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REVIEWING AN EXCEPTIONAL INSTANCE OF EXTRAPONTINE MYELINOLYSIS POST HYPONATREMIA RECTIFICATION

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INTRODUCTION

Extrapontine myelinolysis, also known as osmotic demyelination syndrome, is a rare neurological disorder characterized by the destruction of myelin, the protective covering of nerve fibers, in regions outside the brainstem. This condition typically occurs as a complication of rapid correction of hyponatremia, independent of changes in serum sodium this will cause a rapid change in osmolarity of the extracellular compartments of the brain which lead to dehydration of energy depleted cells with subsequent axonal disfuguration in characteristic areas also[1] low sodium concentration in the blood, which can cause the body to lose or gain water too quickly. Hyponatremia is observed when serum sodium drops to less than 135mmol/L[2] What makes this condition different is the rate and the magnitude of correction of sodium. Over correction can lead to a severe irreversible damage and under correction hangs to potentially damaging clinical manifestations Value less than or in between 115-110mmol/L is considered severe carried with clinical manifestations as gait disturbances, hypoxia, slurring of speech, non cardiac pulmonary edema, increased intracranial pressure, seizures. The final treatment is also aided by the severity of symptoms.[3] Treatment consists of free water restriction and correction of the underlying condition. AVP (vasopressin) receptor antagonists (eg, conivaptan, tolvaptan). However, their mechanism of action poses a risk of overcorrection, as they lead to uncontrolled free water excretion hyponatremia being chronic and acute, chronic hyponatremia is more common. Treatment of chronic hyponatremia has been associated with the development of the osmotic demyelination syndrome (also known as central pontine myelinolysis). To minimize the risk newer guidelines recommend a maximum of 8 mEq/L in the first 24 hours, with a maximum of 6 mEq/L for patients at high risk rate.[4]

EPIDEMIOLOGY

The incidence of CPM is not well known due to underdiagnosis. A 2015 retrospective study shows that the prevalence of ODS is 2.5% between ICU admissions. About 25% of patients with severe hyponatremia have neurological complications after rapid sodium correction. Patients having chronic hyponatremia showed higher rates of neurological complications.[5]

CLINICAL MANIFESTATION

Originally, patients may present with encephalopathy or seizures due to hyponatremia. They might recover quickly as their sodium levels return to normal, only to deteriorate several days later. The initial signs of this second phase of the condition include difficulty speaking and swallowing (related to the involvement of corticobulbar fibers) and weakness in all four limbs.

In cases where an individual who is severely ill due to alcoholism, malnutrition, or another systemic medical condition develops confusion, quadriplegia, pseudobulbar paralysis, and appears comatose (locked-in pattern) over a period of several days, it is reasonable to suspect central pontine myelinolysis (CPM) or extrapontine myelinolysis (EPM). The pathological changes in both conditions are nearly identical, and the lesions often exhibit remarkable symmetry due to their widespread nature. Mutism, parkinsonism, dystonia, and catatonia have all been reported.[6]

A range of encephalopathy severity is observed, from mild to coma and even death. The onset of neurological disturbances can vary but typically occurs 7 to 14 days after an episode of severe electrolyte imbalance.[7]

PATHOPHYSIOLOGY

The pathophysiology of Osmotic Demyelination Syndrome (ODS) involves cerebral cell apoptosis and myelin loss due to abrupt osmotic stress. Consequently, brain regions abundant in oligodendrocytes and myelin are consistently the most affected. ODS cases typically exhibit a two-phase course, with the initial phase reflecting the underlying predisposing condition and the subsequent phase representing ODS itself.[8]

The rapid and excessive movement of water out of brain cells and a reduction in intracellular fluid (ICF) volume occur due to the combination of an abrupt drop in

intracellular osmolality and a rapid increase in serum osmolality. Therefore, overly rapid correction of serum sodium levels can cause an acute reduction in brain cell volume, contributing to the development of ODS or central pontine myelinolysis.

We postulate that readjusting serum sodium levels by using desmopressin and infusing free water can help decrease extracellular osmolarity, which rapidly increases during swift correction, and establish iso-osmolarity between brain cells and extracellular fluid. This, in turn, assists in further expelling water from brain cells.

In patients with acute hyponatremia resulting from intravenous fluid administration, such as in cases of postoperative hyponatremia related to surgery-induced syndrome of inappropriate antidiuretic hormone (SIADH) release, the administration of large volumes of isotonic fluids leads to volume expansion and increased sodium excretion in the urine. However, the excretion of this sodium in concentrated urine causes a further decline in serum sodium levels, a phenomenon referred to as "desalination".[9]

TREATMENT

Our approach to the initial treatment of acutely hyponatremic cases (within the first six hours of diagnosis) depends on the presence or absence of symptoms. In a significant shift in our therapeutic strategy, we now recommend using hypertonic saline gelcaps to treat typical acute hyponatremia instead of continuous saline infusion. This modified approach was initially applied in the management of exercise-induced hyponatremia.

The primary goal of this approach is to achieve a rapid early increase in plasma sodium levels, targeting a rise of 4-6 mmol/L over the initial four hours of treatment. This target is based on data from neurosurgical studies in which a 5 mmol/L increase rapidly reversed clinical signs of trans-tentorial herniation and reduced intracerebral pressure by nearly 50% within an hour. This treatment can be life-saving for cerebral edema secondary to hyponatremia, as the increased extracellular sodium concentration rapidly removes water from the intracellular space.

According to European guidelines, treatment involves administering 150 ml of hypertonic saline over 20 minutes, followed by another infusion of 150 ml of 3% hypertonic saline, which can be repeated up to twice or until a 5 mmol/L increase in sodium levels is achieved.[10]

For patients with even mild symptoms and a serum sodium level below 130 mEq/L that might indicate increased intracranial pressure, we administer a 100 mL bolus of 3 percent saline, followed by up to two additional 100 mL doses if symptoms persist, each infused over 10 minutes. Alternatively, as recommended by European organizations, two 150 mL bolus infusions of 3 percent saline, each given over 20 minutes, can be used.

The objective of this therapy is to rapidly raise serum sodium levels by 4 to 6 mEq/L within a few hours, which should generally alleviate symptoms.

We do not use mannitol or vasopressin antagonists (vaptans) in these patients, either in addition to or instead of hypertonic saline. Mannitol, although used for cerebral edema, can be nephrotoxic and may further lower serum sodium levels, complicating hyponatremia monitoring. Vasopressin antagonists i.e Vaptans, have a very slow onset of action and are not recommended for patients with acute hyponatremia.

For patients with severe symptoms or known intracranial pathology, such as seizures, obtundation, coma, or respiratory arrest, we administer a 100 ml bolus of 3% saline, followed by up to two additional 100 ml doses if symptoms persist, each infused over 10 minutes. An alternative approach, suggested by European organizations, involves infusing 150 mL of 3 percent saline, followed by a second 150 mL bolus 20 minutes later if the serum sodium does not increase by 4 to 6 mEq/L after the initial dose.[11]

Once the targeted daily correction rate of 4 to 6 mEq/L has been achieved, hypertonic saline should be discontinued. Fluid restriction below the level of urine output is recommended for treating typical or severe hyponatremia in edematous conditions like heart failure and cirrhosis, syndrome of inappropriate antidiuretic hormone (SIADH), advanced kidney impairment, and primary polydipsia. Prudent treatment is crucial for all Extrapontine Myelinolysis (EPM) cases. Plasmapheresis may improve the neurological symptoms of ODS, as some reports suggest. Other treatment modalities such as corticosteroids and intravenous immunoglobulin may be beneficial but require further investigation to determine their role in ODS management. Some cases with predominant dystonias and muscle rigidity have shown a significant response to levodopa. In our case, a low dose of carbidopa/levodopa was administered.[12]

DISCUSSION

Extrapontine myelinolysis, also recognized as Osmotic Demyelination Syndrome, is a rare ailment stemming from diminished sodium levels (<120MMOL/L). Specifically, it affects the demyelination of cells within the brainstem's pons region. Individuals who are undernourished, alcohol-dependent, or grappling with conditions like hypokalemia, SIADH, and even pituitary macroadenoma, face an elevated risk of developing this syndrome. The therapeutic guidelines recommend a sodium correction rate of 4-6MMOL/DAY, where the rate of correction takes precedence over the velocity of correction. Symptoms can range from speech impediments to seizures. Treatment alternatives

encompass mannitol, vasopressin, and hypertonic solutions.

LIST OF ABBREVIATION

EPM: Extrapontine myelinolysis CPM: central pontine myelinolysis SIADH: Syndrome of inappropriate anti-diuretic hormone secretion ODS: Osmotic dyelination syndrome.

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