SHORT COMMUNICATIONS

PROTECTION AGAINST PLASMODIUM BERGHEI YOELII IN CHLOROQUINE- AND PYRIMETHAMINE-TREATED MICE

V. R. PRADHAN and D. M. RENAPURKAR

Department of Zoonosis, Haffkine Institute, Parel, Bombay

Abstract. The antimalarial drugs chloroquine and pyrimethamine were observed to afford protection to mice treated with these agents. This protection was observed in mice when given a subsequent challenge infection after they had been radically cured of P. b. yoelii infection.

Antimalarial compounds like pyrimethamine are reported to exhibit immunopotentiating activity (Thong and Ferrante 1980). Several workers have shown that drugs like chloroquine (Lapiere 1954), mepacrine (Cox 1957, 1958, 1959, 1962, 1964), primaquine (Box and Gingrich 1958) induce some degree of protection against subsequent infections with P. berghei in P. berghei-mouse model system.

A study was undertaken to examine whether two of the commonly used antimalarial agents afford any protection against the P. b. yoelii infection in mice after a lapse of eight weeks period.

MATERIAL AND METHODS

A batch of 40 mice (Haffkine strain, average weight 16–18 g, diet consisting of wheat flour 65%, barley flour 15%, yeast powder 10%, skim milk powder 3%, fish meal 3%, complemented by vitamins and common salt was infected with $1 \times 10^6$ parasitized red blood cells of P. b. yoelii per mouse. These were divided into eight groups of five mice each. Each group was separately treated with 3 mg/kg or 10 mg/kg of pyrimethamine or chloroquine, subeutaneously or orally, four hours after infection, once daily for 4 days (Peters' 4-day test, Peters 1965). Blood smears were taken for 7 consecutive days after treatment and later on, on alternate days for 4 weeks. Blood smears of radically cured mice were negative to infection. Only mice that were radically cured were used for this experiment.

Mice that had recovered from the infection were reinfected* eight weeks after the first infection (4 weeks after the radical cure). These mice were further divided into 5 groups according to the drug, dose and route of administration of drug used for the earlier treatment.

A group of five twelve-week-old mice infected with P. b. yoelii was taken as controls for comparison. Mean survival time (MST) of surviving mice was calculated by observing survivors for 11 weeks after the challenge infection.

The experiment was repeated twice to confirm the observation.

* The period of four weeks (after the radical cure) was chosen because it was considered that after four weeks of cure, the host immune mechanisms may not play a significant role in limiting subsequent infections, as has been shown by several studies.
RESULTS

Table 1 shows the MST of chloroquine- and pyrimethamine-treated mice, challenged 8 weeks after the first infection. It will be seen that while the untreated animals died within 8 days of infection (MST = 7.7 days), mice receiving drug treatment survived over 10 times the period of survival of the control mice. Pyrimethamine-treated mice survived longer (MST = 106 days) in comparison to mice receiving chloroquine treatment (MST = 7.5 ± 4.29 days).

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. of mice</th>
<th>Dose mg/kg</th>
<th>Route of administration</th>
<th>MST in days ± 8.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>5</td>
<td>3</td>
<td>po</td>
<td>70.50 ± 6.36</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>10</td>
<td>po</td>
<td>71.40 ± 5.47</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>se</td>
<td>po</td>
<td>75 ± 4.29</td>
</tr>
<tr>
<td>Pyrimethamine</td>
<td>5</td>
<td>3</td>
<td>po</td>
<td>68.50 ± 6.36</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>10</td>
<td>se</td>
<td>106 ± 0</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>7.7 ± 1.4</td>
</tr>
</tbody>
</table>

DISCUSSION

Certain antimalarial drugs are reported to demonstrate immunopotentiating activity and this activity is considered to play an important role in the recovery of a patient suffering from a subsequent attack of malaria in a malaria endemic area. Two such drugs have been studied to see whether such activity occurs in experimental infections after the radical cure. The study showed that pyrimethamine-treated mice when given a challenge infection survived for 106 days and chloroquine-treated mice survived for 75 ± 4.29 days whereas the control mice died within approximately 8 days of infection. Thus survival was longer in pyrimethamine-treated mice than in the control mice. This may be due to the superior immunopotentiating activity of pyrimethamine which appears to be most effective when drug and antigen are administered simultaneously as was done in this experiment.

We therefore believe that the two drugs, pyrimethamine and chloroquine, afford a resistance to reinfection and the infected mice survive much longer than the untreated and infected mice of the same age group. The resistance was found to last as long as 8 weeks after the treatment with dosages as low as 3–10 mg/kg. This resistance to reinfection in mice treated with chloroquine (Thong et al. 1981) and pyrimethamine (Thong and Ferrante 1980) suggests that chemotherapeutic agents may have an important role to play in eliciting protective immune responses against subsequent exposures to blood stages of P. falciparum in infection in mice.

REFERENCES


Received 31 May 1983.

V. R. P., Department of Zoosocia, Haffkine Institute, Parel, Bombay, India.


FIRST RECORD OF THE CESTODE KHAWIA BALTICA SZIDAT, 1941 IN CZECHOSLOVAKIA

During studies on the endobenthos of fluvial fauna of the Mácha Lake fishpond system in northern Bohemia, Czechoslovakia (system of the R. Elbe), carried out in the years 1974—77, cestodes of the family Caryophyllaeidae were found in the intestine of tench (Tinca tinca (L.)). A few young specimens, mounted as stained preparations, were at the disposal of this locality. These were erroneously reported as Caryophyllaeidum anguillae Annenkovas-Chlopina, 1936. In the author’s earlier paper (Jaravay F., Scripta Fac. Sci. Nat. JEPB Brun., Biol. 2, 8: 77—80, 1978) many new species, nearly collected from each of these localities in 1981—82, including gravid specimens, made it possible to study the cestodes in detail. Cross body sections of adult cestodes proved explicitly their belonging to the subfamily Lytocestinae, the general morphology and measurements of these cestodes indicated that they belonged to Khawia botlitsi Szidat, 1941, the species which has not been reported from Czechoslovakia. The body of gravid cestodes is 26—50 mm long, maximum width 1.8 to 2.5 mm. Scolex in compressed, mounted specimens almost always broadening anteriorly, fan-shaped (Fig. 1A), while that in cestodes freely fixed in hot alcohol is relatively narrower, anteriorly rounded and provided with numerous longitudinal grooves (Fig. 1C, D). Vitellaria cortical, forming a layer ensheathing testes which are medulary (Fig. 1E); vitellarium starting anteriorly 2—5 mm from anterior extremity, testes starting a little lower than vitellarium (Fig. 1A). Vitellaria represented by single follicles in ovary region; large postovarian group of follicles present (Fig. 1B). Ovary height, length 2.4—4.7 mm, with elongate, narrow lobes; ends of posterior lobes overlapped by vitellaria. Uterine coiled filling in separate space. Cirrus sac small. Size of eggs 0.060—0.078 x 0.042 to 0.054 mm.

K. botlitsi was originally described from tench of the R. Rossitten in Germany of that time (now the US SSR) (Szidat L., Z. Parasitenk. 12: 129—132, 1941). Later it was reported from barbel and tench from the R. Vistula and R. Oder and from fishponds in Poland (Janeszwacka J., Trav. Zool. Towarz. Sankowo, ser. B, 6: 1—72, 1954). In the US SSR it was found in tench from basins of the Kalinin-Gridzian, from Lithuania and from the R. Dniester basin (Kalukovskaya O. P., Para- stor, zool. Inst. AN USSR 20: 329 to 355, 1961, Bykovskaya-Pavlovskaya I. E., et al. Key to the parasites of freshwater fish of the USSR, Moscow—Leningrad, 776 pp., 1962), both in Russia. In the Mácha Lake fishpond system, K. botlitsi appears to be a rare parasite of tench; of a total of 186 T. tinca