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## Intrathecal Hydrocortisone in the Treatment of Tuberculous Meningitis (Preliminary Report)

by

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### Abstract

*A trial on the treatment of tuberculous meningitis with intrathecal hydrocortisone, beside INH, PAS, and Streptomycin, performed at the Dr. Kariadi General Hospital in October 1972, is reported. Eighteen patients were treated, giving good results; 5.6% mortality were noted. A great number of complications of optic nerve atrophy (61.1%) were found and 22.2% with early atrophy recovered. The results are better compared with those of Choremis et al. (1957) who found a mortality of 13.7% among 29 patients with tuberculous meningitis treated in the same way, except P.A.S.*

## Introduction

Tuberculous meningitis is the most serious complication of primary tuberculosis, which has caused a great number of deaths (Boyd, 1956; Gunadi Santoso and Prajogo, 1968; Lincoln, 1947; Lincoln and Sewell, 1963; Lincoln and Sifontes, 1953; Miller, 1963).

The mortality rate can be reduced by intrathecal hydrocortisone (Bulkeley, 1953; Choremis et al., 1957; Gosh et al., 1971; Roussel, 1972; Szabo et al., 1957). At the Dr. Kariadi General Hospital, Department of Child Health, Medical School, University of Diponegoro, clinical trials were performed to evaluate the effectiveness of intrathecal hydrocortisone against tuberculous meningitis, in addition to Streptomycin injected intramuscularly, Iso Nicotinic Hydrazide and Para Amino Salicylic acid orally.

## Material and methods

Included in this trial were all patients under 14 years of age admitted to the Department of Child Health, Dr. Kariadi General Hospital, in October 1972, with the diagnosis of tuberculous meningitis. The diagnosis was based on the clinical history, physical examination and cerebro-spinal fluid examination. The following examinations were done to confirm the diagnosis: Tuberculin test with alt tuberculin; chest and skull X-ray; cerebro-spinal fluid biochemistry and culture; gastric lavage; Levinson test and Tryptophan test.

According to Levinson (1951) the cerebro-spinal fluid of tuberculous meningitis was clear or opalescent; the cell count was 10 to 350 per ml., the glucose was less than 50 mg.% and the protein was increased (Boyd, 1956; Gunadi Santoso and Prajogo, 1968; Nelson, 1967; Lincoln and Sewell, 1963; Lincoln and Sifontes, 1953; Miller, 1963).

It was divided into 3 groups according to the following stages :

1. Stage I : The prodromal stage of irritability.
2. Stage II : The transitional stage of increased intra-cranial pressure and meningeal symptoms.
3. Stage III : The terminal stage of paralysis and coma (Nelson, 1967; Lincoln and Sewell, 1963; Udani et al., 1972).

The treatment given was :

1. Streptomycin: 50 mg/kg body weight per day intramuscularly, until 30 times or more, according to the patient's condition.
4. Hydrocortisone intrathecally: 10-15 mg per day for 10 days, then 10 mg twice weekly for 3 weeks.

Systemic Corticosteroid treatment was given in conjunction with the preceding treatment:

- 2 mg./kg. body-weight under the age of 3 years;
- 1.5 mg./kg. body-weight between the age of 3 and 8 years;

1 mg./kg. body-weight in older children.

This daily injection, intramuscular or intravenous, should be continued for 2 to 3 weeks (according to the general clinical improvement and the normalization of cerebro-spinal fluid). Then the dose was reduced by 5 mg every 15 days to reach a dose of 10 mg in older children and 5 mg in younger children.

Then the dose was gradually decreased by 1 mg every day until the treatment was stopped.

Evaluation of the cerebro-spinal fluid during the intrathecal treatment was done daily, particularly cells, glucose and protein levels. On admission roentgenograms of the chest and skull were made, and repeated after 30 days. Every patient was consulted to the Ophthalmologic and Neurologic Departments.

## Results

Eighteen patients were admitted, consisting of 11 boys and 7 girls; the average age was between 8 months and 14 years. All of the patients (77.7%) were under 5 years, most of them were 1 to 2 years old (38.8%). The youngest case was an 8-month-old boy and the oldest a 13-year and 9-month-old boy. Most of the patients were in a poor condition and their body-weight was below normal (55.5%). Fifty per cent of the tuberculin tests were positive.

According to the stage of the disease there were :

1. Stage I: 2 patients (11.1%)
2. Stage II : 6 patients (33.3%)
3. Stage III : 10 patients (55.5%)

Chest X-ray, revealed 66.8% pulmonary tuberculosis, 16.6% miliary tuberculosis, and 6.6% were normal. Protein and sugar values of the cerebro-spinal fluid were not rapidly restored to normal. Protein returned to normal in an average of 76.9 days. An average of 44.4 days was required for the abnormally low sugar to return to normal. The average hospitalization of the patients was 120.2 days. Three patients had gone home before the treatment was ended. One patient died within the sixth week of admission. The cause of death was aspiration pneumonia.

Complications :

- Neurological complications: Hemiparesis = 4  
Multiple palsies = 5  
Hydrocephalus = 0
- Ophthalmological complications: Optic atrophy = 11  
Third nerve atrophy = 1
- Ear complication: Slight hearing loss = 1  
Mental disorder was not examined.

## Discussion

Eighteen children suffering from tuberculous meningitis were treated with intrathecal hydrocortisone, in addition to the anti-tuberculous drugs (I.N.H., P.A.S., and Streptomycin). According to some reports, the mortality rate of tuberculous meningitis in Surabaya (1964-1966) was 53.6% (Gunadi Santoso and Prajogo, 1968) and at the Dr. Kariadi Hospital between

1969 - 1971 was 48.6%. Fifty-nine patients with tuberculous meningitis were studied by Ghosh et al. (1971) for 3 years.

Tahernia (1967) found 38 patients during 6 years.

We have found 61.1% boys and 38.9% girls in our study, but we have not read about any prevalence in boys in the literature (Boyd, 1956; Gunadi Santoso and Prajogo, 1968; Nelson, 1967; Lincoln, 1947; Lincoln, and Sifontes, 1953; Miller, 1963). 77.7% of the patients were under 5 years, most of them (38.9%) between 1 to 2 years, the youngest was 8 months. One case under 4 months was found by Lincoln and Sewell (1963). Half of the patients (55.5%) were in a bad condition.

Most of them were admitted during the terminal stage.

Clinical experiences in Surabaya (1964-1966) indicated that 89.7% of the patients were in a bad condition (Gunadi Santoso and Prajogo, 1968). In our study the tuberculous meningitis patients had tuberculosis of the lung (66.8%), and miliary tuberculosis (16.6%). According to Lincoln (1963) most of the tuberculous meningitis patients had tuberculosis of the lung (94%). Nelson (1967) found miliary tuberculosis in 25-30% of his cases. Tuberculous meningitis at the St. Sophie Hospital during a period of 2 years, caused a mortality rate of (Choremis et al., 1957):

16.6% : in cases treated with Streptomycin and INH.

17.2% : in cases where cortisone intramuscularly was added to the above treatment.

13.7% : in cases where cortisone was changed with hydrocortisone intrathecally.

The mortality rate was 6.7%. A similar study was done by Ghosh et al. (1971) between 1966-1969, at the Safsarjang Hospital, New Delhi where 20 children received INH, Streptomycin intramuscularly and hydrocortisone intrathecally; the mortality rate was 55.0%.

Our patients died in the terminal stage; Ghosh et al. (1971) had 3 patients in the 2nd stage and 8 patients in 3rd stage. Choremis et al. (1957) had also 4 patients who died in the third stage. The most frequent sequelae found was optic nerve atrophy (61.1%), of these 22.2% with early atrophy which became normal and 38.9% with irreversible atrophy. Ghosh et al. (1971) had 4 patients (20%) with optic nerve atrophy. Many patients with tetraparesis recovered with physio-therapy.

Kapur (1969) in a study of 103 patients (98 of which were treated with steroids) concluded that the addition of steroids to the treatment of tuberculous meningitis seemed to have significantly reduced the mortality of tuberculous meningitis. She compared this result with 117 patients treated in 1962, of whom only 38 patients had received steroids. Ashby and Grant (1955), Bulkeley (1953), reported a similar improved survival in steroid treated pa-

tients, attributing this to a reduction of the 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. In their double-blind study of 23 patients with dexamethasone as an adjunct to the treatment in 11 patients, he concluded that despite a striking influence of dexamethasone on the cerebro-spinal fluid, an improved survival was related to an amelioration of cerebral oedema. Steroid treatment could lower the cerebro-spinal

fluid protein level in this disorder (Choremis et al., 1957; Johnson et al., 1957; Shane and Riley, 1953).

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