PRE-OPERATIVE CARBAMAZEPINE-INDUCED HYponatraemia: SHOULD WE ACCEPT A RESET HYPO-Osmolar Baseline AND PROCEED WITH SURGERY?

Editor,

Hyponatraemia is an increasingly ubiquitous abnormality that whilst often reversible, is becoming a recognised pre-operative prognostic indicator. A known caveat of subclinical disease, hyponatraemia has been associated with perioperative coronary events, pneumonias and prolonged in-hospital stays, but has not yet been proven to be a causal determinant of mortality1.

We present a 31-year-old Caucasian woman with community-acquired hyponatraemia, whose elective thymectomy for myasthenia gravis has been deferred in light of the perceived hazards of serum sodium less than 130mmol/L.

Further analysis revealed an inability to dilute urine (Ur-Osmolality 561mOsm/kg) despite a serum hypo-osmolality (Sr-Osmolality 265mOsm/kg) and high urine sodium content (160mmol/l), classically in keeping with the syndrome of inappropriate secretion of anti-diuretic hormone.

Physical examination was unremarkable, and the patient was clinically euvoalaemic and asymptomatic throughout. She did however have a complex medical background that included a trans-osseous cerebral arterio-venous-malformation, epilepsy, gastro-oesophageal reflux and depression, as well as myasthenia gravis.

Four Endocrinologists independently concluded on a diagnosis of drug-induced chronic hyponatraemia. Contributory medications included: Carbamazepine (Tegretol-PR 400mg BD), Omeprazole and Fluoxetine; and being seizure-free for many years, there was strong reluctance to stop Tegretol but Omeprazole and Fluoxetine were stopped. In-spite of this and diligent fluid restriction, her serum sodium remained static between 122-128mmol/L.

At this point Demeclocycline (300mg BD) was tried, but was futile and served only to exacerbate symptoms of her myasthenia, a recognised side effect of Demeclocycline. Treatment was escalated to Tolvaptan (15mg twice-weekly). Although it had marginal impact on zenith sodium (129mmol/L) she noted excessive thirstiness and nausea as side effects. Tolvaptan was nonetheless persevered with.

Biochemistry results and treatment timeline are listed in Table 1.

Table 1. Biochemistry Results and Treatment Timeline.

| Year | Date | Sr Na | Sr Osmo | Ur Na | Ur Osmo |
|------|------|-------|---------|-------|---------|
| 2014 | 9-Dec | 131   | 127     | 122   | 129     |
|      | 2015  | 275   | 265     | 160   | 561     |
|      | 2016  | 601   | 561     |       |         |

*May 2015 Fluoxetine/Omeprazole Stopped
**Mar 2015 Demeclocycline Commenced
***Apr 2016 Tolvaptan Commenced

Carbamazepine was initially thought to only potentiate antidiuretic hormone (vasopressin) secretion from the posterior pituitary, but it has been shown to increase the sensitivity of the renal tubule to vasopressin as well, suggesting a duality in cause-effect2. To this effect, Carbamazepine has been used to treat polyuric patients with cranial diabetes insipidus specifically for its anti-diuretic properties.

However, a study by De Braganca et al revealed that Carbamazepine could itself exert an effect on the nephron, independent of vasopressin. Carbamazepine was found to directly stimulate the V2-vasopressin receptor and thus increase aquaporin-2 expression on the membrane of the collecting-ducts, allowing increased osmotic permeability and water absorption leading to a dilutional hyponatraemia.

Furthermore, they realised Carbamazepine could partially recover aquaporin-2 expression in Lithium-induced nephrogenic diabetes insipidus4 (NDI), suggesting a possible novel treatment modality for Carbamazepine in NDI.

Thymectomy can potentially benefit this patient. Whilst unable to forego Carbamazepine, her consequent hyponatraemia, and gradual resetting to a hypo-osmolar state, has become her baseline. Her hyponatraemia will necessitate closer perioperative surveillance, but acknowledging the mechanism for her hypo-osmolar reset should provide the confidence to proceed with surgery.

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The journey through medical training is full of significant transitions and changes in the responsibilities and seniority levels of trainees. Many articles examine the early transition from a medical student to a newly qualified doctor. Nonetheless, few studies were designed to investigate the impact of on-going transitions following the completion of the first year as a postgraduate doctor and transitions at higher levels of training. We aimed to explore the extent to which core medical trainees in their second (final) year (CMT2) feel prepared and confident about starting their higher medical training.

METHODS

In 2013, a pretested questionnaire was sent to all CMT2 in the sector covered by University College London (UCL) partners. The total number of eligible trainees was 88. Thematic analysis was applied to qualitative data.

RESULTS

The survey was completed by 53 trainees (60.2%). While the vast majority of the CMT2s (88.7%) completed the Membership of the Royal College of Physicians (MRCP) exam, 25 (28%) revealed that they had insufficient confidence to become registrars. This confirms the previously reported finding that a positive relationship between competence and self-perceived confidence is often absent.

The trainees expressed concerns across a wide range of clinical and non-clinical domains. It appeared, however, that practical procedures constituted the major area of lack of confidence, followed by managing cardiac arrest calls, running outpatient clinics and responding to referrals from other specialties. The trainees primarily blamed the low volume of exposure to these activities during the training programme. This resembles the association of the lack of confidence with ‘low volume/high impact’ clinical activities described by Kneeborn.

The majority agreed that their job was more of a ‘service provision’, as opposed to being a training one reflecting that the CMT2s are rather distracted by jobs which are less suited for them. The lack of flexibility of placements and inadequate exposure to certain specialties was considered by many trainees as another important reason behind their insufficient confidence.

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