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Cardiovascular effects of serotonin on the pigeon *Columba livia*

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Abstract. The effect of serotonin on the blood pressure and the heart rate of the pigeon *Columba livia* was investigated in anaesthetised condition. The effect of histamine was also investigated to understand the mechanism of action of serotonin. Serotonin and histamine were both depressors. Serotonin produced bradycardia while histamine produced tachycardia. Atropine treatment reversed the serotonin-induced depressor response but only partially blocked the histamine-induced fall in blood pressure. Atropine treatment completely abolished the serotonin-induced bradycardia but partially inhibited the histamine-induced tachycardia. A reflex vagal activity and a direct vasoconstrictor activity were proposed on the action of serotonin.

Keywords. Serotonin; histamine; blood pressure; heart rate; atropin; *Columba livia*.

1. Introduction

The role of humoral agents other than catecholamines that affects avian blood pressure has received little attention. Sturkie and his co-workers (1976) found depressor response in the fowl after serotonin injection at doses ranging from 0·5 μg to 10 μg/kg. Serotonin also produced reflex increase in the heart rate in the fowl which could be blocked by atropine (Woods 1971). Commenting on the mechanism of action, Bunag and Walazak (1962) believed that the depressor response in the chicken was due to the release of histamine induced by serotonin. The authors came to this conclusion after observing a pressor response by serotonin in chicken whose histamine content was depleted by the chemical coded '48/80'. Interestingly, on the other hand, Woods (1971) could not find any evidence of histamine release when the serotonin-induced depressor response reached its lowest value in the fowl.

It is now evident that the mechanism of serotonin induced blood pressure change was examined in the fowl only and the mechanism of action is yet to be determined. Moreover, studies on a single species are certainly not sufficient to reach any general conclusion on any drug action such as serotonin. In order to arrive at an acceptable conclusion, the action of serotonin on the blood pressure and the heart rate of the pigeon *Columba livia* has been studied and is reported in this paper. Cardiovascular action of histamine is also studied to find any similarity in its effects with serotonin in order to reexamine the proposition made by Bunag and Walazak (1962). Atropine treatment prior to serotonin and histamine administration is also made to investigate the possible role of reflex action of vagus to produce the effects.

2. Material and methods

Adult pigeons (250 to 300 g body weight) of either sex were used. The birds were divided into two groups. One group received serotonin injections at doses ranging from 1 to

8 μg/kg through a venous cannula into the brachial vein before and after intravenous treatment of atropine at a dose of 2 mg/kg. Fifteen minutes after atropine treatment, serotonin injections were repeated. The second group received histamine treatment in the same manner. All these treatments were made on animals anaesthetised by intraperitonial injection of pentobarbital sodium (Nembutal, Abbott Laboratories) at a dose of 40 mg/kg. The arterial blood pressure and the heart rate were recorded as described by Banerjee and Ghosh (1982).

Histamine was injected as histamine dihydrochloride (E. Merck), serotonin as serotonin-creatinin sulphate (E. Merck) and atropine as atropine sulphate (Gluconate Limited). All the drugs were dissolved in normal saline except atropine which was purchased as aqueous solution. The doses were expressed as its salt form.

3. Results

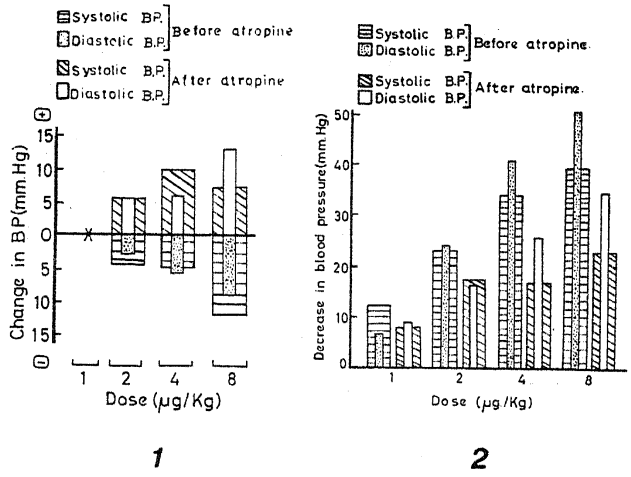
In normal pigeons 1 μg/kg serotonin injection could not produce any change in blood pressure and the heart rate. In some pigeon, the doses of 1 and 2 μg/kg of serotonin produced little rise in the blood pressure. The doses of 2, 4, and 8 μg/kg serotonin produced a fall in the blood pressure (figures 1, 3). This was occasionally followed by a little rise in blood pressure. Histamine also produced a fall in the blood pressure in doses ranging from 1 to 8 μg/kg and was sometimes followed by a slight rise in blood pressure (figures 2, 3). The depressor response produced by histamine was greater than that of serotonin. High doses of histamine (2, 4, and 8 μg/kg) resulted in greater fall in diastolic pressure than systolic.

The effects on the heart rate induced by serotonin or histamine presented some interesting features. Serotonin at doses ranging from 2 to 8 μg/kg produced a fall in the heart rate while histamine at all doses produced a rise of the same (table 1).

Atropine treatment before serotonin injections reversed the depressor response to a pressor one, but the same treatment before histamine could partially inhibit the depressor response (figures 1, 2, 3). The bradycardia induced by serotonin was completely inhibited after atropine treatment while the tachycardia after histamine was partially blocked at high doses and completely suppressed at low doses (table 1).

4. Discussion

The blood pressure response after serotonin in the pigeon was depressor in all the effective doses. Similar findings were reported by Sturkie (1976) in the fowl. The reversal of depressor response induced by serotonin after atropine treatment indicates an unmasking of a direct vasoconstrictor action of serotonin. This serotonin induced vasoconstriction was also observed in the isolated aortic strips of chicken (Moore 1978) and the Chucker, *Alectoris graeca* (Muramatsu and Bern 1979). The partial blockade of histamine induced fall in blood pressure after atropine treatment supports the view of Woods (1971) that histamine was not responsible for the serotonin-induced depressor response. Also, it seems that, histamine acts directly on the blood vessels producing vasodilatation as evidenced from the greater fall in the diastolic blood pressure than systolic. On the other hand, there was a tendency of greater fall in systolic blood pressure after serotonin injection before atropine treatment.



Figures 1, 2. Histograms showing the effect of **1.** serotonin **2.** histamine on the systolic and diastolic blood pressure of the pigeon before and after atropine treatment. The results are expressed as decrease (−) or increase (+) of the blood pressure from the preinjection level, 0. (The dose of 1 μg/kg produced no change (X). figure 1).

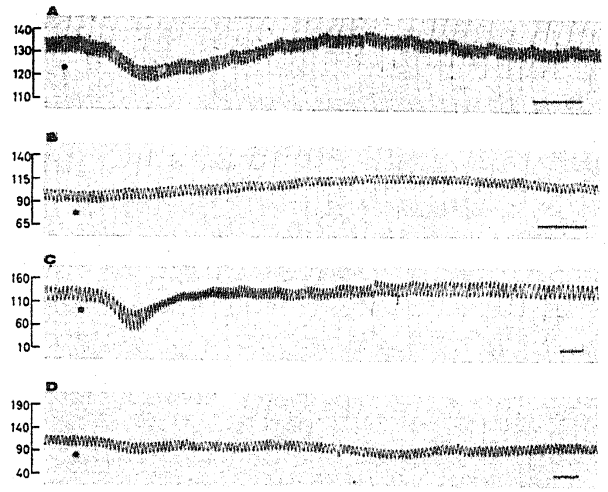


Figure 3. Blood pressure recordings showing the effects of serotonin and histamine on the blood pressure of pigeon. Panels A and B show the effect of serotonin injection (4 μg/kg) before and after atropine treatment respectively, in one animal. Panels C and D show histamine-induced changes in blood pressure at a dose of 8 μg/kg before and after atropine treatment respectively in another animal. Horizontal bars on the right of each panel represent 2 sec time. Vertical calibrations on the left indicate the blood pressure in mm Hg.

Instead of a rise in the heart rate as reported by Woods (1971) in the fowl, a decrease was noted in the pigeon. This was also blocked by atropine indicating a reflex vagal activity induced by serotonin. The positive chronotropic effect induced by histamine was also found in other avian species (Sturkie 1976). The partial inhibition of histamine induced rise in the heart rate by atropine points to a direct action of histamine on the myocardium (at least to some extent). Nothing definite can be said on the possible role of cardiovascular chemoreceptor as its function is yet to be ascertained (Magno 1973).

Table 1. Effects of serotonin and histamine on the percent increase (↑) or decrease (↓) in the heart rate of the pigeon before and after atropine treatment.

	Treatments			
	Serotonin		Histamine	
Doses (μg/kg)	Untreated	Atropine treated	Untreated	Atropine treated
1	0	0	(↑) 9·1 ± 1·6*	0
2	(↓)40·0 ± 3·2	0	(↑)22·4 ± 4·9	0
4	(↓)34·0 ± 3·5	0	(↑)26·9 ± 6·9	(↑) 5·3 ± 1·8**
8	(↓)40·2 ± 6·8	0	(↑)34·1 ± 8·7	(↑)10·9 ± 2·3***

*Mean ± SEM. **$p < 0{\cdot}01$; ***$p < 0{\cdot}05$ after paired student's t test with untreated. 0 indicates no change.

It, therefore, seems quite probable that the depressor response induced by serotonin in the pigeon was principally due to the reflex drop in the heart rate leading to a fall in the cardiac output. On the other hand, the action of histamine was direct and was antagonised by atropine at the receptor level.

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