deaths due to unnatural causes declined from 23.0% in 1997 to 19.9% in 1999, and to 15.9% in 2001. Similarly, for females, out of a total of 128 618 deaths in the sample, the percentage of deaths due to these causes declined from 9.9% in 1997 to 8.1% in 1999, and to 5.5% in 2001.

Ordinarily this would have been cause for celebration, with the various role players identified and given due merit. Unfortunately these gains have been eroded by the rapid rise in natural deaths, with infectious and parasitic diseases accounting for 20.5% of all male deaths in the sample and 21.5% of all female deaths in the sample. In this case the decrease in unnatural deaths pales alongside the increase in natural deaths. This possibly explains the reason for the missed opportunity to celebrate.

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To the Editor: We report on our experience using co-artemether for the treatment of uncomplicated falciparum malaria in subjects exceeding 65 kg body weight.

Co-artemether (Coartem, Novartis), a fixed combination of 20 mg of artemether and 120 mg of lumefantrine, was registered in South Africa on 13 April 2000. The package insert lists as indication the treatment of uncomplicated falciparum malaria in patients up to 65 kg body weight, living in malaria-endemic areas. The insert further states, ‘There is no adequate experience in patients weighing over 65 kg’.

Expatriate workers were classified as non-immune, while Mozambican workers were classified as semi-immune.

The case definition adopted for semi-immune subjects was the presence of a febrile illness together with either a positive rapid antigen test or positive Giemsa-stained peripheral blood smear, where no other obvious cause of illness was apparent. For non-immune subjects the case definition was the presence of either a positive smear or rapid histidine-rich protein II (HRP-II) antigen test for Plasmodium falciparum, with no history...
of malaria in the preceding 4 weeks. Modified World Health Organisation criteria were applied to differentiate complicated from uncomplicated malaria. Informed consent was obtained from all subjects.

From 31 July 2001 to 15 November 2003 inclusive, at an occupational health facility in Mozambique, all adult expatriates who presented to us with uncomplicated falciparum malaria were treated with 6 doses of co-artemether over 3 days (days 0 - 2).

Mozambican adults presenting with uncomplicated falciparum malaria were treated in exactly the same way. Data for this group were available for the period 31 August 2001 to 28 August 2003 inclusive.

Non-immune subjects were assessed on days 0, 1 and 2, both clinically and by means of Giemsa-stained peripheral blood smears. Subjects who failed to improve were switched to quinine therapy and transferred to South Africa for further treatment. Semi-immune subjects were reviewed clinically and by means of Giemsa-stained peripheral blood smears on day 2.

All subjects had 24-hour access to medical attention in the event of need, and were encouraged to report any untoward developments or concerns.

Results

A total of 73 non-immune and 50 semi-immune patients were available for study. Study results including weight data and treatment failures are presented in Table I. All semi-immune patients responded clinically to treatment and were smear-negative on day 2. In the non-immune group 71 of 73 subjects (97.3%) were clinically well and smear-negative by day 2; 2 non-immune patients (2.7%), weighing 88 kg and 108 kg, required quinine rescue.

We were the sole providers of medical care and no subject returned after day 2 with signs or symptoms of malaria.

Discussion

The issues raised by the South African package insert for co-artemether are whether the drug is effective in the treatment of subjects not living in endemic areas, i.e. non-immune patients, and whether the drug is effective in those weighing more than 65 kg.

The term semi-immune is usually taken to mean more than simply ‘living in an endemic area’ and usually implies lifelong residence in a malarious area. Similarly, the term non-immune is usually taken to indicate those who have not grown up in and continued to remain in an endemic area. We have used these terms in the above sense in this communication, understanding the package insert to mean ‘semi-immune’ with its reference to ‘living in an endemic area’.

We have reported elsewhere on our successful deployment of co-artemether for the treatment of falciparum malaria in non-immune subjects. The results reported above, which add body weight data, should reassure those wishing to treat non-immune patients for uncomplicated falciparum malaria using co-artemether.

The addition of body weight data and the zero failure rate among semi-immune subjects should similarly reassure those wishing to treat semi-immune patients for uncomplicated falciparum malaria using co-artemether.

As the authors were the sole providers of medical care to the workforce any return of malaria symptoms, indicating either recrudescence or reinfection, would have come to our attention. The absence of such symptoms after parasite clearance on day 2 leads us to believe that neither semi-immune nor non-immune subjects experienced late co-artemether treatment failures.

Conclusions

The data presented point to co-artemether being effective in the treatment of uncomplicated falciparum malaria in subjects weighing more than 65 kg.

The data similarly point to co-artemether being effective in the treatment of uncomplicated falciparum malaria in subjects ‘not living in endemic areas’, i.e. in non-immune patients.

No funding was received for this work. The authors have been reimbursed for speaking and for conference attendance by Novartis, manufacturers of co-artemether. One of the authors is married to an individual formerly associated with co-artemether.

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Table I. Weight data and treatment failure rates for non-immune and semi-immune subjects treated with co-artemether for uncomplicated falciparum malaria

<table>
<thead>
<tr>
<th></th>
<th>Non-immune subjects</th>
<th>Semi-immune subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>73</td>
<td>50</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>81</td>
<td>71</td>
</tr>
<tr>
<td>Maximum weight (kg)</td>
<td>120</td>
<td>95</td>
</tr>
<tr>
<td>Standard deviation (kg)</td>
<td>11.66</td>
<td>5.99</td>
</tr>
<tr>
<td>Treatment failures (N (0%))</td>
<td>2 (2.7)*</td>
<td>0</td>
</tr>
</tbody>
</table>

*The weights of the 2 patients requiring quinine rescue were 88 kg and 108 kg.

3. Toovey S, Jamieson A. Co-artemether has been used in ambulatory treatment of falciparum malaria. BMJ 2002; 324: 1585.