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ORIGINAL

Hyponatremia in patients with aneurysmal subarachnoid hemorrhage: a literature review

Hiponatremia en pacientes con hemorragia subaracnoidea aneurismática: una revisión de la literatura

Paulo João Ferreira de Almeida[1,2], **Aldair Epalanga Cristóvão**[1,2]

1. Faculty of Medicine, Agostinho Neto University, Luanda, Angola;
2. Nucleus for Scientific Research of Health Students, Angola (NICESA)

Corresponding author
Paulo João Ferreira de Almeida
E-mail: ao.paulojoao@gmail.com

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Abstract

Introduction and objective: Hyponatremia is the most common electrolyte disturbance among patients with aneurysmal subarachnoid hemorrhage (aSAH). In these patients, the diagnosis must be early and the correction of hyponatremia is essential to avoid serious neurological complications and/or death. The objective of this work was to accomplish a bibliographical revision of the literature concerning the hyponatremia in patients with aSAH.
Methods: Using the PRISMA protocol, we performed a literature review through the Medical Literature Analysis and Retrieval System Online (MEDLINE) database. An association between the medical subject headings (MeSH) and the keywords was made using booleans operators, and additionally, a randomized search of clinical guidelines relevant to the study were performed.
Results: Initially, 55 articles were found, and after applying filters, 19 articles were considered eligible for the study.
Conclusion: We conclude that the early approach of patients with aneurysmal subarachnoid hemorrhage is crucial, in the way that late intervention can be associated with adverse outcomes.

Key words: Hyponatremia, aneurysmal subarachnoid hemorrhage, subarachnoid hemorrhage, approach.

Resumen

Introducción y objetivo: La hiponatremia es la alteración hidroelectrolítica más frecuente en pacientes con hemorragia subaracnoidea aneurismática (HSAa). En estos pacientes, el diagnóstico debe ser precoz y la corrección de la hiponatremia es fundamental para evitar complicaciones neurológicas graves y/o la muerte. El objetivo de este trabajo fue realizar una revisión bibliográfica de la literatura referente a la hiponatremia en pacientes con HAAa.
Métodos: Usando el protocolo PRISMA, realizamos una revisión de la literatura a través de la base de datos Medical Literature Analysis and Retrieval System Online (MEDLINE). Se realizó una asociación entre los encabezados de materias médicas (MeSH) y las palabras clave mediante operadores booleanos y, además, se realizó una búsqueda aleatoria de guías clínicas relevantes para el estudio.
Resultados: Inicialmente se encontraron 55 artículos y luego de aplicar filtros se consideraron elegibles para el estudio 19 artículos.
Conclusión: Concluimos que el abordaje temprano de pacientes con hemorragia subaracnoidea aneurismática es crucial, en la medida en que una intervención tardía puede estar asociada con resultados adversos.

Palabras clave: Hiponatremia, hemorragia subaracnoidea aneurismática, hemorragia subaracnoidea, Acercarse.

Introduction

The estimated mortality rate for aneurysmal subarachnoid hemorrhage (aSAH) in patients with hyponatremia is considerably high, and has been associated with high morbidity among survivors. In a patient with aSAH, timely diagnosis and aggressive hyponatremia correction are essential. Studies have shown that aneurysmal subarachnoid hemorrhage is more common in females, and factors such increasing age, smoking and alcoholic habits, hypertension, use of certain drugs and some genetic conditions are associated with these condition[1,2].

Cerebral salt wasting syndrome (CSWS) and syndrome of inappropriate antidiuretic hormone (SIADH) correspond to the main causes of hyponatremia in patients with Ahsa[3]. but it may occurs in patients with traumatic brain injury[4], hypopituitarism and inadequate dietary intake of salt[5,6].

Formulating a correct diagnosis is not always straightforward, as hyponatremia is often multifactorial and there are multiple confounding factors which make diagnosis complex. 1,3,7

When left untreated, hyponatremia in patients with aHSA can lead to serious neurological complications and adverse outcomes, including death[3,8-11]. We performed a literature review about hyponatremia in patients with aneurysmal subarachnoid hemorrhage.

Methods

A descriptive and qualitative literature review was performed using the MEDLINE search engine. As inclusion criteria, we consider full-text articles, articles published in the last 10 years, all types of studies where included, and we did not discriminate the language of publication. The exclusion criteria were duplicate articles.

We used the following search terms and Boolean combination:

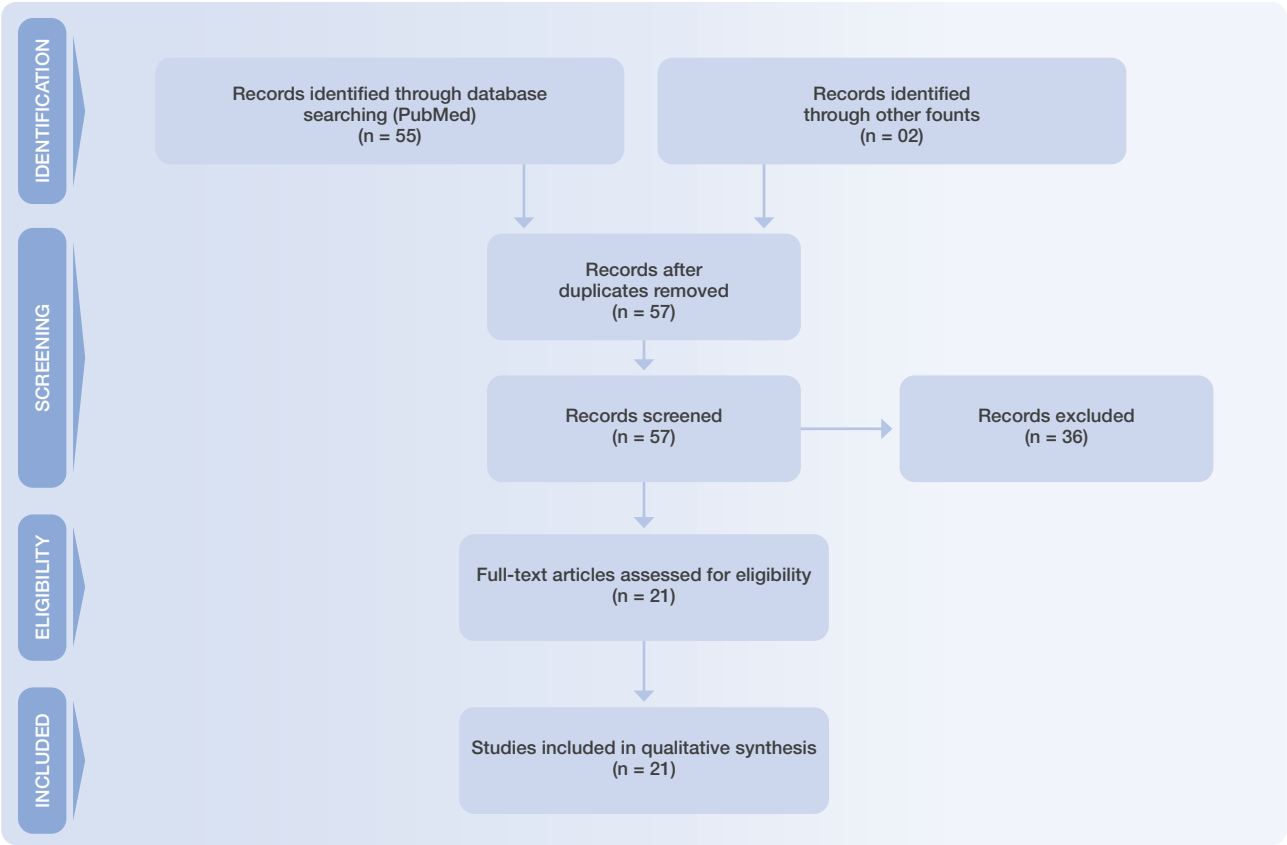
"Symptom Assessment"[Mesh] OR "treatment"[tw] OR "approach"[tw]" AND "hyponatremia""[MeSH] OR "severe hyponatremia"[tw] OR " severe acute hyponatremia"[tw] OR "symptomatic hyponatremia"[tw] AND "Subarachnoid Hemorrhage"[Mesh] OR "Aneurysmal Subarachnoid Hemorrhage"[tw] OR "SAH"[tw] OR "SAHs"[tw]".

Additionally, random searches of clinical guidelines relevant to the study were performed.

Results

Initially, 55 articles were found, and after applying the filters, 19 articles were retrieved, and these, the eligible for the study, as shown in the **figure 1**.

Figure 1: Flow search diagram.



Discussion

Hyponatremia, a serious problem in critically ill patients

Aneurysmal subarachnoid hemorrhage (SAH) has remained one of the most challenging neurosurgical emergencies with continued high mortality[12]. Hyponatremia can be considered an independent risk factor for poor clinical outcomes in patients with SAH2. It is known Hyponatremia is an electrolyte disturbance with a large proportion present in patients with subarachnoid hemorrhage (SAH), and in these patients, has been associated with increased morbidity, including cerebral edema, mental status changes, symptomatic cerebral vasospasm, late cerebral ischemia, representing longer hospital stay and most importantly, resulting in death[1,3,14].

The true contribution of cerebral salt waste (CSW) and syndrome of inappropriate antidiuretic hormone to hyponatremia is unknown, with CSW prevalence estimates ranging from 6% to 75%[3]. Patients with aneurysmal subarachnoid hemorrhage (aSAH) have an estimated 30-day mortality rate of around 35%, with great morbidity among the survivors (a third of whom require full care, and a third are not able to return to work). However, as 15%-30% of deaths occur before hospital admission, the actual incidence of aSAH is likely higher[3].

Risk factors

Some studies have shown that aSAH is more common in females[1,3]. Other factors include increasing age (peaking around 50 years old), hypertension, smoking, alcohol abuse, use of sympathomimetic drugs, family history of aneurysm or subarachnoid hemorrhage (more than two first-degree relatives), and certain conditions genetic (autosomal dominant polycystic kidney disease and Ehlers-Danlos syndrome type IV)[1,2]. As showing in **table I**, formulating a correct diagnosis is not always straightforward, as hyponatremia is often multifactorial and there are multiple confounding factors which make diagnosis complex[7].

Table I: Causes of hyponatremia in neurosurgical patients.

Hypovolemic	Diuretics Insufficient intravenous fluids Cerebral salt wasting
Euvolemic	SIADH Acute adrenocorticotrophic/cortisol deficiency Drugs (e.g., carbamazepine, desmopressin)
Hypervolemic	Excess of IV fluid

Adapted from Cuesta et al., 2016.

Etiology

Hyponatremia often occurs in patients with traumatic brain injury (TBI)4 and the main causes are cerebral salt wasting syndrome (CSW) characterized by depleted intravascular volume, syndrome of inappropriate antidiuretic hormone (SIADH), which occurs with normal intravascular volume, hypopituitarism and inadequate dietary intake of salt[5,6]. Of these, inadequate salt intake can be diagnosed with reasonable certainty if the urine spot sodium is low (below 20 - 40mEq/L) and hypopituitarism can be diagnosed by biochemical evaluation of pituitary hormones. After ruling out these two entities, the clinician is left with cerebral salt waste and syndrome of inappropriate antidiuretic hormone, both of which manifest as hyponatremia with natriuresis (urine spot sodium more than 40mEq/L)[6,15]. CSW is a less common etiology of hyponatremia, occurring in 12% of cases. SIADH has been showed as more common, occurring in 75%[8].

Although these two pathological conditions are notorious (CSW and SIADH), it is difficult to distinguish one from the other, and there is a currently tendency to associate both entities in one. Some claim that since the incidence of SAH is low and it can be difficult to distinguish between[1,5,16].

Some investigators suggest that the underlying etiology of hyponatremia seen in patients with aneurysmal subarachnoid hemorrhage is multifactorial, with different mechanisms occurring at different times. Early-phase hyponatremia is consistent with SIADH, late-phase hyponatremia with CSW Another important difference between CSW and SIADH is that cerebral salt waste involves hypovolemia caused by natriuresis, whereas syndrome of inappropriate antidiuretic hormone is a euvolemic or hypervolemic condition[3,17].

Hoffman et al. suggested that the aneurysm location could affect the risk of developing hyponatremia after aSAH. They reported in a cohort study, that the presence of a ruptured anterior communicating artery aneurysm was associated with the development of hyponatremia, but not the etiology of hyponatremia, and patients with ruptured anterior circulation aneurysms would be more likely to develop SIADH given the closer proximity of the aneurysm to the hypothalamic-pituitary-adrenal axis.

Pathophysiology

When an aneurysm ruptures, blood pours into the subarachnoid space leading to a sharp and sudden increase in intracranial pressure, decreasing cerebral perfusion pressure and leading to global ischemia[1,18]. This event explain the mechanism of loss of consciousness that happens in about 50% of the patients. There is a massive sympathetic tone increase that starts to cause systemic complications and a systemic inflammatory syndrome develops. This series of events is part of what is called early brain injury, a process that starts Just after the aneurysmal rupture and is characterized by microcirculatory constriction, microthrombosis, disruption of the blood-brain barrier, vasogenic and cytotoxic edema, endothelia land neuronal death[1].

The possibility that SAH leads to a generalized stress response that involves the hypersecretion of multiple

pituitary hormones, including antidiuretic hormone is an alternative hypothesis[8].

Diagnosis

The initial assessment of SAH patients, and therefore the grading of the clinical condition, is done by means of a scale based on the Glasgow coma scale (GCS). Early and accurate diagnosis, as well as treatment by specialists is therefore essential[2].

Frequently, the patients refer episodes of headache, described as the worst headache ever felt, which is abrupt and peaks in intensity in one hour at most. Around 10-40% of patients have a warning leak or sentinel episode, which is a similar headache that precedes the bleeding by two to eight weeks. Nausea and vomiting may happen in 77% of the cases, loss of consciousness in 53%, *meningismus* in 35%, focal deficits in 10%, and Terson syndrome (vitreous hemorrhage associated with SAH) in 40% of patients. If computed tomography is negative after high suspicion of aSAH, a lumbar puncture to look for blood or xanthochromia in the cerebrospinal fluid. Computed resonance (CT) and magnetic resonance image should be used in order to look for aneurysms. CT angiography has a sensitivity that approaches 100%[1].

Treatment

Timely diagnosis and aggressive treatment of hyponatremia are recommended regardless of etiology[2,3,19]. In the neurocritical patient, the treatment of hyponatremia requires the identification of the degree of severity, the time evolution, the state of the volume and the severity of the clinical condition. In these patients, the appearance of hyponatremia should be considered, depending on the evolutionary moment, as a true medical emergency that will require the establishment of immediate therapeutic measures[5].

Recent recommendations for managing hyponatremia in cerebral aSAH include (1) avoidance of fluid restriction to prevent cerebral ischemia, (2) use of hydrocortisone or fludrocortisone as an early treatment option, (3) correction of hyponatremia with mild hypertonic saline solutions, (4) avoidance of hypovolemia when using vasopressin-receptor antagonists such as conivaptan, and (5) limiting free water intake via intravenous and enteral routes[13].

Early treatment with mineralocorticoids is used to improve functional outcomes or reduce symptomatic vasospasm[2,3,19]. Studies have shown the benefit of corticosteroids in the management sequelae caused by hyponatremia[20].

Water restriction should be avoided in treating hyponatremia due to the risk of developing delayed cerebral ischemia1.

There are no published data on the appropriate treatment of hyponatremia in patients with aSAH. Studies are needed to establish an adequate management protocol for the maintenance of sodium and water homeostasis in patients with SAH[17]. The unresolved issue with hyponatremia is determine the best method to treat hyponatremia in patients with aSAH, as it can be caused by SIADH, CSW, or a combination of both[13,21].

Conclusions

Early recognition and management of hyponatremia in patients with aneurysmal subarachnoid hemorrhage is critical. Late intervention in these patients can result in a poor prognosis, as hyponatremia can trigger serious neurological complications, which can lead to death. Although certain drugs allow for punctual electrolyte correction, the treatment of hyponatremia in these patients remains a challenge because the underlying etiology of hyponatremia is multifactorial, with different mechanisms and occurring at different times. Therefore, additional studies are needed to improve the management of patients with aSAH and optimize therapeutic measures.

Conflict of interest

The authors declare that they have no conflict of interest.

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