The experience of using Etomidate in the management of severe Cushing's disease and MRSA bacteraemia in a district general hospital in the United Kingdom.

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Introduction

Untreated cases of severe Cushing's disease can lead to an immunocompromised state with various metabolic complications. Aim of treatment is to promptly restore normal cortisol levels while investigating for the primary source of cortisol excess.

This case highlights the use of intravenous Etomidate as an alternative yet effective cortisol lowering medication in a patient with severe Cushing's disease who has developed sepsis and decreased conscious levels thereby limiting administration of oral medications.

Case

History and examination: A 54 year old female with a past medical history of depression presented with symptomatic hyperglycaemia with truncal obesity, proximal muscle weakness, skin bruising, right posterior thorax haematoma. Blood pressure was raised at 163/114mmHg. Later during her admission, she contracted MRSA bacteraemia secondary to infected haematoma.

Results:

- Glycated haemoglobin = 115mmol/mol
- Refractory hypokalaemia on intravenous replacement and Spironolactone
- Peak random Cortisol = above 2000nmol/L
- ACTH = 125pmol/l
- Non-suppressed cortisol levels on overnight, low dose and high dose dexamethasone suppression tests
- Pituitary magnetic resonance imaging revealed a 16x16x18mm hypoenhancing lesion on the right pituitary gland with stalk deviation consistent with Cushing's disease secondary to a pituitary macroadenoma

Treatment: Metyrapone 250mg TDS lowered cortisol levels to nadir of 900nmol/L. A week later, she developed hospital-acquired pneumonia and acute respiratory distress syndrome with hypoxia requiring intubation and ventilation in the intensive care unit. Due to suboptimal administration of Metyrapone capsules and under-dosing of crushed Ketoconazole tablets through a nasogastric tube, cortisol levels rose to a peak of 3319nmol/l. Bilateral adrenalectomy was unsafe, given the degree of metabolic decompensation and severe sepsis.

Intravenous Etomidate was commenced at a rate of 1.25mg/hour, titrating up to 2.5mg/hour. Cortisol was measured every four hours to achieve a target between 600nmol/L and 800nmol/L. Mass spectrometry was used to accurately quantify cortisol levels due to accumulation of 11β-deoxycortisol which interfered with standard laboratory assay, . The infusion was maintained for further 6 days until she was stable to undergo a transsphenoidal hypophysectomy for resection of Cushing's disease.

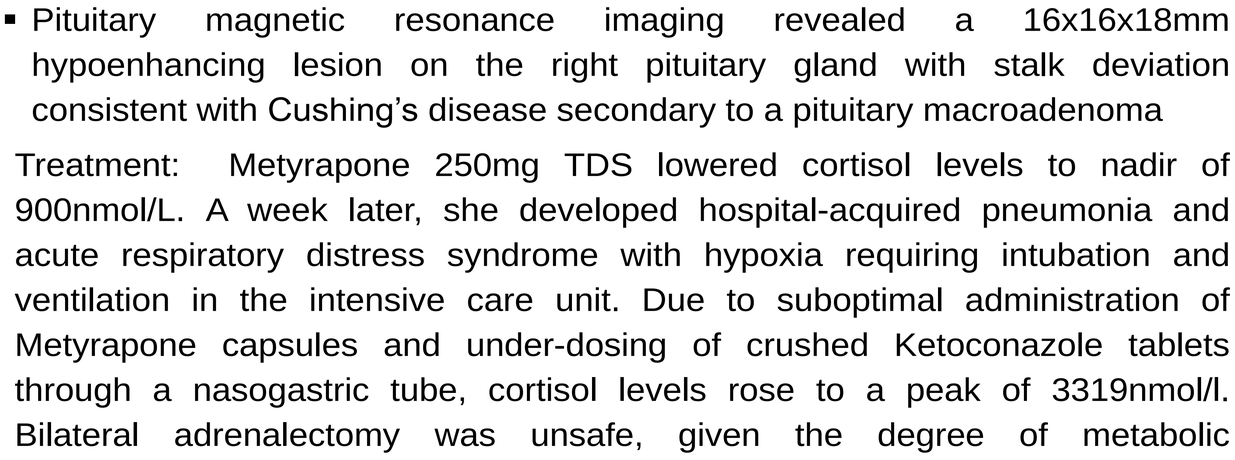

Fig 1: Cortisol values during Etomidate infusion in hours

Discussion

Oral cortisol lowering medications such as Metyrapone or Ketoconazole are commonly used as a medical management of Cushing's disease prior to definitive surgical intervention. However, uniquely to this case, whereby intravenous Etomidate provided the best medical option given the limitations of oral administration of the above medications with urgency to lower cortisol levels to physiological levels.

Historically, Etomidate was often used as an anaesthetic induction agent with it being an imidazole derivative[2]. It works by inhibiting the 11β-hydroxylase and cholesterol side-chain cleavage therefore rapidly decreases steroidogenesis within 12–24 hours[3]. Based on a recommended review paper on using Etomidate for hypercortisolism, it suggest a loading dose of 3–5 mg is followed by a continuous infusion of 0.03 to 0.10 mg/kg/h (2.5 to 3.0 mg/h) for partial blockade [2,4]. Continued monitoring of cortisol levels every 4 to 6 hours is recommended with titration of the infusion rates; with the aim to establish a stable serum cortisol level between 280–560 nmol/L. A block and replace strategy can be also be utilised to achieve a steady cortisol level[2].

Interpretation of cortisol results from standard hospital laboratories must be taken with caution. Lab assay interference with 11β-deoxycortisol resulted in falsely elevated cortisol levels initially. Mass spectrometry would be able to differentiate this precursor and to establish an accurate cortisol level.

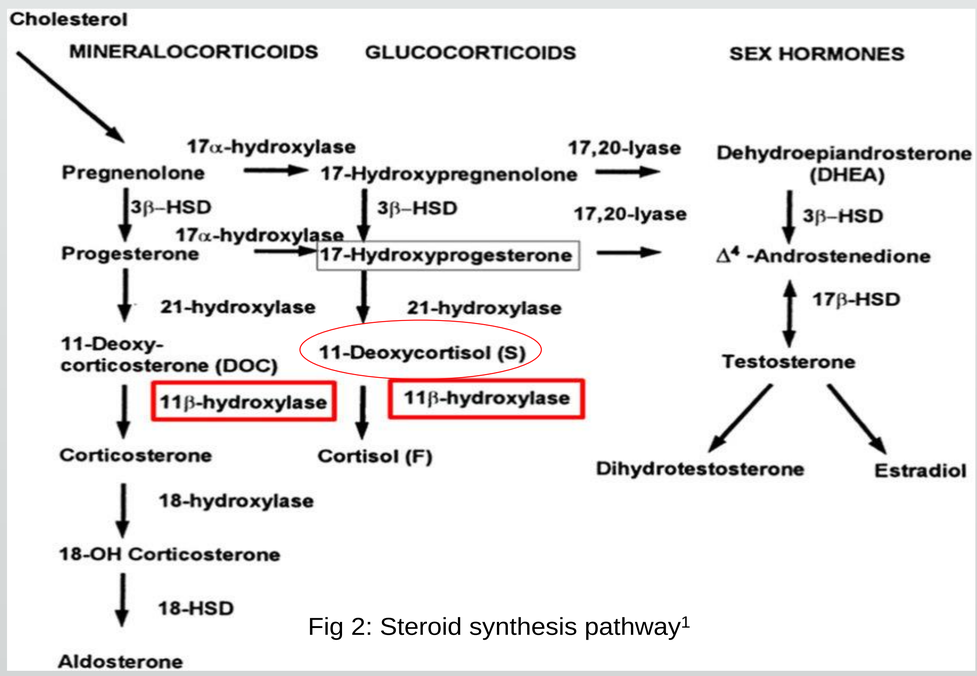

Fig 2: Steroid synthesis pathway[1]

Conclusion

Etomidate can be safely used in patients with concurrent Cushing's disease and severe sepsis in a closely monitored clinical environment.

Additionally, cortisol levels in such cases should be cross analysed using mass spectrometry to minimise measurement interference with precursors such as 11β–deoxycortisol.

References

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