Acute Renal Failure following Massive Mannitol Infusion

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Dear Sir,
Case Report

Mannitol is an osmotic diuretic agent widely used in the treatment of cerebral edema and in the prophylaxis of acute renal failure [1]. The kidneys are the major source of excretion of mannitol (90% excreted within 24 h of intravenous administration) [2]. Renal insufficiency will markedly impair excretion, leading to accumulation in extracellular fluid space [1, 2]. Thus, mannitol intoxication has been reported to be a potentially life-threatening complication when mannitol is used unrestrictedly in patients with established renal failure [3, 4]. The aim of this letter is to report on a patient with diabetic nephropathy and no known other predisposing factors in whom acute oliguric renal failure occurred as a consequence of infusion of massive quantities of mannitol.

A 50 year-old woman arrived at the emergency room with progressive obtundation and right hemiparesis. She had a history of diabetic nephropathy, and 6 months earlier suffered an episode of acute renal failure due to iodine contrast medium, remaining with a creatinine clearance of 18 ml/min. Intracranial haemorrhage was suspected, and 200 g of mannitol was administered as well as thiopental sodium, insulin, ranitidine, and dexamethasone. A computerized tomography scan without contrast medium did not show signs of cerebral bleeding. Serum creatinine was 248 µmol/l, urea 27 mmol/l, Na 130, and K 4.5 mmol/l. Within the first 2 h the patient presented diuresis of 758 ml, though later she was anuric and did not respond to furosemide. Moreover, consciousness decreased progressively until the patient entered profound coma. Haemodynamic stability was maintained throughout. During the following 48 h the patient was anuric and presented hypervolaemic signs which led to the institution of peritoneal dialysis. The patient required mechanical ventilation due to Cheyne-Stokes respiration. Twelve hours after

Table 1. Laboratory data

Parameter
Day

1
2
3a
4
5
6
7
Serum urea nitrogen, mmol/L
27
30
33
30
30
28
23
Serum creatinine, $\mu\text{mol/L}$
248
317
467
481
410
348
253
Diuresis, ml/24 h
750
0
0
5,372
4,705
2,870
2,100
Serum osmolarity (measured), mosm/L
-
322
-
330
324
326
311
Potassium, mmol/L
4.5

4.2

3.9

3.8

3.7

4.5

3.9

Serum sodium, mmol/L

130

119

120

130

133

135

139

Glucose, mmol/L

21

19

16

14

18

19

12

Peritoneal dialysis.

378

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mannitol administration serum creatinine was $317 \mu\text{mol/L}$, urea 30 mmol/L , Na 119, K 4.2, glucose 18 mmol/L , creatine phosphokinase $60 \mu\text{U/L}$, and plasma osmolarity 322 mosm/L . Laboratory data are shown in table 1. On the 4-day polyuria was noted, and renal function progressively recovered. Consciousness and respiratory rhythm simultaneously returned to normal. The patient was extubated 12 h later.

Discussion

This case illustrates the risks of excessive mannitol infusion. The presence of hyponatremia, extracellular fluid volume expansion, hyperosmolarity, and altered mental status were all representative of mannitol intoxication. Since mannitol cannot cross cell membranes, hyponatremia and extracellular fluid volume expansion are secondary to the osmotic effect of mannitol which induces free water movement from intracellular to extracellular spaces. The symptoms of the central nervous system have been attributed to 'brain dehydration' [1]. The most interesting aspect of this report is that onset of oliguria occurred following mannitol administration. There was no evidence implying any agent other than mannitol as the cause of renal function deterioration. Furthermore, in the rabbit mannitol has been reported to induce renal alterations, histologically as vacuolization of proximal and distal tubular cells ('osmotic nephrosis'). This condition is apparently transitory and subsides spontaneously after withdrawal of mannitol [5]. Although literature reporting acute renal failure secondary to mannitol administration is scarce,

large quantities when required should be infused with caution, especially in patients with renal failure, so as to avoid potentially life-threatening complications.

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