Rev. Inst. Med. trop. São Paulo
18(5):298-300, *setembro-outubro*, 1976

UDC 616.995.122

MIGRATION AND FATE OF *SCHISTOSOMA MANSONI* IN MICE TREATED WITH OXAMNIQUINE

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SUMMARY

Two groups of mice were exposed, by the transcutaneous route (shaved abdominal skin, ring technique), to about 600 cercariae of *Schistosoma mansoni* per animal. One group had been treated, 3 hours before, with oxamniquine (6-hydroxymethyl-2-isopropylaminomethyl-7-nitro-1,2,3,4-tetrahydroquinoline; 200 mg/kg x 1, i.m.). Subgroups of 4 mice were sacrificed at different periods after exposure, up to 14 days, for the search of schistosomula or juvenile worms in the skin, lung and hepato-portal system. Mice of the second group (untreated control) were similarly handled. In both groups cercariae penetrated the abdominal skin and in the next day could be collected from skin tissue as active schistosomula. In the second day schistosomula from the oxamniquine-treated mice appeared as round larvae with little or no activity. The first lung schistosomula could be collected starting from the 3rd day, the peak being observed at the 7th day after exposure. It was demonstrated that oxamniquine does not interfer in the process of cercaria-schistosomulum transformation but kills effectively most of the larvae embedded in skin tissue, before reaching the lung.

INTRODUCTION

It has been shown that oxamniquine (6-hydroxymethyl-2-isopropylaminomethyl-7-nitro-1,2,3,4-tetrahydroquinoline) possesses a marked chemoprophylactic activity against *Schistosoma mansoni* infection in laboratory animals (FOSTER [2]; PELLEGRINO, PEREIRA & MELLO [3]; PELLEGRINO et al. [4]; PEREIRA et al. [5]).

In the present paper it was attempted to check the fate of schistosomula in mice exposed to *S. mansoni* cercariae after a previous treatment with oxamniquine (200 mg/kg, single dose, i.m.).

MATERIAL AND METHODS

Infection of mice — The L.E. strain (Belo Horizonte, Brazil) of *S. mansoni*, shed by laboratory-reared and infected *Biomphalaria glabrata*, was used in the present study. Two groups of 50 albino mice, weighing 20 ± 2 gr were exposed to *S. mansoni* cercariae by the transcutaneous route. The abdomen was carefully shaved and cleaned with dechlorinated water. Exposure to cercariae was carried out according to the technique described by SMITHERS & TERRY [6], the metal ring being substituted by a plastic one. A cercarial suspension (300 organisms per ml) was introduced twice in the ring, with an interval of 30 minutes, so

This work was supported, in part, by the "Conselho Nacional de Pesquisas", Brasil, and the World Health Organization, Geneva, Switzerland

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as to have a cutaneous exposure to a total of 600 cercariae per animal.

Treatment with oxamniquine — Oxamniquine was administered in polyethyleneglycol, intramuscularly (200 mg/kg, single dose), 3 hours before exposure of *S. mansoni* cercariae to 50 mice.

Collection of schistosomula and juvenile forms — Schistosomula from skin and lungs were collected according to the technique of CLEGG [1] and counted under a dissecting microscope. Juvenile forms within the hepatic-portal system were obtained by perfusing the liver and mesenteric vessels with saline.

RESULTS AND COMMENTS

The results obtained are graphically summarized in Fig. 1. Schistosomula within skin tissue could be collected up to the 7th day after exposure in both treated and untreated mice. It is important to note that, in the former group, starting from the 2nd day, the larvae appeared as contracted, nearly rounded organisms, with slow movements, in contrast with the larvae recovered from control animals. In lungs, schistosomula were found from the 3rd up to the 14th day (the last day of observation). Lung larvae were more numerous on days 5 and 7 but a great difference was found between the total numbers recovered from the treated and control animals: 112 and 526 schistosomula, respectively. This difference reflects the premature death of most of larvae within the skin, before reaching the lungs. In control mice, juvenile forms were found from the 7th up to the last day of observation (day 14), in sharp contrast to the treated animals from which only a few worms could be recovered. A carefully inspection of Fig. 1 puts in evi-

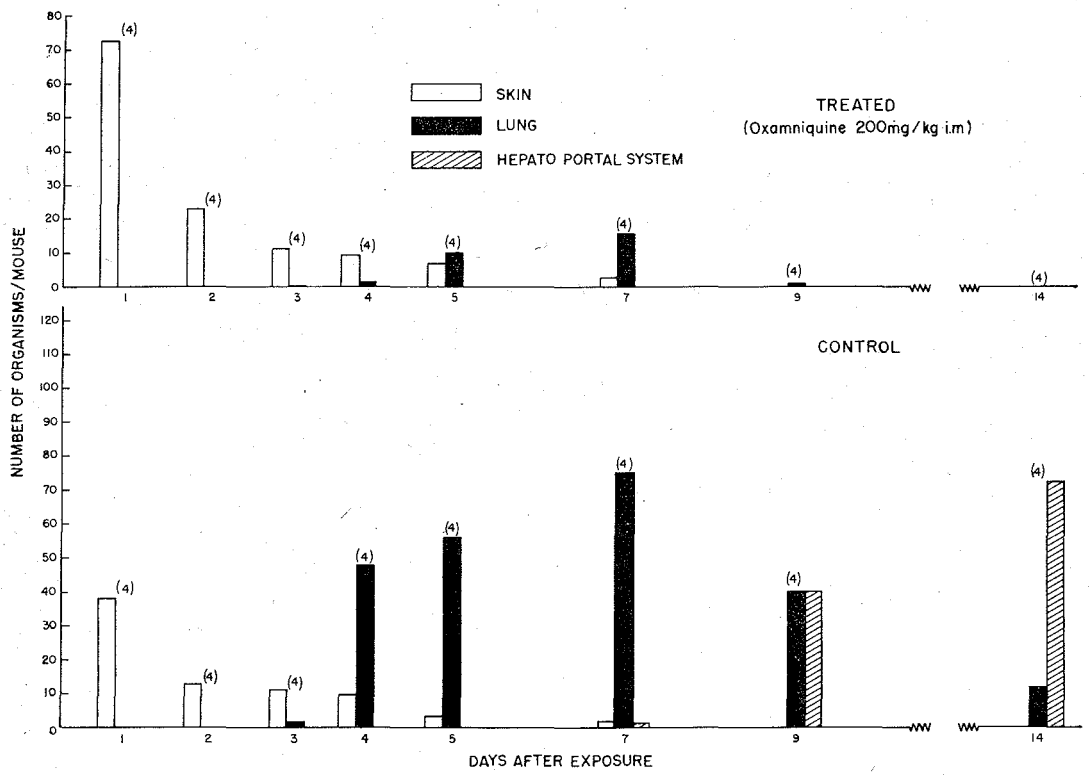

Fig. 1 — Mean number of schistosomula and/or juvenile forms of *Schistosoma mansoni* recovered from the skin, lungs and hepato-portal system of oxamniquine-treated mice and control animals. The numbers in parenthesis indicate the number of animals sacrificed in each particular day.

dence and apparent discrepancy: in control mice, the number of schistosomula recovered from the lungs (5th and 7th days) overcome that recovered from the skin (1st day). This reflects the relative inefficacy of the technique used in recovering early skin schistosomula. In conclusion, oxamniquine administered intramuscularly at the level of 200 mg/kg, as a single dose, does not interfer on the penetration of cercariae through the skin as well as on its further transformation into schistosomula but prevents the accumulation of larvae within the lungs by killing almost all larvae embedded into the skin.

RESUMO

Migração e destino do Schistosoma mansoni *em camundongos tratados com oxamniquine*

Dois grupos de camundongos foram expostos, por via transcutânea (pele do abdomen, técnica do anel) a cerca de 600 cercárias por animal. Um dos grupos havia sido tratado, 3 horas antes, com oxamniquine (6-hidroximetil-2-isopropilaminometil-7-nitro-1, 2,3,4-tetrahidroquinolina; 200 mg/kg x 1, i.m.). Subgrupos de 4 camundongos foram sacrificados em diferentes períodos depois da infecção, até 14 dias, para a coleta de esquistossômulos ou vermes jovens na pele, pulmão e sistema porta. Os camundongos do segundo grupo (controles não-tratados) foram cuidados da mesma forma. Em ambos os grupos as cercárias penetraram através da pele e, no dia seguinte, puderam ser coletadas, no tecido cutâneo, como esquistossômulos ativos. No segundo dia, os esquistossômulos nos camundongos tratados apresentavam-se como larvas arredondadas com movimentos reduzidos ou ausentes. Os primeiros esquistossômulos no pulmão foram encontrados a partir do 3.º dia, sendo que o número atingiu o pico no 7.º dia após a exposição. Foi demonstrado que a oxamniquine não interfere no processo de transformação cercária-esquistossômulo, mas mata eficazmente a grande maioria das larvas localizadas no tecido cutâneo, antes de chegarem aos pulmões.

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Recebido para publicação em 4/8/1975.