

3. Title:

Mannitol - Its Use in Treating Increased Spinal Fluid Pressure in Patients with Malaria and Nervous System Symptoms.

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Reporting Period: 10 January 1966 - 31 March 1966

Objective: This study is designed to compare the effects of mannitol and intravenous quinine in the treatment of increased cerebrospinal fluid pressure in malaria.

Description:

Introduction: Increased spinal fluid pressure occurs in patients who have malaria with nervous system symptoms². Intravenous quinine has been the usual treatment in these cases. The patients' parasitemias are quickly reduced but often neurological symptoms persist. If increased intracranial pressure is indeed responsible for increased morbidity and mortality in "cerebral malaria," then a treatment regimen which combines both treatment of increased intracranial pressure and the parasitemia would be important.

Since 1965, hypertonic solutions have been used to lower cerebro-spinal fluid pressure and decrease brain mass. Recently mannitol has been shown to reduce cerebro-spinal fluid pressure from 30 to 60 percent in two to four hours (Wise and Chater 1962).

Method: All adult patients admitted to the Prabuddhabat Hospital who have a blood smear positive for malaria are seen by the investigators. Those with cerebral symptoms are given a complete history and physical examination. A lumbar puncture is done and if the spinal fluid pressure is over 180 mm CSF the patient is admitted to the study. (All lumbar punctures are done with a 20 g. needle with the patient reclining on his side. After the needle is inserted into the subarachnoid space the patient's legs are extended. No reading is considered valid until complete relaxation is obtained.) No more than 2 ml. of fluid are removed for cells, protein, and sugar determinations.

Treatment: Treatment is given to patients according to one of the two following methods:

A.

1. 0.5 gm. of mannitol (20% solution) per Kilogram over 20 minutes (Weighing of the patient is often impossible. Sixty kilos is taken as the average adult weight at Prabuddhabat Hospital).
2. 10 grams of quinine every eight hours as long as indicated.

B.

1. Placebo (5% Dextrose in saline) equivalent to mannitol.
2. 10 grams of quinine every eight hours as above.

Notes

1. Physician, Prabuddhabat Hospital, Saraburi Province.
2. Chipman, M., Cadigan, F., Benjapong, W., "Malaria and the Nervous System. Clinical Experience with a Hospital Population in an Endemic Area in Thailand."

The bottles of mannitol and placebo are so prepared that the physician administering the treatment will not know what they contain.

During and following treatment, urinary outputs and specific gravities are measured and recorded hourly. Four hours after the start of treatment, the lumbar puncture is repeated and spinal fluid pressure is again carefully measured. No fluid is removed. If the tap is normal no further mannitol is given. If the spinal fluid pressure is not 180 mm CSF or below the mannitol or placebo treatment is repeated and a third lumbar puncture is repeated and a third lumbar puncture is done four hours after the second treatment. If the spinal fluid pressure is still not reduced after eight hours no further taps are done. Daily determinations of serum electrolytes are done on each patient.

Results: To date three patients have been studied. One of these had a subarachnoid hemorrhage which may have been due to a ruptured aneurysm. This patient has been excluded from this study.

The two remaining patients were both female and both had seizures. Patient 276 (age 30) had an initial spinal fluid pressure of 220 mm CSF. The patient diuresed when treated with mannitol. When she was retapped four hours after the start of treatment her pressure was 130 mm CSF. Patient 278 (age 23) had an opening spinal fluid pressure of 230 mm CSF. She was treated with mannitol. She had diuresis but four hours after the start of treatment the cerebrospinal fluid pressure was 226 mm CSF. She was again treated with mannitol, again diuresed and at the end of eight hours the spinal fluid pressure was 160 mm CSF.

No conclusion can at this time be drawn from these two cases. It is anticipated that this study will continue for at least one year.