Post Kala-Azar Dermal Leishmaniasis Following Treatment with 10 mg/kg of Single Dose AmBisome for Visceral Leishmaniasis in Bihar, India

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

In view of the significant role of Post kala-azar dermal Leishmaniasis (PKDL) patients in the transmission/recurrence of visceral leishmaniasis (VL) outbreaks, control of PKDL is among the priorities. As the Single Dose AmBisome 10 mg/kg (SDA) became the obvious choice for the treatment of VL, therefore, in this study, 896 patients were included to explore the probability of developing PKDL. Among the treated patients, 30 (3.35%) of them found confirmed as PKDL with clinical symptoms. Out of the 30 patients, 53.33% male and 46.67% female patients had macular lesions respectively, with a median time (Interquartile range [IQR]) to development of 13.5 (9–23.5) and 23 (9–17) months following treatment. No, significant associations were established concerning any patient's demographics and clinical characteristics. However, with the patients presenting with confirmed PKDL, females were significantly younger than males. This study suggests the rate of PKDL appearance is directly associated with 10 mg/kg of SDA and therefore there is a need for more concerns regarding doses during treatment.

Keywords: Single dose AmBisome; visceral leishmaniasis; PKDL; SDA.

1. INTRODUCTION

In the past few years, due to the high cure rate (95.7%) with 10 mg/kg of AmBisome, patients are regularly treated with a single infusion of 10 mg/kg at different referral centers [1]. It has earlier reported the rate of conversion of VL to PKDL in patients (8311) administered with 20 mg/kg AmBisome was relatively low (0.3%) with an average development period of 1.2 years (0.8–2.2) of following treatment [2-4]. But, risk factors for Single Dose AmBisome (10 mg/kg/body wt) associated with the conversion of VL to PKDL still remains to be elucidated [5]. Here, a field-based cohort study was performed and those patients who received Single Dose AmBisome (i.e. 10mg/kg/body wt) during 2012-2018 were selected. Depending upon the records available at State/District health offices or at RMRIMS about the treatment VL, from endemic regions of Vaishali, Saran, and Muzaffarpur districts were chosen. Spleen or bone marrow test of cure biopsy was adopted only when treatment failure was suspected within the six months after the initial cure from VL.

2. MATERIALS AND METHODS

Among 896 VL SDA treated individuals, 300 individuals were follow-up with both door to door screening method quarterly between 2012-2014 and, rest 596 were selected from indoor patients who came RMRIMS treatment of VL and were received SDA treatment. From these indoor patients, 20 cases were converted to PKDL between 2015 and 2018. After obtaining written and verbal consent from the head of the family and also from each individual, the rK39 test was performed for the detection of anti-leishmanial antibody [6].

3. RESULTS AND DISCUSSION

During follow up, 17 VL treated cases were lost as they moved to other places. The focus was given to the patients who were suspected of lesions. They were examined with a proper record including morphology onset of lesions and history of VL occurrence, and age group. All suspected PKDL cases were referred to RMRIMS for further slit/skin smear examination. The skin biopsies/smears were aseptically collected from the largest and most prominent lesions as per the protocol described earlier [7-10]. Skin smear slides were immediately fixed with methyl alcohol and allowed to dry at room temperature. Slides were stained with diluted (1:9) Giemsa stain for 25 minutes. Smears are examined under the oil immersion objective of the microscope for the demonstration of Leishmania donovani parasites [11,12]. During 36 months follow-up, a sign of PKDL was observed in 30 cases (3.35%) which were further confirmed by demonstration of amastigotes in skin scrapping smear (n=30) (Fig. 1).
The conversion period of VL to PKDL varies from 6 to 29 months. Among 896 VL patients, 577 individuals were male and the rest 319 were females, and only 3.35% of VL cases were converted to PKDL cases. There were no significant associations found regarding any patient demographics (sex, age group, caste, the season of treatment) and clinical characteristics (nutritional status, duration of illness before treatment, admission spleen size, and change in spleen size by the time of preliminary treatment) at time of preliminary treatment and the risk of developing confirmed PKDL. The mean ± standard deviation of time to the onset of lesions of confirmed PKDL as reported by the patients was 14.47±4.08 months [13]. A median (IQR) was used to establish the onset of the lesion, formal diagnosis, and different age groups of PKDL patients, separately for males and females (Table1). The median to the onset of lesion of PKDL (IQR) for males and females is 13.5(9-23.5) and 23(9-17) respectively [2,14]. However, the meantime to confirmation of the diagnosis of PKDL was longer at 6.93 months and correspondingly median (IQR) for males and females is 6.5(4-11) and 5(3-8). The time to onset of PKDL lesions is shown in the Kaplan–Meier graph (Fig. 2) survival distributions showed no significant difference between the sexes. Of the patients presenting with confirmed PKDL, females were significantly younger than males (median age 7 vs 60 years, respectively; p=2) [2,15]. The mean age of males and females in confirmed PKDL is 26.94 vs 25.35 respectively. It is worth emphasizing that the present study...
Table 1. Characteristics of patients with confirmed post-AmBisome PKDL stratified by sex (n = 30)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male (%) n=16</th>
<th>Female (%) n=14</th>
<th>P Mann-Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to onset of lesions, months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12 months</td>
<td>7(43.75%)</td>
<td>6(42.86%)</td>
<td></td>
</tr>
<tr>
<td>12-16 months</td>
<td>3(18.75%)</td>
<td>4(28.57%)</td>
<td></td>
</tr>
<tr>
<td>16-20 months</td>
<td>1(6.25%)</td>
<td>1(7.14%)</td>
<td></td>
</tr>
<tr>
<td>20-24 months</td>
<td>1(6.25%)</td>
<td>2(14.29%)</td>
<td></td>
</tr>
<tr>
<td>≥24 months</td>
<td>4(25%)</td>
<td>1(7.14%)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>13.5(9-23.5)</td>
<td>23(9-17)</td>
<td>64</td>
</tr>
<tr>
<td>Time to formal diagnosis, months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12 months</td>
<td>12(75%)</td>
<td>13(92.86%)</td>
<td></td>
</tr>
<tr>
<td>12-16 months</td>
<td>2(12.5%)</td>
<td>1(7.14%)</td>
<td></td>
</tr>
<tr>
<td>16-20 months</td>
<td>1(6.25%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>20-24 months</td>
<td>1(6.25%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>≥24 months</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6.5(4-11)</td>
<td>5(3-8)</td>
<td>64</td>
</tr>
<tr>
<td>Age group, Years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 years</td>
<td>5(31.45%)</td>
<td>4(28.57%)</td>
<td></td>
</tr>
<tr>
<td>15-25 years</td>
<td>4(25%)</td>
<td>3(21.43%)</td>
<td></td>
</tr>
<tr>
<td>25-35 years</td>
<td>2(12.5%)</td>
<td>2(14.29%)</td>
<td></td>
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<tr>
<td>35-45 years</td>
<td>0</td>
<td>4(28.57%)</td>
<td></td>
</tr>
<tr>
<td>≥45 years</td>
<td>5(31.45%)</td>
<td>1(7.14%)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>19(13.5-45)</td>
<td>23.5(11-37)</td>
<td>64</td>
</tr>
<tr>
<td>Type of lesion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macular</td>
<td>11(68.75%)</td>
<td>10(71.43%)</td>
<td></td>
</tr>
<tr>
<td>Macular-papular</td>
<td>5(31.25%)</td>
<td>4(28.57%)</td>
<td></td>
</tr>
<tr>
<td>Nodular-papular</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

reflects a higher rate of incidence of confirmed PKDL cases following treatment with 10 mg/kg SDA as compared to 20 mg/kg AmBisome. As PKDL possibly serve as potential reservoirs for transmission and remain as a major challenge to the current control and elimination programs [16-19].

4. CONCLUSION

It is concluded that a detailed investigation is urgently required about the higher incidence conversion rate associated with 10 mg/kg Single Dose AmBisome.

CONSENT

After obtaining written and verbal consent from the head of the family and also from each individual, the rK39 test was performed for the detection of anti-leishmanial antibody.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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