Oral Glycerol for the Reduction of Intracranial Pressure*

GIAMPAOLO CANTORE, M.D.,† BENIAMINO GUIDETTI, M.D., † AND MICHELE VIRNO, M.D.‡
Neurosurgical Department, Neurological Institute of Rome University, Rome, Italy

LITERATURE of recent years reports several works on the clinical use of hypertonic solutions administered by slow intravenous infusion for reduction of intracranial pressure. Among the numerous osmotic agents tested to reduce experimentally induced cerebral edema in the animal, glycerol has proved particularly effective both by intravenous and oral route. Considering such experimental results, glycerol has been applied on neurological, ophthalmological, and, chiefly, neurosurgical patients.

Glycerol (1,2,3-propanetriol) is a trivalent alcohol. It is oxidized by the organism through intermediate stages, analogous to those of the carbohydrate-oxidation cycle. As an integral part of fats (glicerides) and phosphatides, glycerol usually is present in the animal tissues at a rate of approximately 1 per cent of body weight. Oxidized to carbon dioxide and water, it produces 4.32 kg. calories per gm. Such value is slightly greater than that produced by glucose. When larger amounts of glycerol are given, however, the drug is not metabolized completely by the organism since part of it is excreted in the urine.

Glycerol increases plasmonic concentration. Its mechanism of action, therefore, would be to draw liquids from the tissues, particularly from those more hydrated.

At convenient doses, glycerol promotes diuresis yet diuresis itself does not condition the action of the drug since reduction of intracranial hypertension in the nephrectomized animal did not differ from that obtained in the normal animal.

In 1929, Ferber and Rabinowitsch described the action of oral glycerol administered as food to 60 patients. No toxic effects or gastrointestinal disorders were noted. In 1933, Johnson et al. studied the replacement of carbohydrate by glycerol in the diet of man and animal and pointed out the absolute tolerance of the drug taken orally. In order to examine the eventual toxicity of higher doses of glycerol, these authors administered daily 9 gm. of glycerol per kg. of body weight to the dog over a period of 1 year. The animals thus treated showed no toxic signs both in vivo and at postmortem examination. Subsequently, a group of students was submitted to a daily treatment of 1–3 gm. of glycerol per kg. of body weight over a period of 50 days. Never were toxic effects noted. Johnson et al., therefore, concluded: “. . . within extensive limits glycerol compares favorably with carbohydrate as a source of energy.”

We are not aware of any work, from a laboratory or clinic, dealing with therapeutic application of glycerol for the reduction of intracranial hypertension, other than those already mentioned, which appeared in 1961.

During this study, oral administration has been applied chiefly, since oral glycerol displays the following qualities (Fig. 1):

1) Promptness and intensity of action in reducing intracranial pressure.

2) Possibility of repeating administration several times over a long period, thus avoiding “rebound overshoot,” common to osmotic substances.

3) Lack of toxicity.

Method

Different kinds of glycerol are supplied. We have always used pure products. Single oral dos.

* “Glycerinum RP” furnished by courtesy of Carlo Eba, Inc., Milan, Italy. Actually, Tubi-Lux Laboratories, Naples, Italy, are supplying 30 per cent glycerol solutions, suitably prepared for oral administration, under the trade name of Luxoral.
Glycerol for Reduction of Intracranial Pressure

Glycerol, 0.8–1 gm. per kg. of body weight, always produced a marked anti-edematous effect, even in the most serious cases. Intravenous infusion, however, has been used only in a limited number of cases because of the frequent occurrence of transient hemoglobinuria. Further studies are being carried out presently in order to prevent hemolysis following intravenous administration.

Results

Glycerol, 1–2 gm. per kg. of body weight, was given to 258 patients, chiefly neurosurgical, from April 1961–April 1963. Oral administration was used in most cases. In a limited number of cases, intravenous infusion was applied. Glycerol was administered before, during and after surgery. In a few instances, the drug was given to patients with nonsurgical lesions of the nervous system.

Sixty-two patients suffering from space-occupying intracranial processes were treated with glycerol before surgical intervention. The doses administered varied according to the patient’s condition. In stuporous and torpid patients, oral glycerol, 0.5 gm. per kg. every 3–4 hrs., reduced intracranial hypertension to an extent that within 30–60 min. from the start of the first administration, the patients’ conditions highly improved and complete responsiveness returned. Solids and liquids were administered at the same time with glycerol, so that a convenient water, salt and protein balance could be maintained.

The most dramatic results with glycerol have been obtained in patients admitted to the hospital in comatose conditions. Administration of glycerol, 1.5 gm. per kg., was

![Fig. 1. Chart of cerebrospinal-fluid pressure in a patient with pinealoma. Cerebrospinal-fluid pressure was measured directly from the right lateral ventricle by means of a polyethylene tube. At “G” oral glycerol, 1.3 gm./kg. of body weight, was first administered; subsequently, 0.6 gm./kg., every 3 hrs., was given. In spite of the marked initial hypertension, repeated administrations of glycerol were able to maintain lower levels of cerebrospinal-fluid pressure, thus allowing the patient to remain fairly vigilant without complaining of cephalalgic crisis.](image-url)