

Treatment of onyalai with prednisolone, intravenous gammaglobulin and ascorbic acid

A prospective clinical trial

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Summary

Forty-two patients in the acute phase of onyalai were admitted to hospital and randomly divided into three groups of 14 to receive prednisolone 3 mg/kg/d for 1 week, intravenous gammaglobulin 100 mg/kg on 2 successive days, or ascorbic acid 1000 mg 3 times a day for 1 week. The groups were comparable with regard to sex and age distribution, initial platelet counts and initial haemoglobin values. No statistical difference was observed between the three treatment groups with regard to changes in the platelet counts during the period of observation. One patient died from haemorrhagic shock. The low mortality rate in this series suggests that admission to hospital and early correction of blood loss are important factors in reducing the mortality rate associated with onyalai.

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the patient is in the acute phase of onyalai may cause a quick rise in the platelet count, but will not always prevent future recurrences and death.⁵ The intravenous administration of very high doses of gammaglobulin in patients with idiopathic thrombocytopenic purpura (ITP) may cause a transient rise in the platelet count.⁶⁻⁸ The infusion of fresh human plasma containing one-tenth of the quantity of gammaglobulin used by Imbach *et al.*⁶ caused a rise in the circulating platelet count in a number of adults with ITP.⁹

Patients and methods

Forty-two patients with onyalai who presented at Rundu State Hospital in Kavango, SWA/Namibia, between December 1982 and September 1983 were sequentially allocated to receive one of the following treatment schedules after informed consent was obtained: schedule A — oral prednisolone 3 mg/kg/d administered in three divided doses for a period of 7 days, followed by the intramuscular injection of 40 IU corticotrophin (Acthar Gel; Armour (Berk)); schedule B — gammaglobulin (Gamma Veinine; Hoechst) 100 mg/kg administered intravenously in a saline drip on day 1 and day 2 after admission; schedule C — oral ascorbic acid 1000 mg 3 times a day for 7 days. All the patients were observed in hospital for a minimum period of 21 days. A blood transfusion was administered whenever the haemoglobin level dropped below 10 g/dl.

The criteria for the diagnosis of onyalai were the presence of haemorrhagic bullae in the buccal cavity, no clinical signs of any other disease, platelet count $< 50 \times 10^9/l$ and the absence of abnormal cells on the peripheral blood film.

Venous blood was obtained on admission and on days 8, 15 and 22 and tested with a Coulter Counter Model DN and a Coulter Thrombocounter C. Giemsa stains of the peripheral blood and a thick smear were examined for abnormal cells and malaria parasites. The urine of every patient was tested for the presence of protein and blood, and examined for bilharzia.

All the patients had haemorrhagic bullae. The presence of petechiae, ecchymoses, epistaxis, melaena, haematemesis, urogenital bleeding and the total duration of haemorrhage in days were recorded for each patient.

Results

The distribution of sex, age and weight in the three groups is presented in Table I. The clinical findings on admission to hospital are presented in Table II. The urine of 3 patients with haematuria contained ova of *Schistosoma haematobium*.

A history of a previous attack of onyalai was obtained in 6 patients in group A, 5 patients in group B and 3 patients in group C. The mean duration of bleeding was 8,8 days (range 2 - 31 days) for group A, 6,2 days (range 1 - 19 days) for group B and 5,1 days (range 1 - 10 days) for group C. A blood

The objective of this prospective therapeutic trial was to compare the short-term effects of prednisolone, intravenous gammaglobulin and placebo (ascorbic acid) on the platelet count in patients in the acute phase of onyalai. Onyalai is an acquired form of chronic immune thrombocytopenia which occurs mainly in the Black population of southern Africa.^{1,2} Many patients experience recurrent episodes of severe bleeding heralded by the appearance of haemorrhagic bullae in the mucous membranes of the mouth. Approximately 10% of patients recorded in the literature died from haemorrhagic shock or cerebral haemorrhage within days of the onset of symptoms.²

Treatment with corticosteroids at a dose of 2 mg/kg/d did not cause a rise in the platelet count in the first days after the onset of symptoms.^{2,3} Ascorbic acid deficiency does not play a role in the disease.⁴ Cerebral haemorrhage may occur despite transfusion with fresh blood.² A splenectomy performed while

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TABLE I. ONYALAI TREATMENT GROUPS — SEX, AGE AND WEIGHT DISTRIBUTION

| | Schedule | | |
|------------------|----------|---------|---------|
| | A | B | C |
| Male : female | 7 : 7 | 7 : 7 | 7 : 7 |
| Mean age (yrs) | 30,2 | 21,6 | 19,6 |
| Range | 2 - 70 | 2 - 67 | 1 - 55 |
| Mean weight (kg) | 46,1 | 41,6 | 35,8 |
| Range | 13 - 70 | 13 - 80 | 11 - 59 |

TABLE II. CLINICAL DATA ON ADMISSION

| | Schedule | | | Total |
|--------------------------|----------|----|----|-------|
| | A | B | C | |
| Haemorrhagic bullae | 14 | 14 | 14 | 42 |
| Petechiae | 9 | 9 | 10 | 28 |
| Epistaxis | 7 | 7 | 5 | 19 |
| Ecchymoses | 4 | 2 | 2 | 8 |
| Urogenital bleeding | 2 | 4 | 0 | 6 |
| Haematemesis/ melaena | 0 | 3 | 2 | 5 |

TABLE III. MEAN HAEMOGLOBIN AND PLATELET VALUES (INTERQUARTILE RANGES GIVEN IN BRACKETS)

| | Schedule | | |
|--|------------|------------|------------|
| | A | B | C |
| Haemoglobin concentration (g/dl) on day 1 | 10,7 (3,8) | 10,6 (8,2) | 10,1 (1,9) |
| Platelet count (x 10 ⁹ /l) | | | |
| Day 1 | 35 (13) | 33 (17) | 36 (11) |
| Day 8 | 138 (175) | 144 (206) | 101 (107) |
| Day 15 | 138 (116) | 193 (247) | 203 (207) |
| Day 22 | 134 (101) | 175 (211) | 176 (155) |

transfusion was necessary in 5 patients in group A, 7 patients in group B and 4 patients in group C. The mean haemoglobin values on day 1 (admission) and the platelet counts on days 1, 8, 15 and 22 are presented in Table III.

The males and females in each group were comparable in respect of platelet and haemoglobin observations according to the Generalized Friedman Test. The data on haemoglobin concentration and platelet count for the three groups for the whole period of observation were then subjected to the multi-

variate multisample median test. No significant differences between the three groups were present (haemoglobin concentration $P > 0,25$, platelet count $P > 0,05$).

A patient in group A died on day 15 from haemorrhagic shock. A patient in group B absconded on day 15 and the blood specimen collected on day 22 from a patient in group C was lost.

Discussion

The short-term rise in the platelet count in two groups of 14 patients treated with prednisolone 3 mg/kg/d for 1 week or intravenous gammaglobulin 100 mg/kg on 2 successive days did not differ statistically from each other or from that in another group of 14 patients who had been treated with ascorbic acid 1000 mg 3 times daily for 1 week as a placebo. Fortunately, cerebral haemorrhage was not encountered among this series of 42 patients. The clinical and laboratory findings were in keeping with those reported by others.²⁻⁴ The very low mortality rate in this series (which might have been nil if the patient who died had been resuscitated more actively) could only be explained by the beneficial effects of hospitalization during the acute haemorrhagic phase of onyalaï and the early correction of blood loss.

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