EFFECT OF ATROPINE AND PHYSOSTIGMINE ON THE HISTAMINE INDUCED GASTRIC SECRETION OF DOG[1]

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Effect of atropine and physostigmine (0.1 mg/kg of each) on histamine (0.06 mg/kg) induced gastric secretion in dogs with gastrostomy was investigated. It was observed that atropine diminished the volume, free and total acidities of gastric secretion, whereas, physostigmine raised the acidity but diminished the volume of gastric secretion possibly, due to increased motor activity of the gut. There was no variation in the total chloride in either case. It was concluded that most likely the parietal gastric cells possess a persistent tonic activity which is essential for the maximum response to histamine. The tonic activity of parietal cells is dependent on the parasympathetic innervation and was thus depressed by atropine and augmented by physostigmine, thereby. modifying the response of histamine.

Histamine is one of the most potent gastric stimulants first described by Popielski (1920). It is generally believed to have a direct action mainly on the acid secreting cells of the stomach, without the participation of nerve, as atropine does not abolish its effect. Babkin (1930) also came to the conclusion that the presence or absence of vagi make little difference on histamine induced gastric secretion. However Keeton *et al.*, (1920), Polland (1930) and Gray (1937) reported that atropine had inhibitory effect on the histamine induced gastric secretion. Sircus (1953) had shown that carbachol augments the effect of physostigmine, a histamine potentiator, indicating the possibility of a parasympathetic nervous influence on histamine effects.

The present work is a part of the studies carried out on gastric secretion and was especially undertaken to note whether atropine and physostigmine have any effect on the histamine induced gastric secretion.

METHODS

This work was conducted on male, healthy dogs operated for gastrostomy by Ssabanjew-Frank Technique (Shackelford, 1955). After this operation when the wound was perfectly healed, experiments were performed on them.

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They were not fed anything except water, eighteen hrs before the experiment. Fasting gastric contents, if any, were aspirated. Histamine acid phosphate was used as a stimulus for inducing gastric secretion. The response of various doses of histamine to evoke gastric secretion was tested, and it was found by trials that 0.06 mg/kg of histamine induced the optimum gastric response without any deleterious effect. Gastric secretion after half an hour of histamine injection was collected by passing a catheter through the stomach opening and was aspirated with a syringe. This secretion served as a control.

In each experiment, fasting half an hour histamine induced gastric secretion was collected for analysis. After the next half hr gastric secretion, if any, was again aspirated and discarded and 0.1 mg/kg of atropine or physostigmiue was administered intramuscularly. The gastric contents were completely evacuated half an hour after injecting the drug and again 0.06 mg/kg of histamine acid phosphate was given. The gastric secretion so induced by histamine when atropine or physostigmine was given before, was collected and analysed.

The volume of each sample was noted and free and total acidities were estimated by titrating against the standard 0.0IN NaOH solution, using Topfer's reagent and phenophthalein as indicators, taking the orange and the pink colours as the end points respectively. The chloride was estimated by Whitehorn-Volhard method (Baldwin and Bell, 1955).

Ten experiments on five dogs were performed.

RESULTS

The following Table shows the results of the mean of ten experiments conducted on five dogs.

TABLE

Effect of atropine and physostigmine on the histamine induced gastric sccretion in dog

Gastric sample	Volume (ml)	Free acidity (mEq/L)	Total acidity (mEq/L)	Total chlorides (mEq/L
Normal	49±1.6	110±1.6	117±1.0	160±0.9
After atropine	23±0.9	94±2.0	106±1.0	160±0.7
After Physostigmine	38±0.9	116±2.2	122±0.8	160±1.1
	Statistical analysis 't' values			
Between normal & after atropine	14.4[1]	2.3[1]	9.1[1]	0.4
Between normal & after physostimine	6.1[1]	2.2[1]	0.2[1]	0.5

1 't' values significant at 5% level mean±S.E.

The above Table shows that atropine reduced the volume and free and total acidities of gastric secretion, and the physostigmine raised the free and total acidities but diminished the volume. There was no variation in the total chloride content in either case.

DISCUSSION

These experiments show that atropine has diminished the action of histamine on gastric secretion, as the volume, free and total acidities indicated a fall in their normal values ; while physostigmine has augmented the action of histamine on gastric secretion as shown by increased free and total acidities. Total chlorides were not affected in either case, as neutral and acid chlorides are inversely related, so the total chloride tends to remain relatively constant (Best and Taylor, 1961). Thus, the response of histamine which acts directly on the gastric oxyntic cells as shown by Babkin (1944) and Kahlson (1948) was modified by these drugs.

Alonso *et al* , (1948) found that the antihistaminic drugs had no inhibitory effect on histamine at those sites where histamine acted indirectly. Hence, histamine must have an indirect influence on the parietal cells. Gray (1937) suggested that atropine by acting on the cell or cell wall nonspecifically did not allow it to react with histamine. Benjamin *et al.*, (1950) had proposed that there had been synergic action between acetylcholine and histamine ; locally released acetylcholine would modify the response of parietal cells to all stimuli including histamine. Born and Vane (1953) concluded that histamine had an indirect effect on oxyntic cells—possibly an interaction between histamine and blood was necessary before secretion could occur, and this required some time. Janowitz and Hollander (1956) also found that atropine in sufficient doses could markedly depress the histamine induced secretion. They were of the opinion that histamine and acetlycholine acted at the same receptor site on the cell. Histamine was the final chemical mediator for the stimulation of the parietal cells. Atropine was unable to differentiate between acetylcholine or vagal stimulation, and especially to histamine stimulation at least in dog so atropine given previously would depress the histamine secretion.

It has been observed that the acidity of the gastric juice increasd with increased rate of gastric secretion. In the case of the histamine induced secretion after physostigmine, the acidity had increased but the volume had diminished. The diminution in volume might be due to increased motor activity of the gut caused by physostigmine so that some of the gastric contents might escape through the pylorus, amounting to diminution in the gastric contents.

Thus it can be concluded that the modification produced by atropine and physostigmine in the response of histamine induced gastric secretion was not direct, they must have acted indirectly, most likely through the innervation of the oxyntic cells and thus had modified their persistent tonic activity, thereby the response to the histamine in the former case had diminished while it had increased in the latter.

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