Prevalence of Hyponatremia in Neurosurgical Patients in South India – An Institution-Based Observational Study

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ABSTRACT

BACKGROUND

Hyponatremia is the most frequently encountered electrolyte abnormality in hospitalized patients, especially those with neurological injury. Acute onset hyponatremia is common in patients with any type of cerebral insult including traumatic brain injury (TBI), subarachnoid haemorrhage (SAH) and brain tumours. Also seen as a complication of intracranial procedures, contributing to increased morbidity and mortality. Early diagnosis and effective management can reduce mortality associated with this condition. This study was done to estimate the prevalence of hyponatremia in neurosurgical patients in our institution.

METHODS

This is an observational study that analysed the adult patients admitted to the neuro intensive care unit (ICU) after having undergone the neurosurgical procedure from January 2019 to July 2019. A structured questionnaire was used for data collection. The prevalence of hyponatremia was calculated with pre-operative serum sodium levels in the study population.

RESULTS

In this study with 61 patients undergoing neurosurgical procedures, the prevalence of hyponatremia was 34.4 %. The majority of patients for surgery comes between 41 to 50 years. 57.4 % cases were with traumatic brain injury, 11.5 % cases were with sub arachnoid haemorrhage and 31.1 % were with intracranial tumour. 26 % of hyponatremia patients belonged to mild grade while 8 % to moderate grade. 62.5 % of patients above 70 years, 44.4 % of patients between 51 to 60 years and 40 % of patients between 61 and 70 years presented with mild hyponatremia. 37.5 % of patients above 70 years and 10 % of patients between 61 and 70 years presented with moderate hyponatremia.

CONCLUSIONS

Our study showed an increased prevalence of hyponatremia in neurosurgical patients which demand effective approaches for an accurate and timely diagnosis of this electrolyte disorder. Hyponatremia frequently occurs in patients with TBI, SAH and intracranial tumours. It is also essential to differentiate between syndrome of inappropriate antidiuretic hormone (SIADH) and cerebral salt wasting syndrome (CSW) as the treatment modalities are entirely different for these two entities. Early detection, close monitoring, etiological evaluation and prompt treatment based on aetiology can reduce the complications and improve patient's outcomes.

KEYWORDS

Electrolyte Abnormality; Brain Injury, Morbidity

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BACKGROUND

Hyponatremia which is defined as serum sodium < 135 mEq/L, is the most common electrolyte abnormality seen in clinical practice.[1] Although it indicates a state of hypotonicity with a relative excess of total body water compared to sodium, however, it does not necessarily imply that the total body water is increased and the patient may be clinically hypovolemic or hypervolemic. It is also the main determinant of serum osmolality, important for fluid transport across the cell membrane and nerve impulse transmission at the time of cell depolarization.[2] According to the plasma level, it is classified as normal 135 to145, mild 130 to 134, moderate 125 to 129, severe when levels are below 125 mEq/L.[3] Hyponatremia can occur in isotonic, hypertonic or hypotonic forms. Hypertonic hyponatremia can occur with hyperglycaemia. Hypotonic hyponatremia can be further classified based on volume status into hypovolemic, isovolumic and hypervolemic hyponatremia. Hypovolemic hyponatremia may be seen in gastrointestinal losses due to vomiting and diarrhoea. While condition like congestive heart failure, nephrosis, liver dysfunction is associated with hypervolemic hyponatremia, SIADH is associated with isovolumic hyponatremia.[4] Arginine vasopressin (AVP) plays an important role in the pathophysiology of hyponatremia. The underlying mechanism for the exaggerated or "inappropriate" AVP response differs in patients with hyponatremia as a function of their extracellular fluid volume. Secondary adrenal insufficiency due to pituitary disease can result in severe hyponatremia. The decreased level of aldosterone in primary adrenal insufficiency causes hypovolemic hyponatremia, while glucocorticoid deficiency in secondary adrenal failure is associated with euvolemic hyponatremia. One of the most common causes of hyponatremia in the hospitalized patient is iatrogenic administration of hypotonic intravenous fluids.

Hyponatremia is frequently seen in patients who have undergone neurosurgical interventions. Acute onset hyponatremia is particularly seen in any patient with cerebral insult or intracranial procedures, results in generalized cellular swelling, due to the movement of water down the osmotic gradient from hypotonic extra cellular fluid (ECF) to intracellular fluid (ICF). Symptoms of hyponatremia are mainly neurological. The initial central nervous system (CNS) response is an increase in interstitial pressure, thereby resulting in the shunting of ECF and solutes from interstitial space into systemic circulation via the cerebrospinal fluid (CSF) and the efflux of major intracellular ions like Na+, Cl- and K+ from the brain cell. When these volume regulatory mechanisms are overwhelmed by a rapid decrease in tonicity, acute cerebral oedema develops resulting in acute hyponatraemic encephalopathy. Early symptoms include nausea, vomiting and headache which can progress to seizures, brainstem herniation, coma and death. In patients with acute hyponatremia, normocapnic or hypercapnic respiratory failure may develop and the associated hypoxia may exaggerate the neurological injury. Perimenopausal women are more likely to develop encephalopathy and severe neurological sequelae.

In patients with persistent, chronic hyponatremia efflux of organic osmolytes (creatine, betaine, glutamate, myoinositol, and taurine) from brain cells occurs thereby resulting in a reduction of intracellular osmolality and the osmotic gradient. The period required for this reduction in intracellular osmolytes is 48 hours. However, the cellular response to chronic hyponatremia does not fully protect patients from symptoms. They manifest subtle gait and cognitive defects that reverse with correction of hyponatremia. They also have an increased risk of developing bony fractures due to hyponatremia-associated reduction in bone density. Therefore, even in the absence of overt symptoms, every attempt should be made to safely correct the plasma Na+ concentration in patients with chronic hyponatremia.

Hyponatremia can also occur following the intake of certain drugs like diuretics, carbamazepine, chlorpromazine, selective serotonin reuptake inhibitors (SSRI), theophylline, amiodarone (K) diuretic-induced hyponatremia is often associated with the use of thiazide or thiazide-like agents while loop diuretics are rarely associated with hyponatremia.[5]

Hyponatremia is a common electrolyte abnormality seen in neurosurgical ICU.[6-8] Acute onset of hyponatremia is usually seen in patients with neurological injury or diseases affecting the central nervous system which includes traumatic brain injury, spontaneous intracerebral bleed, stroke, meningitis, subarachnoid haemorrhage and following surgery for intracranial space-occupying lesions. Acute onset hyponatremia is clinically more dangerous than chronic hyponatremia, as it creates an osmotic gradient between the brain and the plasma, which promotes the movement of water from the plasma into brain cells, causing cerebral oedema and neurological symptoms. Acute hyponatremia needs to be treated promptly to avoid complications like cerebral oedema, increase in intracranial pressure and subsequent manifestations like altered consciousness, seizures and death due to cerebral herniation.[9]

The pathophysiology of hyponatremia in neurotrauma is multifactorial and associated risks of morbidity vary widely. It can be classified as hyponatremia related to normal, high or low osmolality.[10] Neurological dysfunction due to hyponatremia may be aggravated due to underlying conditions or other disease processes, especially in patients with intracranial pathology. Hence it is essential to be aware of all the potential causes of hyponatremia to provide appropriate management and avoid an adverse outcome. Syndrome of inappropriate antidiuretic hormone and cerebral salt wasting syndrome are two potential causes of hyponatremia in patients who have undergone neurosurgery. SIADH is defined as euvolemic hyponatremia with inappropriate urine concentration (urine osmolality > serum osmolality), and oliguria with natriuresis. Whereas, CSWS is defined as hypovolemic hyponatremia resulting in low CVP, diuresis (with urine output > 250 ml/hour) and natriuresis. Hence SIADH is characterized by a volume expanded state, whereas CSWS is characterized by a volume contracted state and the treatment modality varies greatly between these conditions.[11-13] Fluid restriction is the

treatment of choice for SIADH, while salt and volume replacement is the treatment for CSWS.

Hyponatremia is more frequent in patients with subarachnoid haemorrhage (almost 50 %) when compared to traumatic brain injury. Some retrospective studies strongly support SIADH as the predominant cause of hyponatremia. In the largest prospective study done to date also support SIADH as the leading cause of hyponatremia in SAH patients. Management of hyponatremia is relatively simple if detected early. Early complications can be reversed with the infusion of sodium-containing solutions.[14-17]

Hyponatremia is a negative prognostic factor in patients with ischemic or haemorrhagic stroke.[18] It is associated with increased length of hospital stay and a higher rate of short term and long-term mortality compared to patients with normal sodium levels. Dysnatremia and water balance disturbances go hand in hand. Hence patient's hydration status should always be assessed while managing dysnatremias. Change in water balance is usually the cause for short term changes in serum sodium concentration, although in some cases, salt balance also contributes to this change.[19,20]

Salt balance is about the maintenance of volume whereas water balance is more associated with osmolality. Hyponatremia and hypernatremia may therefore occur in presence of positive, negative or zero salt balance. If the change in water balance is known from serial weighing, then by calculating the change in serum sodium concentration over the same period, we can know the day to day balance of sodium.

Severe hyponatremia (serum Na+ < 120 mmol/l) is associated with the development of cerebral oedema and brain damage especially in extremes of age. Acute symptomatic hyponatremia may require an infusion of 3 % hypertonic saline for rapid correction of serum sodium level. However rapid correction of severe hyponatremia may cause neurological damage due to osmotic demyelination. To avoid this, hyponatremia should be corrected at a rate not exceeding 10 mmol/l/day. False hyponatremia should always be excluded before making a diagnosis of hyponatremia. In pseudo hyponatremia, plasma osmolality will be normal whereas it will be reduced in true hyponatremia. In conditions like severe hyperlipidaemia with milky serum, serum sodium may be falsely low as lipid expands ECF but contains no sodium. Similarly, when there is hyperglycaemia, ECF expands due to the osmotic action of glucose and as the blood glucose falls with treatment, water passes from the ECF to the ICF, thereby increasing the sodium concentration in the cell. Serum sodium falls by 1.6 mmol/L for every 5.6 mmol/L increase in plasma glucose. In case of hyperglycaemia, therefore, serum sodium should be corrected upwards appropriately and the corrected value should be used to guide fluid replacement.

Symptoms of hyponatremia depend on the development of cerebral oedema, increase in intracranial pressure and the rapidity with which hyponatremia occurs. Acute onset of symptoms like headache, agitation, confusion, vomiting and lethargy occurs when serum sodium level is as low as 120 to 125 mEq/L (higher in children and perimenopausal females). More severe symptoms like seizures and coma occur when Na+ concentration is less than 110 mEq/L. High levels of atrial natriuretic peptide and brain natriuretic peptide are found to be associated with the incidence of hyponatremia and natriuresis in patients with SAH. ANP and BNP produce natriuresis by increasing the glomerular filtration rate via a direct effect on the renal medullary collecting ducts, and suppression of the renin-angiotensin-aldosterone axis.[21]

While managing hyponatremia, other potential underlying causes such as steroid deficiency, renal disease, and cardiac disease should be identified and treated. Patients with chronic hyponatremia (> 48 hours or of unknown duration) may be asymptomatic even at Na+ concentrations less than 120 mEq/L due to the adaptive mechanism. However, it should be treated very cautiously because of the cerebral compensation that may occur due to the hypo-osmolar state. Hence a sudden increase in osmolarity can lead to cerebral water loss and osmotic demyelination (central pontine myelinolysis).[22-25] Although patients with euvolemic hyponatremia due to SIADH, hypothyroidism, or secondary adrenal failure may respond to successful treatment of the underlying cause, some causes of SIADH are not immediately reversible and may require pharmacological therapy to increase the plasma Na+ concentration. Many of them respond to combined therapy with oral furosemide, 20 mg twice a day (higher doses may be necessary for renal insufficiency), and oral salt tablets. In patients whose Na levels do not increase in response to furosemide and salt tablets, demeclocycline (a tetracycline derivative) which is a potent inhibitor of principal cells can be used. Vasopressin antagonists like conivaptan and tolvaptan which block receptors for arginine vasopressin also may be used as an alternative to fluid restriction in patients with euvolemic or hypervolemic hyponatremia. Hence, hyponatremia should be managed according to the patient's intravascular volume status, chronicity of onset and presence of symptoms.[26]

Aim

This study aimed to estimate the prevalence of hyponatremia in neurosurgical patients in our institution.

METHODS

This is an observational study done in the Department of Anaesthesiology, Government Medical College Thrissur, Kerala in association with the Department of Neurosurgery of the institute. 61 patients undergoing elective & emergency neurosurgical procedures at all age groups were included. The study period was from January 2019 to July 2019. Patients on pharmacotherapy affecting body electrolytes, those who had comorbidities with associated sodium abnormality and spine surgeries were excluded from the study. To diagnose hyponatremia, the serum sodium cut off level was taken as less than 135 mEq/L.

The sample size was calculated as 61 with a prevalence of 62 % from a study.[27]

$4pq/d2P$

Where
P = prevalence = 100-p, and d = absolute precision (taken as 20 % of prevalence)
q: 100-p = 38, d: 20 % of prevalence = 12.4.4*62*38/12.4*12.4 = 61

After obtaining ethical committee clearance, the patients were recruited by the primary investigator (PI). Informed consent was obtained from each patient. All relevant data as per the structured questionnaire was used for data collection. This includes a detailed history of comorbidities and assessment of the general physical status of the patient along with complete physical and systemic examination. Basic & relevant investigations were noted for confirmation of diagnosis and preoperative workup.

Pre-operative serum sodium was noted in all patients undergoing both elective and emergency neurosurgeries. Duration of surgery, type and amount of IVF given were noted. Majority of our patients had mild hyponatremia who were managed with avoidance of hypotonic intravascular fluid and drugs causing electrolyte imbalance. Patients with decreasing trend in serum sodium levels associated with clinical deterioration were managed with hypertonic saline. A structured questionnaire was used for data collection.

Statistical Analysis

The statistical analysis was done by entering data into a Microsoft Excel sheet and analysed using Statistical Package for Social Sciences (SPSS) software**.** Descriptive statistics frequency analysis and percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables.

RESULTS

Demographic Data

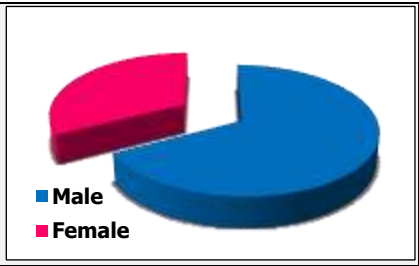

Figure 1. Gender Distribution

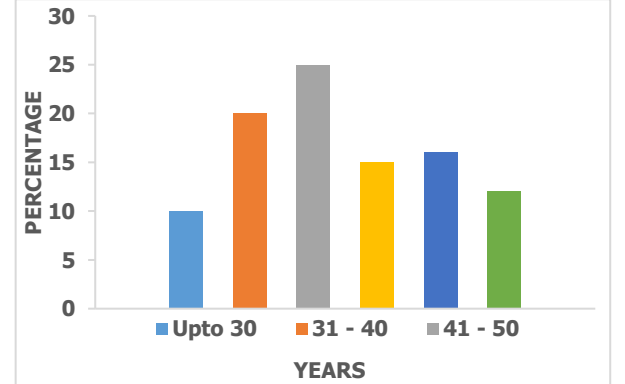

Figure 2. Age Distribution

Majority of patients came between 41 to 50 years, of which 37 (60.7 %) were emergency cases and 24 (39.3 %) were elective.

Diagnosis	Frequency	Percent
Traumatic brain injury	35	57.4
Subarachnoid haemorrhage (non-traumatic)	7	11.5
Intracranial tumours	19	31.1
Total	**61**	**100.0**

Table 1. Diagnosis Distribution

The prevalence of hyponatremia among the study population was found to be 34.4 % pre-operatively. To diagnose hyponatremia, the serum sodium cut off level was taken as less than 135 mEq/L.

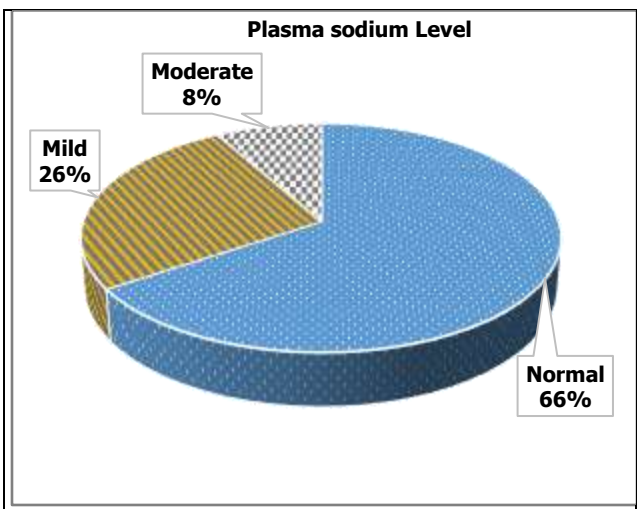

Figure 3. Distribution of the Study Population According to Different Levels of Serum Sodium

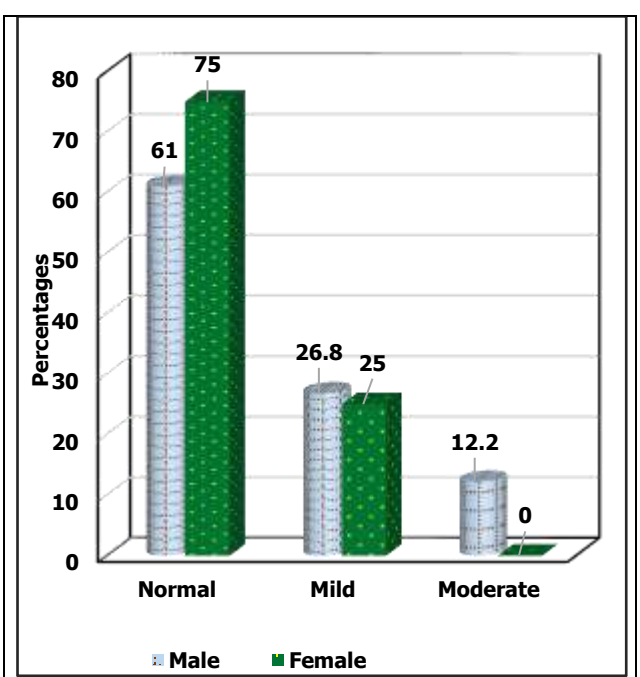

Figure 4. Distribution of the Serum Sodium Concentration According to the Gender

In the above figure, hyponatremia was found to be higher among males 16 (39 %) compared to females 5 (25 %).

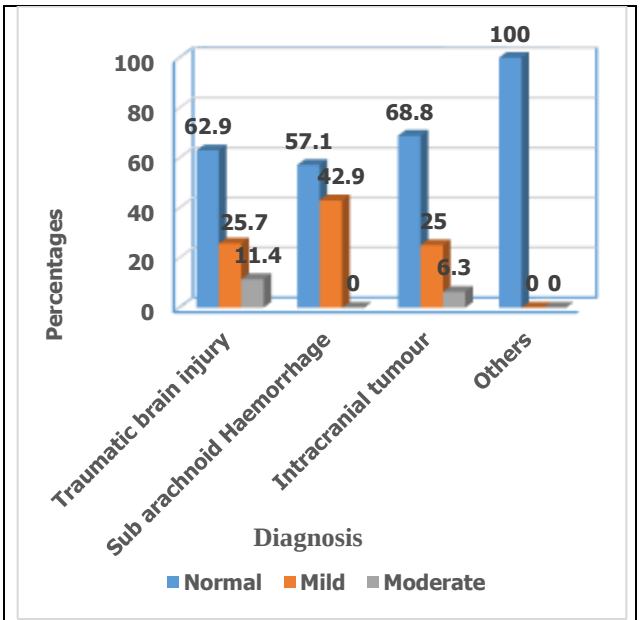

Figure 3. Distribution of Sodium Concentration According to the Different Brain Pathology

The above figure shows that mild hyponatremia was found to be higher among SAH patients whereas moderate hyponatremia was found to be higher among TBI patients. It was found that the prevalence of hyponatremia was higher among patients above 60 years 13 (72.2 %), P value < 0.01. 62.5 % of patients above 70 years, 44.4 % patients between 51 to 60 years and 40 % of patients between 61 and 70 years presented with mild hyponatremia. 37.5 % patients above 70 years and 10 % patients between 61 and 70 years presented with moderate hyponatremia.

DISCUSSION

In critically ill adult neurological patients, sodium and water imbalance is a very common finding. It has been associated with increased morbidity and mortality, especially in neurotrauma. The mortality rate in hospitalized patients with severe hyponatremia (serum Na < 130 mmol/L) associated with brain injury was found to be 50 times higher than in patients with normal sodium level.[28] The majority of the patients in the study 26.2 % belonged to middle age (41 - 50 years), 41 (67.2 %) were male and 20 (32.8 %) were females. This relates to the fact that traumatic brain injury was the most common reason for surgery 35 (57.4 %), and male patients under 45 years of age are more prone to the injuries. Among hyponatremia patients, males contributed 26.8 % of the mild grade, 12.2 % of moderate grade and females contributed 25 % of the mild grade. There were no cases of severe hyponatremia observed in males and no cases of moderate or severe hyponatremia noted in females.

In our study, the prevalence of hyponatremia was found to be 34.4 %.

A similar study of hyponatremia in neurosurgical patients conducted by Rocha–Rivera et al. where a total of 79 patients were included to assess the incidence, most frequent diagnosis was a head injury which is comparable with our study but the incidence of hyponatremia was 25.3 %. The median age was 40 years, 73.4 % was male. They also observed that patients with a diagnosis of subarachnoid haemorrhage were 8 times more likely to have hyponatremia.[29] Prevalence of hyponatremia in ambulatory hospital care setting ranges between 11 % to 21 % and increased to 28.2 % in acutely hospitalized patients. The lower limit of sodium taken in our study was 135 which justifies the higher prevalence of hyponatremia in the preoperative period. Our hospital is a tertiary care referral Centre which explains the higher prevalence of hyponatremia in the study population.

Our study population included patients with traumatic brain injury (57.4 %) non-traumatic subarachnoid haemorrhage (11.4 %) intracranial tumours (31.1 %) and pituitary surgery.

A similar study by Zahra chitsazian et al. conducted in 2012 on 95 patients with various types of brain injuries showed a prevalence of 31.6 % of hyponatremia which is comparable with our study. They also observed that it was developed during the second week of hospitalization.[30]

Sherlock et al. in a study on 1698 patients with brain injury also showed a 41.7 mean age for hyponatraemic patients, they couldn't find any meaningful correlation between hyponatremia age and sex.

A study conducted by Mark J Hannon in 2014 concluded that hyponatremia is associated with increased morbidity and mortality in hospitalised patients and is common in neurosurgical patients. They also concluded that the most common cause following neurotrauma being SIADH and cerebral salt wasting is very rare in this setting.

A study in patients with intra cranial haemorrhage Joji B Kumarastu and associates revealed that hyponatremia is associated with an increase in hospital and short term mortality. Patients with TBI in which hyponatremia was linked to disease severity. Hyponatraemic patients showed higher intracerebral haemorrhage scores and were more frequently anaemic on admission which is independently associated with poorer functional long term outcomes.[31] Our study showed an increased prevalence of hyponatremia in patients above 60 years when compared to less than 60 years (72.2 % versus 18.6 %) which is much higher than the prevalence seen in elderly patients with hip fracture. In another study, the prevalence of hyponatremia in 334 elderly patients with hip fracture admitted to San Giovanni di Dio e Ruggid' Aragona Hospital of Salerno in Italy is 19 %.[32] In a prospective observational study conducted in adult patients aged ≥ 65years with a fragility fracture to a university hospital in 2013 showed a point prevalence of hyponatremia on admission was 13.4 %.[33]

CONCLUSIONS

Our study showed the prevalence of hyponatremia in 34.4 % of neurosurgical patients which is more than orthopaedic and general surgery patients, which demands effective approaches for an accurate and timely diagnosis of this electrolyte disorder thereby preventing the occurrence of life-threatening complications due to a low serum sodium concentration. Although hyponatremia is often mild and self-

limiting, treatment with fluid restriction is generally unsatisfactory. The use of hypertonic saline is still the treatment of choice for acute symptomatic hyponatremia. It is also essential to differentiate between SIADH and CSW as the treatment modalities are entirely different for these two entities. Hyponatremia frequently occurs in patients with TBI, SAH and intracranial tumours and there is evidence that it is associated with increased morbidity. However, further prospective studies are needed for aetiological evaluation and development of a protocol based management.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
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