GONADAL INFLUCENCES ON GASTRIC SECRETION

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Grossman *et al* (12) noted that sex and age have known influences on acid secretion of gastric juice, and reported that males secreted more acid than females. Diminished incidence of peptic ulceration in women compared to men, had been described (7, 8, 9, 16). They suggested a correlation between sex hormones and gastric secretion (7, 9, 16). Reduction in the acid and pepsin contents of gastric juice during pregnancy had been noted (4, 15, 23). Strauss and Castle (26) found that gastric functions which were diminished during pregnancy, returned to normal after delivery, and rose again during puerperium. McCarthy *et al* (22), however, did not detect any variation in gastric secretion during pregnancy, but did record enhanced activity during lactation. Griffen and his co-workers (11), on administering sex hormones, observed aggravation in the condition of the histamine induced gastric ulcers. On the other hand, Kowalewski (18) noted that testosterone treated rats, compared to normals, were resistant in developing cortisone induced ulcers. Singh and Shukla (25) discovered that oophorectomy in rats, augmented gastric ulceration and secretion as well, while orchidectomy was ineffective. Other workers failed to detect any appreciable alteration in the secretion and composition of gastric juice in intact or castrated rats (2, 10).

Though majority of investigators suggested a definite correlation between sex hormones and gastric secretion, yet conflicting results have been reported by others, so, this work of studying the effect of gonadal hormones on gastric secretion has been undertaken.

MATERIALS AND METHODS

These studies were conducted on rats and dogs.

Studies On rats : Normal, healthy, albino rats of either sex, weighing between 120-150 *gm* were fed milk, germinated gram and liver, and were divided as :

I. FEMALE RATS : (1) *Normal*—consisted of 12 rats and were injected 0.05 ml Ovocyclin solvent (Ciba) daily for 10 days. They were taken as control as no difference was detected between the normal and the solvent treated rats. (2) *Oestrogen treated normal*—consisted of 14 rats injected with Ovocyclin (Ciba), 0.005 *mg*/100 *gm* body weight daily for 10 days. (3) *Spayed*—consisted of 17 rats, used a fortnight after oophorectomy. (4) *Oestrogen treated ovariectomized*—consisted of 13 rats, which 1 month after castration were treated daily with 0.005 *mg*/100 *gm* body wt. of Ovocyclin for 10 days.

II. MALE RATS : (1) *Normal*—11 rats were injected 0.1 ml Perandren Solvent (Ciba) daily for 10 days, and were treated as control. (2) *Testosterone treated normal*—14 rats were treated daily with 0.01 *mg*/100 *gm* body wt of Perandren (Ciba) for 10 days. (3) *Castrated*—15 rats operated for orchidectomy were used 15 days after the operation. (4) *Testosterone treated castrated*—18 rats, one month after orchidectomy were injected 0.01 *mg*/100 *gm* body weight Perandren for 10 days.

Control as well as the expreimental rats were kept under identical conditions. Tendency towards coprophagia was avoided. Their meals were restricted 24 hours before gastric analysis, but had a free access to water. They were anaesthetized by intraperitoneal nembutal (Abbott), 4*mg*/100*gm* body weight. Abdomen was opened, cardiac and the pyloric ends ligated, avoiding injury to the nerves and vessels. After ensuring that the stomach was empty and free from solid material, 0.1 *mg*/100 *gm* body weight of histamine (BDH) was injected subcutaneously to stimulate gastric secretion. After 4 hours blood from the heart for glucose estimation (13) was withdrawn, animal sacrificed and gastric contents were measured and collected for analysis. Gastric samples, if contaminated with blood or contained a fair amount of solid residue, were discarded. Gastric contents were measured, free and total acidities by titrating against 0.01 N sodium hydroxide solution, were determined, total chlorides (6) as well as the peptic activity (14) were also estimated.

Studies in dogs : Healthy, mongrel dogs of either sex, weighing between 8-15 *kg* were used in these studies. They were fed 500 *gm* boiled meat daily with biweekly supplements of 100 *gm* liver and 1 table of multivitamin (Becadex-Glaxo). Each dog, prior to starting the experiemtns, was administered anti-rabic and anti-helminthic treatments. They were operated for gastrostomy by Ssbanajew-Franck stomach cone transfer technique (24). Experiments were performed only after the complete healing of the wound had occurred.

These animals were divided into 2 groups : (I) 12 male, and (II) 11 female dogs. Both these groups were studied as : (1) Their normal histamine induced gastric secretion was studied. (2) Sex hormones were administered daily for 10 days. On 11th day the histamine induced gastric secretion was studied. 2.5 *mg* Ovocyclin (Ciba) to female, and 5.0 *mg* Perandren (Ciba) to male, dogs was injected daily for 10 days. (3) These animals were castrated and gastric secretion was studied a fortnight after the operation .(4) One month after castration, dogs were injected Ovocyclin (female) and Perandren (male) for 10 days, after which gastric secretion was studied.

They were fasted for 18 hours before gastric analysis, but were allowed to drink water *ad libdum*. Blood for glucose estimation (13), before and after the treatments, was withdrawn. Fasting gastric contents, if any, were discarded. Half an hour histamine induced gastric secretion was measured, and analyzed for free and total acidities, total chlorides (6) and the peptic activity (14).

RESULTS

Significant diminution in free acidity and peptic activity associated with hyperglycemia was noted on injecting estrogen to female rats (Table I). In dogs similar results were obtained (Table II), but, in addition, total acidity was also diminished. Oophorectomy enhanced gastric acidity, more so, the free acidity which was significant statistically in both the species. Oestrogen treated spayed animals showed normo -or hypogastric activity.

TABLE I

Effect of oestrogen, testosterone and castration in rats

Treatment	Volume ml	Free acidity mEq/l	Total acidity mEq/l	Total chlorides mEq/l	Peptic activity unit/ml	Blood glucose mg%
I FEMALE RATS :						
1. Control (12)	0.5 ±0.1	15.7 ±2.2	29.9 ±3.8	125.4 ±2.9	9.6 ±1.2	68.7 ±1.8
2. Oestrogen treated normal (12)	0.4 ±0.1	8.9 ±1.9	20.4 ±2.1	122.5 ±1.8	4.5 ±1.9	78.5 ±1.6
3. Oophorectemized (17)	0.6 ±0.1	19.8 ±1.2	32.1 ±2.9	126.1 ±2.3	11.5 ±1.5	61.2* ±1.9
4. Oestrogen treated castrated (13)	0.5 ±0.1	14.7 ±1.9	28.1 ±2.8	124.6 ±2.1	8.4 ±1.9	71.1 ±1.9
II MALE RATS :						
1. Control (11)	0.5 ±0.1	17.2 ±2.1	31.2 ±2.6	126.1 ±2.6	10.2 ±1.4	69.1 ±2.1
2. Testosterone treated normal (14)	0.5 ±0.1	21.4 ±2.2	36.2 ±1.7	128.2 ±2.1	11.5 ±1.2	63.5* ±1.9
3. Orhidectomized (15)	0.5 ±0.1	13.2 ±1.2	22.1 ±1.9	124.9 ±1.8	8.8 ±1.5	74.2 ±2.1
4. Testosterone treated castrated (18)	0.5 ±0.1	18.9 ±1.7	32.8 ±2.1	126.2 ±1.8	10.0 ±1.1	64.9 ±1.2

Values are Mean ± SE; Figures in parentheses refer to the number of animals used; Significant 't'-values*

TABLE II

Effect of oestrogen, testosterone and castration in dogs

Treatments	Volume ml	Free acidity ml	Total acidity mEq/l	Total chlorides mEq/l	Peptic activity unit/ml	Blood glucose mg%
I FEMALE DOGS : (11)						
1. Normal	20.3 ±3.4	97.4 ±4.7	108.4 ±5.1	15.83 ±2.9	11.5 ±1.4	60.2 ±3.7
2. After oestrogen	16.8 ±1.9	68.2* ±3.9	84.1* ±3.7	154.7 ±2.1	8.1* ±2.6	72.9* ±2.9
3. After ovarectomy	21.9 ±2.6	102.7 * ±3.9	118.4 ±4.8	159.4 ±3.9	11.9 ±1.4	58.5 ±3.1
4. After oestrogen to spayed dogs	19.5 ±2.1	89.6* ±2.6	107.5 ±1.9	156.9 ±1.2	10.9 ±1.2	63.7 ±2.9
II MALE DOGS (12)						
1. Normal	20.9 ±2.8	99.7 ±3.1	112.6 ±2.9	159.4 ±2.1	12.2 ±1.8	60.1 ±1.2
2. After testosterone	21.4 ±2.1	109.1* ±2.7	118.9 ±2.1	160.6 ±1.9	12.8 ±1.9	58.7 ±1.7
3. After orchidectomy	18.5 ±1.9	80.2* ±2.4	100.1* ±1.5	158.2 ±1.7	19.8 ±1.2	61.9 ±1.5
4. After testosterone to castrated dogs	20.8 ±2.3	100.4 ±1.6	115.8 ±2.3	159.5 ±2.2	12.5 ±1.8	59.4 ±1.2

values are Mean ±SE; Figures in parentheses indicate the number of dogs used; *significant 't'-values.

In male rats, testoestrone produced a significant rise in the free and total acidities, and castration produced a fall. (Table I). In male dogs testosterone produced a rise only in the free acidity, while orchidectomy resulted in a fall in free and total acidities, as well as the peptic activity (Table II). Testosterone treatement after castration, tried to restore the original level of gastric activity, with a tendency towards hypersecretion.

DISCUSSION

In the present studies, it has been observed that administration of oestrogen produced a marked diminution of gastric secretion in rats as well as in dogs. An associated rise in the blood glucose has also been noted. Depression of gastric functions noted in this work was in corroboration with the observations of Arzt (3) and Labate (19). Vinogradava (27) suggested that ovarian hormone was responsible for the lowered gastric acidity, while Murray *et al* (23) attributed this depression to alteration in the reactivity of the parietal cells, whereas others (20) reported it to be due to rise in the histaminase content of the stomach. MacDonald (21) considered the possibility of fluctuating level of adreno-cortical hormones during pregnancy and suggested them to be the cause of gastric variations. However, Baker (5) failed to detect any change in th structure of the chief cells after overiectomy.

Testosterone caused an augmentation of gastric secretion in both the species and has an effect opposite to that of the oestrogen. These hormones brought about gastric changes, either when they were in excess as by injecting them from outside, or when they were deficient as produced by castration. These altered levels of sex hormones must had influenced the gastric secretion through the pituitary-adrenal axis (17). Abrahamson and Hinton (1) also noted that disproportion between the levels of oestrogens and androgens was of greater importance than the activity of individual hormone. Hyperglycemia associated with hypogastric secretion, however, was not constant in all cases. Thus, depression of gastric secretion produced by oestrogen, and the augmentation by testosterone, was due to altered levels of sex hormones which influenced the gastric secretion through the hypophysis-adrenal axis.

SUMMARY

Effect of castration and of injecting sex hormones (oestrogen in females, and androgens in males) to normal as well as to castrated animals (ligated rats and gastrostomized dogs), on the histamine induced gastric secretion, was studied. Oestrogen in female rats and dogs caused depression of gastric secretion, while testosterone in male rats as well as dogs augmented it. Castration had the reverse effect in both the species of animals. These changes, possibly, were brought about through the hypophysis adrenal axis.

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