Evaluation of Corticosteroids in Treatment of Tuberculous Meningitis

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Ghosh, S., Seshadri, R., and Jain, K. C. (1971). *Archives of Disease in Childhood*, 46, 51. **Evaluation of corticosteroids in treatment of tuberculous meningitis.** 98 patients with tuberculous meningitis were studied with a view to assessing the value of steroids as an adjuvant to antitubercular drugs. The patients were divided into three groups irrespective of the clinical stage of the disease. One group received antitubercular drugs alone, the second oral prednisolone, and the third intrathecal steroids, in addition to the antitubercular drugs. There was no significant difference in the mortality rate in the different groups. Oral steroid treatment lowered the CSF protein more rapidly, but did not influence the outcome nor prevent the formation of spinal block.

Steroids have been used as an adjuvant in the treatment of tuberculous meningitis since 1953. Experimentally, steroids suppress certain aspects of the inflammatory response in tuberculosis (Ebert, 1952) and have been proposed as an adjuvant in the treatment of tuberculous meningitis. Steroids have been administered either orally, parenterally, or intrathecally. Reports on the therapeutic efficacy of steroids are conflicting, with only two attempts at a controlled study (Lepper and Spies, 1963; O'Toole *et al.*, 1969). This study was undertaken to assess the value of steroids, either oral or intrathecal, as an adjuvant in the treatment of tuberculous meningitis.

Material and Methods

This study concerns 98 patients under the age of 12 years admitted in Safdarjang Hospital, New Delhi, between 1966 and 1969. The following investigations were done to confirm the diagnosis: tuberculin test with PPD; chest and skull x-rays; CSF biochemistry, cellular reaction, direct smear for acid-fast bacilli (AFB) and culture using Krischner media and guinea-pig inoculation; laryngeal swab for AFB; and gastric lavage for AFB.

The CSF examination was done on admission, every fortnight till it became normal, and thereafter every month. The disease was classified into three stages according to the M.R.C. (U.K.) classification at the time of admission. Stage I: the prodromal stage of irritability (27 patients); Stage II: the transitional stage of increased intracranial pressure and meningeal symptoms

(49 patients); and Stage III paralysis and coma (22 patients). The patients were divided into three groups for the purpose of treatment, irrespective of the clinical stage of the disease. *Group I:* (a) intramuscular streptomycin sulphate (40 mg/kg per day); (b) isonicotinic acid hydrazide (20 mg/kg per day orally); (c) after discontinuation of the streptomycin, thiacetazone 3.5 mg/kg per day orally.

Group II: (a) antitubercular treatment as in Group I above; (b) prednisolone (2 mg/kg per day orally for six weeks).

Group III: (a) antitubercular treatment as in Group I; (b) hydrocortisone intrathecally (25 mg/kg per day for 6 days).

Table I shows the distribution of patients according to the treatment groups, with the mortality.

When first seen, of the 98 cases, 50 had convulsions, 31 generalized spasticity. Other neurological complications are detailed in Table II.

TABLE I
Treatment Group and Mortality

Groups	No. of Patients	Died	%
I	36	14	38.8
II	42	12	28.5
III	20	11	55.0
Total	98	37	37.8

Results

Of 98 patients, 37 died (14 of Group I, 12 of Group II, and 11 of Group III). 22 patients died

FIG.—The response of CSF protein to treatment in various groups. The protein level fell more rapidly in the patients treated with oral steroids.

of steroids to the treatment of tuberculous meningitis seemed to have significantly reduced the mortality from tuberculous meningitis. She had compared this result with that of 117 patients treated in 1962, of whom only 38 patients had received steroids. Ashby and Grant (1955), Bulkeley (1953), and Voljavec and Corpe (1960) reported similar improved survival in steroid treated patients, attributing this to the reduction in the meningeal inflammation and to a decrease in the reduction of spinal block. Lepper and Spies (1963) on the other hand were unable to detect any effect after 14 days of steroid therapy in 19 patients compared with controls. O'Toole *et al.* (1969), in their double-blind study of 23 patients with dexamethasone as an adjunct to the treatment in 11 patients, concluded that despite a striking influence of dexamethasone on the CSF, an improved survival was related to an amelioration of cerebral oedema. They felt that the administration of steroids in high doses was clearly indicated in the treatment of cerebral oedema associated with tuberculous meningitis. Other investigators have modified the initial enthusiasm for the routine use of the steroid therapy, reserving them for use in desperate situations (Wasz-Höckert, 1962). Toole and McCall (1969) postulated that dehydrating agents might be as use-

ful as steroids in treating the secondary effects of inflammation of the meninges and the brain.

The mortality rate in the present series is 38% and there is no significant difference in Groups I and II statistically ($\chi^2 = 0.93$). The higher mortality in Group III appears to be due to more patients in Stage III being included in this series. The mortality rates in Stage III in Group II and III are about the same. Again there is no significant difference between the deaths that occurred within one week in the various groups (8 of the 36 in Group I; 6 of the 42 in Group II; 8 of the 20 in Group III). Thus steroids failed to alter the outcome during the acute phase.

In terms of recovery, patients in Group II showed a slightly increased recovery rate compared to Group I, but this was not statistically significant ($t = 0.2309$). As follow-up was achieved in only 5 patients of Group III, no comment can be made about the recovery rate.

That steroid treatment lowers the CSF protein level in this disorder (Chromis *et al.*, 1957; Johnson *et al.*, 1957; Shane and Riley, 1953) was confirmed. But whether this reduction in the protein decreases the incidence of spinal block has not been shown. In this study two patients developed spinal block during treatment with steroids (Group II) and the simultaneous administration of intrathecal steroid did not affect the course.

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