The Effects of Isosorbide on Serum and Cerebrospinal Fluid Osmolality and on the Spinal Fluid Pressure in Man*

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Isosorbide is a dihydric alcohol with a molecular weight of 146, formed by the removal of 2 molecules of water from 1 molecule of sorbitol. We recently reported that orally administered isosorbide lowered cerebrospinal fluid (CSF) pressure in dogs. This paper reports our findings when this osmotic diuretic was administered orally to humans.

Methods

A dose of 2 gm/kg body weight was chosen as being probably both safe and effective. The 50% isosorbide solution† was administered via nasogastric tube to comatose patients; conscious cooperative patients drank the iced solution. The CSF pressure was measured with a water manometer attached to a needle in the lumbar subarachnoid space. Osmolality of samples of serum and CSF were determined by the method of freezing point depression.‡

Results

Case 1. A 32-year-old woman with a presumptive diagnosis of "pseudotumor cerebri" possibly related to Griseofulvin. She was given 2 gm/kg of 50% isosorbide every other day for three doses. The effect of the first treatment is shown in Fig. 1. The serum electrolyte concentrations were normal several hours after this study, and her headache and visual obscurations subsided progressively. On examination 6 months later, she was free of symptoms, and the papilledema had disappeared completely.

Case 2. A 21-year-old man with a head injury and parietal skull fracture. On the fifth day post-injury, a right-sided subdural hematoma was evacuated. There was also evidence of temporal-lobe contusion. The study illustrated in Fig. 2 was done 2 days later.

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‡ Advanced Osmometer, Model 31-L.
Case 3. A 55-year-old man with a head injury and occipital skull fracture. His conscious state was impaired for 5 days, followed by gradual recovery. The study illustrated in Fig. 3 was done on the seventh day following injury.

Case 4. A 45-year-old man who had had a partial temporal lobectomy for glioblastoma multiforme several weeks before this study (Fig. 4). The osmotic gradient between serum and CSF reached a maximum of 28 milliosmols (mOsm) at 90 min.

Case 5. A 53-year-old man who had had several cerebral infarcts in the several months preceding this study (Fig. 5). Maximum osmotic gradient of 21 mOsm was reached at 120 min.

Case 6. A 77-year-old man who had had partial resection of a parietal glioblastoma multiforme 2 months before this study (Fig. 6). Maximum osmotic gradient of 35 mOsm was reached at 90 min.

Case 7. A 30-year-old man who had extensive brain trauma with an acute subdural hematoma. This study (Fig. 7) was done 3 days postoperatively while the patient was hypothermic and had been receiving dexamethasone in large doses for 2 days.

Case 8. A 27-year-old man who had had a severe head injury with drainage of an acute subdural hematoma 2 days previously (Fig. 8).

The following three patients received isosorbide without CSF pressure measurements:

Case 9. A 25-year-old woman with “pseudotumor cerebri” who received two doses of isosorbide, 3 gm/kg, in 3 days. Symptoms improved at the time. When seen 1 year later, the papilledema had subsided completely.

Case 10. A 65-year-old man who had had persistent CSF otorrhea for 8 days after a basal skull fracture. On the ninth day, he received 2 gm/kg of isosorbide; the otorrhea ceased within 2 hours and did not recur.

Case 11. A 50-year-old woman who was receiving radiation therapy for an unverified malignant glioma deep in the motor area. She was given 1.5 gm/kg of isosorbide, which did not produce any obvious alteration of findings.

Discussion

The onset of action of isosorbide in lowering CSF pressure appears to be very prompt after oral administration although this may vary with the speed of absorption from the intestine. Studies in animals have shown that,