Dangers of overtreating “mild” hyponatremia?

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Are patients with chronic asymptomatic hyponatremia (hypoNa) with serum sodium of 125 meq/L and higher at risk for osmotic demyelination syndrome (ODS) with rapid correction of their serum sodium? This question was recently posed in an ASN Communities discussion thread.

The question was asked because the poster’s Pharmacy and Therapeutics Committee at a local hospital had noticed that following the use of tolvaptan for hypoNa, 3 of 45 patients had an increase in plasma sodium concentration (PNa) of 6–12 meq/L and 3 had an increase >12 meq/L, within a 24-hour period. The average PNa pre-tolvaptan was 127. The committee wanted to know if those patients needed a maneuver to re-lower their post-tolvaptan Na to avoid risking ODS.

Query and Hypothesis

Is the risk of ODS the same at all levels of starting PNa levels? And if not, perhaps we do not need to re-lower the PNa if starting in the mid-120s?

Discussion

The discussion focused on several points:

1. The relative change in serum osmolality (and therefore shifting of brain water) is not the same with a 12 meq/L PNa change when you consider, for example, starting at a PNa of 110 vs. 125. Thus, you would not expect the risk of ODS to be the same in those two patients. This is confirmed by the fact that most cases of ODS have been reported at lower starting PNa levels. Other ODS risk factors should be considered such as cirrhosis, alcoholism, hypoK, hypophosphatemia, and malnutrition.

2. The discussants found one case of ODS following tolvaptan, but the PNa went from 126 to 167 over 3 days before tolvaptan was stopped: https://www.ncbi.nlm.nih.gov/pubmed/24511399. However, this was felt to be a mismanagement issue more than due to tolvaptan itself.

3. Even though ODS is rare following the treatment of “mild” hypoNa, cases of ODS have been reported with acute hyponatremia https://www.ncbi.nlm.nih.gov/pubmed/29277507 and hyperglycemia https://www.ncbi.nlm.nih.gov/pubmed/19565558 in which the starting PNa was relatively normal.

4. There was no consensus about whether or not you need to re-lower the PNa following an overly rapid correction in mild hypoNa. Data simply do not exist to guide us. However, the point was made that acute changes in brain water are always risky and that perhaps you should try to avoid these rapid changes when using tolvaptan for SIADH (syndrome of inappropriate antidiuretic hormone secretion). In that regard, there are two recent papers that report this phenomenon when using a starting dose of 15–30 mg: http://www.ajkd.org/article/S0272-6386(18)30004-0/fulltext and http://journals.sagepub.com/doi/full/10.5301/jon.5000025. Both papers suggested using a starting dose of 7.5 mg.

Conclusion

ODS may be rare when using tolvaptan for mild hypoNa, and it is unknown if the PNa needs to be lowered in cases where the PNa increase exceeds standard recommendations. Using lower starting doses of tolvaptan may make this discussion moot.

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