Successful co-artemether (artemether-lumefantrine) clearance of falciparum malaria in a patient with severe cholera in Mozambique

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Received 16 June 2003; received in revised form 2 September 2003; accepted 3 September 2003

KEYWORDS
Cholera; Co-artemether; Falciparum malaria; Artemether

Summary
Background. Both falciparum malaria and cholera occur in Mozambique and other resource poor African countries. We report successful parasite clearance by oral co-artemether of coincidental falciparum malaria in a patient suffering severe cholera.

Methods. A case report.

Results. Parasite clearance was observed at day 3.

Conclusions. Oral artemether is sufficiently absorbed in the face of co-existent severe cholera to effect parasitological clearance of P. falciparum. This may be of relevance in resource poor tropical settings when a malaria patient presents with a simultaneous secretory diarrhoea, and a limited drug choice is available.

Introduction

Falciparum malaria is a problem of massive proportion in tropical developing countries, causing approximately one million deaths every year. Ninety per cent of these deaths occur in Africa, and malaria is responsible for approximately 10% of the continent’s total disease burden.1 The emergence of drug resistance has led to the increasing use of newer agents such as the artemesinins for treatment, and this group of drugs is being increasingly deployed in Africa. Additionally, many malaria endemic African countries are prone to cholera outbreaks. Mozambique provides a good example of this, officially reporting a total of 4124 cases of cholera, which included a total of 31 deaths, in Maputo province for the period January 1st to June 15th 2003.2 Treatment of malaria and cholera in Africa is frequently undertaken in resource poor settings, and it would be useful to know whether cholera, and by implication secretory diarrhoea, interferes with the absorption of artemisinins.

Case report

The subject, a 67 kg 32-year-old Negroid Mozambican male labourer presented on 8th March 2003 in Maputo, with a one day history of physical weakness, vomiting, profuse watery diarrhoea with a ‘rice water’ appearance, and marked abdominal colic. On examination, the patient appeared ill and...
was noted to be severely dehydrated with decreased skin turgor, dry mucus membranes, and sunken eyes. He was unable to walk unaided, requiring support. He was apyrexial and had a regular heart rate of 72 beats per minute; supine blood pressure was 90/60 mm Hg. The abdomen was noted to be soft with tenderness in the left upper quadrant, with the spleen palpable 1 cm beyond the costal margin. Auscultation of the abdomen revealed markedly increased and very active bowel sounds. Further physical examination revealed no positive or other contributory findings.

Immediate investigation revealed the following:

1. Capillary haemoglobin of 13.5 g/dl (Omron BMS Portable Haemoglobinometer; Model 10-101, USA)
2. Blood glucose of 5.1 mmol/l (Lifescan SureStep, Johnson & Johnson, USA)
3. Rapid stool test for cholera antigen positive (Kat-Quick, Kat Medical Pty Ltd, South Africa)
4. Giemsa stained peripheral blood smear positive for falciparum malaria with <0.1% parasitaemia. Ring forms were observed.

A diagnosis of severe cholera accompanied by falciparum malaria was made. Intravenous fluid and electrolyte replacement was instituted, and oral co-artemether administered (six doses over three days), as facilities for parenteral antimalarial therapy were not available. A single dose of hyoscine (20 mg) was administered intramuscularly for relief of abdominal cramps. The patient was admitted and discharged upon cessation of his diarrhoea and completion of rehydration 3 days later. A follow up blood smear on 10th March 2003, on day three of his illness was negative for malaria, and as the patient was clinically well he was returned to duty (see Table 1).

Discussion

The patient’s lifelong residence in a malaria endemic area would have endowed him with a degree of premunition, classifying him as ‘semi-immune’ with respect to falciparum malaria. The lack of pyrexia and the low level of the parasitaemia led to the conclusion that the malaria finding was coincidental in this patient. What we believe to be of interest is that clearance of the parasitaemia indicates that co-artemether, or at least artemether, was absorbed from the gastrointestinal tract despite simultaneous severe cholera.

The importance of ingesting co-artemether with food has been emphasised, as this increases the bioavailability of both the artemether and lumefantrine component. It is known that artemether bioavailability doubles when ingested with food, and it is the artemether component of co-artemether that is responsible for early parasite clearance. The course of artemether prescribed was the standard six dose three day regimen, and for at least the first day the patient had no solid food intake. Despite this, the patient appears to have absorbed adequate artemether to give early clearance of his parasitaemia.

The importance of ingesting co-artemether with fatty food has also been emphasised, but this relates to the absorption of the lipid soluble lumefantrine component. The lumefantrine component of co-artemether is included for its long half-life, and is intended to mop up parasites not killed by the faster acting artemether component. The principal role of the lumefantrine is to prevent recrudescence, and not to effect early parasite clearance. As a 28 day smear was not taken, we are unable to state with confidence that a recrudescence of parasitaemia did not occur in this patient, but as the sole providers of medical care, symptomatic malaria would have been brought to our attention. Nevertheless, we cannot rule out a recrudescence of asymptomatic parasitaemia, or indeed even reinfection. What is reasonable to conclude is that the artemether component of the co-artemether was absorbed, as evidenced by the parasite clearance in the day 3 smear.

We would not suggest that it is reasonable to extrapolate from this case that co-artemether or oral artemisinins be administered in similar circumstances to returned travellers, or to non-immune

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<tr>
<th>Date</th>
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<td>8 March 2003</td>
<td>Presentation 1 day history of weakness, vomiting, diarrhoea</td>
<td>Afebrile dehydrated HR 72, BP 90/60 mm Hg splenomegaly</td>
<td>Cholera Ag + Pf smear + , Hb 13.5 g/dl, blood glucose 5.1 mmol/l</td>
<td>Treated with IV fluid and co-artemether</td>
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<tr>
<td>10 March 2003</td>
<td>Follow up examination and smear</td>
<td>Full clinical recovery</td>
<td>Pf smear negative</td>
<td>Patient discharged</td>
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patients with falciparum malaria and cholera. This case report may be of relevance when treating semi-immunes in tropical regions, however. In such settings, coincidental diarrhoea is not uncommon, and our experience may lend some confidence to clinicians who either wish or are obliged to prescribe oral artemisinins to malaria patients with a secretory diarrhoea syndrome.

**Conclusion**

Despite severe simultaneous cholera, sufficient artemether was absorbed after oral administration to effect parasite clearance in a semi-immune adult with falciparum malaria. Oral artemisinins could be used to effect early parasite clearance in malaria patients simultaneously suffering secretory diarrhoea.

**References**