

STUDY ON MODIFICATION OF HYPOGLYCAEMIC EFFECT OF QUININE BY DOXYCYCLINE IN ALBINO RATS

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Hypoglycemia has been reported to occur in the patients and animals infected with various species of plasmodium (1). The use of quinine has been associated with significant decrease in blood sugar level, thus worsening the prognosis (2). In such a situation cautious thinking of possible drug interaction which may, further, aggravate the hypoglycemia is mandatory. But the data of the drug interaction of the combination of quinine and doxycycline in the treatment of chloroquine or multi-drug resistant falciparum malaria are not available. This study was aimed to find out whether this combination can cause more hypoglycemia when compared to quinine alone.

METHODS

Thirty albino rats (100-180 g) of either sex were divided into three groups. Rats were starved for 18 hours, but had free access to water. Blood samples (0.5 ml) were collected from the orbital sinuses before the drug treatment. In the animals of group (i), ip distilled water injection was immediately followed by oral 2% gum acacia suspension; in group (ii), ip injection of 0.3% quinine hydrochloride solution (120 mg/kg) followed by oral gum acacia; in group (iii), quinine combined with oral 1% doxycycline

suspension (200 mg/kg). The collection of blood samples were again done at 1, 2 and 3 hr after the feeding of the drugs. The estimation of blood sugar level was done by glucose oxidase peroxidase method (3). The statistical significance was calculated by Student's 't'-test.

RESULTS

Quinine produced significant hypoglycemia at 1, 2 and 3 hr. In group (iii), doxycycline antagonised hypoglycemic effect of quinine (Table I).

TABLE I : Alterations in blood sugar level following the treatment with quinine alone and in combination with doxycycline.

	<i>Blood sugar in mg% Mean ± SEM</i>			
	<i>0 hr</i>	<i>1 hr</i>	<i>2 hr</i>	<i>3 hr</i>
Control	95.1 ± 1.8	95.5 ± 3.8	90.2 ± 3.1	88.8 ± 3.0
Quinine	92.1 ± 2.3	66.8 ± 5.3***	63.8 ± 5.3***	70.2 ± 3.7**
Quinine + Doxycycline	94.1 ± 1.9	79.5 ± 4.3	79.6 ± 2.6*	83.8 ± 2.2**

n = 10 in each group, *P 0.02, **P 0.01 and ***P 0.001.

DISCUSSION

The blood sugar levels of the control albino rats were within the normal range (4). Quinine *per se* can produce the hypoglycemic effect in conformity with the findings of other workers.

Doxycycline can potentiate the hypoglycemic effect of glibenclamide. Here, the inability of doxycycline in potentiating the hypoglycemic effect of quinine may be due to less plasma protein binding nature and higher volume of distribution of quinine compared to glibenclamide.

Quinine has glucose like activity in releasing insulin from the isolated β -cell (5) and availability of calcium ion and its influx are also very important for the release of insulin. The antagonistic effect of doxycycline on the hypoglycemic action of quinine may be due to the calcium chelating effect of doxycycline, thereby reducing availability of calcium for influx into β -cell for the release of insulin.

In conclusion, doxycycline antagonises hypoglycemic effect of Quinine and this combination is safe.

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