GENDER DIFFERENCES IN INTOLERANCE TO MULTI-DRUG THERAPY (MDT) FOR LEPROSY

Giselda Trigueiro Hospital – Natal, RN (Brazil)
Leprosy elimination

MDT: side effects FAQ

Questions and answers

Does MDT expose patients to a higher risk of serious side-effects?

When more than one drug is used, naturally there is a risk of side-effects from each of the drugs used in the combination. However, in practice, the side-effects reported from the use of MDT in several hundreds of thousands of patients around the world show that most of them are mild and major side-effects are rare.
Side effects to MDT

• Some authors have reported that between 37% and 45% of patients have side effects.
• The percentage requiring a change in MDT regimen is smaller, from 5 to 24%.

Objective

To characterize and identify potential risk factors for intolerance to multi-drug therapy (MDT) which prompted a medication change in a leprosy referral center in northeastern Brazil.
Giselda Trigueiro Hospital – Natal, RN (Brazil)
Design

• A retrospective chart review of leprosy patients treated at a state referral center in Natal, Rio Grande do Norte, Brazil.

• Chart review focus was on adverse effects necessitating modification of MDT regimen.
Outcomes for people starting MDT therapy for leprosy at the Giselda Trigueiro Hospital from 1999 to 2008

711 people started MDT

- 47 Transferred care to another center
- 14 Defaulted on MDT (1.9%)
- 4 Deaths
- 4 Misdiagnoses stopped therapy

642 completed MDT

- 30 Charts not located

612 charts available for review

- 521 cases completed standard MDT therapy
- 91 cases of medication intolerance leading to change in MDT regimen

(14.9%)
### Most common causes* of medication intolerance leading to change in MDT regimen

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Ratio Female: Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>305</td>
<td>307</td>
<td>612</td>
<td>1,0</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>41 (3-93)</td>
<td>44 (8-82)</td>
<td>42 (3-93)</td>
<td>1,1</td>
</tr>
<tr>
<td>Any Cause of Medication Intolerance</td>
<td>8.9%</td>
<td>20.8%</td>
<td>14.9%</td>
<td>2,4</td>
</tr>
<tr>
<td>Anemia</td>
<td>5.2%</td>
<td>12.1%</td>
<td>8.7%</td>
<td>2,3</td>
</tr>
<tr>
<td>Headache</td>
<td>2.3%</td>
<td>6.2%</td>
<td>4.2%</td>
<td>2,7</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>0.6%</td>
<td>2.9%</td>
<td>1.8%</td>
<td>4,5</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>0.3%</td>
<td>2.9%</td>
<td>1.6%</td>
<td>9,0</td>
</tr>
</tbody>
</table>

* A person may have had more than one reason for change in regimen.
Gender and MDT intolerance

• Women were 2.4 times as likely as men to have MDT intolerance ($p<0.0001$).

• Within the PB subgroup, women were twice as likely as men to have MDT intolerance ($p=0.0148$).

• Within the MB subgroup, women were 2.4 times as likely as men had MDT intolerance ($p=0.0197$).

• In a multiple logistic regression analysis, female sex (OR=2.63, $p<0.001$) and age < 42 years (OR=2.7, $p<0.001$) remained associated with medication intolerance.
Gender and anemia

• 58.2% of people who changed their MDT regimen had anemia.
• Anemia was 2.3 times as frequent in women as in men \((p=0.0037)\).
• In a multiple logistic regression analysis female gender \((OR=2.36, m CI: 1.25-4.44, p=0.007)\) and age less than 42 years old \((OR=1.86, CI: 1.02-3.39, p=0.041)\) remained associated with anemia.
Discussion

• We found a rate of adverse events requiring change in MDT of 14.9%, which is the same percentage reported by Goulart (2002) in another study in Brazil.

• 81% of medication intolerance occurred within the first three months which has operational implications and suggests that close monitoring is most important at the time of initiation of MDT.
Discussion

- In a Sri Lanka study, those with adverse events were more likely to be women than men (Kaluarachchi et al, 2001).
- In a Brazilian study, there was a slightly higher percentage of anemia related to dapsone in women compared with men (9.4% vs 7.3%) (Goulart et al, 2002).

Could this association of anemia with female gender and age less than 42 years may be a reflection of blood loss during menstruation in pre-menopausal women?
Discussion

• Singh (2011) reported an association between any type of MDT-related adverse event in MDT regimen and body mass index less than 18.5.

*In our study, could a difference in BMI be related to the association of female gender and age less than 42 years old and medication intolerance?*
Discussion

- It has been suggested that drug allergy in general occurs more frequently in young and middle-aged rather than older adults, and that it is more common in women than men.

Could this be related to allergic mechanisms involved in anemia caused by dapsone?

Conclusion

• Few studies have looked at the association of side effects from MDT and patient demographics as gender and age.

• Our findings showing association of MDT side effects (especially anemia) with female gender and age less than 42 years have operational implications for monitoring drug intolerance during therapy for leprosy, and should be verified by other leprosy services.
Thank you!
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