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Research Article

PROSTAGLANDINS AND 5-HT RESPONSE ON GASTRIC SECRETION IN ALBINO RATS

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ABSTRACT: Prostaglandins (PGE_1) 0.1, 0.2 and 0.4 mg/kg and 5-hydroxytryptamine (5-HT) 1, 2.5 and 5 mg/kg dose dependently inhibited gastric secretion in pyloric legated rats model While $PGF_2\propto$ 0.1, 0.4 and 1mg/kg inhibited gastric acid secretion. Methysergide in the dose 0.05 mg/kg significantly stimulated the gastric secretion. When non-inhibitory dose of PGE_1 (0.1) and 5-HT (1.0 mg/kg) are injected simultaneously there were potentiation of inhibitory activity on gastric secretary response on volume, acid output, chloride output and pepsin output. The inhibitory activity of both PGE_1 (0.4 mg/kg) and 5-HT (5.0 mg/kg) including the inhibitory potentiating activity could not be modified by the pretreatment of methysergide (0.05 mg/kg). Similarly stimulatory dose of $PGF_2\propto$ (0.4) mg/kg) and inhibitory dose of PGE_1 (0.4 mg/kg) administered together inhibitory response of PGE_1 (0.4 mg/kg) were also not modified by methysergide pretreatment.

Key words: Prostaglandins, 5-HT, Gastric Secretion, Methysergide.

INTRODUCTION

Prostaglandins (PGs) and 5-Hydroxytryptamine (5-HT) both are found throughout the central nervous system (CNS) and gastro-intestinal tract (GIT) with synthesizing and metabolizing distinct PG and 5-HT type. Although, they show similar activity but their role in GIT and CNS are not well understood. PGE type and PGF type showed opposing effect in various experimental models both in CNS and GIT. Therefore, rather antagonistic effect of PGE_1 and $PGF_2\propto$ were obvious. PGE_1 and 5-HT both inhibit gastric secretion while $PGF_2\propto$ stimulate gastric secretion and in higher doses inhibit gastric secretion (Guha *et al*., 1979, Goel and Sanyal, 1983). In CNS level PGE_1 potentiate morphine analgesia and per se antinoceceptive action of PGE_1 was found to be nhibited by $PGF_2\propto$ (Bhattacharya *et al*., 1978; Sanyal *et al*., 1977).

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$PGF_2\propto$ is known to inhibit the effects of several centrally acting drugs, namely hexobarbitone hypnosis, anticonvulsant effect of phenobarbitone and antonociceptive effect of cannabis where as these are potentiated by PGE_1. Further, $PGF_2\propto$ activity was also inhibited by PGE_1 induced potentiation on the effects of these centrally acting agents. In the present study inter-relationship on the effect of Prostaglandins (PGE_1 and $PGF_2\propto$) and 5-hydoxytryptamine (5-HT) on gastric secretion in pyloric ligated rats were determined**.**

MATERIALS AND METHODS

The effect of drugs was studied on gastric secretion in 4 h pyloric ligated rats. The stomach was removed after 4 h pyloric ligation and the gastric juice was collected and filtered through glass wool and centrifuged at 3000 rpm for 5 min. Supernatant was collected from centrifuged juice and its volume was expressed as ml/100g body weight. Total acid was determined by titrating the gastric juice with N/100 NaOH using phenolphthalein as indicator and concentration was expressed as µEq/ml and output as uEq/4h (Hawk 1965, Sanyal *et al.,* 1971). The peptic activity was determined using hemoglobin as substrate as per the method described earlier (Debnath *et al.*, 1974) and concentration was expressed as µmol tyrosine/ml and output as µmol of tyrosine/4h.

Drugs and Pre-treatment: PGE_1, $PGF_2\propto$ (Upjohn Company, USA) and 5-HT (Sigma) used 30 min and methysergide (Sandoz Basal) 60 min before pyloric ligation.

RESULTS AND DISCUSSION

Prostaglandin PGE_1 0.1, 0.2 and 0.4 mg/kg and 5-HT 1, 2.5 and 5 mg/kg dose inhibited gastric secretion dose-dependently. The dose of PGE_1 (0.1 mg/kg) and 5-HT (1 mg/kg) showed no appreciable inhibition. While $PGF_2\propto$ 0.1 and 0.4 mg/kg stimulated the gastric acid secretion on the contrary 1.0 mg/kg inhibited the gastric secretion. Methysergide in the dose 0.05 mg/kg stimulated the gastric acid secretion significantly. When non-inhibitory dose of PGE_1 and 5-HT are injected simultaneously there was potentiation of inhibitory activity of gastric secretary response on volume, acid output, chloride output and pepsin output. However, the inhibitory activity of both PGE_1 (0.4 mg/kg) and 5-HT (5 mg/kg) could not be modified by the pretreatment with methysergide (0.05 mg/kg). Similarly, when stimulatory dose of $PGF_2\propto$ (0.4 mg/kg) and inhibitory dose of PGE_1 (0.4 mg/kg) were administered together, the inhibitory response of PGE_1 (0.4 mg/kg) could not be modified. Further, the gastric inhibitory potentiating activity of non-inhibitory dose PGE_1 (0.1 mg/kg) and 5-HT (1 mg/kg) could not also be modified by methysergide (0.05 mg/kg) in its stimulatory dose (Table 1).

In the present study gastric secretary response of 5-HT, PGE_1 and $PGF_2\propto$ were screened. While $PGF_2\propto$ showed stimulation of gastric acid secretion in small doses and inhibition in higher doses. Significant stimulatory and inhibitory dose of $PGF_2\propto$ and PGE_1 respectively when administered together showed inhibitory activity. The inhibitory effect of PGE_1, 5-HT and $PGF_2\propto$ or in combination could not be modified by methysergide. PGE_1 induced inhibition of gastric secretion has been shown to be 5-HT mediated response. $PGF_2\propto$ on the other hand stimulate basal and pentagastrin stimulated gastric acid secretion in anaesthetized and in conscious rats (Guha *et al.*, 1979; Goel and Sanyal 1983).

Table 1: Effect of Prostaglandins and 5-Hydroxytryptamin response on gastric secretion in Albino rats.

Group* Dose mg/ kg	No	Volume ml/100g	Free acid mEq/l	Total acid mEq/l	Total acid output ìEq /4h	Chloride Concen-tration mEq/l	Chloride output mEq/4h	Pepsin Concent ration ìmol/ tyrosine	Pepsin Output
Control	28	2.97 ±0.25	58.4 ± 6.2	89.6 ±4.3	291.7±31.5	134.5±4.7	389.1±41.5	409 ±34	1023 ±97
PGE_1 0.1	10	2.90±0.20	63.7 ±9.9	98.2 ±6.9	262.4±54.4	139.9±4.8	374.0±25.2	420 ±26	1206 ±91
0.2	8	2.18 ±0.19	46.1 ±7.3	93.9 ±7.5	203.1±27.8	146.4±3.5	326.2±34.7	511±29	1083 ±9
0.4	20	1.37 ±0.24[b]	21.6±4.6[a]	47.4 ±4.4[b]	66.7±9.1	124.5±3.6[a]	174.2±16.6[a]	588 ±29[a]	758 ±61[a]
PGF2 á 0.1	10	3.10 ±0.24	61.2 ±6.3	83.7 ±7.2	358.3±21.7	142.2±6.4	402.7±31.2	483±39	1289 ±97
0.4	8	4.61 ±0.31[a]	69.3 ±7.8	96.2 ±7.4	411.1±30.3[a]	159.3±5.2	624.1±37.7[a]	431 ±26	1675±104[a]
1.0	8	1.90 ±0.25[b]	58.7 ±5.2	83.2 ±6.1	202.2±19.4[a]	127.7±4.9	267.2±29.3	540 ±31[a]	1081 ±63
5-HT 1	8	2.37 ±0.25	57.7 ±7.5	86.3 ±6.8	201.6±28.1	124.8±4.3	289.3±21.9	504 ±46	1114 ±87
5	9	1.59 ±0.20[b]	34.8 ±6.6[a]	63.6 ±6.1[a]	103.9±17.9[a]	114.5±4.6[a]	181.5±60.9[a]	538 ±40	780 ±79[a]
Methy 0.05	10	4.10 ±0.24[a]	63.7 ± 6.3	101.8±4.0[a]	420.5±37.2[a]	161.5±3.4[a]	665.1±49.5[a]	447 ±38	1795±150[a]
5-HT + PGE 1 + 0.1	12	1.52 ±0.29[a]	54.0 ± 6.7	79.6 ±5.8	126.4±22.1[b]	110.0±2.7[a]	167.9±21.4[a]	532 ±40	692±134[a]
PGF_2á + 5-HT 0.4 + 5	10	1.61 ±0.26[a]	56.0 ± 6.5	79.6 ±5.8	101.4±23.1[b]	108.0±2.5[a]	157.9±20.2[b]	512 ±41	632±124
PGE_1 + PGF_2 á 0.4 + 0.4	10	1.66 ±0.25[a]	51.2 ± 4.9	86.4±6.3	86.3±18.3[b]	114.4±4.5[a]	156.8±34.6[b]	542 ±38	748 ±86
Methy + 5-HT 0.05 + 5	8	1.13 ±0.22[b]	26.4±3.8[b]	54.2±2.1[a]	71.3 ±15.2[b]	114.3±7.2[a]	148.2±31.3[b]	481±38	627 ± 59[a]
Methy + PG E_1 0.05 + 0.4	15	2.30 ±0.21	53.4 ±4.1	76.4±4.5	177.7±20.6a	139.6±2.7	314.3±36.1	560 ±63[a]	1573±161
Methy + 5HT+PGE_1 0.05 1 0.1	8	1.51 ±0.43[a]	44.2 ±7.1	63.3 ±6.82	106.8±46.6[a]	103.4±1.7[a]	159.2±44.4[a]	532 ±42[a]	692 ±134

* Single dose treatment ; Values are mean ± S E. P value a <0.05, b <0.01 in comparison to control Prostaglandin E_1 (PGE_1), Prostaglandin F2∝ (PGF_2 ∝) ,5-hydroxytryptamine (5-HT), Methysergide (Methy).

The effect of PGE_1 on steady state level of 5-HT increased in brain but not in stomach and intestine. On the contrary, turn over of rat brain and stomach correlated well with the pharmacological activity to gastric secretion and CNS parameters. PGE_1 enhanced the rate of accumulation of serotonin in pargyline treated rats (Debnath *et al.,* 1978) confirming an earlier report (Haubrich *et al.,* 1973) in brain. $PGF_2\propto$ *per se* in the dose 0.5, 1.00 and 2.0 mg/kg decreased the steady state level of brain 5-HT but the differences are significant only at the dose 1.0 and 2.0 mg/kg. The brain turn over was studied on accumulation of 5-HT at 30 min and 45 min with tranylcypromine were significantly increased while at 60 and 90 min came to normal level. In stomach tissue turn over is increased at 15, 30, 45 and 60 min, but came to normal by 90 min (Goel *et al.*, 1985). The morphine analgesics (7.5 mg/kg) was antagonized by $PGF_2\propto$ in the dose 2.00 mg/kg at 15 min while at 75 min potentates the analgesic activity (Katiyar and Debnath, 2013) corroborate with its effect on brain 5-HT turn over. In another study (Bhattacharya 1982) showed that centrally administered $PGF_2\propto$ at the dose decreased the brain serotonin.

The higher dose of $PGF_2\propto$ (1.0 mg/kg) did not show stimulatory activity on gastric secretion rather showed inhibition of gastric acid secretion of 5-HT type response. There is report of auto-conversion of prostaglandin one type to another (Ricciotti 2011). When PGE_1 inhibitory dose and stimulatory dose of $PGF_2\propto$ were administered together, in-spite of antagonism rather showed potentiating of inhibitory response. In smaller dose stomach 5-HT was decreased while in higher dose increased (Sanyal and Debnath, 1974; Debnath 1977). The inhibitory response of 5-HT and PGE_1 could not be blocked.

The alteration of 5-HT metabolism could produce clinical symptoms. Similarly, after small bowel resection, hyperacid secretion appear in man due to reduction in 5-HT secreting area (Aber *et al.*, 1967).

Further, on continuous administration of pentagastrin the peak gastric secretary response is always followed by decrease in the secretary activity. It has already been shown in cats, rats and in man, this phenomenon of pentagastrin could be modified by drugs like methysergide, cyproheptadine, reserpine and pCPA suggesting the involvement of 5-HT after pentagastrin (Sanyal and Waton 1972, 1976, Debnath *et al.*, 1975, Goel *et al.,* 1983). Rats pretreated with indomethacin, a potent drug known to significantly inhibit the biosynthesis of PGE_1, modified the phenomena of pentagastrin. Inhibitory response of PGE_1 was also blocked by pretreatment with reserpine and pCPA suggesting that the absence of optimal concentration of tissue 5-HT the inhibitory activity of PGE_1 was annulled (Goel *et al.,* 1983; Debnath *et al.,* 1975). Thus, the findings from the present investigation indicate that prostaglandin's and 5-hydroxytryptamine work in conjunction to control the gastric secretary process. Both these mediators, when augmented reduce gastric secretion.

In certain clinical situations. increase or decrease concentration of PG and 5-HT could be correlated with gastric hypo and hyper secretion (Prasad *et al.*, 1977, Gupta *et al.*, 1977, 1980). Cyproheptadine, apart from being a 5-HT antagonist, also possesses prostaglandin antagonist properties (Acharya *et al.*, 1977). The exact nature of interaction between PGs and 5-HT and the receptor sub types involved in such interactions need to be delineated Keeping in

cognigence of earlier studies and in conjunction with the present investigation with clinical conditions on gastric secretion and on tissue and blood 5-HT levels extend support to fulfill the aims with objectivity for bridging the gaps on the role of PGs and 5-HT on the inhibition of gastric secretion.

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