Rebound phenomenon complicating cerebral dehydration with glycerol

Case report

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A patient with glioblastoma multiforme of the brain was treated with both intravenous and oral glycerol as well as intravenous mannitol in an attempt to reduce increased intracranial pressure. After an initial lowering of the cerebrospinal fluid (CSF) pressure to near normal values during continuous glycerol administration, a secondary rise in CSF pressure above the initial level occurred despite a persistent elevation of plasma osmolality (315 mOsm/kg) and glycerol level (30 mmole/l). Similarly, 4 hours after the administration of a single oral dose of glycerol, CSF pressure increased to levels higher (700 mm H2O) than the original baseline (400 mm H2O).

KEY WORDS • increased intracranial pressure • glycerol • rebound phenomenon

GLYCEROL, a low molecular weight alcohol, has been used extensively in attempts to reduce increased intracranial pressure in man.1,4,5,9,11 We recently treated a patient with increased intracranial pressure secondary to cerebral malignancy, and tried to lower the elevated cerebrospinal fluid (CSF) pressure with glycerol, while studying the effects of such therapy. We are reporting the results of this treatment here.

Case Report

A 57-year-old man became progressively disoriented, with impaired memory for recent events and occasional loss of sphincter control. Examination revealed mild disorientation to time and place and mild dementia, but the rest of the general and neurological examinations were unremarkable. Brain scan and bilateral carotid angiograms revealed two hypervascular space-occupying lesions, one in the right frontal and the other in the left parietal area; during the next few weeks, bilateral papilledema developed. During the first 2 weeks after admission, CSF pressure fluctuated around 300 mm H2O, with a maximum of 405 mm H2O. Dexamethasone (Decadron, 4 mg orally every 6 hours), was given for 10 weeks, but no significant change in CSF pressure, mental, or neurological status was noted.
The nature of the procedures (spinal taps, subarachnoid space cannulation, glycerol and mannitol infusion) were fully explained to both the patient and his wife and informed consent was obtained. Oral glycerol was prepared as a 50% solution and a 10% solution of glycerol in 0.15 M sodium chloride was administered intravenously with an IVAC 500 infusion pump.* For the continuous recording of CSF pressure, a polyethylene catheter (Portex Epidural cannula No. A109)t was introduced under appropriate sterile conditions at L3–4 level, and advanced into the subarachnoid space to T-5. The CSF pressure was measured via a three valve Morse Manifold‡ connected to a Statham SP 37 pressure transducer.§ and was recorded by a Hybrid Systems Electromanometer.** The correct position of the catheter in the subarachnoid space was ascertained by observation of both respiratory and cardiac pulse fluctuations, and the response to a quick, unilateral jugular vein compression. Serum Na⁺, K⁺, Cl⁻, bicarbonate, and osmolality were frequently determined during glycerol infusion, and glycerol levels were determined as described by Eggstein and Kreutz.§

Glycerol was given intravenously at an initial rate of 0.03 mmole/kg/min to increase plasma osmolality by 15 mOsm/kg and plasma glycerol level to 5.3 mmole/l. During the initial 8 hours of the infusion, the CSF pressure fell from 400 to about 200 mm H2O. After 24 hours of the same rate of infusion, CSF pressure gradually rose from 200 to 600 mm H2O; this rise persisted even though plasma glycerol concentration was raised to 16 mmole/l. After termination of infusion, CSF pressure rose to 900 mm H2O in 6 hours. The plasma glycerol was then increased to 30 mmole/1 for the next 8 hours. CSF pressure initially fell by 750 mm H2O but then rose to 400 mm H2O (Fig. 1). CSF pressure fell from 450 to 260 mm H2O 30 minutes after the oral administration of 10 mmole/kg of glycerol. Two hours later, however, the CSF pressure had risen to 700 mm H2O, which persisted for the next 3 hours of observation, at which time serum and CSF glycerol levels were 6.3 mmole/1 and 3.5 mmole/l, respectively.

Since we were unable to control the patient’s elevated CSF pressure with glycerol, we tried administering intravenous mannitol at a rate of 0.11 mmole/kg/min for 3 hours. The CSF pressure initially fell from 700 to 350 mm H2O in 90 minutes but was followed by a secondary rise up to 900 mm H2O, 4 hours after initiation of the infusion.

No significant hemolysis was seen during the administration of glycerol orally or intravenously, as evidenced by a constant hematocrit, bilirubin levels, normal urinary urobilinogen and blood haptoglobin levels, and absence of free serum hemoglobin. There was no significant change in serum Na⁺, K⁺,
Cl, or bicarbonate levels during the period of glycerol administration as compared with the levels before treatment.

Course of Treatment

Hyperosmolar agents were discontinued and a total tumor dose of 4000 rads was given, but the patient continued to deteriorate and died 3 months after admission. Necropsy revealed two large foci of glioblastoma multiforme in the right frontal and left parietal lobes, but no gross or histological evidence of edema or increased intracranial pressure.

Discussion

The rebound phenomenon reported here with glycerol has previously occurred in association with urea, mannitol, and hyperonic glucose, but not with oral or intravenous glycerol administration. The presence of an intact or only partially damaged blood-brain barrier may explain the absence of a rebound phenomenon in these cases; on the other hand, our patient had an extensive blood-brain barrier defect. We have recently presented evidence for a secondary rise in CSF pressure despite continuous intravenous infusion of glycerol; this occurs in experimental animals with brain edema induced by means of a cold lesion.

Since interest in the use of glycerol in a variety of neurological diseases is growing, one should appreciate the possibility of the rebound phenomenon. Until more is known about the metabolism and mechanism of action of this substance, its unrestricted use in man cannot be advocated.

References


Supported in part by Public Health Service Research Grant No. CA-15924-01 from the National Cancer Institute.

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