



## Hyperkalemia after Administration of Hypertonic Mannitol: Two Case Reports

Hsuan-ling Chen, Bin Zhu\* and Lan Yao

Department of Anesthesiology, Peking University International Hospital, Beijing, China

### Introduction

20% mannitol is used commonly to reduce intracranial pressure [1]. The dehydration effect of 20% mannitol was fast strong and long lasting. After 10 min~20 min administration, the intracranial pressure begins to decrease, after 0.5 h to the lowest level. It can decrease 50~90% of the intracranial pressure. After 1 h of the administration, the intracranial pressure begins to increase and about 4~8 h can return to the premedication level. The general dosage: 15%~25%, 0.25 g/kg~2 g/kg, i.v.in 30~60 min [2]. Mannitol serves as an osmotic diuretic, shifting water out of the cells and into the plasma. This movement of water acts to lower Intracranial pressure (ICP) and improve visualization of the field for the surgeon. Complications associated with mannitol infusion include temporary intravascular volume expansion, vasodilation, decrease in blood pressure (BP), metabolic acidosis, and electrolyte disturbances [3]. Here, we reported two cases of hyperkalemia, which were highly suspected caused by the administration of mannitol solution without the obvious T wave changes. The Internal Review Board exemption from Peking University International Hospital was obtained for the presented cases.

### Case Report

#### Case 1

A 69-year-old, 170-cm, 63-kg man with History of present illness of “dizziness with nausea and vomiting for 5 days”, was admitted to our hospital for right cerebellar space-occupying lesion excision under general anesthesia. MRI showed “space occupying lesion of cerebellum”. Previous surgical procedures include Lumbar endoscopic resection with postoperative

pathology suggesting “schwannoma”. Preoperative laboratory values ECG and chest radiography showed no abnormalities. BP was 134/83 mmHg, heart rate 64 beats per minute.

In the operating room, initial 5 leads ECG, oxygen saturation via pulse oximetry (SPO<sub>2</sub>), peripheral vein, central venous and radial artery catheterization were placed. No premedication was provided. General anesthesia was induced with midazolam, sufentanil, propofol and cisatracurium. Anesthesia was maintained with propofol, sufentanil and cisatracurium. Bispectral Ixex (BIS) was used for anesthesia depth monitoring and maintained at 40~60. After tracheal intubation, lungs were ventilated using oxygen in air (FiO<sub>2</sub> 0.7) and end-tidal carbon dioxide was maintained at 36~38 mmHg.

The patient was hemodynamically stable throughout induction and at the beginning of the surgery. 30 minutes later, the surgeon asked for 20% mannitol solution 250 ml i.v. 25 minutes after the complete administration, patient’s BP began to decrease to 56/39 mmHg, with the lowest to 39/31 mmHg. Heart rate dropped to 42 beats per minute and subsequently ECG showed ventricular fibrillation. The operation was suspended. Patient was covered and turned over to supine position for cardiopulmonary resuscitation. External chest compression, electric defibrillation and HCO<sub>3</sub><sup>-</sup> solution (250 ml) was infused and intravenous adrenaline injected 1~3 mg per time. Results of ABG before and after mannitol infusion are presented in Table 1. Transesophageal echocardiography (TEE) was placed during the resuscitation. TEE found left ventricle, left atrium enlargement and asystole. Cardiologist was called for urgent consultation, temporary pacemaker was placed, had pace signal, but there was still no

**Table 1:** Results of ABG analysis before and after infusing mannitol solution.

Mannitol	PH	PaCO <sub>2</sub>	PaO <sub>2</sub>	Na <sup>+</sup>	K <sup>+</sup>	Ca <sup>2+</sup>	Hb	FI <sub>O</sub> <sub>2</sub>
Before	7.414	34.0	242.0	142.0	4.23	1.28	109	70
After 15 min	7.356	40	256.3	143.5	6.03	1.17	103	70
After 30 min	7.136	44.9	287	140.0	5.65	0.78	97	100
After 50 min	6.990	50	186.5	142.2	5.78	0.77	94	100
After 120 min (ICU)	7.36	46	204	154	7	1.17	98	100

effective contraction. Heart rate was 20~30 per beats, BP 52/30 mmHg. Since the patient was hemodynamically unstable, after the urgent Multiple Disciplinary Team (MDT) consultation, the surgery was called off. The patient was transferred to ICU for further observation and treatment. For this patient, intraoperative fluid infusion was 4200 ml (crystalloid solution 3100 ml, colloidal solution 1000 ml, 20% albumin 100 ml) Blood lost was about 1000 ml and clear urine was about 2000 ml. In ICU, BP was 40/20 mmHg and no respiratory was observed. 3 hours after the resuscitation initiation, further treatment was discontinued and the patient was dead.

## Case 2

A 69-year-old, 170-cm, 79-kg man, had two months of intermittent headache aggravating with dizziness for one day was admitted to our hospital for clipping of artery aneurysm under general anesthesia. MRI showed "space occupying lesion of cerebellum". The patient has a history of hypertension for 40 years, coronary heart disease 30 years. Preoperative laboratory values and chest radiography showed no abnormalities. BP was 134/83 mmHg, heart rate 64 beats per minute. ECG showed atrial premature beats and ST-T changed.

In the operating room, initial 5 leads ECG, oxygen saturation via pulse oximetry (SPO<sub>2</sub>), peripheral vein, central venous and radial artery catheterization were placed. No premedication was provided. General anesthesia was induced with midazolam, sufentanil, propofol and rocuronium. Anesthesia was maintained with propofol, sufentanil and rocuronium. Bispectral Index (BIS) was used for anesthesia depth monitoring and maintained at 40~60. After tracheal intubation, lungs were ventilated using oxygen in air (FiO<sub>2</sub> 0.6) and end-tidal carbon dioxide was maintained at 31~36 mmHg.

The patient was hemodynamically stable throughout induction and at the beginning of the surgery. Around 14 minutes later, the surgeon asked for 20% mannitol solution 250 ml i.v. BP and heart rate remained unchanged when the full dosage of mannitol was given, but the routine ABG showed hyperkalemia. Results of ABG before and after mannitol infusion are presented in Table 2. After 4 U insulin was intravenously administered, serum potassium gradually returned back to normal level. The surgery was completed after six hours. The patient was extubated and transferred to ICU for further observation. Intraoperative fluid infusion

was 3870 ml, including crystalloid solution 2370 ml, colloidal solution 1500 ml. Blood lost was about 300 ml, urine about 2200 ml, clear. Next day, the patient was transferred back to inpatient ward and after 8 days discharged from hospital.

## Discussion

We reported two cases of hyperkalemia after administration of hypertonic mannitol. One was dead despite of resuscitation. Therefore, neurosurgeon and anesthesiologist must pay full attention to hyperkalemia after administration of hypertonic mannitol.

There are several case reports about hyperkalemia after administration of hypertonic mannitol. In 1987, the infusion of high-dose mannitol (2 g/kg) results in significant changes in serum electrolytes, including hyperkalemia [4]. This research suggested that with low-dose (1 g/kg) mannitol, there was a slight decrease in serum K<sup>+</sup> (mean, 0.5 mEq/L). In contrast, with high-dose mannitol (2 mg/kg), a statistically significant increase in serum K<sup>+</sup> (mean, 1.5 mEq/L) level occurred after completion of the mannitol infusion.

Nakasuji, et al. [5] found that serum potassium concentration in each patient was reaching 6.0 mEq/L and 5.7 mEq/L, respectively, at 2 hours after completion of infusion of 45 and 30 g mannitol. The research recommended that patients with potassium concentration more than 4 mEq/L before infusion, should undergo repeated ABG analysis until at least 2 hours after completion of mannitol infusion. It also summarized the features of the nine published cases of mannitol-induced hyperkalemia and found out that when ABG showed hyperkalemia, the ECG also showed peaked T wave (Our two cases didn't appear). Sharma [6] reported that 30 min after infusing 1.5 g/kg mannitol, the patient's ECG showed peaked T waves and widening of QRS complexes, with ABG showing hyperkalemia. Hassan [3] reported the case of infusing mannitol twice because of the surgical field. First dose of mannitol was 0.5 g/kg and was finished in 25 minutes, serum potassium was normal. Because the surgeons complained of poor visualization, they requested a second dose of mannitol (0.5 g/kg). 80 g of mannitol was infusing in 45 minutes and after 15 minutes of administration, the patient's ECG showed peaked T wave and ABG showed hyperkalemia. Although all these cases reported hyperkalemia after administration of hypertonic mannitol, but adequate attention has not been drawn

**Table 2:** Results of ABG analysis before and after infusing mannitol.

Mannitol	PH	PaCO <sub>2</sub>	PaO <sub>2</sub>	Na <sup>+</sup>	K <sup>+</sup>	Ca <sup>2+</sup>	Hb	FIO <sub>2</sub>
Before	7.428	30.1	275.1	136.7	4.35	1.26	138	60
After 120 min	7.378	35.1	253.8	138.5	6.41	1.24	122	60
After 3 h	7.304	42.3	259.3	139.1	5.16	1.23	119	60
After 4 h	7.362	36.5	240.4	136.5	5.09	1.20	115	60

yet. Even the medication introduction provided by the pharmaceutical company only mentioned “sometimes could cause hyperkalemia”. In addition, to obtain better effect of reducing intracranial pressure, neurosurgeon prefer to rapid infusion of hypertonic mannitol [7]. The relationship between infusion speed and hyperkalemia still needs further studies.

The etiology of hyperkalemia is classified into three categories: increase intake, decreased urinary excretion, and transcellular redistribution of potassium [8]. In our two cases, we didn't use medication which caused hyperkalemia, like, succinylcholine, angiotensin converting enzyme inhibitors, digoxin etc. In addition, hyperkalemia could be observed in adrenal metastases and tumor lysis syndrome (associated with certain abnormalities such as hyperkalemia, hyperphosphatemia, hypocalcemia, hyperuricemia, and increased serum blood urea nitrogen levels), but our two patients did not have such kinds of disease. Moreover, two patients underwent no blood transfusion. Urine output was maintained at 0.5 ml/kg.min<sup>-1</sup> and clear, so we can exclude hyperkalemia caused by rhabdomyolysis and hemolysis [8,9]. And lastly, for the consideration of possible anaphylactic reaction, in case one, while the circulation collapsed, there was no rash, skin change and other signs related to allergic reaction, so anaphylaxis, for the first underlying reason, might be excluded. As for the reason of ventricular fibrillation, caused by hypotension or hyperkalemia, can not be definitely articulated because of the unexpected emergency. Even if hyperkalemia was not the driving reason for ventricular fibrillation, it exacerbated the resuscitation. Under the ECG and TEE monitoring, we found that the pace maker generated clear pace signal but failed to produce effective ventricular contraction.

After excluding all the factors that may cause hyperkalemia, we speculate that the administration of hypertonic mannitol caused hyperkalemia. As previously mentioned, mannitol induced hyperkalemia was not uncommon. About the reason, two hypotheses are raised. One is after infusing mannitol, the increase of plasma osmolality lead potassium transfer from intracellular to extracellular [8]. Second is the frictional forces between solvent (water) and solute (potassium) can result in potassium being carried out through cell membrane, a process called solvent drag [3]. All these hypotheses have not been elucidated, still no exact mechanism can explain why hyperkalemia will appear after the administration of mannitol solution. After administration of hypertonic mannitol, early correction of hyperkalemia must be done. Procedure as follows: Stop infusing mannitol solution immediately and infusing with bicarbonate calcium, insulin and glucose [9].

To avoid hyperkalemia after the administration of mannitol solution, some research suggested infusing

hypertonic saline substituted with infusing mannitol solution as to prevent the imbalance of electrolyte [5], but the effect of reducing intracranial pressure is inferior to mannitol solution. Sharma, et al. [6], suggested that the infusing dose of mannitol solution should be in low-dose (0.75-1 g/kg), Seto, et al. [10], are more conserved, suggested dose should be in low-dose (0.25-0.5 g/kg). It is essential to observe changes in the ECG, vital sign, plasma electrolyte concentration and plasma osmotic pressure after administering hypertonic mannitol.

In conclusion, we suggested that we should pay close attention to the infusion of mannitol solution. During and after the administration of mannitol solution, it is essential to monitor closely for changes in the ECG, vital sign, plasma electrolyte concentration and plasma osmotic pressure to detect and treat possible adverse cardiovascular events induced by hyperkalemia early.

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**Corresponding Author:** *Dr. Bin Zhu, Department of Anesthesiology, Peking University International Hospital, Beijing, China, E-mail: [zhubin@pkuih.edu.cn](mailto:zhubin@pkuih.edu.cn)*

**Editor:** *Renyu Liu, MD, PhD, Associate Professor, Department of Anesthesiology and Critical Care, Perelman School of Medicine at the University of Pennsylvania, 336 John Morgan building, 3620 Hamilton Walk, Philadelphia, PA 19104, Phone: 2157461485, Email: [liur@uphs.upenn.edu](mailto:liur@uphs.upenn.edu)*

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