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Mannitol Induced AKI in a Patient with CVA - A Rare Case Report

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ABSTRACT

Mannitol is an osmotic diuretic which is used in various indications like treatment of oliguric acute kidney injury, cystic fibrosis, irrigation of urinary bladder, measuring of creatinine clearance, treatment of elevated intracranial and intraocular pressures, treatment of intracranial tumour and subdural hematomas. It stimulates the diuresis by raising the osmolarity of the glomerular filtrate and thus blocking the tubular reabsorption of water. Generally, the lower doses of the drug leads to renal vasodilation and higher doses lead to renal vasoconstriction leading to acute kidney injury. Serum osmolarity above 320 mosm/lit is related with the development of acute kidney injury. The criteria for diagnosing a patient with the Mannitol induced acute kidney injury is greater than or equal to 0.3 mg/dl rise in the serum creatinine level from the baseline and greater than or equal to 50% raise in blood urea nitrogen levels. The chief risk factors associated with the reaction includes presence of diabetes, lower glomerular filtration rate during the initial presentation, co-administration of the diuretics, greater NIHSS scores at the initial presentation, dehydration and older age. Generally the incidence of Mannitol induced acute kidney injury in patients presenting with cerebral stroke is 6-7% and in particular 6.2-6.4% in ischemic stroke patients and 6.6- 6.8% in patients presenting with haemorrhagic stroke.

INTRODUCTION

In patients presenting with stroke elevated ICP due to hydrocephalus is one of the chief complication leading to severe neurological illness and mortality.[1]Mannitol is known to reduce the elevated ICP by raising the osmotic difference between the brain tissue and blood thereby drawing the water from the tissue into the blood circulation and decreases the elevated ICP. This effect of decreasing the ICP is chiefly dose-dependent, so the bolus doses has a greater effect compared to the continuous infusions of the drug in reducing the elevated ICP. This drug is also known to induce volume and electrolyte disturbances.[2] Greater doses of hypertonic Mannitol when given to a patient with preexisting renal failure leads to the accumulation of the drug in the blood due to decreased clearance leading to increased osmolarity causing the movement of water and potassium to the extracellular compartment leading to extracellular fluid expansion, metabolic acidosis, hyperkalemia, hyponatremia. Mannitol induced acute kidney injury is chiefly associated with the dose of the drug administered. Lower doses of the drug causes renal vasodilation and higher doses are linked to renal vasoconstriction. Dosing greater than 200gm/day or 400gm/48 hrs is linked to development of acute kidney injury. It can also induce AKI if the serum osmolarity is above 320 mosm/lit. The chief risk factors associated with the reaction includes presence of diabetes, lower glomerular filtration rate during the initial presentation, co administration of the diuretics, greater NIHSS scores at the initial presentation, dehydration and older age[3]. Generally the incidence of Mannitol induced acute kidney injury in patients presenting with cerebral stroke is 6-7% and in particular 6.2-6.4% in ischemic stroke patients and 6.6- 6.8% in patients presenting with haemorrhagic stroke. The criteria for diagnosing a patient with the Mannitol induced acute kidney injury is greater than or equal to 0.3 mg/dl rise in the serum creatinine level from the baseline and greater than or equal to 50% raise in blood urea nitrogen levels. In some indications, it is a well-known reno protective drug.[4]We present a case of Mannitol induced AKI in a patient diagnosed with CVA with bilateral cerebellar infarct with sub-acute haemorrhage in left cerebellum presenting with hydrocephalus.

CASE REPORT

A 58-year-old male patient weighing 70 kgs was presented to the Neurology OP with the complaints of loss of consciousness 3 days back which lasted for 10 minutes associated with 1 episode of vomiting at that time. The patient also had a history of similar episode 10 days back. The patient is a known case of type 2 diabetes mellitus and hypertension. On

examination patients cerebellar signs include ataxic gait and swaying. The patient was advised to admit in the ward for further evaluation. The patient was immediately diagnosed with CVA with the confirmation from the MRI indicating acute infarct in the bilateral cerebellum with sub-acute haemorrhage in the left cerebellum and operated for Post decompressive craniotomy. On the postoperative day 1 the patient was on ventilator, a febrile with pulse of 90 bpm, BP of 160/90 mmhg, haemoglobin of 11.1 gm%, random blood sugar- 236 mg/dl, BUN- 35 mg/dl, Creatinine – 1.5 mg/dl, serum sodium- 136 meq/lit, serum potassium- 3.4 meq/lit and ESR of 59 mm/hr. On the postoperative day 2 the patient was on ventilator, with the pulse of 90 bpm, BP of 150/80 mmhg, random blood sugar- 120 mg/dl, serum sodium- 130 meq/lit, serum potassium- 3.2 meq/lit and haemoglobin of 10.5 gm%. On the postoperative day 3 the patient was drowsy and on ventilator, developed pyrexia and with a pulse of 81 bpm, BP – 140/80 mmHg, serum sodium- 133 meq/lit, serum potassium- 3.2 meq/lit, Hb- 8.9 gm%, Total WBC count- 12100 cells/cumm and ESR- 56 mm/hr. On the postoperative day 4 the ventilator was removed and the patient continued to be febrile, with a pulse of 70 bpm, BP- 120/70 mmHg, random blood sugar- 151 mg/dl, haemoglobin of 8.6 gm%, WBC- 12700 cells/cumm, ESR- 91 mm/hr, Creatinine 1.7 mg/dl, BUN- 50 mg/dl, sodium 135 meq/lit, and potassium- 3 meq/lit. On the post-operative day 5 the patient was afebrile, with a pulse of 99 bpm, BP – 120/80mmHg, WBC- 12900 cells/cumm, Creatinine 1.8 mg/dl, BUN- 56 mg/dl, ESR- 118 mm/hr. On the post-operative day 6 the patient was afebrile with a pulse of 92 bpm, BP 120/80 mmHg. On the postoperative day 7 the patient looks dehydrated with sunken eyes and dry skin and tongue with a pulse of 84 bpm, BP- 120/80 mmHg, creatinine 1.9 mg/dl, urea- 78 mg/dl, sodium 131 meq/lit, potassium 3.2 meq/lit and was diagnosed with Mannitol induced AKI and the Mannitol injection was stopped and was given NS. On the postoperative day 8 the patient was a febrile with the pulse of 95 bpm, BP- 130/80 mmHg, creatinine- 1.7 mg/dl, BUN- 60 mg/dl. On the postoperative day 9 the patient was a febrile with the pulse of 90 bpm, BP- 130/80 mmHg, creatinine- 1.5 mg/dl, BUN- 44 mg/dl, Sodium 138 meq/lit and potassium of 3 meq/lit. On the postoperative day 10 the patient was a febrile with the pulse of 97 bpm, BP- 130/80 mmHg with decreased bilateral plantar reflexes, presence of finger nose in coordination and positive Romberg's sign. On the post-operative day 11 the patient was a febrile with the pulse of 92 bpm, BP- 120/80 mmHg. On the postoperative day 12 the patient was a febrile with the pulse of 78 bpm, BP- 130/80 mmHg. On the postoperative day 13 the patient was a febrile with the pulse of 90 bpm, BP- 130/80 mmHg with intact higher mental functions, negative cerebellar signs, and presence of postural instability. On the postoperative day 14 the patient was afebrile with

the pulse of 91 bpm, BP- 150/80 mmHg with intact higher mental functions and bilateral hand grip of 3/5 and improved general health condition so the patient was discharged. The medications prescribed to the patient in the course of treatment were Normal saline @50 ml/hr from day 1 to day 3, Inj Enoxaparin 0.4 cc once a day subcutaneous from day 1 to day 5, InjMannitol @ 1.5 gm/kg/d intravenous thrice daily from Day 1 to day 7, Tab Clopidogrel+ Aspirin 75+150 mg once daily from day 1 till discharge, Tab Atorvastatin 40 mg every night from day 1 till discharge, Tab Citicholine 500mg twice daily from day 1-2, Inj Human insulin according to the sliding scale from day 1-3 and later continued with Metformin 500 mg twice daily, Tab Cilnidipine 10 mg once daily from day 1-3, Inj Ceftriaxone 2 gm intravenous twice daily from day 1-10, Inj Levetiracetam 1 gm intravenous twice daily from day 1-10, Inj Furosemide 20 mg intravenous twice daily from day 3-11, 0.9% NS @ 50 ml/hr on day 7 after diagnosing drug induced AKI. The discharge medications included Tab Atorvastatin, Tab Clopidogrel+ Aspirin, Tab Metformin.

DISCUSSION

The patients development of the AKI can be due to the presence of the risk factors of the patient like diabetes, decreased GFR at the baseline (the patients GFR was 50.6%- Stage III kidney failure), co-administration with diuretic like furosemide, higher NIHSS score at the baseline.[5] The patients with diabetes are more prone to kidney injury because chronic uncontrolled hyperglycemia is known to adversely affect renal hemodynamics. Patients with decreased GFR there would be decreased clearance of the drug leading to accumulation and the half-life of the drug may increase up to 30-38 hrs and decreases the reabsorption of sodium and water in the entire renal tubule in this patient it is evident by hyponatremia and signs and symptoms of dehydration. The co-administration with diuretics further increases the diuretics and leads to severe volume depletion and AKI, in this scenario the patient was also prescribed with Inj Furosemide further making the AKI more severe. The patient was also associated with higher NIHSS scoring at the baseline. Even though the patient received less than the maximum safe daily dose of the drug AKI was evident due to decreased GFR, presence of diabetes, concomitant administration with the diuretics. The patient met both the criteria for diagnosing him as Mannitol induced AKI like elevation of Serum creatinine from 1.5 to 1.9 mg/dl (Greater than or equal to 0.3 mg/dl of serum creatinine from the baseline) and BUN level from 35 to 78 mg/dl (Greater than or equal to 50% raise in BUN level). The mechanism of Mannitol induced AKI in this patient includes any of the following three

mechanisms like 1) High dose/high concentration of the drug resulting in renal vasoconstriction, 2) Intense Natriuresis and diuresis, 3) Structural changes happening in the proximal convoluted tubule where vacuolization and swelling of the cells of the tubule are seen in the presence of Mannitol and this phenomenon was termed as Osmatic Nephrosis (ON)[6]. Generally, the increase in renal blood flow after the administration of drug is followed by redistribution of the renal blood flow causing diminished supply of oxygen to the renal medulla and causes renal damage due to ischemia. Patient's hyponatremia and signs and symptoms of dehydration can be attributed to the action of Mannitol and Furosemide combined. Here the patient was diagnosed with the drug induced AKI within a week and the patients clinical condition and laboratory parameters improved once the drug was withdrawn and treatment with normal saline was started, Patients creatinine and BUN started to lower gradually and improvement in serum sodium level was evident after discontinuation. General treatment of Mannitol induced kidney injury includes drug withdrawal, dialysis based on the symptom severity and presentation[7,8]. Untreated AKI leads to deterioration of the patient's condition and can lead to death.

CONCLUSION

This case report provides useful insights for the diagnosis, monitoring, treatment of AKI induced by Mannitol which has both nephrotoxic and nephroprotective properties.

ABBREVIATIONS

AKI: Acute Kidney Injury

BP: Blood Pressure

BUN: Blood Urea Nitrogen

CVA: Cerebrovascular Accident

GFR: Glomerular Filtration Rate

Hb: Haemoglobin

ICP: Intra Cranial Pressure

MRI: Magnetic Resonance Imaging

RCC: Renal cell carcinoma

WBC: White blood cells

NIHSS: The National Institutes of Health Stroke Scale

NS: Normal Saline

CONSENT

Written informed consent was obtained from the patient for publication of this case.

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Ethical approval: Not required

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