

THE EFFECT OF PALUDRINE ON HUMAN GASTRIC SECRETION

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(Received July 22, 1948)

Burn and Vane (1948) have reported that paludrine depressed gastric secretion in cats after histamine stimulation. This was worth investigating in man, as paludrine is comparatively non-toxic and a means of reducing gastric secretion might be of value in the treatment of peptic ulcer.

Doses of up to 1.5 g. a day have been given without producing serious toxic effects. Abdominal discomfort, nausea, and vomiting have been noted by Fairley (1946) and Maegraith (1946) with doses of 1.0 g. a day, and Fairley also observed diarrhoea and haematuria. The toxic symptoms usually subsided without reduction of the dose as the malaria for which the paludrine was given was relieved.

We have studied the effect of paludrine on gastric secretion in man by two methods, giving it orally before a gruel test meal and intravenously with subcutaneous injections of histamine.

Twenty patients (11 men and 9 women) were given gruel test meals on two consecutive days, on one of which they received 1.0 g. paludrine hydrochloride by mouth 2 hours before the meal began. One man and one woman were excluded from the series on account of achlorhydria in both test meals, and the tests could not be completed in two women who vomited after the paludrine. The results in 16 cases are available for analysis.

Paludrine was given before the first meal in half the cases and before the second in the other half. The resting juice was drawn off immediately before the meal was started, and samples were taken at half-hourly intervals up to two and a half hours. The concentration of free acid after paludrine was compared with that of the sample drawn off after the same interval in the control meal. The averaged results for the 16 cases are shown in Table I.

TABLE I

The effect of 1.0 g. paludrine hydrochloride on the concentration of free HCl after a gruel test meal. Mean results for 16 patients.

Time	C.C. N/10 HCl per 100 c.c. gastric juice		B—A	“t”
	A Control	B Paludrine		
½ hr.	18.1	7.7	—10.4	2.01
1 hr.	30.8	17.3	—13.5	2.17
1½ hrs.	37.7	25.4	—12.3	2.31
2 hrs.	30.6	25.5	—5.1	1.12
2½ hrs.	22.3	23.7	+1.4	—
Average	27.9	19.9	—8.0	3.78

Individual results varied from an increased concentration of acid after paludrine to the production, in four cases, of achlorhydria. Considering them as a whole, the average depression of free acidity after paludrine was 8.0 c.c. N/10 HCl per 100 c.c. juice. Applying the “t” test to the 80 individual differences between comparable specimens, the probability of obtaining such differences due to chance on the hypothesis that paludrine had no effect is less than 0.01 ($t=3.78$, $n=79$). The depression can therefore be considered to be real. If the results at each period after the start of the meal are considered separately a significant depression with paludrine was found at 1 and 1½ hours ($0.02 < P < 0.05$), while after a half-hour the depression was just too small to be considered significant. No effect was demonstrated at 2 and 2½ hours.

Repetition of the test meal had no effect on the acidity of the gastric secretion. The average acidity of all the samples drawn off during the second meal was 0.3 c.c. N/10 HCl per 100 c.c.

* While working with a grant from the Medical Research Council.

less than the average of the samples of the first meal.

In contrast to the results with oral paludrine and gruel test meals, no effect was demonstrated when paludrine was given intravenously and gastric secretion was stimulated with histamine subcutaneously; 0.5 mg. histamine was given initially, with a further 0.5 mg. after 60 to 80 minutes. Doses of up to 400 mg. paludrine acetate were given intravenously immediately before the second injection of histamine. The stomach was emptied at 10 min. intervals, and the effect of the paludrine was determined by

comparing the amounts and average concentrations of free acid secreted in the hours following the first and second injections of histamine. The results in the 4 subjects given 400 mg. are shown in Table II.

The amount of paludrine given intravenously was small in comparison with that used by Burn and Vane in cats, but it was comparable with the oral dose which was effective in depressing acid secretion in response to a gruel test meal in man. The reason for the conflicting results is not clear.

SUMMARY

1.0 g. paludrine hydrochloride given 2 hours before the start of a gruel test meal produced a significant depression of more than 33 per cent in the concentration of free acid during the first 1½ hours of the meal. No consistent effect was observed with doses of up to 400 mg. paludrine acetate given intravenously on the gastric secretion in response to histamine.

We should like to express our thanks to Dr. F. Avery Jones, under whose direction the work was carried out, for his help and advice.

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TABLE II

The amount and concentration of free acid secreted in one hour after 0.5 mg. histamine (1st hr.) and 0.5 mg. histamine S.C. and 400 mg. paludrine I.V. (2nd hr.).

Subject	Amount of free acid, c.c. N/10 HCl			Average concentration of free acid, c.c. N/10 HCl % (v/v)		
	1st hr.	2nd hr.	Difference	1st hr.	2nd hr.	Difference
1	202.1	155.4	-46.7	59.0	59.1	+0.1
2	203.0	181.9	-21.1	67.9	65.7	-2.2
3	14.1	19.9	+5.8	20.0	37.0	+17.0
4	254.7	323.3	+68.6	107.0	113.2	+6.2