The Response of Focal Ischemic Cerebral Edema to Dexamethasone

A. Fenske1*, M. Fischer1, F. Regli2, and U. Hase3**

1 Department of Neurology, University Hospital, Mainz (Head: Prof. Dr. med. H. C. Hopf), Langenbeckstr. 1, D-6500 Mainz, Federal Republic of Germany
2 Head of the Department of Neurology, University Lausanne, CH-1011 Lausanne, Switzerland
3 Department of Neurosurgery, University Hospital Mainz, Langenbeckstr. 1, D-6500 Mainz, Federal Republic of Germany

Summary. Twenty-four h after permanent occlusion of the middle cerebral artery (MCA) in the cat, the hemispheric swelling due to edema is markedly reduced under treatment with large doses of dexamethasone than is the case with the untreated group. The increase of regional water and sodium content in the MCA territory is less in the dexamethasone treated group, whereas the potassium changes in the ischemic tissue showed only small differences between the two groups. The potassium content of the non-ischemic tissue is slightly increased in the dexamethasone treated animals when comparing with the untreated group. RISA activity in the tissue is increased in the grey and the white matter of both groups. The less marked RISA-131 activity in the cortical grey matter of the treated animals indicates blood-brain barrier damage of a smaller degree due to dexamethasone. These findings indicate a beneficial effect of dexamethasone on local ischemic edema. Regarding our results and the pharmacokinetics of this steroid the dexamethasone loading of a patient has to be in the range of about 100 mg per day for the adult, and has to be started immediately after the onset of a stroke.

Key words: Ischemia focal – Cerebral edema – Blood-brain barrier – Dexamethasone – Stroke.

Zusammenfassung. Vierundzwanzig Stunden nach permanentem Verschluß der Arteria cerebri media der Katze ist die ödembedingte Volumenzunahme der geschädigten Hemisphäre unter hochdosierter Dexamethasonbehandlung gegenüber nichtbehandelten Tieren deutlich geringer. Auch der Vergleich der regionalen Wasser- und Natriumzunahme ergibt für die behandelten Tiere

* Corresponding author
** Present address: St.-Elisabethen-Krankenhaus, Department of Neurosurgery, Elisabethen-strasse, D-7980 Ravensburg, Federal Republic of Germany
gingere Werte. Gleichzeitig findet sich ein nur geringerer Kaliumverlust aus dem geschädigten Gewebe, während sich unter Dexamethasongabe in den ungeschädigten Hirnregionen eine erhöhte Kaliumkonzentration nachweisen läßt. Die RISA$^{131}$-Aktivität im Hirngewebe, Indikator für eine Blut-Hirn-Schrankenschädigung, ist 24 h nach Ischämiebeginn sowohl in der grauen als auch der weißen Substanz in beiden Gruppen erhöht, wobei das Ausmaß der BHS-Schädigung im betroffenen Cortexareal der behandelten Gruppe gegenüber den Kontrollen wiederum geringer ist. Diese Befunde sprechen unter Berücksichtigung der Pharmakokinetik des Steroids für eine günstige Wirkung bei der Therapie des lokalen ischämischen Hirnödems. Voraussetzung scheint jedoch die frühzeitige, hochdosierte Steroidgabe zu sein, wobei eine Tagesdosis entsprechend über 100 mg Dexamethason beim erwachsenen Menschen erreicht werden sollte.

Introduction

Although good results have been obtained with dexamethasone in the treatment of local cerebral edema, such as perifocal tumor edema, the benefit of steroid therapy for focal ischemic edema following acute cerebral vascular occlusion still remains contradictory. This applies to experimental and also to clinical investigations [6, 7, 8, 10, 28, 39, 41].

It is possible that the varying duration and method of administration of the treatment, as well as inadequate consideration of its biological activity, are responsible for the variation in the results. In addition, the mechanism of the effect of steroids on cerebral edema is still not completely known and only few data about pharmacokinetics of this steroid and the dose/effect relationship are known [9, 24, 35, 40, 43].

The present experimental investigation had as its objective a study of the effect of large doses of dexamethasone on the focal cerebral edema resulting from permanent occlusion of the middle cerebral artery (MCA).

Method

Adult cats (weighing between 2.6 and 3.4 kg) were anesthetized with sodium pentobarbital. A femoral artery and a femoral vein were catheterized for continuous measurement of the mean arterial blood pressure (MABP) with a pressure transducer, to collect blood samples for gas analysis, and to inject drugs.

With the animal in the prone position, its head was immobilized in a special holder. A left supraorbital marginal incision was made, the orbital cavity enlarged, the left eye enucleated and the roof and median wall of the orbital cavity were dissected free. The optic canal was enlarged with the aid of the operating microscope and a drill and, after opening the dura and the arachnoid, the MCA was exposed and occluded by bipolar electrocoagulation applied directly at the point of its origin from the internal carotid artery. Electrocoagulation was effected without causing any damage to the brain tissue during the process [8, 29]. The dura and the optic foramen were then closed, the orbital cavity filled with Epoxy cement and the margins of the eyelids sutured together.