Mannitol and Glycerine Combination Causing Hypokalemia in Post Neuro-Surgical Patient: A Case Report

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ABSTRACT - Linsol infusion is a combination of mannitol and glycerin, where mannitol is an osmotic diuretic which draws water out of tissue in the brain and decreases swelling around the brain. The relative therapeutic benefit of glycerine is not exact but based on observation they found that glycerin prevents rebound swelling which may possibly occur with plain mannitol. Hypokalemia is a condition where serum potassium levels are lower than normal range. It usually results from increased potassium excretion or intracellular shift and less commonly from reduced potassium intake. It is a common electrolyte disturbance, especially in hospitalized patients, due to various causes and sometimes requires urgent medical attention in which patient should be placed on a cardiac monitor; establish intravenous (IV) access and assess respiratory status. If cardiac arrhythmias or other life threatening complications are present, more aggressive therapy is needed. This is a case report of Linsol infusion induced hypokalemia in a geriatric person.

KEYWORDS - Mannitol, Glycerin, Case report, Hypokalemia, Potassium, Infusion and Electrolyte.

I. INTRODUCTION

Hypokalemia is a condition where serum potassium levels are lower than normal concentrations (normal range: 3.5-5.1 mmol/L). It usually results from increased potassium excretion or intracellular shift and less commonly from reduced potassium intake. It is a common electrolyte disturbance, especially occurring in hospitalized patients, due to various causes and sometimes requires urgent medical attention. Severe and life-threatening hypokalemia is defined as serum potassium levels found below 2.5 mmol/L. The incidence of hypokalemia is almost 14% in out-patient; 20% in hospitalized patients, out of which only 4-5% is clinically significant. Approximately 80% of patients receiving diuretics become hypokalemic. Hypokalemic manifestation can be categorized in accordance to the organ system affected. Renal system: metabolic acidosis, rhabdomyolysis (in severe hypokalemia) and rarely impairment of tubular transport, chronic tubulointestinal disease and cyst formation. Nervous system: leg cramps, weakness, paresis or ascending paralysis. Gastrointestinal system: Constipation or intestinal paralysis.[1] Respiratory system: Respiratory failure. Cardiovascular system: Electrocardiogram (ECG) changes, cardiac arrhythmias and heart failure.[2] Clinical features of severe hypokalemia include muscle weakness, polyuria and cardiac hyper excitability. Hypokalemia can be diagnosed by routine serum electrolyte measurement. It should be suspected in patients with typical changes on an ECG or with muscular symptoms and risk factors and confirmed by blood testing. [3] Mannitol and glycerin combination commonly available with a brand name Linsol. Mannitol is an osmotic diuretic which draws water out of tissue in the brain and decreases swelling around the brain. The relative therapeutic benefit of glycerine is not exactly known but it is found that glycerine prevents rebound swelling which may possibly occur with plain mannitol. [1] The above combination is administered intravenously; confined to the extracellular space; metabolized by liver and rapidly excreted by the kidney. Approximately 80% of a 100 g dose appears in the urine in 3 hours after administration. The drug is freely filtered by the glomeruli with less than 10 % tubular re-absorption. It is not secreted by tubular cells and induces diuresis by elevating the osmolarity of the glomerular filtrate. Glycerine is a potent osmotic dehydrating agent with additional effects on brain metabolism. In doses of 0.25 - 2.0 g/kg glycerol decreases intracranial pressure (ICP) in various disease states like stroke, road traffic accidents (RTA) with neurological injuries, traumatic brain

injury and intra cranial hemorrhage. Intravenous doses of 1 – 2 g/kg every second hourly can be administered safely in severe cases of elevated ICP. Thus combination of mannitol and glycerine decreases the dose of mannitol and its effects like diuresis and asthenia. In addition, glycerine also helps in neural recovery and sustained resolution of cerebral edema thus ensuring prompt resumption of Central Nervous System functioning without alteration in mental capability and intelligent quotient (IQ) or residual paresis. [4] Diuretics filtered into the renal tubules undergo minimal reabsorption and accomplish diuresis in part due to their physical presence in the tubular lumen. Because osmotic diuretics are mostly not reabsorbed, their presence in the tubular lumen limits the osmosis of water into the interstitial space. This results in dilution of the luminal electrolyte concentrations to the point that the reabsorption of electrolytes is reduced. As osmotic diuretics have a limited cellular permeability, their presence in the blood causes osmotic extraction of water from cells; a process that expands the extracellular fluid volume, decreases blood viscosity, inhibits rennin release, and increase renal blood flow. These changes can also contribute to the osmotic diuretics' ability of inducing diuresis. Osmotic diuretics act both in the proximal tubule and loop of Henle, probably the main site of action; and they increase urinary excretion of most electrolytes (including sodium, potassium, calcium, magnesium, and chloride), bicarbonates and phosphates. [5] Treatment of hypokalemia includes oral (for acute cases) or IV (for severe cases) potassium supplementation. Potassium supplementation can cause gastrointestinal irritation and occasional bleeding when used in high single doses. Hence given in multiple divided doses. Liquid potassium chloride (contains 40 mmol of potassium per 15 ml) given orally elevates serum potassium concentrations within 1 to 2 hours administration but has a bitter taste. Microencapsulated potassium chloride preparations contain 8 or 10 mmol/capsule. Because a 1mmol/L decrease in serum potassium levels correlates with about a 200 to 400 mmol deficit in total body potassium stores, a total deficit should be estimated and replaced over a period at 20 – 80 mmol/day. [3]

II. CASE STUDY

A 55 year old male patient was admitted in hospital with chief complaints of loss of consciousness, vomiting and involuntary urination after a fall at home and was diagnosed to be suffering from Saccular right posterior communicating artery aneurysm and Supraclinod internal carotid artery aneurysm. He was treated with diuretics (mannitol + glycerine), antibiotics (cefpodoxime), antiepileptic (levetiracetam), analgesics (paracetamol) and antipsychotics (resperidone). The patient had a history of status post Appendicectomy. On examination, his body temperature was 98.6F, blood pressure was 130/90 mmHg, pulse rate was 88 bpm and respiratory rate was 20/minute. On day 3 and 4, serum potassium levels were 3.3mmol/L and 3.1mmol/L respectively. Offending drug was ruled out to be the combination of mannitol and glycerine. Dose of mannitol was altered from 100 ml to 75 ml. The resulted hypokalemia was treated with an intravenous infusion of potassium chloride, (2 mmol/min on Day-3); followed by oral supplementation of potassium chloride, (40 mmol/TID for 4 days).

III. DISCUSSION

The risk of brain swelling in patients with stroke, traumatic brain injury, hemorrhage and patients after undergoing neurosurgery is common. Brain swelling results in increased intracranial pressure. Mannitol is recommended as a first-line osmotic treatment to reduce brain edema and enable brain relaxation. The effect of mannitol on intraoperative brain relaxation has been increasingly studied in recent years. High osmotic pressure in the blood vessels after the infusion of mannitol drives water molecules from the brain tissue to blood vessels and results in brain tissue dehydration. The repeated intraoperative use of large doses of mannitol may precipitate serious side effects like electrolyte abnormalities, renal and cardiac dysfunctions. [6] A previous study undertaken by Seo et.al, to evaluate, whether significant alterations in serum osmolarity [Na^+] and [K^+] occur after the repeated dosing of mannitol and whether these imbalances increased accordingly with the progress of mannitol administration. The study was conducted by performing a

retrospective medical record review of brain injury patients who were admitted to the neurological intensive care unit. Osmolarity levels were recorded from the first to the seventh day of mannitol administration. Their results showed that the highest rate of hyperosmolarity occurred on the Day-1 of mannitol administration which subsequently reduced, although still maintained high. The most notable finding was that high rate of hypokalemia observed in 22 % of subjects on the Day-1and continuously increased to 52.3 %, and this increase was significant. Their findings appear to provide clear evidence of electrolyte imbalances after repeated mannitol administration. Accordingly, careful monitoring of electrolyte status is essential when repeated doses of mannitol are given. [7] In a study, undertaken to evaluate the effects of adding potassium sparing diuretics to mannitol therapy on potassium urinary excretion; in patients treated with mannitol, the urinary excretion of potassium was stable over the first 3 days and then significantly increased. In patients receiving mannitol and potassium sparing diuretic combination, the potassium urinary excretion decreased. The incidence of new cardiac arrhythmias was higher in the mannitol group than the mannitol plus potassium sparing diuretic group [8].

IV. CONCLUSION

Since mannitol was noted to reduce brain edema almost a century ago, osmotic agents including mannitol have represented standard care in the management of intracranial hypertension, recommended by consensus guidelines. Geriatrics may be more prone to electrolyte disturbances after receiving mannitol. This case study suggests that patients receiving mannitol 2 to 4 times a day require monitoring for potential electrolyte disturbances especially for incidence of hypokalemia. In case patient experiences electrolyte disturbance, necessary precautions should be taken (to avoid complications) which may include one or more of the following: withdraw or alter the dose of suspected drug; provide symptomatic and supportive treatment. According to other studies, patients receiving neurocritical care with mannitol can be given an adjunct of potassium sparing diuretic to reduce potassium urinary loss, prevents hypokalemia and reduce the incidence of hypokalemia related effects.

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