

Commentary

Predictors of outcome in myxoedema coma

Jennifer Beynon, Simeen Akhtar and Tara Kearney

Endocrinology Department, Salford Royal NHS Foundation Trust, Stott Lane, Salford, M6 8HD, UK

Corresponding author: Jennifer Beynon, jenniferarnott@doctors.org.uk

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See related research by Dutta *et al*, <http://ccforum.com/content/12/1/R1>

Abstract

Myxoedema coma is a rare and life-threatening illness the outcome of which has not been robustly studied in large numbers, partly due to its low incidence. Dutta and colleagues have explored outcome predictors in a developing country where access to thyroid function tests is more limited than in the Western world. Cardio-vascular instability, reduced consciousness, persistent hypothermia, and sepsis all contributed to a poorer outcome, as has been demonstrated before, but a generic outcome predictor model was shown to be useful in this group of patients. Unfortunately, this observational study was unable to show differences in outcome based on replacement treatment methods and the mortality remains at 40%.

Myxoedema coma is a rare endocrine emergency resulting from decompensation of severe hypothyroidism, as Dutta and colleagues [1] rightly comment in their recent article. It can be the presenting feature of hypothyroidism or occur in previously diagnosed individuals who either have been partially treated or have been exposed to some form of stress. Diagnosis is difficult due to the rarity of the condition and its insidious onset but is suggested clinically by the presence of altered mental state, dysthermoregulation, and a precipitating factor such as cold exposure, sepsis, or drugs [2-4]. Biochemically, serum thyroxine (T_4) and triiodothyronine (T_3) concentrations are reduced, with either elevated thyroid-stimulating hormone (TSH) in primary hypothyroidism or low or normal TSH in secondary hypothyroidism. One of the pitfalls in diagnosis is that 'coma' is a misnomer as patients may present only with signs of cognitive deterioration, such as lethargy, confusion, or disorientation. The other characteristic clinical features of severe hypothyroidism are often present, including dry skin, sparse hair, a hoarse voice, periorbital oedema, non-pitting peripheral oedema, macroglossia, and delayed deep tendon reflexes. Biochemically, anaemia, hyponatraemia, hypoglycaemia, hypercholesterolaemia, and high serum lactate dehydrogenase and creatine kinase concentrations may be evident [5].

Due to the rarity of myxoedema coma, very few randomised controlled trials have been undertaken to look at the treatment and outcome; however, myxoedema coma remains an important entity to diagnose. The prevalence of hypothyroidism is likely to increase with advancements in diagnostic tools and the increased practice of offering definitive treatment for hyperthyroidism in the form of radioactive iodine treatment and thyroidectomy. Clinicians need to have a high index of clinical suspicion to make an early diagnosis when myxoedema coma is present. Mortality has fallen from 80% to 20%-40% in treated individuals partly due to increased awareness of physicians, improved diagnostic testing, and advances in intensive care [3]. However, these statistics are based on developed countries and Dutta and colleagues raise a pertinent point in highlighting the differences in the developing world, where ready access to laboratory tests is not always possible and education for the primary physician, who does not have to deal with large numbers of thyroid conditions, remains important.

It is evident that these patients need to be treated in an intensive care setting with close monitoring of their cardiovascular status. Ventilatory support is often needed because of decreased level of consciousness, respiratory depression secondary to drugs, underlying pneumonia, or sometimes macroglossia or myxoedema of the larynx resulting in airway obstruction [3]. Hypothermia, besides conventional treatment with warm blankets and fluids, requires replacement with thyroid hormones to normalise thermoregulation. There is consensus that all patients should be given glucocorticoids as these patients may have coexistent adrenal insufficiency; thyroid hormone replacement may result in increased metabolism of cortisol, thereby precipitating adrenal crisis. However, controversy regarding optimal replacement regimens persists due to the paucity of large clinical trials [6-10]. Three different regimens have been advocated: (a) intravenous (IV) or oral T_4 , (b) IV T_3 , or (c) a combination of T_4 and

IV = intravenous; T_3 = triiodothyronine; T_4 = thyroxine; TSH = thyroid-stimulating hormone.

T₃. Unfortunately, the work of Dutta and colleagues has not moved the debate forward with a definite answer; no clinical or biochemical differences were observed between those patients who initially received IV compared with oral T₄. Arlot and colleagues [6] demonstrated that although oral absorption of levothyroxine was variable, the clinical response occurred promptly, even in a case of myxoedema ileus. A prospective study by Rodríguez and colleagues [7] found that the administration of higher doses of levothyroxine appeared to reduced mortality, although statistical significance was not reached. All studies are limited by small sample size.

Predictors of poor outcome in patients with myxoedema coma include increased age, cardiovascular compromise, and reduced consciousness. In the study by Rodríguez and colleagues [7], mortality rates for both primary and secondary hypothyroidism were similar and survival was independent of the mean free T₄ and TSH concentrations. The analysis of Dutta and colleagues of *de novo* subjects compared with treatment defaulters is interesting epidemiologically and again highlights the importance of education. Nevertheless, this information is not useful in determining the outcome once the patients have reached the intensive care setting, unlike the SOFA (Sepsis-related Organ Failure Assessment) score, which provides a more dynamic approach in predicting outcome by regularly analysing six systems, namely respiration, cardiovascular, liver, coagulation, renal, and neurological [11].

Competing interests

The authors declare that they have no competing interests.

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