Neurochemical Monitoring of Glycerol Therapy in Patients With Ischemic Brain Edema

Christian Berger, MD; Oliver W. Sakowitz, MD; Karl L. Kiening, MD; Stefan Schwab, MD

Background and Purpose—Osmotic agents such as glycerol are used to treat brain edema in stroke patients. We investigated the pharmacokinetics of glycerol in brain tissue by cerebral microdialysis.

Methods—Patients experiencing large middle cerebral artery infarction were included in this prospective study. The following variables were assessed before and every 10 minutes until 80 minutes after intravenous administration of 25 g of glycerol: intracranial pressure (ICP), serum osmolarity, and cerebral microdialysate concentrations of glycerol, glutamate, pyruvate, and lactate.

Results—During 16 ICP crises in 7 patients, cerebral glycerol concentrations (baseline 73.9±17.0 μmol/L) increased immediately after glycerol administration by up to 350%. Conversely, ICP (baseline 25±2.4 mm Hg) rapidly decreased by almost 50%. Both effects lasted for 70 minutes. Serum osmolarity (baseline 305±5.6 mOsm/L) was only briefly raised, whereas glutamate, lactate, and pyruvate remained unaffected.

Conclusion—Treatment of stroke patients with intravenous glycerol has only a brief effect on plasma osmolarity, but a more sustained effect on ICP, which is, however, accompanied by a rapid glycerol accumulation in brain tissue. (Stroke. 2005;36:e4-e6.)

Key Words: brain edema • infarction • intracranial pressure • middle cerebral artery
Microdialysate concentrations for glutamate, pyruvate, and lactate were within normal ranges and remained unchanged during the measurements (Figure 2) as did blood gases, hemoglobin, hematocrit, pH, electrolytes, and mean arterial blood pressure (Table). No hemolysis or electrolyte disturbances were noted.

**Discussion**

Intravenous glycerol reduces ICP promptly and significantly for up to 60 minutes without large and long-lasting effects on serum osmolarity. Instead, glycerol rapidly accumulates in brain tissue until 20 minutes after the infusion, before it subsequently decreases gradually and almost linearly to previous concentrations.

These results suggest that glycerol readily moves across the blood brain barrier into the brain. This was confirmed in a study using glycerol as enema for paralytic ileus in brain-injured patients, though after oral administration the peak concentration occurred 3 to 5 hours later. In CSF, rapid glycerol accumulation after intravenous infusion preceded a temporary reversal of the serum/cerebral spinal fluid concentration gradient during glycerol elimination. This reversal may be the cause of a rebound effect that describes an increase in ICP after repeated administration of an osmotic agent. The brief ICP rebound at 40 minutes in our series may be indicative of this effect.

No changes in cerebral glutamate, lactate, and pyruvate concentrations occurred after glycerol administration, which may argue for a pharmacological rather than ischemic effect. The latter would have been accompanied by an increase in glutamate and lactate and by a decrease in pyruvate concentration in ischemic brain tissue. Potentially, the implantation of microdialysis probes altered the blood brain barrier, which may have alleviated the permeation of a hyperosmotic solution into brain tissue. However, animal experiments suggest that glycerol readily enters even intact brain tissue. Other than a potential adverse rebound effect, glycerol may also be beneficial for ischemic brain tissue: first, by offering an alternative source of energy for neuronal tissue which can metabolize glycerol if glucose is lacking; second, by redistribution of cerebral blood flow with increase in regional cerebral blood flow and regional cerebral blood volume in ischemic brain secondary to reduction in focal cerebral edema, though no reduction of healthy brain volume was observed in MRI studies; and third, glycerol may modulate the leukocyte-endothelium interaction by preventing leukocytes from interfering with the blood cell and plasma flow, thus improving cerebral blood flow.

In conclusion, glycerol can reduce ICP in stroke patients though its main mechanism does not consist of creating a sustained osmotic gradient. Instead, glycerol accumulates in brain tissue with potential rebound effects on ICP if frequently administered. Therefore, its general use in stroke therapy with a lack of evidence of benefit in long term survival cannot be recommended.

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References

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