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In Context

IN CONTEXT

Treating hyponatremia fast but modestly: counterbalancing risks and the fear of osmotic demyelination syndrome

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Hyponatremia is the most common electrolyte abnormality, affecting among 20%–30% of hospital admissions [1]. Hyponatremia is acute if it develops in less than 48 h and chronic when >48 h have passed since its occurrence. This 48-h period is the time needed for adaptation mechanisms to normalize cell volume. The symptoms of hyponatremia are mainly due to brain edema in the acute phase and include nausea, vomiting, confusion, headaches, somnolence, seizure, coma and even death. Whereas proper correction of acute symptomatic hyponatremia may substantially decrease morbidity and mortality, fear of osmotic demyelination syndrome (ODS), which develops as a result of a too rapid increase in serum sodium concentration, confounds treatment applications. ODS is generally delayed, presenting 2–6 days after the too rapid correction of hyponatremia. Its clinical manifestations are dysarthria, dysphagia, paraparesis, quadriparesis, seizures, lethargy and coma [2]. ODS can be irreversible, and thus, should be avoided. Prevention of ODS is achieved by limiting the correction rate of hyponatremia, especially for chronic hyponatremia. However, accurate incidence of ODS and the safe but effective pace of sodium increase to prevent its occurrence are not very well known. Defined risk factors for ODS include: (i) too low serum sodium levels at which to start correction (e.g. <110 mmol/L), (ii) hypovolemia, (iii) alcohol use, (iv) malnutrition and (v) hypokalemia [3]. Diagnosing ODS is not easy because imaging including magnetic resonance imaging (MRI) findings may not be visible until weeks after rapid correction–associated brain injury.

In a recent study, MacMillan *et al.* aimed to evaluate the incidence of ODS in a large sample of more than 22 000 hospitalized patients who were admitted with hyponatremia (<130 mmol/L) [4]. They defined rapid correction as more than 8 mmol/L increase in serum sodium concentration in any 24-h period during hospital stay. Rapid correction happened in 17.7% of the patients. However, ODS was diagnosed in only 12 patients, i.e. 0.05% of the entire cohort, and 7 of these patients (58%) had a sodium correction rate <8 mmol/L in 24 h. The investigators suggested that there might be factors other than rapid sodium correction that resulted in ODS, including hypokalemia and concurrent circulating alcohol, which were found more frequently in these patients. Predictably, patients with serum sodium level <110 mmol/L at therapy start significantly more frequently developed ODS than patients without (58% vs 1.1%). Yet, 86.9% of the patients in the study cohort had a serum sodium >120 mmol/L and almost none (five or fewer) developed ODS. While the rate of ODS was 0.05% in the entire cohort, it increased to 0.3% and 2.6% in patients who had an initial sodium level of <120 mmol/L and <110 mmol/L, respectively.

The study by MacMillan *et al.* may imply that fear of ODS is somewhat exaggerated in real world scenarios. However, hypertonic sodium infusion rate and type of replacement fluids were not reported in this study. Additionally, it was not known whether patients had acute or chronic hyponatremia. The risk of ODS has been reported to be much lower in acute hyponatremia including those with too rapid correction rates, so that

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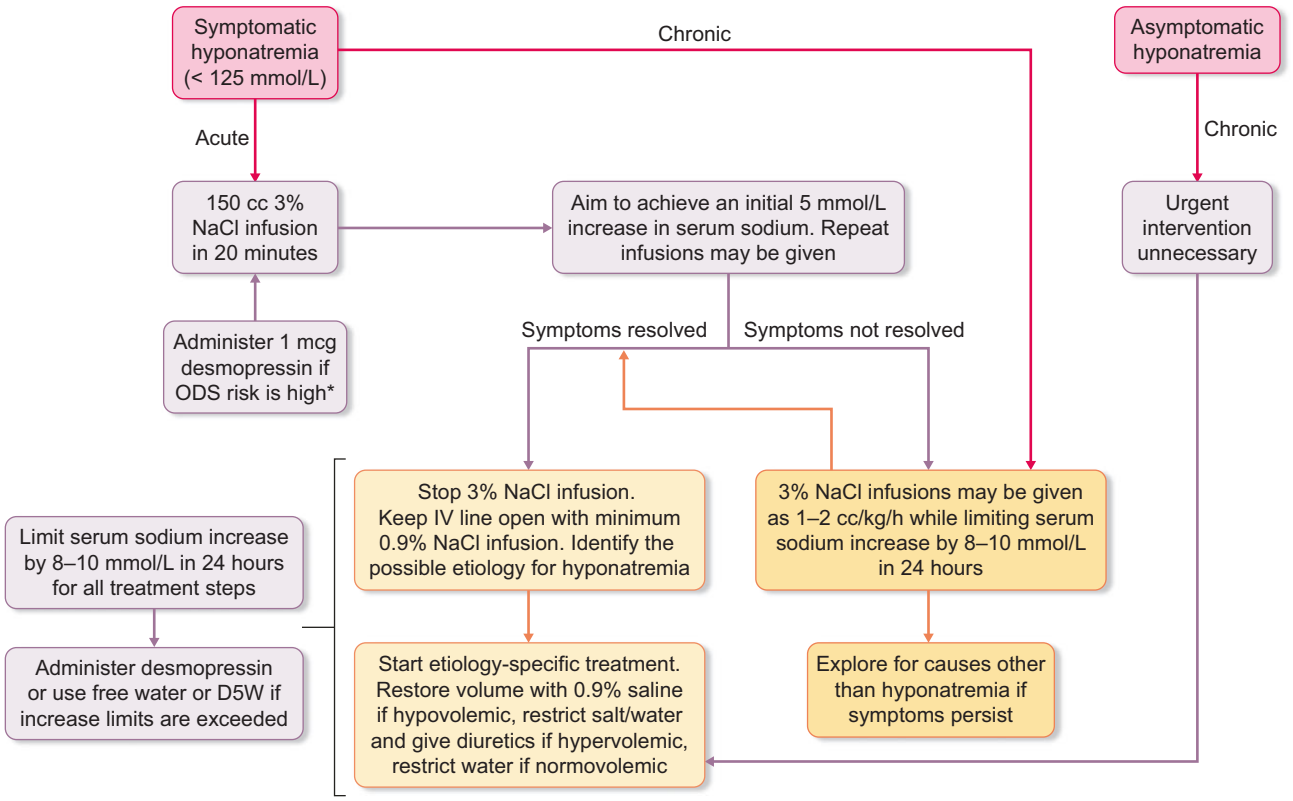

Figure 1: Treatment algorithm of hyponatremia with focus to prevent ODS. D5W: 5% dextrose in water. *Please refer to the text for conditions that increase ODS risk.

if patients in this study had mostly developed acute hyponatremia, it is not surprising to observe that just a handful of patients developed ODS. Moreover, the vast majority of their cohort had initial sodium of >120 mmol/L, which is already related to lower ODS risk. Previous studies reported higher ODS incidences (as high as 11%–25%) when initial sodium levels of <120 mmol/L and <105 mmol/L were overcorrected [5, 6]. We also doubt that some ODS diagnosis might have been missed as a median of only 3.4 days (IQR 1.6–7.3) had passed before MRIs were ordered to diagnose ODS. The authors, however, suggest that they did not leave any ODS undiagnosed given that all-cause mortality and hospital readmissions were not inappropriately high in the group that experienced rapid correction.

Because length of hospital stay and discharge to a nursing facility rather than to home is substantially higher among patients with ODS, even in the study by MacMillan *et al.* with a very low rate of ODS, we suggest that physicians should take necessary precautions to avoid practices with high risk of ODS, especially when hyponatremia is chronic. An effective strategy to treat symptomatic hyponatremia, taking practice guidelines into account [3, 7], is summarized in Fig. 1.

CONFLICT OF INTERESTS STATEMENT

The authors declare that they have no conflicts of interest.

AUTHORS' CONTRIBUTIONS

A.M. and K.K.-Z. designed the work. A.M. drafted the first version of the manuscript. K.K.-Z. critically revised the first version. Both authors contributed to the consecutive versions of the manuscript and approved the final version.

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