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Histamine Affects Blood Flow through the Reproductive Organs of the Domestic Hen (*Gallus domesticus*)

Anna HRABIA, Helena PACZOSKA-ELIASIEWICZ, Józef NIEZGODA and Janusz RZĄSA

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The study was undertaken to determine the effect of histamine on blood flow to the ovary and oviduct in the domestic hen (*Gallus domesticus*). Cardiac output and blood flow were measured with ^{86}RbCl through the ovarian stroma, white ovarian follicles, yellow preovulatory follicles, postovulatory follicles and four oviductal parts: infundibulum, magnum, isthmus and shell gland 1 min and 5 min after histamine treatment. In comparison with control hens which received 0.9% NaCl, histamine significantly increased (by 21.4%) cardiac output exclusively 5 min after its treatment. Blood flow (ml/min/g tissue) through the stroma, the infundibulum and the shell gland was significantly elevated both 1 min (54.3%, 84.3% and 64.2%, respectively) and 5 min (87.1%, 111.5% and 70.4%, respectively) after histamine administration and through the ovarian follicles (29.3%-61.9%) exclusively 5 min after histamine treatment. The increase in blood flow through the ovarian stroma, follicles and the oviductal parts following the administration of histamine was not the result of increased cardiac output but the consequence of local histamine action on blood flow through the ovary and oviduct. The results of the present study indicate that histamine, by influencing the hemodynamics of blood vessels and in consequence changing the blood flow through the reproductive organs, participates in the processes taking place in the ovary during growth, maturation and regression of the follicles, and in the oviduct during formation of the egg.

Key words: Histamine, blood flow, ovary, oviduct, chicken.

Anna HRABIA, Helena PACZOSKA-ELIASIEWICZ, Józef NIEZGODA, Janusz RZĄSA, Department of Animal Physiology, Agricultural University of Cracow, Mickiewicza Av. 24/28, 30-059 Kraków, Poland
E-mail: rzhrabia@cyf-kr.edu.pl

Histamine is present in all compartments of the chicken ovary (PACZOSKA-ELIASIEWICZ & RZĄSA 1998) and the oviduct (MEYER & STURKIE 1974; PACZOSKA-ELIASIEWICZ *et al.* 1998; HRABIA *et al.* 2001) and its level changes significantly during sexual maturation, lay and pause in lay (HRABIA *et al.* 1997, 1998; PACZOSKA-ELIASIEWICZ 1999; PACZOSKA-ELIASIEWICZ & RZĄSA 1997, 1998; PACZOSKA-ELIASIEWICZ *et al.* 1998).

In the ovary of a laying hen, within the hierarchy of yellow preovulatory F7-F1 follicles, the initial decrease in histamine concentration from the F7 to the F4 is followed by a gradual increase as the follicle matures. After ovulation there is a significant decrease in histamine concentration of the postovulatory P1 follicle (PACZOSKA-ELIASIEWICZ & RZĄSA 1998). On the other hand, the histamine level changes in the oviduct according to the stage of the egg formation cycle. Just before ovulation, the histamine concentration significantly increases in the infundibulum. In the magnum and the shell gland histamine concentration elevates when the ovum enters the segment (PACZOSKA-ELIASIEWICZ *et al*. 1998). Moreover, administration of histamine receptor blockers causes a gradual delay of oviposition time (PACZOSKA-ELIASIEWICZ 1999; PACZOSKA-ELIASIEWICZ *et al.* 2000). These results indicate that histamine is involved in local regulation of ovarian and oviductal activity connected with growth, maturation and regression of the ovarian follicles and formation of the egg in the oviduct.

As in mammals, histamine is considered a mediator of ovarian hyperaemia, increases blood flow through the ovary induced by LH (SZEGO & GITIN 1964; WURTMAN 1964; KRISHNA *et al.* 1986), and affects blood flow through the uterus (DYNAROWICZ *et al.* 1988). It seems likely that in birds the action of this amine as an intra-ovarian and intra-oviductal regulator may occur via its association with regulation of blood flow. Therefore, the aim of the present study was to examine the effect of

histamine on cardiac output and blood flow through the ovary and four oviductal parts of the domestic hen.

Material and Methods

The experiment was carried out on 35 week old Hisex Brown laying hens (n=32) caged individually under a photoperiod of 14 h light/10 h dark with free access to food and water. Birds at 0.5 h before the expected time of ovulation were divided into control (n=16) and experimental (n=16) groups. Experimental hens received histamine (5 μg/kg b.wt, i.v.), while control hens received 0.9% NaCl. Cardiac output and blood flow through the ovarian stroma (STR), white ovarian follicles (small SWF, atretic AWF, large LWF), yellow preovulatory follicles (F5-F1; F5<F4<F3<F2<F1), postovulatory follicles (P1-P3; P1>P2>P3) and four oviductal parts (infundibulum, magnum, isthmus and shell gland) were measured 1 min (n=8) and 5 min (n=8) after histamine or NaCl treatment.

Cardiac output and blood flow were measured with ^{86}RbCl using the method of SAPIRSTEIN (SAPIRSTEIN 1958) with minor modification (NIEZGODA *et al.* 1979). Anaesthesia was induced by injection of sodium pentobarbital (12 mg/kg body weight, i.v.). The femoral artery was catheterised for blood collection. One or 5 min following histamine administration, radioactive rubidium (30 μCi ^{86}RbCl/ 0.5 ml of physiological saline) with heparine (5 mg) was injected into the wing vein and immediately after isotope injection the arterial blood was collected at a rate of 15-20 samples per 1 min in a volume of 0.2 ml. Immediately after blood collection the hens were decapitated and the ovary and oviduct were isolated. Each part of the ovary and oviduct was weighed, homogenised and their radioactivity was measured using a γ-counter (LKB). The cardiac output was calculated from the curve relating the radioactivity of the arterial blood to the time. The fraction of the cardiac output perfusing the measured tissue was calculated by dividing the radioactivity of the tissue by the total activity administrated. Blood flow through the organ was expressed as ml/min/g tissue.

For statistical evaluation of the results, a two-way ANOVA followed by Duncan's multiple range test was used. Differences were considered significant at the level of P<0.05.

Results

It was found that 1 min after histamine administration cardiac output did not change significantly in comparison with control hens, while 5 min after histamine treatment a significant increase in cardiac output (21.4%) was observed (Table 1).

Table 1

Effect of histamine on cardiac output (mean ± SE)

Time after treatment	Cardiac output (ml/min)	
	Control (0.9% NaCl)	Histamine (5 μg/kg)
1 min	287.4 ± 19.47[a]	333.1 ± 28.20[a]
5 min	305.7 ± 18.80[a]	371.1 ± 15.81[b]

N=8; [a, b] – means marked with different superscripts differ significantly at P<0.05.

1 min after histamine administration in the ovary a significant (P<0.01) increase (54.3%) in blood flow was observed through stroma, whereas blood flow through ovarian follicles did not change (data not shown). Changes in blood flow (ml/min/g) through the ovary 5 min after histamine treatment are presented in Table 2. In comparison with control hens histamine administration significantly (P<0.01, P<0.05) increased blood flow through the stroma and each class of ovarian follicles, except white atretic follicles (AWF), in which blood flow in control and experimental group did not differ significantly. In comparison with the control group, blood flow through the stroma increased by 87.1%. Blood flow through the ovarian follicles increased as follows: small white – 61.9%, large white – 42.5%, yellow preovulatory (F5-F1) – 29.3% to 35.0%, postovulatory (P1-P3) – 37.5% to 42.8% (Fig. 1).

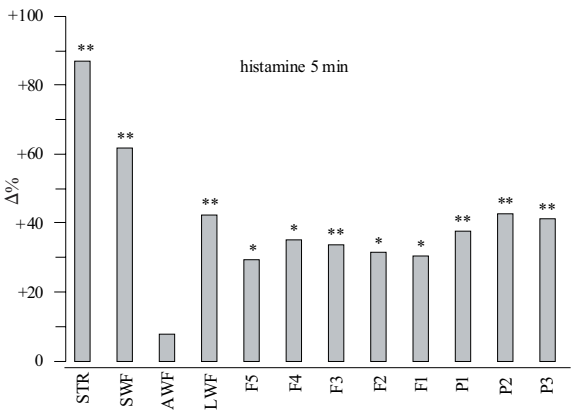

Fig. 1. Blood flow through the ovary 5 min after histamine administration expressed in relative values (△%). Values (ml/min/g tissue) in control group = 100%. STR – stroma; SWF – small white follicles; AWF – atretic white follicles; LWF – large white follicles; F5, F4, F3, F2, F1 – large preovulaory follicles (F5<F4<F3<F2<F1); P1, P2, P3 – postovulatory follicles (P1>P2>P3).
**P<0.01, *P<0.05 – in comparison with control group with unrelated values.

Table 2

Blood flow through stroma (STR) and white (SWF, AWF, LWF), yellow preovulatory (F5-F1) and postovulatory (P1-P3) chicken ovarian follicles 5 min after histamine administration (mean ± SE)

Tissue type	Blood flow (ml/min/g)	
	Control (0.9% NaCl)	Histamine (5 μg/kg)
STR	0.31 ± 0.035^{a}	0.58 ± 0.065**
SWF	0.42 ± 0.037^{ac}	0.68 ± 0.070**
AWF	0.13 ± 0.015^{b}	0.14 ± 0.014
LWF	0.47 ± 0.047^{cd}	0.67 ± 0.058**
F5	0.58 ± 0.045^{de}	0.75 ± 0.056*
F4	0.60 ± 0.048^{de}	0.81 ±0.067*
F3	0.65 ± 0.047^{e}	0.87 ± 0.061**
F2	0.70 ± 0.051^{e}	0.92 ± 0.071*
F1	0.69 ± 0.043^{e}	0.90 ±0.073*
P1	0.32 ± 0.020^{a}	0.44 ± 0.035**
P2	0.21 ± 0.017^{ab}	0.30 ± 0.025**
P3	0.17 ± 0.013^{b}	0.24 ± 0.020**

N=8; $^{a, b, c, d, e}$ – within control group means with different superscripts differ significantly at P<0.05; **P<0.01, *P<0.05 – in comparison with control group.

Histamine administration in the oviductal parts significantly increased blood flow through the infundibulum and shell gland 1 min as well as 5 min after its administration (P<0.01, P<0.05, Table 3). One minute after histamine treatment the increase in blood flow to the infundibulum was 84.3% and 64.2% to the shell gland. After 5 min the increase was 111.5% and 70.4%, respectively (Fig. 2).

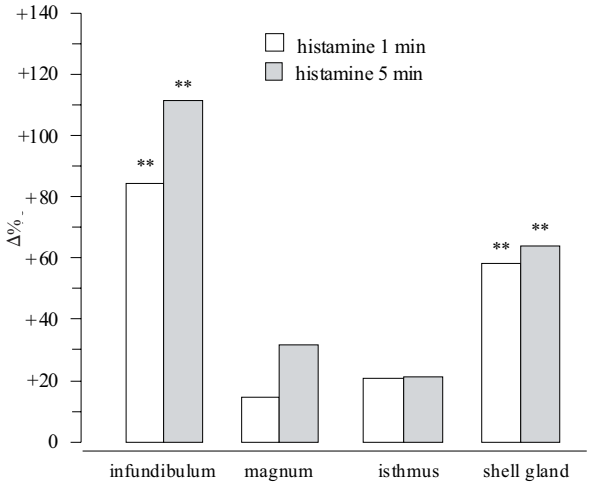

Fig. 2. Blood flow through the oviductal parts 1 min and 5 min after histamine administration expressed in relative values (△%). Values (ml/min/g tissue) in control group = 100%. **P<0.01 – in comparison with control group with unrelated values.

Discussion

An important role in the normal functioning of the avian ovary and oviduct is played by the blood supply which changes according to ovarian and oviductal activity (MOYNIHAN & EDWARDS 1975; NIEZGODA *et al.* 1979; NIEZGODA *et al.* 1982). In a laying hen, 20% of cardiac output perfuses the ovary (NIEZGODA *et al.* 1982) and 15% the oviduct (MOYNIHAN & EDWARDS 1975), which indicates high rate of metabolic processes in these organs. Ovarian activity in birds is connected mainly with vitello- and steroidogenesis, while oviductal activity pertains to the formation of the egg during its passage through the oviductal parts. During each ovulatory cycle of 24 h the hen lays an egg weighing 50-70 g, composed of 15-17 g yolk formed in the ovary, 25-35 g egg white and 5-6 g shell synthesised in the oviduct. The presence of the egg in a given oviductal segment significantly (3-4 times) increases blood flow to this part (BOELKINS *et al.* 1973). As changes in ovarian and oviductal functions are accompanied by changes in histamine levels, in the present study cardiac output and blood flow through the ovary and ovi-

Table 3

Blood flow through oviductal parts 1 min and 5 min after histamine administration (mean ± SE)

Oviductal parts	Blood flow (ml/min/g)			
	1 min		5 min	
	Control (0.9% NaCl)	Histamine (5 μg/kg)	Control (0.9% NaCl)	Histamine (5 μg/kg)
Infundibulum	0.41 ± 0.024^{a}	0.75 ± 0.043**	0.43 ± 0.053^{a}	0.91 ± 0.034**
Magnum	0.54 ± 0.070^{ab}	0.62 ± 0.056	0.51 ± 0.051^{a}	0.68 ±0.077
Isthmus	0.59 ± 0.067^{b}	0.73 ± 0.077	0.58 ± 0.052^{ab}	0.72 ± 0.079
Shell gland	0.71 ± 0.059^{b}	1.16 ± 0.120**	0.71 ± 0.050^{b}	1.21 ± 0.110**

N=8; a, b – within control group means with different superscripts differ significantly at P<0.05; **P<0.01 in comparison with control group.

duct were measured 1 and 5 min following histamine administration.

In control hens values of cardiac output were in accordance with earlier studies (MOYNIHAN & EDWARDS 1975; NIEZGODA *et al.* 1979; NIEZGODA *et al.* 1982; NIEZGODA *et al.* 1990). Histamine significantly increased cardiac output 5 min after its administration. Blood flow expressed as ml/min/g tissue through the ovary in the control group increased gradually along with the maturation of the follicles, reaching the highest level in yellow preovulatory follicles, among which statistically significant differences were not present. A similar lack of differences in blood flow among the hierarchical follicles was revealed by previous investigators (MOYNIHAN & EDWARDS 1975; SAPIRSTEIN 1958; SCHAYER 1962). White atretic follicles in which vascularity is disrupted (GILBERT *et al.* 1985), were characterised by the lowest blood flow, i.e. from 2.4 to 7.7 times lower than in stroma, growing white follicles and hierarchical yellow follicles. On the other hand, in postovulatory follicles possessing a well developed system of blood vessels functioning at least 6 days after ovulation (MOYNIHAN & EDWARDS 1975), blood flow gradually decreased with progressing regression of these follicles. In the largest postovulatory follicle (P1), blood flow was more than 2 times lower than in the largest preovulatory follicle (F1), which seems clear because this follicle does not accumulate yolk and steroidogenesis is at a very low level (HUANG *et al.* 1979).

The present study has shown that histamine significantly increased blood flow through the ovarian stroma 1 min after administration, and 5 min following treatment through the stroma and each class of the ovarian follicles except white atretic. During this time cardiac output increased by 21.4% as compared to the control, whereas blood flow to the stroma and populations of the follicles increased from 29.3% to 87.1%. Changes in blood flow may be the result of an increase in cardiac output or local histamine action in the ovary. Calculation of blood flow as a percent of cardiac output per gram of tissue revealed an increase in blood flow through the stroma of 54.4%, the SWF – 33.6%, the LWF – 16.9%, the F5 to F1 follicles – 6.3%-11.2% and post ovulatory follicles P1 to P3 – 12.4%-16.1%. This may suggest that the remarkable increase in blood flow in the stroma and SWF was not the result of increased blood cardiac output but the consequence of the local histamine action on blood flow through the ovary.

An increase in blood flow was revealed through two parts of the oviduct, the infundibulum and the shell gland, 1 min as well as 5 min following histamine administration. This amounted to an 84.3% and 111.5% increase in the infundibulum and a 64.2% and 70.4% increase in the shell gland, respectively. Notably, measurement of blood flow was carried out in hens just after oviposition, i.e. about 0.5 h before the expected time of ovulation. Therefore, an increase in blood flow in the infundibulum may be connected with its higher activity around the time of ovulation (CROSSLEY *et al.* 1975; RZĄSA 1981), while an increase of blood flow through the shell gland may be connected with the oviposition process. The experimental treatment did not affect the magnum and the isthmus, however, it would be interesting to see whether the presence of the egg in particular segments of the oviduct changes the influence of histamine. As has been previously reported (MOYNIHAN & EDWARDS 1975; NIEZGODA *et al.* 1982; WOLFENSON *et al.* 1982), the highest blood flow through the oviductal parts occurs before, during or after the passing of an egg through a given segment.

To sum up, the results of the present study indicate that histamine influences the hemodynamics of blood vessels and consequently modifies blood flow through the ovary and oviduct, thereby participating in the processes taking place in the ovary during growth, maturation and regression of the follicles and in the oviduct during formation of the egg.

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