
ORIGINAL ARTICLE

Heparin in the Treatment of Cerebral Malaria

by

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Abstract

Cerebral episodes in malaria are considered to be due to thrombin in the cerebral capillaries. Heparin is beneficial in arterial thrombosis, not only on account of its anticoagulating property, but also by virtue of its slight vasodilating effect which promotes collateral circulation. Based on these, a study was undertaken with the objective of finding out the effect of heparin in the treatment of cerebral malaria.

Thirty-three cases admitted to the Child Health Department, Medical School, Sam Ratulangi University/Gunung Wenang Hospital, Manado from July 1, 1973 until October 31, 1977 were divided into 2 groups: a study group receiving 300 u/kg bw/day of heparin either intramuscularly or intravenously for 3 consecutive days along with antimalarial drugs; and a control group receiving only antimalarial drugs.

Thirteen out of 17 patients of the control group succumbed (76.5%) as compared to 2 out of 16 patients of the heparin group (12.5%). This study shows that heparin seems to be of real benefit in the treatment of cerebral malaria in children, since not only the mortality rate reduced significantly but the general condition improved rapidly.

Introduction

Malaria constitutes one of main diseases in children. Repeated attacks may lead to severe anemia, wasting, stunted growth, enlargement of the spleen and nutritional disturbances. One of the most serious complications, which is almost always caused by *Plasmodium falciparum* infection, is cerebral malaria. In children the clinical manifestation can be very acute and rarely present a classical picture.

The cerebral episode is thought to be due to cerebral intravascular thrombosis. Heparin, a well-known antithrombotic agent, has been considered effective in the prevention of capillary sludging and thrombosis (Smitskamp and Wolthuis, 1971).

The purpose of this study is to find out whether or not heparin is really useful in lowering the mortality of cerebral malaria in children.

Materials and methods

All patients admitted to the Child Health Department, Medical School, Sam Ratulangi University/Gunung Wening Hospital, Manado from July 1, 1973 until October 31, 1977 with the diagnosis of cerebral malaria, were subjected to this study.

The diagnosis was based on the following criteria :

1. Hyperpyrexia.
2. Cerebral manifestations with or without convulsion, e.g. :

- a. disturbances of mental alertness :
apathy to coma, excitement
- b. behavioral changes or psychotic syndrome
- c. convulsive seizures.

3. Negative cerebrospinal findings, e.g. : negative Nonne/Pandy reaction, normal cell count, normal glucose and protein content.

Patients showing abnormal cerebrospinal fluid findings were excluded from the study. Those fulfilling the above mentioned criteria were divided into 2 groups by labeling with a number according to the sequence of admission, an odd number being the control group and an even number the study or heparin treated group. There were totally 33 patients, 17 of them belonged to the control and 16 to the study group. Each group was given the same treatment and management except for the additional heparin in the study group. Details of this procedure has been previously described (Munir et al., 1976).

Results

Thirteen out of 17 patients of the control group succumbed as compared to 2 out of 16 of the heparin group. This gives a mortality rate of 76.5% and 12.5% respectively (Table 1). One of the heparin group patients' death was due to severe anemia before blood transfusion could be given. And the other one was moribund when admitted.

TABLE 1: *Mortality rates of the control and heparin groups.*

G r o u p	No. of cases	Died	Mortality
Control	17	13	76.5%
Heparin	16	2	12.5%

Discussion

Sensorium disturbances and convulsions were the main features which brought our patients to the hospital. All showed mental disturbances ranging from lethargy to coma. Only a few showed excitement. Nineteen patients showed convulsive disorders either prior to admission or during hospitalization.

The pathogenesis of cerebral episodes has been described by Maeraith (1948) who considered anoxia to be of primary importance. This primarily effects the endothelial lining of capillaries and leads to increased permeability of the capillary wall and cell diapedesis. The fluid loss produces intravascular concentration of cells, agglutination and sludging which in turn lead to stasis and anoxia. A vicious cycle thus occurs. Sludging and thrombosis are found especially in the cerebral capillaries (Smitskamp and Wolthuis, 1971). This is in accordance with the opinion of Devakul et al., (1966), that intravascular coagulation may be important in producing intravascular changes in *Plasmodium falciparum* infection.

Smitskamp and Wolthuis (1971) believed that the benefit of heparin in preventing occlusion of cerebral capillaries by anticoagulation outweighs the risk of haemorrhage. This has also been stated by Devakul et al., (1966) and later suggested by Borochoviz et al., (1970) and Jaroonsama (1972). On the other hand, Howard and Collins (1972), based on their result in the absence of a controlled trial in man, stated that heparin therapy must be regarded as experimental in human malaria and potentially harmful. Adverse reactions by heparin in our study have not been encountered.

One of the causes of the death from cerebral malaria is severe anemia and delay in giving blood transfusion (Munir et al., 1976). This was the case in one of our heparin group patients.

The significant difference in mortality ($p < 0.0001$) between the 2 groups in this study revealed that heparin proved to be useful in lowering the mortality of cerebral malaria in children. Beside that the patient's general condition also rapidly improved.

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