

## Furosemide- and Mannitol-induced Changes in Intracranial Pressure and Serum Osmolality and Electrolytes

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The effects of furosemide and mannitol on intracranial pressure (ICP), serum osmolality, and electrolytes were measured preoperatively, after induction of anesthesia, at the onset and peak of diuresis, at the completion of diuresis, and postoperatively. After mannitol, ICP increased significantly at the onset of diuresis ( $15.7 \pm 4$  torr) and decreased significantly at the completion of diuresis ( $7.25 \pm 2.4$  torr), and postoperatively ( $6.1 \pm 2.4$  torr). After furosemide, ICP decreased at peak diuresis ( $5.4 \pm 1.4$  torr), at completion of diuresis ( $4.7 \pm 1.7$  torr), and postoperatively ( $2.6 \pm 1.3$  torr). Serum osmolality increased significantly following mannitol at onset ( $302.1 \pm 4.4$  mOsm), peak ( $299.8 \pm 2.2$  mOsm), and completion of diuresis ( $296 \pm 2.3$  mOsm), and postoperatively ( $294.1 \pm 2.4$  mOsm). Furosemide did not significantly alter serum osmolality or electrolyte values. After mannitol, serum potassium was significantly decreased at the end of diuresis ( $4.0 \pm 0.2$  mEq/l) and postoperatively ( $3.9 \pm 0.2$  mEq/l), while serum sodium was decreased significantly at the onset ( $132.4 \pm 1.3$  mEq/l), peak ( $133.8 \pm 1.1$  mEq/l), and completion of diuresis ( $134.9 \pm 0.8$  mEq/l) and postoperatively ( $135.8 \pm 0.9$  mEq/l). Because of these changes, it is recommended that furosemide be used instead of mannitol when diuresis is desired in patients with increased ICP, and in those who have pre-existing cardiac and electrolyte abnormalities. (Key words: Kidney, diuretics, furosemide; Kidney, diuretics, mannitol; Cerebrospinal fluid, pressure; Blood, serum osmolality.)

THE ADMINISTRATION of mannitol to decrease brain size in neurosurgical patients may cause adverse effects, such as: rebound of intracranial pressure<sup>1</sup>; transient increases in cerebral<sup>2</sup> and circulating blood volumes<sup>3</sup>; changes in blood coagulation and blood viscosity; increased serum osmolality and decreased serum electrolyte concentration.<sup>4</sup> Furosemide, a sulfonamide diuretic that inhibits distal tubular reabsorption, is said to decrease brain water content without adverse effect and therefore may be a suitable substitute for mannitol.<sup>¶</sup> This study compares the effects of furosemide and man-

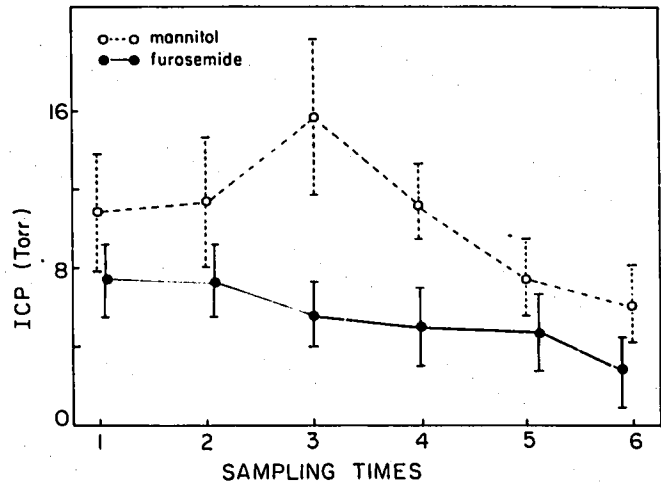


FIG. 1. Changes ( $\bar{X} \pm SE$ ) in ICP after mannitol and furosemide. Sampling times are as follows: 1 = preoperative; 2 = after induction of anesthesia; 3 = at the onset of diuresis; 4 = at peak diuresis; 5 = at the completion of diuresis; 6 = postoperatively.

nitol on intracranial pressure (ICP), serum osmolality, and serum electrolytes in a group of patients scheduled for craniotomy for clipping of an aneurysm, repair of an arteriovenous malformation, or resection of a tumor.

### Methods and Materials

Twenty patients scheduled for craniotomy were anesthetized with a halothane-nitrous oxide-oxygen mixture after placement of arterial, right atrial and bladder catheters. No patient had clinical evidence preoperatively of increased ICP. Respiration was controlled with an Air Shields ventilator to maintain the arterial partial pressure of carbon dioxide between 25 and 30 torr. ICP was measured with a Richmond bolt that was inserted before induction of anesthesia. The pressure signal was transduced by a Statham (P23) transducer, amplified and recorded on an Electronics for Medicine VR-6 monitor. Calibrations were performed with the use of a sphygmomanometer. The control ICP was made when the inspired halothane concentration had been stable for at least 30 minutes. Airway pressure was measured with an aneroid manometer. At the start of the skin incision, mannitol (1 g/kg) or furosemide (1 mg/kg) was given by bolus intravenous injection in a randomized sequence. Arterial blood was drawn preoperatively (1), after induction of anesthesia (2), at the onset (3), peak (4), and com-

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Received from the Departments of Anesthesiology and Neurosurgery, New York University Medical Center, 560 First Avenue, New York City, New York 10016. Accepted for publication March 7, 1977. Presented at the Annual Meeting of the American Society of Anesthesiologists, San Francisco, California, October 12, 1976.

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pletion (5) of diuresis, and postoperatively within one hour (6). Hematocrit, serum osmolality, sodium, potassium, and arterial blood-gas values ( $pH$ ,  $P_{CO_2}$ ,  $P_{O_2}$ ) were measured using standard methods.

Using Student's  $t$  test for paired data, no significant difference was found for any variable for the two randomly selected groups either preoperatively or pre-diuretic administration.

### Results

Mannitol significantly increased ICP at the onset of diuresis ( $15.7 \pm 4$  torr) and significantly decreased ICP at the completion of diuresis ( $7.25 \pm 2.4$  torr) and postoperatively ( $6.1 \pm 2.4$  torr). Significant decreases in ICP following furosemide were seen at the peak of diuresis ( $5.4 \pm 1.4$  torr), at the completion of diuresis ( $4.7 \pm 1.7$  torr), and postoperatively ( $2.6 \pm 1.3$  torr). No increase in ICP was seen at any time with furosemide (fig. 1).

Significant increases in serum osmolality following mannitol were seen at the onset of diuresis

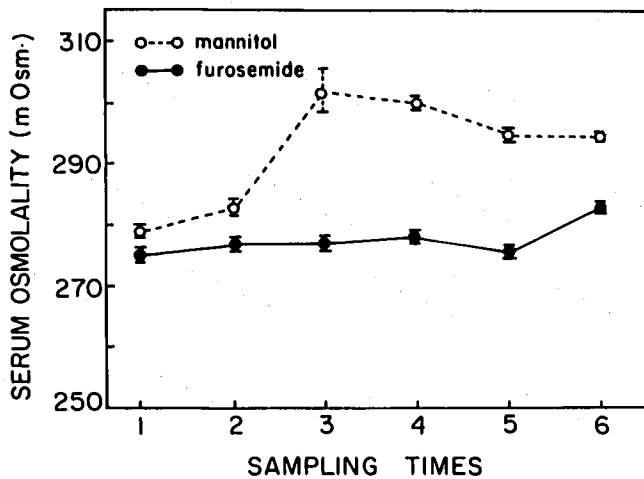


FIG. 2. Changes ( $\bar{X} \pm SE$ ) in serum osmolality after mannitol and furosemide.

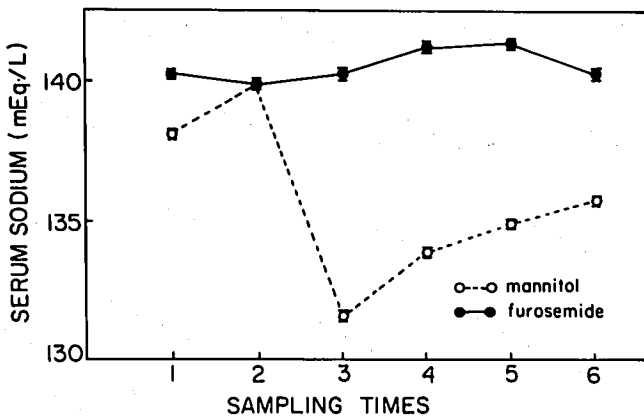


FIG. 3. Changes ( $\bar{X} \pm SE$ ) in serum sodium after mannitol and furosemide.

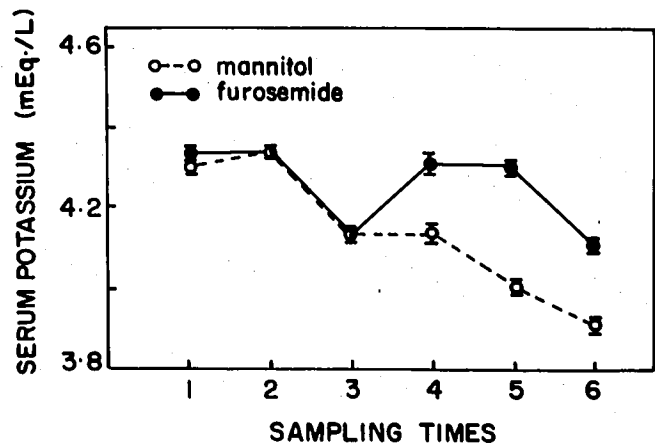


FIG. 4. Changes ( $\bar{X} \pm SE$ ) in serum potassium after mannitol and furosemide.

( $302 \pm 4.4$  mOsm), the peak of diuresis ( $299.8 \pm 2.2$  mOsm), the completion of diuresis ( $296 \pm 2.3$  mOsm), and postoperatively ( $294.1 \pm 2.4$  mOsm). A significant increase in serum osmolality following furosemide occurred postoperatively ( $282.7 \pm 2.4$  mOsm) (fig. 2).

Serum sodium decreased significantly following mannitol at the onset of diuresis ( $132.4 \pm 1.3$  mEq/l), the peak of diuresis ( $133.8 \pm 1.1$  mEq/l), the completion of diuresis ( $134.9 \pm 0.8$  mEq/l), and postoperatively ( $135.8 \pm 0.9$  mEq/l), while no significant change occurred following furosemide (fig. 3).

Significant decreases in serum potassium occurred after mannitol at the completion of diuresis ( $4.0 \pm 0.2$  mEq/l) and postoperatively ( $3.9 \pm 0.2$  mEq/l), while no significant change occurred following furosemide at any sampling time (fig. 4).

### Discussion

Osmotic diuretics have been used in neurosurgery for many years to decrease ICP by decreasing brain size. Mannitol depletes intracellular and extracellular fluid volume by increasing plasma osmolality. Plasma volume increases faster than renal clearance of the additional fluid can occur, which may cause transient increases in cerebral blood volume and intracranial pressure. Hyperosmolar solutions such as mannitol have direct vasodilating properties that can also result in increases in cerebral blood volume and pressure.<sup>5</sup> When ICP is already increased because of pre-existing disease, the ICP increase induced by mannitol may cause cerebral ischemia or brain-stem compression from herniation.

Our results show that osmotic diuretics may also cause passive changes in serum sodium and potassium. These changes may produce arrhythmias, precipitate digitalis toxicity, or even increase the likelihood of heart failure in certain patients. We did not encounter these untoward cardiovascular reactions in our patients.

Changes in serum osmolality, electrolytes, circulating blood volume, and ICP observed with mannitol were not seen following the use of furosemide at the onset and peak of diuresis. There was, however, a significant decrease in ICP starting with the peak of diuresis, which persisted post-operatively.

Differences in brain size and pliability could not be distinguished by the neurosurgeon when furosemide was used instead of mannitol. The decrease in ICP observed with furosemide is due to the diuretic effect of furosemide on renal tubules and also has been attributed by Buhley *et al.* to a direct reduction of sodium transport into the brain, thus decreasing brain size and ICP.<sup>6</sup>

Since ICP consistently decreased with usual therapeutic doses of furosemide, and since electrolytic and osmolality changes were less with furosemide than with mannitol, we recommend that furosemide replace mannitol in neurosurgery, especially when the patient already has increased ICP, an altered blood-brain barrier, or increased pulmonary water content,<sup>7</sup> and for those patients who have pre-existing cardiac and electrolytic abnormalities.

### Endocrinology

**PROPRANOLOL AND HYPERTHYROIDISM** The use of propranolol to treat hyperthyroidism and prepare patients for thyroidectomy has become increasingly popular. The authors describe two patients with known hyperthyroidism who were to undergo termination of pregnancy. One patient had been taking propranolol, 40 mg, four times daily for the preceding four weeks. The patient was alert and oriented, but had eye signs consistent with hyperthyroidism, as well as diffuse muscle weakness and resting tremor. Propranolol was continued at the same dosage, and two days later dilatation and curettage was performed with local anesthesia. Over the next seven hours, the patient became febrile (38.9 C), tachycardia (120/min) developed, and she became confused and obtunded. Therapy for thyroid storm was begun, and pulse rate and mental status returned to normal with 48 hours. The other patient had been started on the same dose of propranolol as well as propylthiouracil (PTU), 300 mg, every six hours. A

The authors gratefully acknowledge the expert technical assistance provided by Judith Katz, B.A., and Anne Klein, C.R.N.A., in the performance of these studies.

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week later (without surgery having been performed), she became febrile (40.6 C) and had a pulse rate of 132/min, with a markedly abnormal mental status. Propranolol dosage was doubled and PTU increased from 300 to 500 mg every six hours. Sodium iodide, 1 g every 12 hours, hydrocortisone, 100 mg every six hours, fluids, glucose and vitamins were also administered. The patients' mental state returned to normal within 12 hours, and temperature returned to normal within two days. The authors conclude that these two cases "demonstrate that despite the apparently salubrious effect of propranolol on cardiovascular signs and symptoms in patients with hyperthyroidism propranolol does not prevent thyroid storm." (*Eriksson M, and others: Propranolol does not prevent thyroid storm. N Engl J Med* 296:263-264, 1977.)  
**ABSTRACTER'S COMMENT:** It might have been more accurate to say that this particular dosage of propranolol does not necessarily prevent thyroid storm.