Treatment of resistant intracranial hypertension with hypertonic saline

Report of two cases

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The authors describe two patients with traumatic cerebral edema and intracranial hypertension in whom the continued use of mannitol and furosemide resulted in a progressive lessening of the effect of these agents on the intracranial pressure (ICP) and caused prerenal failure. Intravenous administration of hypertonic saline (50 ml and 20 ml of a 5-mmol/ml saline solution over 10 minutes in Cases 1 and 2, respectively) produced a prolonged reduction in the ICP and improved renal function in both cases. It is suggested that if a reduction in ICP without diuresis is required in patients with traumatic cerebral edema, treatment with intravenous hypertonic saline should be considered.

KEY WORDS • hypertonic saline • intracranial pressure • head injury

Cerebral edema associated with head injury often required nonsurgical management to increase the removal or decrease the formation of cerebrospinal fluid (CSF). Experimental studies with intravenous hypertonic solutions have demonstrated a decrease in cerebral volume, reduction of CSF production, and lowering of intracranial pressure (ICP). These studies have stimulated clinicians to use hypertonic sucrose, glucose, glycerol, urea, and mannitol to lower the ICP in patients with cerebral edema.

Glucose and sucrose are rapidly metabolized, and thus their effect on ICP is often transient. Intravenous glycerol may cause hemolysis, hemoglobinuria, and renal failure; urea often produces a rebound rise in ICP, and hyperoncotic albumin requires the concomitant administration of furosemide to achieve consistent ICP reduction. While mannitol has become widely accepted as the hypertonic solution of choice in the management of cerebral edema, its use has been associated with acute renal failure, hypertonicity, and factitious hyponatremia, indicating that it is also not without hazard.

Hypertonic saline reduces the CSF pressure and brain water content in experimental animals, but it is rarely used to reduce ICP in clinical practice unless hyponatremia is present. In this paper we describe the use of hypertonic saline to reduce the ICP in two patients with intracranial hypertension that was unresponsive to mannitol and furosemide.

Case Reports

Case 1

This 47-year-old man was admitted to the hospital after a motor-vehicle accident in which he sustained a closed head injury. Because he was sweating profusely, hyperventilating, and exhibiting spontaneous decerebrate posturing, he was paralyzed with 8 mg pancuronium, intubated, and mechanically ventilated. A cranial computerized tomography (CT) scan showed symmetrical compression of the lateral ventricles with no mass lesion or midline shift. Subdural, radial artery, and subclavian vein catheters were inserted for continuous monitoring of ICP and arterial and central venous pressure (CVP), and 200 ml of 20% mannitol was administered intravenously. The patient was maintained on a ventilator with arterial blood gas values as follows: pCO₂ 33 mm Hg, pO₂ 132 mm Hg, and pH 7.55. Plasma biochemical tests revealed the following values:
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Fig. 1. Intracranial pressure (ICP) in Case 1 before and after administration of 250 mmol of intravenous hypertonic saline (50 ml of 5 mmol/ml saline). The artifact just before saline administration was due to flushing and calibration maneuvers.

sodium 135 mmol/liter, potassium 4.3 mmol/liter, urea 4 mmol/liter, and creatinine 0.1 mmol/liter; osmolality was 282 mOsm/kg, and there was an osmolar gap of 4 mOsm/kg.

During the first 24 hours the mean ICP varied between 12 and 20 mm Hg, the mean arterial blood pressure (MABP) between 75 and 90 mm Hg, and the CVP between 5 and 8 mm Hg. Thirty-six hours after injury the mean ICP rose to 40 mm Hg while the MABP remained at 83 to 85 mm Hg. The ICP elevation was treated with 20-mg boluses of mannitol every 2 hours as required. The first two doses of mannitol reduced the ICP to a mean of 17 mm Hg; however, after administration of a total of 140 gm of mannitol during the next 12 hours and recording of a negative fluid balance of 2200 ml, the ICP became resistant to the effect of mannitol. The patient became oliguric, with a blood pressure of 110/85 mm Hg, a CVP of 2 mm Hg, a plasma creatinine level of 0.28 mmol/liter, and osmolality of 305 mOsm/kg. The serum sodium concentration had decreased to 131 mmol/liter and the osmolar gap increased to 27 mOsm/kg due to the retention of mannitol. A CT scan was performed which showed no change when compared to the initial scan.

Ventilation was increased to reduce the arterial pCO₂ to 25 mm Hg, and 100 ml of mannitol and 40 mg of furosemide were administered. Following this, the mean ICP decreased from 45 to 32 mm Hg, but increased 20 minutes later to 53 mm Hg. Fifty milliliters of a 5-mmol/ml hypertonic saline solution (250 mmol) was administered intravenously over 10 minutes, which reduced the mean ICP from 53 to 10 mm Hg (Fig. 1). One hour later blood pressure was 140/80 mm Hg, CVP was 6 mm Hg, plasma sodium level was 137 mmol/liter, and osmolality was 317 mOsm/kg. The mean ICP remained between 8 and 12 mm Hg for the next 24 hours, at which time the subdural catheter was removed. The patient's urine output increased from between 5 and 10 ml/hr to between 50 and 80 ml/hr, and his serum creatinine returned to normal 4 days later. During the next 3 months he slowly recovered until he was able to feed himself and respond to commands, although he still required nursing help for complex tasks.

Case 2

This 17-year-old youth was admitted to the hospital after a motor-vehicle accident in which he sustained a closed head injury. On examination the patient flexed his limbs nonpurposefully to pain and both pupils reacted to light. Within the 1st hour after admission the left pupil became fixed and dilated and he was treated with 200 ml of 20% mannitol, paralyzed with 6 mg pancuronium, and artificially ventilated. A CT scan revealed a small hematoma in the orbital apex, subarachnoid blood around the brain stem, and multiple widespread contusions in the right frontal and left parietal lobes with no midline shift. A subdural catheter was inserted over the right frontal lobe for continuous ICP measurement, which varied between 25 and 30 mm Hg with plateau waves rising to 60 mm Hg and lasting 10 to 15 minutes. An additional 200 ml of 20% mannitol was administered, and this dose was repeated 2 hours later. Both doses had little effect on the ICP or urine output. At this stage the blood pressure was 125/90 mm Hg, CVP was 0 mm Hg, and plasma biochemistry revealed a sodium concentration of 139 mmol/liter and a creatinine level of 0.21 mmol/liter. Twenty milliliters of a 5-mmol/ml hypertonic saline solution (100 mmol) was administered intravenously over 10 minutes, reducing the ICP to 10 mm Hg where it remained for the next 12 hours (Fig. 2). The CVP increased to 4 mm Hg, and 2 days later the patient's renal function was normal. Two months after the accident the patient was able to talk and feed himself; a left-sided hemiparesis required him to use a walking frame.
Fig. 2. Intracranial pressure (ICP) in Case 2 before and after administration of 100 mmol of intravenous hypertonic saline (20 ml of 5 mmol/ml saline).

Discussion

Intravenous hypertonic solutions reduce intracerebral volume and ICP in patients with cerebral edema by reducing brain water content and CSF production. When mannitol is used, the initial dose of 0.25 to 1.0 gm/kg infused over 10 minutes produces a maximum ICP reduction at 14 to 17 minutes. Five hours later most of the mannitol is excreted and the associated positive free water clearance usually results in a return of the body osmolality to a slightly higher value, with the ICP reverting to its previous level.

In the two cases described here, mannitol produced a fall in ICP and diuresis. However, with its continued administration the patients became progressively dehydrated. The effect of mannitol (and subsequently furosemide) on lowering the ICP was reduced and prerenal failure developed. In Case 1, factitious hypotension also occurred. While a reduction in ICP was still required, we believe that an increase in intravascular volume was also needed to improve renal function. Intravenous hypertonic saline increased the intravascular volume and improved renal function, as assessed by the increase in CVP and the reduction in the serum creatinine level, respectively. The reduction in ICP and increase in serum osmolality was prolonged, and the change in osmolality was easily assessed from the rise in plasma sodium values.

To provide the osmolar gradient of 10 to 30 mOsm that is required to mobilize brain water, 100 mmol of hypertonic saline was administered in Case 2 and 250 mmol was given in Case 1, achieving an osmolar amount equivalent to 36 gm and 91 gm of mannitol, respectively. A concentration of 5 mmol/ml was chosen since it enabled osmolar amounts to be calculated easily and has been used previously in patients with hypotensive cerebral edema.

In patients with cerebral edema the ideal hypertonic agent should reduce the CSF content without producing adverse systemic effects. In a controlled study, Albright, et al., compared mannitol, furosemide, concentrated albumin, and concentrated albumin with furosemide in dogs with cerebral edema induced by a cold lesion in the left parietal area. They noted that the ICP was significantly reduced by all agents except concentrated albumin, although a negative fluid balance without an increase in hematocrit or vasopressin secretion occurred only in the animals given concentrated albumin with furosemide. They concluded that the more desirable effect of a reduced intracellular CSF volume without a reduction in intravascular volume occurred only in this group. However, albumin solutions may on rare occasions produce severe elevations of ICP and are not generally used in the treatment of intracranial hypertension. If diuresis is considered to be undesirable and maintenance of the extracellular fluid volume is required, then hypertonic saline, which can reduce the ICP and is monitored easily from serum sodium estimations, may have advantages when compared to concentrated albumin with either furosemide or mannitol.

References

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