Hemolytic anemia in patients receiving daily dapsone for the treatment of leprosy

PATRICIA DEPS, PATRÍCIA GUERRA, SOFIA NASSER & MARISA SIMON
Department of Social Medicine, Federal University of Espirito Santo, Vitória-ES, Brasil

Accepted for publication 03 October 2012

Summary
Introduction: Multidrug therapy for leprosy is currently done with dapsone, clofazimine and rifampicin. Dapsone is known to cause hemolytic anemia (HA) and this adverse event during MDT seems to be more frequent than reported. The aim of this report is to discuss and grade HA due to dapsone during MDT treatment for leprosy.
Methods: This is a retrospective study of 194 leprosy patients from a Leprosy Control Programme Unit in Vitória-ES, Brazil.
Results: HA was observed in 48 (24·7%) patients and occurred within the first 3 months in 51% of these. Mean hematocrit levels fell from 38·5 to 31·5 and hemoglobin from 12·8 to 10·3.
Conclusion: Dapsone used in the MDT regime for leprosy decreases the hematocrit and hemoglobin levels due to a low grade hemolysis, which can result in significant anemia.

Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae that leads to neurocutaneous damage in susceptible patients. In 1981 the World Health Organization officially recommended multidrug therapy (MDT) in a regimen that includes dapsone 100 mg/day for 12 months in multibacillary leprosy and 6 months in paucibacillary leprosy.1–2 Despite efforts to eliminate leprosy and the continued reduction in its prevalence, leprosy remains a public health problem in many countries in Africa, Asia and Latin America. Brazil still ranks second in the number of reported cases and first in the prevalence of the disease.3 Interruption of treatment is an obstacle to eradication.

Dapsone, a sulfone, inhibits bacterial synthesis of dihydrofolate acid. According to WHO, the drug is very safe in the dosage used in multidrug therapy for leprosy.2–4 The main side-effects usually described are allergic, such as itchy rash and exfoliative dermatitis, hemolytic anemia (HA), jaundice, methemoglobinemia and dapsone syndrome.5–7
Individuals deficient in erythrocytic glucose-6-phosphate dehydrogenase (G6PD) are at risk of severe and potentially fatal hemolysis due to dapsone. It has been reported that HA can lead to dapsone being stopped during leprosy treatment.

Methods

This study was carried out in a Leprosy Control Programme Unit of Maruípe, located in Vitoria, State of Espirito Santo, Brazil. Data from 194 patients who were treated between 1998 and 2003 were collected, and SPSS version 14 for Windows was used as a data base and for statistical analysis. Ethical approval was granted by the Ethical Committee in Research of the Biomedical Centre from the Espirito Santo Federal University, Vitoria, Brazil. Blood tests were performed in all 194 patients before start the MDT and repeated in 48 patients who presented one of the following symptoms: fatigue, weakness, shortness of breath, mild jaundice, enlarged spleen and abdominal discomfort. The diagnosis of HA was made in those patients who had hemoglobin (Hb) level of 12·7 g/dl or less for men and 11·5 g/dl or less for women, and/or a hematocrit (Htc) less than 42% for men and 36% for women. Definitions of side effects found in this study were described previously.

Results

The onset of symptoms related to HA occurred within the first three months in 51%, 4–6 months in 26·7%, 7–9 months in 13·3% and after the 10 month in 9% of the patients who developed HA.

The mean of the hemoglobin and hematocrit levels were higher before taking dapsone as compared to the means obtained after starting dapsone (Table 1).

There was a fall in the mean of hematocrit levels, which decreased from 38·5 to 31·5, as well as a decrease in hemoglobin levels from 12·8 to 10·3.

Discussion

Although there is a possibility that there could be other causes of anemia, a strong association between cause and effect was established taking into account the start of MDT and the onset of the clinical symptoms.

Alterations in hematocrit and hemoglobin might be more frequent than detected here, as blood tests were only requested for patients with symptoms and/or signs of anemia.

Table 1. Hemoglobin and hematocrit levels from 48 leprosy patients before and after starting dapsone

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb – BT</td>
<td>45</td>
<td>10·25</td>
<td>14·90</td>
<td>12·81</td>
<td>1·09</td>
</tr>
<tr>
<td>Hb – AT</td>
<td>48</td>
<td>8·14</td>
<td>11·60</td>
<td>10·29</td>
<td>0·84</td>
</tr>
<tr>
<td>Htc – BT</td>
<td>46</td>
<td>30·10</td>
<td>46·50</td>
<td>38·46</td>
<td>2·62</td>
</tr>
<tr>
<td>Htc – AT</td>
<td>48</td>
<td>24·57</td>
<td>35·43</td>
<td>31·46</td>
<td>3·22</td>
</tr>
</tbody>
</table>

Legend: Hb – hemoglobin; Htc – hematocrit; BT – before treatment with dapsone; AT – after treatment with dapsone.
In 1991, Byrd and Gelber reviewed the records of 100 patients and found a fall in haemoglobin concentration of 1 g/dl or more in 83% of patients, and the mean hemoglobin concentration of all patients decreased from 14·25 g/dl to 12·31 g/dl. The authors then emphasized that the decreasing of hemoglobin in patients taking MDT for leprosy is very frequent. However, the present study indicates when and by how much dapsone decreases the hematocrit and hemoglobin levels.

Unfortunately, haptoglobin, reticulocyte and G6PD levels and RBC morphology, which could help or confirm the diagnosis of HA, were not provided in this study. This study was retrospective and patients from the LCP had no access to those laboratory tests, unless they needed to be hospitalised.

Although, anaemia can be from many causes, in a poor population, the most important cause is iron deficiency due to monthly periods, malnutrition, intestinal parasites, gastrointestinal blood loss, chronic kidney diseases and other less common causes. In leprosy patients we must include in that list ENL, hepatitis or other liver disease. However, those patients described here underwent a detailed clinical examination prior to starting MDT, and presented no associated comorbidities or other condition which could explain the quick fall in their hematocrit and hemoglobin levels following the start of MDT.

The somewhat more profound reduction found in hematocrit and hemoglobin in this study as compared to Byrd et al., may be the result of the fact that the study only included patients with signs and symptoms which might suggest anemia, while Byrd et al. looked at all patients treated with DDS.

Acknowledgements

The authors are thankful to Dr R. H. Gelber from the University of California at San Francisco, CA, USA, for helpful suggestions to this manuscript; and Dr Rita de Cássia Birschner from the Health Unit of Maruipe for helping the authors accessing the patients records.

References