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A FIELD TRIAL ON THE EFFECT OF A COMBINATION OF CYCLOGUANIL PAMOATE AND CHLOROQUINE AGAINST *P. FALCIPARUM* IN BANDAR ABBAS, SOUTHERN IRAN, 1970*

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ABSTRACT

Cycloguanil Pamoate was intramuscularly injected into semi-immune people living in a hyper-endemic malarious area. The results showed that a single dose of Cycloguanil Pamoate by intramuscular injection together with an oral dose of Chloroquine, 10 mg/kg body weight, suppressed *P. falciparum* for ath least 3½ months and P. *vivax* for 5 months in southern Iran.

INTRODUCTION

The anti-malarial activity of cycloguanil pamoate has been studied in experimental clinical trials with non-immune subjects and has been shown to have the capacity to exert at least six months' protection against vivax and falciparum malaria.[1,2,3,4]

Under field conditions, cycloguanil pamoate was injected into Africans and New Guineans living in malarious areas.[5,6] The duration of protection in these trials was less than that observed in the above-mentioned clinical trials, and

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it was about 120 and 150 days in Tanzania and New Guinea, respectively. The anti-malarial effect of cycloguanil pamoate with Amodiaquine was studied in New Guinea[7] and the *P. falciparum* parasite was first seen on day 150. In areas where *P. falciparum* is resistant to proguanil and pyrimethamine, the duration of protection was about 30 to 43 days. [8,9]

The present trial was designed to study the suppressive effect of cycloguanil pamoate against *P. falciparum* in Siahou village, which is situated in the highland area, 108 km N.E.O. of Bandar Abbas, southern Iran.

History of Malaria and the Anti-Malaria Campaign

For many years, Bandar Abbas has been a malarious area nd the disease has been prevalent there in hyperendemic form . Anti-malaria measure were begun in 1950, and up to 1957 the area was regularly under DDT insecticide coverage, 2 gm/m^2 of w.w.p., one round per year.

In 1957, *A. stephensi mysorensis* developed resistance to DDT, and thus all southern parts of Iran were sprayed with Dieldrin at 500 mg/m^2, two cycles per year. In 1959, indication of resistance of *A. stephensi* to DLD was detected. Since 1964, the area has been under Malathion spraying twice a year.

In this area, the malaria vectors are *A. stephensi, A. fluviatilis* and *A. dthali*[10] and, in spite of intensified anti-malaria measures (two rounds of DDT and two rounds of Malathion spraying, treatment of positive cases, introduction of Gambusia fish in active and potential breeding places, etc.), due to the exophilic and exophagic tendency of *A. fluviatilis* and *A. dthali* as well as outdoor sleeping habits of the local population during the transmission season, the transmission of malaria has not been interrupted. The number of positive cases during 1964, 65, 66, 67, 68 and 1969 were 376, 599, 188 26, 57 and 166 respectively. In 1964-1965, about 50 and 51% of positive cases were *P. falciparum* and in 1968-1969, 100% of positive cases were *P. falciparum*.

MATERIAL AND METHOD

Siahou village was chosen for this trial. This village is situated in the highland area, 108 km N.E.O. of Bandar Abbas port, has an altitude of 800 m above sea level, and has a population 1050 persons Malaria in this village is in hyperendemic form with the transmission season from June to November. In early May 1970, before starting the trial, 750 blood samples were taken from the inhabitants; 3 cases of *P. vivax* were found and these cases were excluded from the trial. One hundred forty subjects were chosen for this study; 89 were between 5-10 years of age and 51 between 11-20. On th 5th, 6th and 7th of May 1970, cycloguanil pamoate (Camolar) was intramuscularly injected into these children on the basis of the following schedule : 280 mg for 5-10 years and 350 mg for subjects older than 10 years, together with, in all cases, the oral administration of chloroquine, based on 10 mg/kg of-body weight. In the meantime, 137 persons from the smae age group who served as "control"

received an injection of 2cc vitamin A each.

Immediately prior to use, the vial containing the drug was immersed in hot water and shaken vigorously to ensure full particle suspension.

After the injection of Camolar and vitamin A in the buttocks of the subjects, both groups were under daily observation for the first week and then bi-weekly. During the study, thick blood film samples were taken every 15 days from both groups and examined for malaria parasites.

RESULTS AND DISCUSSION

During the first 3 days, about 80% of the subjects who received an injection of Camolar showed a local reaction and mild tenderness; this was reduced to about 20% on the seventh day. After 2 weeks, localized side-effects at the injection site included one or more of the following : tenderness, swelling, heat, induration and erythema, which begun in 16 subjects (6 in age group 11-20 and 10 in age group 5-10 years). Only one person developed an abcess after 60 days.

In the treatment of urban custaneous leishmaniasis in Iran with cycloguanil pamoate, the most commonly observed side-effects were tenderness at the injection site (83%), induration (27%), fever (6%) and abscess (2%).[11]

In the control group, which received only an injection of vitamin A, local reaction and tenderness was observed in 41% of the individuals during the first 3 days and it then decreased to 33%; on the seventh day it was less than 20% and atfer 30 days it was reduced to 2.4%.

Blood samples taken from the subjects who received an injection of Camolar together with oral administration of chloroquine, showed no malaria parasites up to 105 days after injection. On the 120th, 135th and 150th days, 6, 6 and 9 cases of *P. falciparum*, respectively, were observed, and only after 150 days was one case of *P. vivax* found.

In the control group, 2 cases of *P. vivax* and 8 cases of *P. falciparum* were found 45 and 60 days after the beginning of the study, and within 105 days 21% of the persons showed parasitaemia with *P. falciparum*.

It should be mentioned that the pilot project was originally planned for two injections, one in early May and the other in August, 1970. However, because of the attitude and resistance shown by the majority of the target population, the second injection was cancelled. It is our opinion that the use of cycloguanil pamoate as a prophylactic agent in malaria control programs, at least under the prevailing conditions of the pilot area and similar zones, is of limited practical value, but in special cases such as army personnel or workers it might be valuable.

Drug susceptibility tests by the WHO standard method[12] on subjects whose blood showed *P. falciparum*, on a control group, on a drug injectee group and on the positive cases found among villagers older than 20 years of age, showed that the local strain of *P. falciparum* was susceptible to chloroquine. In the

case of proguanil, which was administered at 300 mg/kg body weight daily for five days[13] to 15 cases with *P. falciparum* and to drug injectees, the blood of these subjects was cleared of a sexual parasites, and thus they were considered susceptible to proguanil.

The results obtained from this study showed that a single dose of cycloguanil pamoate by intramuscular injection together with an oral dose of chloroquine, 10 mg per kg body weight, suppressed *P. falciparum* for at least 3½ months and *P. vivax* for 5 months in southern Iran.

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