs; thyroiditis is self-limiting and could be treated symptomatically with non-steroidal anti-inflammatory drugs, steroids or beta-blockers. Effective management of this disorder during Ramadan depends on the severity of the symptoms.

Thioamides are frequently used in the treatment of hyperthyroidism. However, the main limitation of propylthiouracil in Ramadan is that dosing might be required every 4-6 hours. On the other hand, methimazole has long-term action and could be administered in single or divided doses at different times of the day (19). Therefore, patients receiving methimazole

therapy require no treatment adjustment in Ramadan.

In this regard, use of carbimazole is similar to methimazole, while the required dose is approximately 40% higher. In other words, 10-20 mg of carbimazole is equal to 6-15 mg of methimazole, respectively. Maximum effect of carbimazole is achieved within a week; therefore, beta-blockers are added to this drug regimen for immediate symptomatic relief. Other treatment options for hyperthyroidism are radioactive iodine and surgery, which could be delayed until after Ramadan in case the patient fasts.

Adrenal insufficiency

Patients with adrenal insufficiency are more likely to develop adrenal crisis or acute adrenal insufficiency in Ramadan. Acute adrenal insufficiency is a medical emergency characterized by nausea and vomiting, abdominal pain, hyperkalemia, hyponatremia, hypotension, dehydration, weakness and lethargy. Furthermore, it is usually associated with primary adrenal insufficiency (i.e., adrenal gland disorders) rather than secondary adrenal insufficiency (i.e., pituitary or hypothalamic disorders). Acute adrenal insufficiency may occur following the abrupt cessation of long-term glucocorticoid use at high doses (20). This is because mineralocorticoid secretion remains intact in secondary adrenal insufficiency, while it is disturbed in primary adrenal insufficiency.

The most common cause of primary adrenal insufficiency is autoimmune adrenal disease in developed countries, whereas tuberculous adrenalitis has been proposed as the most common cause of this condition in underdeveloped countries. Therefore, in case they are willing to fast, patients with adrenal insufficiency need proper advice and training in order to prevent adrenal crisis.

Choice of medication

Hydrocortisone is the preferred medicine for adrenal insufficiency despite its short biological half-life (<12 hours), while the duration of fasting is usually longer (approximately 15 hours). Therefore, prednisolone and dexamethasone, which have longer half-life, are considered better options to improve patient compliance during Ramadan.

Combination of prednisolone (in the morning)

and hydrocortisone (in the evening) could be effective in order to match the cortisol day curve. This drug replacement should be initiated a few weeks prior to Ramadan, and the clinical symptoms (e.g., lethargy, fatigue, dizziness) and signs of the patient (e.g., blood pressure and postural drop) should be monitored for dosage adjustment. Moreover, timing of drug intake at Iftar and Sohur must be adjusted in order to match the cortisol day curve. However, measurement of plasma adrenocorticotropic hormone and/or serum cortisol is not required.

Mineralocorticoid replacement is not required in secondary adrenal insufficiency, while the mineralocorticoid dose must be adjusted in primary adrenal insufficiency, depending on the used corticosteroid preparation.

Hydrocortisone has glucocorticoid and mineralocorticoid activities, whereas prednisolone has lower mineralocorticoid activity compared to hydrocortisone, and dexamethasone has no mineralocorticoid activity.

With respect to anti-inflammatory properties, cortisol is one, prednisolone is three, and dexamethasone is 26. The dosage is adjusted based on blood pressure measurements, serum Na⁺, and serum K⁺ (20-25). In addition, proton-pump inhibitors may be required to prevent gastritis, mostly due to the consumption of fatty food in Ramadan apart from steroids.

Patient education

Patients should be educated regarding the alarming symptoms of acute adrenal insufficiency (e.g., fatigue, nausea and vomiting). Training is also required for the family, friends, and caregivers of these patients, so that they would be able to identify the signs and symptoms of adrenal crisis and perform emergency management.

It is recommended that patients with acute adrenal insufficiency carry an emergency medical card, containing information such as daily medication doses, and name and contact number of the physician or family members in case an emergency arises. As another precaution, these patients should always carry a vial of hydrocortisone or dexamethasone and a syringe, which should also be available at home.

In the presence of the signs and symptoms of adrenal insufficiency, patients should be instructed to take an extra dose of steroids. Moreover, a family member or friend should be

trained on the intramuscular injection of steroids (usually in the thigh) in case of adrenal crisis, especially if the patient becomes unconscious. It is noteworthy that in the event of adrenal insufficiency, the patient must be referred to a medical facility immediately.

Sick day management

In case of minor illnesses (e.g., cold, flu, diarrhoea and vomiting), patients should be instructed to double or triple their daily dose of corticosteroid. Once the stressful medical condition is over, patients can return to the routine medication dosage. However, in case of severe diseases, intravenous corticosteroids are required and medical consultation must be provided.

Dietary advice

Patients with adrenal insufficiency should adhere to a healthy diet and avoid the consumption of sugar, refined carbohydrates, caffeine and nicotine. Since the majority of patients with primary adrenal insufficiency are "salt-losers", they should avoid intense physical exertion and exposure to hot climates while fasting. After sunset and fast break at Iftar, these patients are advised to consume large proportions of fluids with added salt in order to prevent adrenal crisis. It is also noteworthy that excess salt may lead to diarrhoea and must be avoided.

On the other hand, patients with adrenal insufficiency should be examined for ankle edema, which is likely to occur due to insufficient salt intake and could be resolved within 2-3 days with adequate salt replacement.

Physical activity

Patients with adrenal insufficiency should avoid strenuous physical exertion, sleeplessness and stress as far as possible. Furthermore, they need adequate, long rests during fasting hours, as well as proper night's sleep.

Conclusion

With regard to the treatment protocols for patients with thyroid diseases during Ramadan, it is suggested that fasting hypothyroid patients use thyroxine at bedtime instead of half an hour before Sohur. As for hyperthyroid patients, methimazole therapy with 1-2 daily doses is recommended in Ramadan. On the other hand,

patients with mild-to-moderate hyperthyroidism are able to fast safely, while patients with severe hyperthyroidism are considered high-risk for Ramadan fasting.

With reference to patients with primary adrenal insufficiency, they are medically advised to avoid fasting. However, if they insist on fasting, they should be provided with proper education and training regarding the choice of drug regimen in Ramadan, alarming signs of adrenal crisis, sick day rules, possession of a medical information card, suitable dietary plan, and physical activity. Furthermore, these patients must be instructed on self-treatment skills in the presence of alarming signs.

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