EFFECT OF ESTROGEN AND TESTOSTERONE ON THE GASTRIC SECRETION OF RATS AND CONCIOUS RABBITS

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Summary: Shay rats and conscious rabbits were used to study the effect of sex hormones on gastric secretion. Daily injections of estradiol-di-propionate and testosterone-propionate were given separately to each set of animals, while the control animals received solvent alone for the same duration of time. Estrogen inhibited gastric acid output but augmented the mucus secretion as evidenced by increased hexosamine and fucose contents; and testosterone had the reverse effects. The effect of estrogen was more potent than that of testosterone. An inverse relationship between gastric acid and mucus secretion has been noted. Peptic activity varied independently of the acid output. These hormones seemed to vary the acid output by modifying the composition of mucus secretion.

Key words: Shay rats, acid output, peptic activity, sex hormones, glycoproteins, hexosamine, fucose, augmented histamine, stimulated gastric secretion

INTRODUCTION

A correlation between sex hormones and gastric secretion has been described (1,19). In cat, estrogen was shown to reduce gastric acid secretion (6). No such effect was reported in monkey (9), dog (7) and rat (5). Under conditions of maximal histamine stimulation male guineapigs secreted significantly higher amounts of gastric acid than the females (23). Stilboesterol therapy depressed gastric secretion in cats of either sex (17), but not in dogs (3). Myhre (16) reported that estorgen produced no demonstrable effect on the healing of experimental gastric ulceration in rats, while Griffen *et al.* (7) observed that histamine induced ulcers in dogs were enhanced by it. A promoting effect of female sex hormone on the development of gastric ulcer has been claimed in pylorus-ligated rats (2). Kowalewski *et al.* (12) recorded that androgens enhanced the susceptibility of rat's gastric mucosa to peptic action of gastric juice.

In view of these conflicting reports regarding the action of sex hormones on gastric secretion, this study was conducted in rats and rabbits.

MATERIALS AND METHODS

Studies in rats : Normal, healthy, adult, albino rats weighing between 200-250 *g* were used. They were divided into (i) male, and (ii) female groups. Each group was

further subdivided into the following subgroups of 10 rats each: (a) Normal, treated as control, (b) Estrogen treated, and (c) Testosterone treated. Estrogen treated rats were injected im estradiol-di-propionate (Ovocyclin-Ciba), 10 $\mu g/kg$/day. and testosterone treated rats received testosterone propionate (Perandran-Ciba), 100 $\mu g/kg$/day for 10 days. For control experiments the solvent used for dissolving these hormones was injected for the same duration of time. Gastric juice in 24-hr fasted rats was collected by ligating the cardiac and pyloric ends as described by Shay *et al.* (20). Kay's augmented histamine stimulated gastric secretion (10) was collected for 2 hr and its volume, total acid output (TAO), and peptic activity (8) were determined.

Studies in rabbits : Normal, healthy, albino, adult rabbits of either sex, weighing between 1.5-2.0 *kg* fed on Hind Lever feeds and green foliage, were used. 10 rabbits of each sex underwent three types of treatments, hence were classified into: (a) normal, (b) estrogen treated, and (c) testosterone treated animals. Normal group were injected with the solvent of these hormones for 15 days. Then they were injected 20 $\mu g/kg$/day of Ovocyclin for 15 days, and constituted the estrogen treated group. After this therapy, their gastric samples were analysed, and they were given a rest for 10 weeks to enable them to restore their normal original gastric parameters. In the third stage, they received 200 $\mu g/kg$/day of Perandren for 15 days, and formed the testosterone treated group.

After each treatment, Kay's augmented histamine stimulated gastric secretion (10), was collected from conscious, 24-hr fasted rabbits by passing 3-mm polythelene tube orally by the technique developed in this laboratory. Gastric samples for 2 hr was collected and pooled. Its volume, free acid output (FAO), total acid output (TAO), pepsin (8), hexosamine (25) and fucose (4) contents were estimated.

Under both these groups the animals were not used during estrous, and the dosage and duration of therapy were established after trial and error to yield the optimum results.

RESULTS AND DISCUSSION

Table I shows that estrogen in male rats caused significant reduction in gastric secretion volume and its acid output. Similar results were obtained in female rats except for the fact that the volume of gastric secretion was not reduced significantly. In female rats, testosterone produced a significant rise in acid output and a fall in peptic activity but the changes were not significant in male rats.

Table II also indicates that estrogen inhibited significantly the volume, free and total acid outputs but augmented the hexosamine and fucose fractions of gastric juice in both the

TABLE I: Effect of sex hormones on gastric secretion of rats.

Group	Volume ml/2 hr	TAO mEq/2 hr	Peptic activity units/ml
		FEMALE RATS	
Normal	0.93±1.210 (0.5—1.5)	0.026±0.0045 (0.012—0.045)	105.5±9.56 (70—150)
Eestrogen treated	0.73±0.101 (0.5—1.5)	0.011±0.0012 (0.007—0.020) *	109.9±4.17 (90—134)
Testosterone treated	0.99±0.127 (0.8—1.8)	0.035±0.0032 (0.019—0.052) *	95.8±5.05 (66—120) *
		MALE RATS	
Normal	0.92±0.190 (0.5—2.5)	0.035±0.0048 (0.014—0.064)	119.1±16.79 (50—192)
Oestrogen treated	0.62±0.057 (0.5—1.0) *	0.024±0.0022 (0.017—0.040) *	112.5±9.02 (70—150)
Testosterone treated	0.94±0.086 (0.6—1.2)	0.028±0.0030 (0.020—0.040)	110.5±12.48 (56—180)

Total number of rats in each group were 10; Values are Mean ±SE;
Figures in parentheses indicate the range. *denotes significant p values.

sexes of rabbits. Testosterone significantly elevated the FAO in female rabbits and reduced the fucose contents of gastric juice in both the sexes of animals.

In both the species of animals studied, estrogen inhibited the gastric secretion and testosterone augmented it, though the former exercised more potent effect than the latter. An inverse relationship between gastric acid output and mucus secretion has been noted. Peptic activity varied independently of the acid secretion. Hexosamine and fucose fractions of gastric secretion has been identified as major constituents of gastric mucus and both these glycoproteins represented biochemically the amount of mucus present in it (12). Due to lesser volume of gastric secretion in rats, these fractions could not be estimated.

Several reports (1,13,19) indicated that estrogen exerted inhibitory effect on gastric secretion, while testosterone had the reverse effect. Our study also corroborated these findings, though contrary results in dogs (24) and rats (2) have been mentioned, and even some

TABLE II : Effect of sex hormones on gastric secretion of rabbits.

Group	*Volume ml/hr*	*FAO mEg/hr*	*TAO mEq/hr*	*Pepsin unit/ml*	*Hexosamine mg/100 ml*	*Fucose mg/100 ml*
			FEMALE RABBITS			
Normal	15.1±0.2 (14—16)	0.9±0.3 (0.8—1.2)	1.1±0.1 (1.0—1.3)	45±1.3 (37—51)	14.1±0.2 (13.2—15.4)	17.1±0.3 (15.7—19.2)
Estrogen treated	14.1±0.2 (13—15) *	0.7±0.1 (0.5—0.8) *	0.8±0.1 (0.6—0.9) *	43±1.5 (37—51)	20.8±1.7 (16.2—28.8) *	23.1±1.6 (18.1—30.8) *
Testosterone treated	16.2±0.2 (15—17)	1.1±0.3 (0.9—1.5) *	1.2±0.2 (0.9—1.6)	41±1.9 (31—48)	13.4±0.1 (13.0—14.1)	15.6±0.2 (15.0—16.9) *
			MALE RABBITS			
Normal	16.8±0.4 (15—19)	1.2±0.2 (0.9—1.6)	1.4±0.1 (1.0—1.7)	45±1.6 (40—55)	14.1±0.1 (13.1—14.7)	20.9±0.6 (18.0—23.8)
Estrogen treated	14.3±0.3 (13—16) *	0.9±0.1 (0.6—1.1) *	0.9±0.1 (0.7—1.2) *	50±1.8 (38—59)	20.6±1.7 (15.6—28.8) *	23.9±1.5 (18.9—31.0) *
Testosterone treated	16.4±0.4 * (14—18)	1.2±0.2 (1.0—1.6)	1.4±0.2 (1.1—1.8)	48±2.0 (42—60)	13.0±0.3 (11.2—14.1)	15.8±0.3 (14.5—18.1) *

10 rabbits of either sex were used: Values are Mean ±SE: Figures in parentheses indicate range; *denotes significant p values.

authors described them to be without effect in dog (7), monkey (9) and man (18,21). Singh and Shukla (22) demonstrated correlation between sex hormones and gastric mucus secretion. Kowalewski (11) noted diminution in the secretion of mucopolysaccharides in rat's stomach after androgens. Menguy (15) reported that some hormones were known to influence the 'protective gastric mucus barrier' and androgen was labelled to be one of them. There are two mechanisms (14) responsible for bringing about variations in gastric acid secretion : (i) changes in mucus, and (ii) changes in parietal cell mass. In this study estrogen caused reduction in acid output and a rise in mucus secretion, while testosterone produced the opposite effects. These hormones, thus seemed to modify the gastric acid secretion by varying its mucus secretion. Peptic activity, however, varied independently of the acid secretion.

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