Haematological adverse reactions to MDT in children with leprosy: A retrospective study

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Abstract

Leprosy is a chronic infection which causes significant morbidity. It is also associated with social and psychological burden and is engulfed with myths. With the advent of Multi Drug Therapy outlook of the disease has significantly changed. Combination of these drugs is known to cause common and rare side effects.

A retrospective study was carried out to find out prevalence of Multi Drug Therapy (MDT) related adverse effects among children for last 5 years duration (2010-2014). Data were collected from clinical records and leprosy register using a comprehensive data sheet. Dapsone induced haemolysis, liver function alteration, dapsone hypersensitivity syndrome, methemoglobinaemia and agranulocytosis were considered as MDT related adverse effects.

172 patients were registered during the period of study. Only 55 were eligible for study due to incomplete data. 29 were males and 26 were females. Males (89.6%) showed higher rate of adverse effects compared to females (84. 6%). Reported adverse effects were: Haemolysis (81.18%), liver function alteration (14.54%), both haemolysis and liver function derangement (9%), dapsone hypersensitivity syndrome (3.6%). Adverse effects related to MB and PB had no significant difference (83% and 81.6%). Majority of adverse effects were reported within 1st two months (75%).

MDT related adverse effects are higher among children. Haemolysis remains the leading cause.

Introduction

Leprosy is a chronic infection which causes significant morbidity. Disease is also associated with social and psychological burden and is also engulfed with myths. With the advent of Multi Drug Therapy (MDT) in 1981, outlook of the disease has significantly changed. These changes include better compliance and better clinical outcome.

Recommended multi-drug therapy is a combination of rifampicin, dapsone and clofazimine. MDT is of two types, Multibacillary (MB) and Paucibacillary (PB). Combination of these drugs is known to be associated with common and rare side effects. These include haematological side effects of dapsone and hyperpigmentation included by clofazimim. Dapsone is known to cause both idiosyncratic and dose related adverse effects. Former includes dapsone hypersensitivity syndrome and latter includes haematologically mediated side effects such as hemolytic anemia and methaemoglobinaemia.

In recent clinical practice we have encountered a rising trend of MDT related adverse effects among children. There is a paucity of studies related to this entity.

Objectives

General

1. Find out prevalence and severity of MDT related haematological adverse effects among children.

Specific

1. To find out adverse effects related to type of MDT
2. To find out adverse effects related to age of the child
3. To compare hematological adverse effects of MDT between adults and paediatric age group

Methodology

Study design: Retrospective study conducted for last 5 years (2014-2010).

Study setting: Dermatology Unit, Lady Ridgeway Hospital for Children.

Eligibility criteria

1. All patients with leprosy who attended clinic during period of study were included.
2. Patients with incomplete data were excluded.

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Methodology

A comprehensive data sheet was prepared for data collection. All relevant demographic, clinical and biochemical data were collected using individual clinic records and leprosy register. Hemolytic anemia, liver function alteration, methaemoglobinaemia, agranuloctosis and dapsone hypersensitivity syndrome were considered as main MDT related haematological adverse effects. Full blood count (FBC) and blood picture (BP) findings were used to assess haemolysis and considered as significant if Hb drop is more than 2g/dl. Elevation of SGOT and SGPT were used to assess liver function tests and elevation more than 3 times of basal value was considered as significant.

Results

172 children with leprosy had attended clinic during the period of study. Only 55 were eligible due to incomplete data. 29 were male and 26 were females. Majority have received MDT-PB (48/87.2%) compared to MDT MB (7/12.72%).

Age of the study group distributed between 3 to 12 years and the majority belonged to 9 to 12 years of age (61.1%). Males showed higher rate of adverse effects (89.6%) compared to females (84.6%).

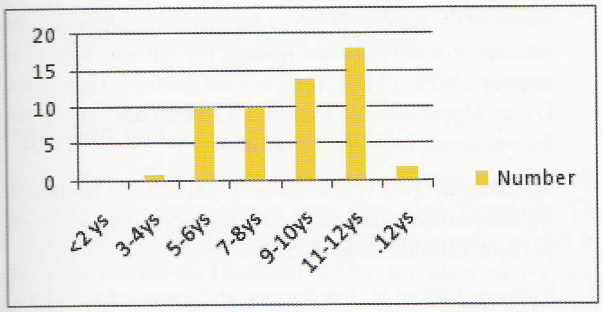


Figure 1. *Age distribution of the sample.*

Haemolysis was the commonly encountered adverse effect (45). Other reported adverse effects are liver function derangement (10) and dapsone syndrome (2). Agranulocytosis and methaemoglobinaemia were not recorded. Three (3) patients (5.4%) had none of the above. Adverse effects related to MDT were nearly equal among MB (6/83%) and PB (40/81.63%) treatment categories.

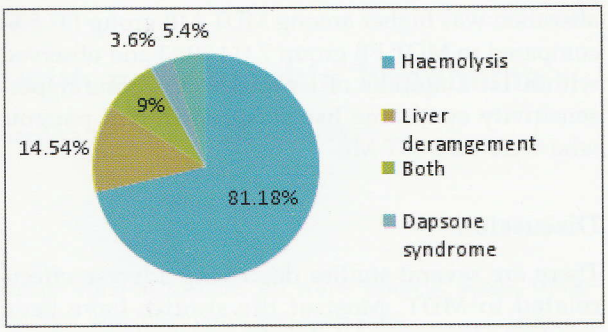
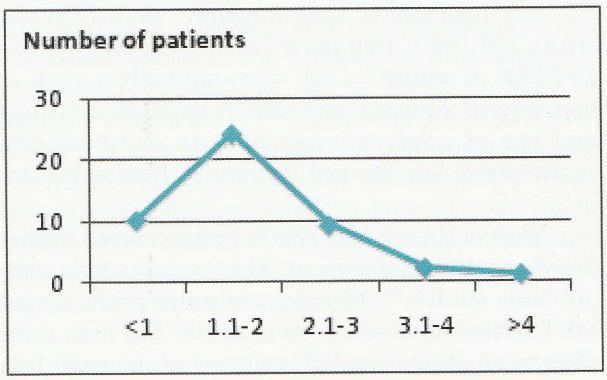


Figure 2. *Adverse effects.*

Brewer's test was performed in 51 patients and positivity observed only among 3 patients. Significant (> 2g/l) Hb drop was observed in 13 (28.8%). Males (86.2%) had higher rate of haemolysis than females (76.92%).

Hb drop g/dl	*No*	*Percentage*
< 1	10	22.2
1.1-2	22	48.8
2.1-3	08	17.7
3.1-4	04	8.88
4,1-5	00	00
>5	01	2.2



Haemolysis has occurred within 3-4 weeks of therapy in majority (25). Late onset haemolysis was reported among six patients.

Alteration of liver functions were observed among 10 (18, 18%) patients but significant elevation (>3* of basal value) was seen only in three (30%). Liver function

alteration was higher among MDT MB group (37.5%) compared to MDT PB group 7 (14.89%) and observed within 1st 2 months of treatment. Dapsone hypersensitivity syndrome has occurred in two patients who were on MDT MB.

Discussion

There are several studies describing adverse effects related to MDT. Most of the studies have been conducted among adults. Haemolysis has been reported as the leading cause in most studies. It has occurred in those with normal G6PD level and those with deficient G6PD level but more severely with latter group. Other reported adverse effects are mild and transient elevation of liver function tests, dapsone syndrome, allergic reactions to MDT (dapsone and rifampicine) and methaemoglobinaemia. Most of the adverse effects have occurred in females.

Total number of adverse effects is higher among children (87.2%). The incidence of total adverse effects reported in previous studies (mainly adults) varies from 45.3%-63.6%[1,5]. Haemolysis the commonest adverse effect in our study (81.18%) was higher than that of adults[2,6]. Dapsone is thought to be the offending drug as haemolysis has occurred equally among both MB and PB therapy. Lower efficacy of detoxification and excretion of hydroxylamine metabolites in children may contribute to oxidative damage and early onset acute haemolysis. Mild G6PD deficiency causes late onset haemolysis which was low in our study due to routine screening (Brewer's test) before starting treatment.

Derangement of liver function was less in our study (18.18%). Reported incidence varies from 15-23.5% in adults[6,8]. Lack of co-morbidities such as hepatorenal diseases, concurrent hepatotoxic drugs and use of relative lower dose in children may contribute to less marked increase in liver enzymes.

Most of the adverse effects have occurred during first 2 months of treatment. This is compatible with previous studies[2,6]. Females are more prone to get MDT related adverse effects in adults[2] but both sexes were more or less similarly affected in children. This may be due to lack of hormonal influence on drug metabolism in children.

Limitations

There is paucity of studies related to paediatric age group for comparison. All possible adverse effects were not evaluated (eg. Agranulocytosis and methaemoglobinaemia).

Suggestions

More studies have to be conducted among children to find out prevalence of MDT induced adverse effects. The studies should be directed towards looking for new strategies which can be used to minimize MDT related adverse effects.

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