



THERAPEUTIC TRIALS OF CHLOROQUINE SILICATE
IN TANGANYIKA

by

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Therapeutic trials of the tasteless chloroquine preparations naphthoate and tannate have been reported from Tanganyika by Clyde, Mzoo & Mluba (1963). A more recent development is a silicate salt of chloroquine with a remarkable thermal stability.¹ This tasteless preparation has been found in human trials by the manufacturers to be excreted (and therefore absorbed) to the same extent as chloroquine diphosphate.

This report deals with therapeutic trials of chloroquine silicate among semi-immune children living near Morogoro, Tanganyika. The trials were of two kinds: (1) screening to ascertain the smallest single dose capable of clearing asexual parasitaemia, and (2) treating children with small doses repeated daily, in simulation of the amounts that might be taken in the form of medicated salt.

METHOD

The subjects were semi-immune Bantu children aged 6-12 years, all carriers of various species of malaria parasites, in some cases mixed infections being present in the same child. Although most of the subjects could be considered to be asymptomatic carriers, and the infections were usually in low density, there were some febrile cases attributable to Plasmodium falciparum in high density.

¹ The author is indebted to Professor Dr R. Gönner of the Bayer Laboratories, Elberfeld, for supply of the chloroquine silicate (Resochin "S") used in this trial.

No distinction has, however, been made between these differing degrees of density, because it has been shown before that the smallest amount of chloroquine capable of clearing trophozoites of P. falciparum in symptom-free carriers is equally effective among clinical cases (Clyde, 1961).

Chloroquine silicate and diphosphate were supplied in the form of tablets each containing 0.0375 gram base chloroquine. The silicate was almost tasteless, although a slightly bitter after-taste lingered in the mouth. The tablets were swallowed with water by every child under direct supervision, and the mouth then searched. Following ingestion of the drug all children remained seated in front of the investigator for half an hour (as this has proved to be a useful precaution against vomiting of the dose outside) and then returned to their normal activities in classroom and football field.

TOXICITY

No vomiting or nausea occurred with chloroquine silicate, nor were toxic side-effects observed or reported. With the higher doses of the contrast drug, chloroquine diphosphate, these symptoms sometimes arise.

RESULTS

1. Screening trials

One hundred and twenty children carrying trophozoites of all four species of human malaria parasite were each given a single dose of chloroquine silicate, and examined by means of interval and final blood slides for seven days following the treatment. The results obtained include (a) the proportion of asexual infections cleared within seven days by various single doses of the preparation, and (b) the speed of clearance, that is, the number of hours elapsing before parasites were cleared. Results were compared with those of chloroquine diphosphate.

(a) The proportion of asexual infections cleared by various single doses of chloroquine silicate is shown in Table 1. The examinations were made seven days following treatment. Of these infections, 91 were P. falciparum alone, three P. malariae alone, 22 P. falciparum mixed with P. malariae, and four P. falciparum mixed with P. vivax/ovale. In the mixed infections, P. falciparum always predominated.

TABLE 1. EFFECT ON MALARIA INFECTIONS
USING CHLOROQUINE SILICATE AND DIPHOSPHATE

Dose of chloroquine base in grams	Number of cases treated	Number of cases cleared	Percent cleared
Silicate			
0.075	61	61	100.0
0.1125	22	22	100.0
0.150	37	37	100.0
Diphosphate			
0.075	16	16	100.0
0.150	19	18	94.7

It will be observed in the table that the results obtained with chloroquine silicate were as good as with the diphosphate; the single failure of the latter at the higher dosage may have been due to delayed vomiting. Of eight infected cases given a single tablet of the silicate containing as little as 0.375 gram base, five were cleared. This is similar to the activity of the diphosphate in the same low dosage.

(b) The speed of clearance of asexual P. falciparum parasites from the peripheral blood was ascertained by twelve-hourly examination of 24 ambulant children receiving 0.150 gram base of chloroquine silicate, contrasted with 15 receiving the same dose of chloroquine diphosphate. The mean clearance time for trophozoites proved to be 38 hours for the silicate and 40 hours for the diphosphate (in another trial with a larger series, the mean clearance time for chloroquine diphosphate had been 36 hours). These times do not differ significantly.

2. Trials with small daily doses

In order to simulate the small daily intake of chloroquine when used as medicated salt, chloroquine silicate was administered in a dose of 0.0375 gram base every morning to children carrying asexual malaria parasites. The dose was given daily for four days, all 41 children treated being cleared of parasites within seven days. A similar dose given for only three, instead of four, consecutive days cleared the blood of 10 of the 11 children treated. From these results it is apparent that small daily doses of chloroquine silicate are as effective as are those of the diphosphate.

CONCLUSIONS

These trials among human carriers of malaria show that chloroquine silicate is the equal of chloroquine diphosphate in its ability to clear parasites from the blood, and takes the same length of time to do so. When given in small daily doses the effect is similar for both products. Two advantages possessed by chloroquine silicate are: first, this salt is almost without the bitter taste that makes the standard chloroquine preparations difficult to use among children or mixed in salt; second, when administered in high dosage it may not be as likely to induce vomiting.

SUMMARY

1. Chloroquine silicate was tested in Tanganyika among semi-immune children aged 6-12 years, carriers of all four species of malaria parasite.
2. Single doses containing 0.075 gram base invariably cleared asexual parasitaemia, as did larger doses, and toxic side-effects were absent.
3. Small daily doses of 0.0375 gram base content given for four, but not for three, days invariably cleared asexual parasitaemia.
4. In these respects, as well as in the speed of parasite clearance, chloroquine silicate appears to be as effective as chloroquine diphosphate with which it was compared.

REFERENCES

- Clyde, D. F. (1961) Amer. J. trop. Med. Hyg. 10, 1
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