Mannitol-Induced Acute Renal Failure

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Dear Sir,

Although mannitol is widely used in the clinical practice, the potential nephrotoxic effects of this drug have only recently been observed. We herein report one more case of acute renal failure temporally associated with mannitol administration.

A 71-year-old man was admitted to hospital because of obtundation. He had a longstanding history of hypertension, which was managed with clonidine, and mild chronic renal failure felt to be secondary to nephroangiosclerosis.

At the time of admission (day 0) the patient appeared quite confused. Blood pressure was 160/90 mm Hg, pulse 80/min and the temperature 36.2°C. The lungs, heart and abdomen were normal. The findings of the neurologic examination and EEG were unremarkable. A grade II Keith-Wegener optic fundus was demonstrated. His serum creatinine was 1.8 mg/dl (normal values 0.4-1.3); other laboratory investigations were normal. A transient ischemic attack was diagnosed and 400 g of mannitol were administered intravenously in the 48 h after admission. During the next 2 days he became increasingly lethargic and experienced nausea and vomiting. A computed tomographic cranial scan, performed without the intravenous injection of contrast material, disclosed no evidence of cerebral abnormalities.

The nephrologist was consulted on day 4 of hospitalization. At that time, oliguric acute renal failure had developed: serum creatinine had risen to 6.1 mg/dl and the urine output was 10-15 ml/h. The patient appeared to have a normal volume status; his blood pressure was 165/100 mm Hg, pulse 85/min and temperature 36.8°C. Other laboratory investigations included a serum sodium of 111 mEq/l and a measured serum osmolality of 327 mosm/kg {calculated 256 mosm/kg}; urinary sodium was 9 mEq/l and urinary osmolality was 363 mosm/kg; a fractional sodium excretion of 0.7% was calculated. Urinalysis was unremarkable. Urinary concentrations of α -r microglobulin and β -2-microglobulin were normal [7 mg/l (normal values 0-8) and 0.15 mg/l (normal values 0.02-0.23), respectively]. Renal ultrasonography did not demonstrate any evidence of obstruction.

Intravenous infusion of dopamine (1.5 μ g/kg/min) was started and by the next day urine output exceeded 75-100 ml/h. Consciousness readily ameliorated and returned to normal. Creatinine values gradually fell and returned to the baseline value within day 8.

In brief, we present one case of acute renal failure that developed shortly after infusion of mannitol. In view of the close time relationship between the two events in the absence of other recognizable causes, we attributed this patient's renal dysfunction to the drug he received. The

presence of neurologic disturbances, hyponatremia, hyperosmolality and an increased osmolal gap were all representative of mannitol intoxication.

There is already a number of anecdotal reports in the earlier literature of acute renal failure solely attributable to mannitol therapy [1-6]. Acute renal failure occurred in the oliguric form in patients who received mannitol in doses ranging from 200 to 2,050 g over 1-3 days.

Interestingly, removal of the offending drug by dialysis or renal excretion turned out to be curative, leading to immediate renal functional recovery in all cases.

The mechanism(s) by which mannitol leads to acute renal failure are not clear. Time-honoured experimental studies provided convincing evidence that mannitol can induce vacuolization of proximal and distal tubular cells ('osmotic nephrosis') and lead, in certain instances, to tubular obstruction as the result of cell swelling. However, these morphologic changes are difficult to recon-

cile with the very prompt reversibility of this form of renal insufficiency. More recently, Goldwasser and Fontino [2] reported an alternative hypothesis for the pathogenesis of acute renal failure secondary to mannitol therapy. They suggested that the increased urinary solute excretion caused by mannitol may trigger an intense tubuloglomerular feedback culminating in afferent arteriolar vasoconstriction. Therefore, the consequent renal ischemia, rather than substantial histo-logic alterations in the kidney, would be responsible for the acute renal failure occurring in the setting of mannitol intoxication. In our patient urinary indices were compatible with renal ischemia; extrarenal causes of renal hypoperfusion excluded, it is likely that such a functional mechanism was indeed involved in this case. The therapeutic response to low-dose dopamine, which acts primarily by modifying the afferent arteriolar tone, further supports this possibility.

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