Editorial

Hyponatraemia in older people is usually multifactorial and commonly iatrogenic

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Keypoints:

Hyponatraemia in older people is usually multifactorial

SIADH is frequently considered the commonest cause but may be over-diagnosed

Medication-associated hyponatraemia is extremely common and may be reversible

Hyponatraemia is most frequently found in older people [1] and the commonest cause of hyponatraemia is usually cited as the syndrome of inappropriate diuretic hormone (SIADH) [2]. However, studies in the frailest and most elderly subjects suggest hyponatraemia is frequently multifactorial, with medications playing a key role [2,3]. Therefore, it is time to re-evaluate whether diagnostic assessment of the aetiology of hyponatraemia in older adults needs to move on from elucidating a single cause or pathological mechanism, such as SIADH. A similar approach already exists within geriatric medicine as all the 'geriatric giants', such as delirium or falls, tend to be multifactorial in origin. Rarely is a single disease or entity attributed as directly causal to the development of geriatric syndromes, precisely because of their complexity and multifactorial nature. Should hyponatraemia be the same? It shares all the essential criteria for a 'geriatric giant' – common, complex, of multifactorial aetiology, often iatrogenic and with a tendency to cluster along with the other giants such that once a patient develops one, others often follow. Hyponatraemia is associated with poor balance, falls, reduced cognition and stroke, so this clustering effect is particularly marked [4]. A diagnosis of SIADH, a condition with no universally approved definition [5], may be unhelpful when an alternative approach of listing contributing factors and treating those that are reversible may be much more informative and fruitful.

Jun et al [6] report novel research that supports the need for sea change in the assessment of hyponatraemia in older adults. Firstly, they found hyponatraemia-inducing medications (HIMs) were prescribed in 77% of older people with hyponatraemia. Although there is no comparator arm (prevalence of HIMs in those that did not develop hyponatraemia), it seems certain that medications must have contributed. Moreover, this will be an underestimate because they did not count loop diuretics on the basis they may have been used appropriately to treat chronic hypervolaemic hyponatraemia, but loop diuretics themselves frequently cause hyponatraemia. Secondly, they tackled the problem of potential confounding by indication (i.e. that medications are associated with hyponatraemia because they are prescribed for a condition that itself causes hyponatraemia). Their analysis adjusting for co-morbidity still shows a profound effect on the risk of development of hyponatraemia for those prescribed HIMs. This strongly suggests the medications themselves are driving hyponatraemia, immediately providing a potential target for remedial intervention through medical optimisation. Finally, the proportion of those with hyponatraemia that still had HIMs on discharge fell only to 70%. This hints at a significant educational gap, potentially a failure to recognise the multifactorial and potentially iatrogenic nature of hyponatraemia in this group. Current guidelines on the assessment of hyponatraemia do not help, relying on an out-dated 'Ockham's razor' paradigm to hone in on a single-cause diagnosis [7,8]. They also rely heavily on determination of volaemic assessment of the patient, but this is notoriously challenging and unreliable in older people [9]. Perhaps unsurprisingly therefore, hyponatraemia frequently fails to improve in clinical practice and becomes chronic or recurrent.

Jun et al [6] demonstrate that attention to HIMs and medical optimisation must be a key component of any treatment strategy for correction of hyponatraemia in older people. They show how prescription of multiple HIMs results in additive risk, especially in combination with thiazide diuretics. The importance of thiazide diuretics cannot be overstated. Whilst scoping the extent of SIADH in older people with fragility fractures (a population where SIADH is supposedly common), the predominant form of hyponatraemia was actually hypovolaemic, with thiazides the commonest predisposing factor [3]. Misdiagnosis of diuretic-induced hyponatremia as SIADH is worryingly common, a phenomenon I label tongue-in-cheek as an example of 'syndrome of appropriate antidiuretic hormone' [10,11]. Treatment with fluid restriction is likely to cause further dehydration and sodium loss into hyper-

concentrated urine. One silver living is that almost half of all those with thiazide-induced hyponatraemia had their thiazide diuretics discontinued [6]. However, prescribing of most other HIMs, including commonly prescribed antidepressants and analgesics did not decrease. More worryingly, prescribing rates of antipsychotics almost doubled. This probably suggests treatment of hyponatraemia-associated delirium with medications that may exacerbate the condition, instead of a non-pharmacological approach that included avoidance of delirium-promoting medications.

Adequate diagnosis of all the precipitant causes of hyponatraemia really matters. Hyponatraemia in older people is associated with a range of adverse outcomes, including falls, fractures, delirium, longer hospital stays and death [4]. Although some debate remains about how much this reflects hyponatraemia acting as a marker of poor outcome, there is evidence correction of hyponatraemia improves balance and cognition [4,12]. Inevitable age-related changes in physiology predispose to hyponatraemia, particularly decreases in glomerular filtration rate, urinary concentrating ability, sensitivity of the thirst mechanism and free water clearance and alterations in production of key hormones such as arginine vasopressin, aldosterone and atrial natriuretic peptide [13]. However, hyponatraemia is uncommon in otherwise well older people, and its presence strongly suggests the presence of disease/s or other external stressor on homeostatic mechanisms, such as HIMs. Therefore, the discovery of hyponatraemia in an older patient merits careful consideration of underlying causes and attempts at correction should be encouraged, even when hyponatraemia is mild [4]. Future research should focus on verifying whether correction of hyponatraemia improves important clinical outcomes such as mortality or length of stay in hospital. However, any strategy for correction of hyponatraemia will rely on clinicians being competent to identify all reversible causes, undertake appropriate risk/benefit evaluations of prescribed medications and be prepared to minimise use of HIMs. Though the results of the study by Jun et al [6] come only from a Korean population, they are likely to be generalisable to a wider international audience. There is much to do in improving the identification, assessment and management of medication-induced hyponatraemia in older people.

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