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Letter to the Editor

Drug-associated hyponatraemia in Internal Medicine: Interpreting real-world clinical data

Hiponatremia asociada a fármacos en Medicina Interna: interpretando resultados de la práctica clínica real

Dear Editor,

We thank Cárdenas Durán and Lorences Noguera for their interest in our work and for their comments, which allow us to clarify several methodological aspects relevant to the study of drug-associated hyponatraemia (DAH).

Regarding causality attribution, our retrospective observational study of real-world clinical practice did not systematically use standardised causality assessment tools such as the Naranjo or WHO-UMC algorithms.[1] Instead, we identified DAH through individual review of the clinical and medication history. DAH was considered when hyponatraemia had been attributed to medication in the discharge report or, when no aetiology was explicitly documented, when exposure to one or more potentially causative drugs was present and no alternative cause better explained the episode. For this purpose, we reviewed volume status, renal function, thyroid and adrenal function, plasma and urine osmolality, and urinary electrolytes as available.[2]

We agree that a standardised causality assessment tool would have allowed more precise characterisation, particularly in patients simultaneously exposed to several potentially implicated drugs.[1] However, comparisons between our cohort and data from the Spanish Pharmacovigilance System should be interpreted with caution, as these sources are inherently different. Our series comprises patients admitted to an Internal Medicine department, with a median age of 87 years and a high burden of multimorbidity and polypharmacy, whereas pharmacovigilance systems rely on spontaneous reporting and may therefore be subject to different patterns of selection and reporting.[2,3] Thus, the higher frequency of antidepressants observed in our series should be understood as a description of the drugs implicated in this specific hospitalised population, not as evidence of a greater intrinsic causal risk associated with this drug class. Our primary objective was to characterise DAH in patients admitted to Internal Medicine, not to compare the risk associated with different drug classes.

Regarding volume status assessment, we agree that clinical examination alone has limitations, particularly in older patients with multiple comorbidities.[4,5] In our study, patients were retrospectively classified as euvolaemic, hypovolaemic, or hypervolaemic based on physical examination, vital signs, and the clinical assessment documented during hospitalisation. Biochemical measurements were not uniformly available because, given the retrospective nature of the study, we collected the tests performed as part of routine clinical care, without a diagnostic protocol specifically established for the study: plasma osmolality was available in 46 patients (28.9%), and urine osmolality or urinary electrolytes in 83 (52.2%). Therefore, the 69.8% of patients classified as euvolaemic should be understood as a clinical categorisation rather than a complete biochemical phenotype.[2] Regarding the potential influence of this classification on therapeutic management, the 23.9% of patients in whom no specific therapeutic intervention was recorded should also be contextualised. Of the 38 patients in this group, 36 (94.7%) had DAH as a secondary diagnosis, and all had mild or moderate hyponatraemia – 18 mild and 18 moderate. Thus, the absence of a specific intervention should be interpreted in light of the lower severity of these episodes and the fact that, in most cases, DAH was not the primary reason for admission.[2]

We again thank the authors for their comments. We agree that prospective incorporation of standardised causality assessment algorithms and systematic biochemical characterisation would improve the aetiological precision of DAH and facilitate comparisons across cohorts. Our study aims to describe the presentation and management of DAH in routine Internal Medicine practice and to serve as a starting point for prospective, multicentre studies using a more standardised methodology.

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