

The Management of Coma in Falciparum Malaria

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OBJECTIVE: To establish the optimum management of coma in falciparum malaria.

BACKGROUND: Cerebral malaria is common in falciparum malaria and usually occurs in patients with high parasite counts; however, occasionally, patients present in coma with low parasite counts. Coma is the most serious manifestation of cerebral malaria in adults. Epilepsy is also a grave complication especially in small children. Other forms of cerebral malaria include delirium, confusional states and stupor. Often the patients enter hospital seriously ill and stuporous and lapse into coma soon afterwards or after therapy. Often the patients appear to lapse into coma or to come out of coma following minimal therapy. In some patients, therefore, the cerebral malaria is short-lived, whereas in others coma is deep and irreversible.

Quinine is the most effective drug in therapy. Corticosteroids were first recommended in 1967 but have never been subjected to a controlled clinical trial. The anticoagulant heparin has been recommended because some investigators consider disseminated intravascular coagulation to be a common complication of severe falciparum malaria. The plasma volume expander, Dextran, has also been recommended for falciparum coma as has the osmotic diuretic, Mannitol.

DESCRIPTION: Between January 1973 and July 1974 at Trad Provincial Hospital about 40 patients with the various types of cerebral malaria were treated. Further experience has been gained at the Prachinburi Hospital since the project was initiated there in February 1975. The clinical evaluation of the patients has consisted of close observation by the study physicians. Detailed clinical notes have been maintained on specific study sheets. The rate of intravenous therapy has been monitored at regular intervals, usually every 30 minutes. The state of consciousness, pulse rate, and blood pressure were also regularly monitored when indicated. Complete physical examination was regularly performed. If bladder distension occurred, a urethral catheter was passed and the bladder continuously drained into a measured bottle. The rate of urine production was recorded at frequent intervals. Laboratory investigations included a parasite count at least twice daily and a daily hematocrit. Urinalysis was performed on admission and whenever subsequently indicated. Serum was taken for biochemical analysis on admission and at regular intervals thereafter. Relevant investigations were performed a few weeks later at the SEATO laboratory in Bangkok and usually comprised a total serum bilirubin, serum creatinine and serum glutamic oxaloacetic transaminase (SGOT). A serum alkaline phosphatase was also occasionally determined. Serial serum quinine concentrations were determined on most patients. The technique consisted of extraction of the quinine with benzene followed by sulfuric acid and estimation of the fluorescence of the quinine in a spectrofluorophotometer.

PROGRESS: Three case histories are given to illustrate the successful management of cerebral malaria.

Case 1: A 42 year old man (a tree worker) was brought to Trad Hospital at 2000 hours on 11 May 1974. He had been in coma since 1700 hours. The history was of vomiting and anorexia for three days. He consulted a physician in Trad city at midday on the day of admission and a 500 ml unit of intravenous fluid was administered as well as one tablet orally. The patient went home and then lapsed

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into coma. He gave a history of malaria two years previously. His temperature was 38.5°C and pulse rate 120. The parasite count was 62,000 per cu.mm. He was in coma but reacted to pain. He was sweating profusely. The obvious question arose as to whether the patient had received quinine in the private clinic earlier in the day. For this reason he was given a half dose of quinine (250 mg) in 500 ml normal saline, infused over five hours. The next morning, 10 hours later, he was awake. A half-dose of quinine was given orally (270 mg) and eight hours later a full dose (540 mg). A full dose of Fansidar (three tablets) was administered in the evening. The patient made a satisfactory recovery and his parasitemia cleared in 83 hours.

His sera were analyzed two weeks later. Surprisingly, the serum was free of quinine on admission. On the morning after receiving the half-dose of intravenous quinine his serum quinine level was 4.2 mg. per L.

Case 2: A 21 year old farmer was admitted in a stuporous condition. His parasite count was 250,000 per cu.mm. but his vital signs were satisfactory. We decided to treat him with intravenous quinine in the standard 500 mg doses in 500 ml normal saline—at 12 hour intervals. The first dose was given in two hours. The serum quinine was 9.0 mg per L at the end of the infusion (Figure 1) and had decreased to 3.6 mg. per L at hour 17 when the second infusion was commenced. This was infused in three hours and raised the serum quinine to 9.3 mg per L. The third infusion was begun at hour 24 for four hours and increased the serum quinine to 10.3 mg per L. The final infusion was begun at hour 38 and infused in five hours. The serum quinine then peaked at 11.0 mg per L. No further quinine was given until hour 71 when three doses of oral quinine were administered over a 15 hour interval. A dose of Fansidar (three tablets) was administered at hour 98. The patient's parasitemia remained high until hour 38 when a steady decrease began. The patient became completely conscious about hour 43. Another notable feature of this case was that the patient had evidence of a bleeding disorder on admission. He had a large amount of recently dried blood in his nostrils and bleeding about venipuncture sites. These signs rapidly cleared with the successful management of his disease.

Case 3: This patient represented a very successful therapeutic result because he appeared moribund on admission. He was in deep coma and flaccid. His respiratory rate was increased at 40 per minute and his heart rate was 130 per minute. There was a loud systolic murmur. There was bleeding about venipuncture sites. The Thai physician gave the relatives a very serious prognosis. The initial parasite count was about 95,000 per cu.mm. The patient's progress can be seen in Figure 2. Doses of intravenous quinine were administered at 0, 16 and 23 hours following admission. The patient's consciousness returned towards the end of the third infusion. He received a dose of oral quinine on hour 20 and another dose of intravenous quinine at hour 49. A dose of Fansidar (three tablets) was administered at hour 62. During the first 50 hours the serum quinine concentration remained in the 4-12 mg per L range. The patient made an uneventful recovery.

DISCUSSION: A system for managing severe falciparum malaria has been established by our investigations. Most patients recover with quinine therapy alone but it is important to avoid overdosage. Twenty milligrams per kilogram daily is the maximum safe dose and this is administered intravenously not more frequently than every 12 hours. As discussed elsewhere, fluid input should be restricted to prevent pulmonary edema. Corticosteroid therapy has not been discussed in this paper and its value is difficult to determine.