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HAEMATOLOGICAL ALTERATIONS IN LEPROSY PATIENTS TREATED WITH DAPSONE
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HAEMATOLOGICAL ALTERATIONS IN LEPROSY PATIENTS TREATED WITH DAPSONE

N.K.D. HALIM and E. OGBEIDE

ABSTRACT

Objective: **To evaluate the haemoglobin concentration (Hb); total white blood cell count (WBC), differential WBC count; platelet count and reticulocyte count in leprosy patients already treated with dapsone.**
Design: **A case-control study.**
Setting: **Specialist Hospital Ossiomo, which is a Leprosarium and Haematology laboratory, University of Benin Teaching Hospital (UBTH), Nigeria.**
Subjects: **Seventy six leprosy patients (forty males and thirty six females) age range 13-40 years on single dose dapsone.**
Results: **The haemoglobin concentration showed a marked decrease while the reticulocyte count was markedly elevated which was suggestive of haemolytic anaemia. There was also lymphocytosis in patients during pre and post dapsone therapy.**
Conclusion: **Leprosy patients on a dosage of 100mg dapsone, are prone to haemolytic anaemia. Leprosy patients should routinely have their Hb, WBC, platelet count and reticulocyte count determined, while on dapsone therapy in order to ascertain the presence of haemolysis.**

INTRODUCTION

Alteration in the Hb concentration, WBC (total and differential) platelet count, and reticulocyte, usually occurs in dapsone treated leprosy patients(1,2). Leprosy is a chronic granulomatus disease which occurs worldwide(3), and it is caused by *Mycobacterium leprae,* an acid and alcohol fast bacilli. There are three clinical types of leprosy. These are the lepromatous type, characterised by widespread involvement of organs such as the skin, the mucous membranes, the kidneys; the tuberculoid type characterised by skin and nervous system involvement and the borderline type, which has clinical manifestations bordering on both the lepromatous and the tuberculoid types.

The drug dapsone (4,4' diaminodiphenlyl sulphone) is used for the treatment of leprosy worldwide. Dapsone is an oxidative drug, which produces side effects of methaemoglobinaemia and haemolysis. The latter finding has been reported by Queiroz *et al*(3) and Byrd *et al*(4). The latter author has reported a decrease in haemoglobin concentration in leprosy patients on dapsone. Menezes *et al*(5) in India, reported a 60.7% incidence of anaemia in patients on dapsone therapy.

The Hb concentration, WBC (total and differential) platelet count and reticulocyte count tend to be altered in patients on dapsone therapy. This alteration has not been documented in this environment. The possible haematological alterations in leprosy patients are documented and discussed on this study.

MATERIALS AND METHODS

Seventy six leprosy patients (forty males and thirty six females) age range, 13-40 years, on single dose of dapsone 100 mg daily (sixty one patients) and dapsone 50 mg daily (fifteen patients), were studied over a six month period from February to July 1996, at the Specialist Hospital Ossiome, Edo State, Nigeria and at the Haematology laboratory of UBTH, Benin. Consent was obtained verbally from all patients before the tests were performed. The Hb concentration, WBC count, platelet count and reticulocyte were performed as described by Brown *et al*(6), within six hours of blood sample collection, at the Haematology laboratory UBTH, Benin City, Nigeria.

The Haematological tests were performed prior to commencement of dapsone therapy, on each patient (control) and six months after (study group) commencement of dapsone therapy.

Patients recruited were those commencing dapsone for the first time. All patients were recruited after the diagnosis of leprosy was confirmed by the second author(6), following history taking, physical examination and laboratory investigations, which revealed the presence of numerous acid fast smears. All patients recruited (study and control groups inclusive) were screened for Glucose-6-phosphate dehydrogenase (G-6-PDH) activity(7);

causes of anaemia such as sickle cell anaemia, hook worm infestation(8) and conditions associated with blood loss from the gastrointestinal tract.

Patients with low G-6-PDH activity, were excluded from the study because G-6-PDH deficiency increases the lysis of the red cell membrane by dapsone. It was also necessary to exclude anaemia and ensure adequate nutritional status of the patients. Patients with the genotype Hbss, were excluded from participating in the study, after subjecting their blood sample to electrophoresis using cellulose acetate strip at PH 8.6(9). The Hbss genotype is associated with haemolysis, which would alter the results significantly. Patients with intestinal blood loss as shown by a positive occult blood test(10) were also excluded.

Fifteen patients that developed malaria within one month of the study, were allowed to continue. However, due to difficulty in recruiting new patients and the probable adverse clinical manifestations when placed on 100mg dapsone, it was decided to place these patients on a lower dose of 50mg. This served the purpose of ascertaining the presence of dose-dependent haematological alternations, when comparisons were made between patients on 100mg dapsone and 50 mg dapsone for a duration of six months.

The study group patients were monitored during the six months study period, by routine clinical and laboratory checks at four weeks interval and patient had a history taken to exclude drugs that would significantly alter the haematological values. A physical examination was also performed to exclude signs of anaemia. Laboratory tests performed at each clinic visit included a PCV, WBC count, platelet count and reticulocyte count. Patients were also advised verbally on the need to ensure adequate nutrition and the need to report any untoward adverse reaction or symptoms during the period of the study. Subsequently, 3mls of blood was obtained from the ante-cubital vein, using a syringe and needle in all patients. Haematological tests performed on each blood sample, included the microhaematocrit tube method(6), for the PCV. The WBC count was performed using the method described by Brown *et al*(6). A 1 in 20 dilution of blood mixed with glacid acetic acid was used, after which a haemocytometer was used to view and count the WBC, under the microscope. The platelet count was also performed using the method described by Brown *et al*(6). A dilution of 1 in 100 of blood mixed with ammonium oxalate solution was made, after which a haemocytometer was used to view and count the platelets. The reticuloyte count was performed(6) by initially mixing the blood sample and methylene blue solution. Smears were made and viewed under the microscope.

The student's t-test was used to determine the statistical significance. P value of less than 0.05 was considered significant.

RESULTS

Table 1 shows the mean±standard deviation (SD), for Hb, WBC, percentage neutrophil count, percentage lymphocyte count, platelet count and reticulocyte count (pre-dapsone and post-dapsone therapy) in 161 patients on 100mg daily. The mean ± SD for Hb, was significantly lower (P<0.05), in patients post-dapsone therapy (10.1±0.9mg/dl) compared to pre-dapsone therapy (12.3 ± 0.6mg/dl). The mean ± SD for WBC count, was slightly higher in patients post-dapsone therapy, but was not significant (P>0.05). The values were 9010 ± 426cu.mm and 9561 ± 607 cu. mm for pre and post-dapsone therapy. The mean ± SD for differential neutrophil count was 27.2 ± 3.5% for pre-dapsone therapy, compared to 27.5 ± 3.8% for post-dapsone therapy (p>0.05).

Table 1

Mean ± SD for Hb, WBC, platelet, Reticulocyte count for patients on 100 mg dapsone

Parameter	Pre-dapsone group n=61	Post-dapsone group n=61	Significance (P-value)
Mean Hb (mg/dl)	12.3 ± 0.6	10.1 ± 0.9	P>0.05
Mean WBC (cu.mm)	9010 ± 607	9561 ± 607	P>0.05
Differential neutrophil count	27.2 ± 3.5	27.5 ± 3.8	P>0.05
Differential lymphocyte count	72.7 ± 4.6	72.1 ± 4.9	P>0.05
Differential eosinophil	Nil	Nil	
Mean platelet count (cu.mm)	103000± 52 000	103400 ± 56000	P<0.05
Mean reticulocyte count %	0.6 ± 0.1	7.3 ± 1.0	P<0.05

Table 2

Mean ± standard deviation for Hb, WBC count, platelet count and reticulocyte count in patients on dapsone 50mg daily.

Haematological parameters	Pre-dapsone therapy n=15	Post-dapsone therapy n=15	Significance P-value
Mean Hb (mg/dl)	11.3 ± 1.3	11.1 ± 1.2	p>0.05
Mean WBC count	8500 ± 600	8400 ± 450	P>0.05
Mean differential neutrophil count	28.7 ± 2.4	29.6 ± 3.1	P>0.05
Mean differential lymphocyte count	85.8 ± 5.2	86.2 ± 4.8	P>0.05
Mean platelet count (cu.mm)	87000 ± 33000	86500 ± 32500	P>0.05
Reticulocyte count	0.5 ± 0.1	1.4 ± 0.3	P<0.05

The mean ± SD for differential lymphocyte count was 72.7 ± 4.6% for pre-dapsone therapy patients compared to 72.1 ± 4.9% for post-dapsone therapy patients (p>0.05). The mean ± SD for platelet count, for the pre-dapsone therapy patients was 103000 ± 52000 cu.mm compared to 103400 ± 56000 for the post-dapsone therapy patients (p<0.05).

Table 2 shows the haematological values for fifteen patients with other associated illness, such as malaria, which necessitated a lower dose of 50mg daily. The values pre and post-dapsone therapy were not significantly different (p>0.05), for the Hb concentration, WBC count, mean differential neutrophil, mean differential lymphocyte count and platelet count.

DISCUSSION

This study reveals a marked decrease in Hb concentration in patients on dapsone, 100 mg daily. The

Hb dropped 2.2 mg/dL from the initial value of 12.3 mg/dL predapsone therapy, to 10.1 mg/dL post-dapsone therapy ($p<0.05$). It was also observed that fifteen patients, on a lower dose of 50mg daily, had only a drop of 0.2 mg/dL from an initial pre-dapsone therapy value of 11.3 mg/dL, to 11.1 gm/dL.

We suggest that the decrease in Hb concentration is dose dependent. It has been observed, that higher doses of dapsone increased the direct oxidant effect on the red blood cell membrane(4,5), we are in support of this observation. We observed that doses above 50 mg daily were associated with a greater likelihood of a decrease in Hb concentration. This may be attributed to other factors which already exist in the environment, such as poor nutritional status and malaria infection. Previous studies(11) in Nigeria corroborate our observation. There was no significant alteration in the value of WBC count pre and post-dapsone group of patients.

Approximately 98% of patients did have a lymphocytosis, pre and post therapy. This finding occurs in chronic bacterial infections such as leprosy and tuberculosis. Leprosy may be a cause of lymphocytosis, by a similar mechanism to tuberculosis(12). This may involve the mobilisation of lymphocytes. The mean differential neutrophil count was low, both in the pre-dapsone and post-dapsone group of patients. This may be attributed to the finding of lymphocytosis as previously highlighted.

There was absence of eosinophilia. This is contrary to severe eosinophilia, obtained by Queroz *et al*(2) in a study in Brazil. The reasons for the eosinophilia in the latter study were due to the high incidence of allergy and asthma. The mean platelet count was significantly different in the pre and post dapsone patients on 100 mg daily. However there was no significant difference in pre and post dapsone platelet counts in patients on 50 mg daily. We wish to postulate that the former observation, is as a result of dose dependence where a higher dose of dapsone resulted in a fall in platelet count probably by bone-marrow suppression, or by an immune mediated mechanism. The reticulocyte count had a greater than ten fold increase during the study period. The reticulocyte count was elevated to $7.3 \pm 1.1\%$ in the post-dapsone patients. This finding was suggestive of dapsone induced haemolysis. Previous studies(2,4) corroborate our findings.

We observed that no significant alteration in haematological values occurred in leprosy patients on a lower dose of 50mg dapsone. We are of the opinion that leprosy patients on 100 mg dapsone daily are at greater risk of haemolysis, when compared to patients on 50 mg daily. Thus haemolysis appears to be dose dependent. We recommend routine determination of Hb concentration, WBC count, platelet count and reticulocyte count for leprosy patients prior to dapsone therapy, and subsequently. Secondly, the dosage of dapsone should be reduced from 100 mg daily, if features of haemolysis develop.

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