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BRIEF REPORTS

DRUG-INDUCED HYPONATREMIA: NSAIDS, A NEGLECTED CAUSE THAT SHOULD BE CONSIDERED

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Abstract: Hyponatremia is the most common electrolyte disorder. It may have serious consequences in asyntomatic patients with a mild disease. Therefore, an evaluation of unsual causes is of paramount importance. Polypharmacy is highly prevalent in older people and many drugs can cause hyponatremia as a collateral effect. In our retrospective analysis of geriatric medical records dated 2015 we found that 39 out of the 273 hospitalized patients had hyponatremia. Polipharmacy was highly prevalent, especially in hyponatremic patients. Non-steroidal anti-inflammatory drugs, which are seldom considered as a cause of hyponatremia were instead found to be associated to an increased risk of the disorder (adjustedOR 3.61, 95% CI 1 – 12.99, p = 0.05). In-hospital mortality was higher in patients with moderate or severe hyponatremia at hospital admission. Our study underlines the importance of considering rare but potentially reversible causes of hyponatremia, which can lead to serious consequences.

Key words: hyponatremia, NSAIDs, polypharmacy.

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Hyponatremia, or sodium serum concentration [Na] <135 mEq/L, is the most common electrolyte disorder in clinical practice (1).

Its prevalence increases with age; the causes can be: senescence related changes in homeostatic mechanism, polypharmacy and comorbidities which alter the body fluid balance (2).

In community dwelling elderly the prevalence varies between 7.2 and 11% (3), whereas for older people hospitalized in geriatric wards seems to be higher: 22.2%, at hospital admission and 14.8% during hospital stay (4).

Hyponatremia is very heterogeneous both in term of aetiology and symptoms (ranging from complete asymptomaticity to life threating coma) (5). Since even mild forms have been associated with bad clinical outcomes (i.e. mortality, longer hospitalization, readmissions, falls, osteoporosis, cognitive impairment) (6), it is of utmost importance to approch this disorder appropriately. Even if several diagnostic algorithms exist, the assessment remains far from optimal in most clinical settings especially in complex older people (7). Physicians often fail to give the proper attention to drug-induced hyponatremia and they pay low attention to pharmacological rare causes. This can be very dangerous because the association of drugs which may cause hyponatremia increases the risk of developing the elecrolyte disorder up to 10 folds (8).

We conducted a retrospective analysis of medical records of patients hospitalized in the Geriatric Unit of a tertiary hospital in Milan between January and December 2015.

Among the 273 hospitalized patients we found a prevalence of hyponatremia reaching 14.3% at hospital admission. Hyponatremia was mild in most cases (30 patients = 11%), moderate in 6 patients (2.2%) and severe in only 3 cases (1.1%).

Polipharmacy was highly prevalent at hospital admission (mean number of drugs ± SD: 6.7 ± 4.2) and slightly more frequent in hyponatremic patients than in normonatremic ones (mean number of drugs ± SD: 7.4 ± 3.7 vs 6.6 ± 4.2, p=0.19).

Moreover we found that the use of anti-inflammatory drugs (NSAIDs) was associated with an increased risk of having hyponatremia at hospital admission (adjustedOR 3.61, 95% CI 1 – 12.99, p = 0.05).

Drug-induced hyponatremia can be caused by various medications that can affect sodium or water homeostasis (6, 9, 10), but NSAIDs are rarely reported (11, 12). The mechanism by which NSAIDs cause hyponatremia is the reduction of renal prostaglandins. Prostaglandins exert an inhibition on the activity of the antidiuretic hormone; thus their reduction can cause free water retaintion (13) and hyponatremia. This collater effect is more frequent in those conditions characterized by high and relatively nonsuppressible levels of ADH like the use of other drugs. This can cause an inappropriate secretion of the antidiuretic hormone, or effective volume depletion, which is quite frequent among older people. Both non-selective and selective cyclooxygenase inhibitors can cause hyponatremia, even though they are administered for few days. Awareness of this adverse effect is particularly important since NSAIDs are frequently used in the older population. A rational clinical management and a proper medication review are advisable at hospital admission since the discontinuation of the therapy is

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the first step to treat drug-induced hyponatremia. This reduces the possibly serious consequence of increased mortality. Indeed, our study confirmed that the in-hospital mortality was higher in patients who were admitted with a moderate or severe hyponatremia (4). Thus the treatment and the prevention of reversible causes is of paramount importance.

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