The Effect of Glucocorticoids on CSF Flow in Dogs

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In the 23 years that have elapsed since Prados, et al., demonstrated that adrenal cortical extract mitigated against the development of “brain swelling” upon exposure of the cerebral cortex, the use of glucocorticoids as an adjunct to treatment of intracranial pressure problems has gained wide acceptance by the neurosurgeon. The availability of commercially synthesized glucocorticoids following 1950 made such agents readily available to the clinician, and further refinements in the synthetic products have helped to minimize some of the undesirable side effects of chronic administration of these drugs in therapeutic doses. Although these agents are widely employed in efforts to alleviate increased intracranial pressure, their mechanism of action remains incompletely defined. Most studies have been directed at the evolution of “cerebral edema” and its consequences. The work of Long, et al., on the experimental use of glucocorticoids has demonstrated a decrease in the amount of intracellular swelling with virtually no enlargement of the extracellular space in experimental cerebral edema. Kullberg and West, employing chronic intraventricular recording in a series of patients with increased intracranial pressure, were able to demonstrate a decrease in the mean intracranial pressure within 2 days after the administration of the steroids. This was manifested primarily as a reduction in the periodic high pressure waves, so that the pressure recordings were relatively free of wide fluctuations.

There has, on the other hand, been surprisingly little interest in a second possible effect of glucocorticoids, namely, upon the production and absorption of cerebrospinal fluid (CSF). Garcia-Bengochea administered cortisone to non-castrated cats for 2 weeks and found a small but significant decrease in the flow of CSF from the lumbar theca when compared with pretreatment levels. Sato has described a significant fall in CSF production in four dogs observed for 50 to 110 minutes after rapid intravenous infusion of dexamethasone. We are aware of no other publications referring to this effect upon CSF dynamics.

Our investigation was undertaken in an effort to define further the acute effect of glucocorticoids on the flow of CSF and to establish the role of certain parameters that could possibly influence this phenomenon.

Material and Method

We used 14 adult mongrel dogs weighing 12 to 17 kg in a study divided into two series.

First Series of Experiments. The first series employed six dogs that had been made hydrocephalic by the intracisternal injection of 12.5% suspension of Kaolin to isolate the ventricular system from the over-all subarachnoid space. After an appropriate period of time to develop hydrocephalus (confirmed by air contrast study in vivo and later at autopsy), a Holter silicone ventricular catheter was inserted into the right lateral ventricle and attached to a capped Rickham reservoir which was secured in position beneath the scalp in the subgaleal space. The dura at the point of insertion of the ventricular catheter was cauterized to encourage subsequent adhesion to the underlying pia arachnoid, thereby isolating the catheter tract from the surrounding subarachnoid space. The catheter was inserted through a dural opening that was originally slightly smaller than the diameter of the catheter itself, thereby assuring a snug fit. No leakage around the catheter was noted in any of the experiments.

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After the dogs had recovered, they were anesthetized with pentobarbital sodium (30 mg/kg), intubated endotracheally, given intravenous injections of Flaxedil (1 mg/kg), and placed on a Harvard respirator to maintain controlled ventilation. Supplemental pentobarbitol and Flaxedil were administered as needed throughout the course of the experiment to maintain an even level of anesthesia.

Animals were placed in the right lateral position with their heads at the level of the right atrium. Access to the right lateral ventricle was easily obtained by percutaneous puncture of the Rickham reservoir with a No. 22 needle, attached to siliconized tubing (1 mm in internal diameter), which, in turn, led to a collecting vessel placed 30 cm below the level of the right atrium.

Second Series of Experiments. The second series included eight normal dogs, similarly anesthetized, intubated, and positioned. A 2-inch No. 20 LP needle was then placed in the cisterna magna, and the same collecting system was used as described above.

The animals were allowed to equilibrate CSF flow for 90 min, after which samples were taken at 10-min intervals in tared covered flasks, which were then carefully weighed on a balance accurate to the fourth decimal place. During the course of each experiment, the animal was given 275 to 325 cc of lactated Ringer's solution via a slow intravenous infusion. Respirations were maintained constant for each animal, depending on its size, ranging from 18 to 22 per min with a tidal volume of 250 cc. Pulse and blood pressure were monitored via an indwelling femoral artery catheter attached to a Statham transducer and recorded on a direct writing oscillograph. At the conclusion of each experiment the animal was allowed to recover. There were no observed effects from the procedure.

Results

First Series of Experiments. In these experiments dealing with the monitoring of isolated ventricular CSF flow, three animals were treated with steroids and three served as controls. As indicated by the graphs in Fig 1, the control animals maintained a relatively constant flow of CSF which averaged 0.028 cc/min with an average standard deviation of ± 0.0020 throughout the 6- to 8-hour periods of observation. The treated animals were allowed control periods of 45 to 90 min (after an initial 90-min period for equilibration), at which point they were given dexamethasone (0.25 mg/kg) via a rapid infusion. As indicated in the curves plotted in Fig. 2, there was a rapid fall-off in the flow of CSF which was evident within the first 10 min and reached a peak in 30 to