SUSCEPTIBILITY OF MASTOMYS NATALENSIS TO BRUGIA MALAYI FOLLOWING PRETREATMENT WITH ANTIFILARIALS

K. TYAGI, P. K. MURTHY and A. B. SEN

Division of Parasitology, Central Drug Research Institute, Lucknow, India

Abstract. Mastomys natalensis pretreated with diethylcarbamazine (DEC), levamisole or 2-phenoxacin were exposed to the standard inoculum of infective larvae of Brugia malayi. Percentage ‘take’ of infection, duration of prepatent period, course of microfilaraemia and number of adult worms recovered were compared with those of untreated infected Mastomys (control). DEC and 2-phenoxacin did not alter the ‘take’ (DEC: 100%; control: 88.24%) and the average prepatent period (DEC: 105.44 days; control: 105.18 days), but 2-phenoxacin (100.18 days) with extended prepatent period (125.87 days). However, unlike 2-phenoxacin and control, the course of microfilaraemia was similar in DEC and levamisole pretreated animals. The average adult worm recovery was significantly lower in 2-phenoxacin treated animals being 14.69 as against 8.12, 7.46 and 8.42 in DEC, levamisole pretreated and control animals, respectively.

Available evidences indicate that certain antifilarials might act by modulating the host’s immune response. Of those, diethylcarbamazine (DEC), the drug of choice for filariasis, has a suppressive action on specific antibody mediated immune response (Sawada et al. 1968, Katiyar et al. 1974, Murthy et al. 1978, Misra et al. 1982, Tyagi et al. 1986), while levamisole, a well known broad spectrum anthelmintic, possesses immunostimulatory action on cell mediated immune response (Merluzzi et al. 1975, 1976, Renoux and Renoux 1977). However, it is not yet known whether prolonged administration of these drugs in endemic areas, modifies the host defense mechanism with particular reference to susceptibility of the host. The present study is, therefore, designed to investigate the effect of pretreatment with DEC, levamisole and a candidate antifilarial, 2-phenoxacin, on the susceptibility of Mastomys natalensis to filarial infection by Brugia malayi. The criteria used for assessing the susceptibility were (i) percentage ‘take’, (ii) duration of prepatent period, (iii) course of microfilaraemia, and (iv) worm burden.

MATERIALS AND METHODS

Seventy eight male M. natalensis (8 weeks old) were used for the study. The animals were grouped into four groups, of which group I, II and III received DEC (Heterzan, Cynamid India Ltd.), levamisole (Vermisole-100, Knodels Laboratories) and 2-phenoxacin (Saxena et al. 1970), respectively, at 12.5 mg/kg (base), 20 mg/kg and 10 mg/kg orally for 13 consecutive days. Group IV was left untreated. The doses of the drugs employed were intentionally kept below the therapeutic dose in order to clearly demarcate the effects of prolonged treatment on the defense system, if any, from the known antifilarial effects. Seven days after the last dose, the animals were inoculated with 100 infective larvae of B. malayi per animal through subcutaneous route. Tail blood of all the animals was examined for microfilariae (mf), initially on day 90 post inoculation and thereafter at fortnightly intervals, as described elsewhere (Murthy et al. 1983). The prepatent period was determined on the basis of the first appearance of mf in the peripheral blood. All the surviving ani-
mals were sacrificed after day 360 post larval inoculation and worm burden was assessed as described by Murthy et al. (1983).

Statistical analysis. Test of proportionality and one way analysis of variance was carried out. Individual comparisons were done after the significant evidence of variation test.

RESULTS AND DISCUSSION

Table 1 and 2 and Fig. 1 depict the results of the effect of pretreatment with antifilarials on the susceptibility of host. It was observed that the differences in the number of animals surviving beyond the prepatent period in the pretreated groups (I, II and III) was insignificant (P > 0.05) when compared with the control group (IV). However, the mortality in animals of groups I and III was higher (p < 0.05) in comparison with group II following larval exposure. Regarding the 'take' of infection, no significant (P > 0.05) difference amongst all four groups could be found. Longer prepatent period observed in animals pretreated with levamisole was highly significant in comparison with animals pretreated with either DEC or centiperazine (P < 0.01). However, it was less significant when compared with control (P < 0.05).

The recoveries of adult worms in the pretreated and control groups separately and amongst the pretreated groups were compared. It was observed that female and total worm recovery was significantly higher in group III than in the remaining 3 groups (Table 1). Most of the female worms obtained from animals pretreated with DEC were sterile. Regarding the male worm recovery, apparently no difference could be exhibited when pretreated groups were compared with control separately. But amongst pretreated groups, group III showed significantly higher worm recovery than groups I and II. (P-values are shown in Table 2).

![Fig. 1. Course of microfilaraemia (H. malayi) in pretreated and untreated M. natalensis](image-url)
course of microfilaraemia in untreated control and centaperazine pretreated *M. natalensis*, increased continuously up to day 360 post inoculation. Whereas in untreated mice with leishmanial infection, the *M. natalensis* count remained suppressed throughout the observation period, the immune response, including an increase in antibody titers, was also observed. In the case of DEC pretreated animals, the course of microfilaraemia in them was similar to that observed in leishmanial infected mice, and the response was to the often reported immunosuppressive effects of DEC (Sadwala et al. 1968, Katiyar et al. 1974, Murthy et al. 1978, Misra et al. 1982, Tyagi et al. 1986).

Table 2. Statistical analysis of comparative worm burden from pretreated and control groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Significance in adult worm recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male, Female, Total</td>
</tr>
<tr>
<td>I vs IV</td>
<td>NS, NS, NS</td>
</tr>
<tr>
<td>II vs IV</td>
<td>NS, NS, NS</td>
</tr>
<tr>
<td>III vs IV</td>
<td>NS, P &lt; 0.01, P &lt; 0.01</td>
</tr>
<tr>
<td>I vs III</td>
<td>P &lt; 0.05, P &lt; 0.01, P &lt; 0.01</td>
</tr>
<tr>
<td>I vs III</td>
<td>P &lt; 0.01, P &lt; 0.01, P &lt; 0.01</td>
</tr>
</tbody>
</table>

I — pretreated with DEC; II — pretreated with leishmanial; III — pretreated with centaperazine; IV — untreated control; NS — not significant

Moreover, no explanation can be offered for the presence of sterilized female worms in DEC pretreated *M. natalensis*, as DEC has a comparatively short half-life (Harned et al. 1948). Similarly, centaperazine which had been found to have an immunostimulatory action on filaria-specific cell-mediated immune response (Tyagi et al. 1986) has no effect on any of the above mentioned criteria taken for the study of susceptibility of the host to filarial infection. Thus, from the present study it appears that the pretreatment with either DEC or leishmanial has an adverse effect on the susceptibility of the host and might check a mass spread of filarial infections.

Acknowledgements. The award of a Senior Research Fellowship by Indian Council of Medical Research, New Delhi, India, to first author is gratefully acknowledged.

ЧУВСТИТЕЛЬНОСТЬ *MASTOMYS NATALENSIS* К ЗАРАЖЕНИЮ *BRUGIA MALAYI* ПОСЛЕ ОБРАБОТКИ АНТИФИЛАРИЯННЫМИ ПРЕПАРАТАМИ

K. Tyagi, B. K. Murthy, and A. B. Sen

Резюме. *Mastomys natalensis* обработанные диэтилбарбамидом (DEC), левамизолом или центаперазином имели более высокую инфекционную активность по сравнению с контрольной группой инфицированных животных. DEC и центаперазин не влияли на приживаемость инфекции (ДИС/пентерации: 100%, контрольная группа 88,24%) и на среднюю продолжительность превентивного периода (DEC: 105,4, пентерация: 105,18, контроль: 109,20 дня). С другой стороны, у животных обработанных левамизолом приживаемость инфекции была гораздо ниже (68,18%), чем у животных с ДИС/пентераций в 3 группы с более продолжительным превентивным периодом (125,87 дня). В отличие от контрольной группы и от группы обработанных DEC и левамизолом, среднее количество ядерных червей было статистически достоверно выше у животных обработанных центаперазином — 4,9, по сравнению с 8,12, 7,60 и 8,20 в группах животных обработанных DEC, левамизолом и контрольной группой соответственно.

REFERENCES


Received 29 February 1948

K. T., Division of Parasitology, Central Drug Research Institute, P. B. 173, Lucknow 226 001, India

264

265