CORTISONE IN THE TREATMENT OF POSTOPERATIVE CEREBRAL EDEMA

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Modern surgical and anesthetic techniques have diminished markedly the desperate problems of postoperative cerebral edema that plagued the pioneer neurological surgeons, but cerebral edema of lesser degree remains an important factor in postoperative morbidity and mortality following many intracranial operations. The introduction of intravenous urea has been a major contribution in the prevention or temporary alleviation of the mechanical complications of brain swelling, but does not prevent or relieve the neurological deficits associated with cerebral edema that are not caused by brain-stem herniation and other mechanical complications of the swollen brain.

Although there has been evidence in the literature over the past 20 years that the anti-edema and anti-inflammatory effects of adrenal cortical steroids extend to cerebral tissue, this present attempt to evaluate the effectiveness of cortisone in the prevention and amelioration of the neurological symptoms of postoperative cerebral edema actually was undertaken because of an incidental observation made during an analysis of the endocrinological aspects of pituitary tumors and other tumors of the sellar region. This analysis showed that the protective effect of cortisone in operations in and about the sella was equally dramatic in those patients who had little or no preoperative hypopituitarism as in those with marked hypopituitarism. This raised the possibility that part, at least, of the well-known protective effect of cortisone in reducing the mortality and morbidity following these operations might be ascribable to a nonspecific effect of cortisone in reducing cerebral edema in a critical area of the brain rather than to the specific effect of supporting the pituitary-adrenal axis.

Since temporal lobectomy for focal cerebral seizures involves a reasonably standard amount of surgical manipulation of the brain, it seemed worth while to compare the effects of prophylactic administration of cortisone in a series of patients, undergoing temporal lobectomy, with a similar series of patients, operated upon by the same surgeon (T.R.), in whom cortisone had not been administered. It was hoped that a comparison between these two groups of the incidence and severity of the temporary postoperative symptoms which we attribute to postoperative cerebral edema might give an indication as to whether or not cortisone was of value in affording some protection against these postoperative problems.

REVIEW OF LITERATURE

The striking effect of cortisone in reducing the mortality and morbidity of operations about the sellar region became apparent soon after cortisone became generally available.9,10,18,24,25 In this connection it is of interest that Adson, in a discussion on surgery of sellar and suprasellar lesions at the St. Louis meeting of the Society of Neurological Surgeons on April 29 and 30, 1940, reported beneficial effects from the use of adrenal cortical extract for "pituitary asthenia" in the early postoperative period.

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The earliest pertinent study on cerebral edema, however, is that of Prados et al.,16,17 who studied the effect of subcutaneous injection of extract of anterior pituitary lobe (prepared in the Research Institute of Endocrinology of McGill University) on experimental cerebral edema produced by exposure of the cat brain to air. They concluded that adrenal cortical extract and extracts of the anterior lobe of the pituitary gland containing the corticotrophic factor prevent or minimize the swelling of the brain, the changes in permeability of cerebral capillaries and the electroencephalographic alterations that follow exposure of the brain to air. Similar conclusions were reported by Grenell and McCawley1 in a study using a similar model. In a subsequent related study, Grenell and Mendelson7 showed that Cortisal was more effective in preventing cerebral edema than either ACTH or cortisone.

Foley et al.2 studied the effect of cortisone on early repair of brain wounds in guinea pigs. Whereas an appropriate inflammatory response appeared in control animals the first week, in the cortisone-treated animals there was a pronounced inhibition of this inflammatory response. There was no edema about the wound, no extravasation of serum into adjacent tissue, and no fibrin formation. Dr. Aronson,1 in discussion of this paper, remarked that after a certain amount of time, whether or not cortisone was continued, the reactive elements managed to catch up to those of the control animals.

In recent years cortisone has been tried out in a number of neurological conditions in which suppression of edema and/or inflammatory response was felt to be therapeutically important. Of particular importance to this study are the reports of Russek et al.20,21 and Roberts19 who used cortisone in the immediate therapy of apoplectic strokes. Within 24 hours of commencement of therapy, the majority of patients were reported to show significant lessening of paresis, increased sense of well-being and improved motivation.

Similar but temporary improvement in neurological status was reported by Kofman et al.15 in their report of 15 cases of cerebral metastases from carcinoma of the breast treated with Prednisolone. They reported remarkable temporary improvement in 14 of these 15 patients. This was attributed to the anti-inflammatory effect on the cerebral edema surrounding the metastatic lesions, since these patients all had had previous adrenalectomy and the metastatic tumors themselves, therefore, probably were not hormone-dependent at this time, and also because a similar improvement occurred in 3 cases of cerebral metastases from bronchial carcinoma. Galicich et al.4,5 reported similar dramatic clinical improvement in cases of recurrent gliomata treated with large doses of Dexamethasone. In some of their patients, in addition to improvement in consciousness and reduction of other neurological deficits such as hemiparesis and papilledema, there was objective evidence of reduction of intracranial pressure with bulging decompressions becoming flat and soft, and in 2 patients, angiographic evidence of reduction in size of the expanding lesion. Säker and Rust22 also reported on the use of Prednisolone as an anti-inflammatory and anti-edema agent in patients with brain tumors, and recommended the combination of Prednisolone with Marsalid.

Gurdjian and Webster8 commented on the use of cortisone and Prednisolone in the treatment of severe head injuries. It was their impression that cortisone produced marked improvement in some of their deeply comatose patients, with the result that patients unconscious for several days as a result of head injuries but without intracranial mass lesions seemed to become ambulatory more quickly when treated with cortisone than similar patients who did not receive cortisone.

Smith and Ross23 studied the effect of steroids on meningeal inflammation caused by injection of small amounts of Pantopaque into the brains of rabbits and guinea pigs. They found that cortisone and Prednisolone given by mouth or parenterally were effective in preventing chronic adhesive arachnoiditis by inhibiting the production of