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ACTION OF CHEMICALLY DIFFERENT PROSTAGLANDIN BLOCKERS ON THE ADRENAL HORMONES IN PIGEONS DURING STRESS

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Abstract : The effect of prostaglandin (PG) inhibitors differing in their chemical nature, viz. Aspirin (acetylsalicylic acid), Mefenamic acid (fenamates), Diclofenac (phenylacetic acid derivative) and Piroxicam (oxicam derivative) on the adrenal hormones was studied in acutely stressed pigeons. None of these PG blockers exerted any significant effect on the catecholamine and corticosterone content of the control, i.e. unstressed pigeon adrenal gland excepting mefenamic acid which caused a release of epinephrine. Aspirin, diclofenac and piroxicam did not modulate the catecholamine or corticosterone secretion whereas mefenamic acid caused a released of both epinephrine and norepinephrine and increased the adrenal corticosterone content in the acutely stressed pigeons. These results were compared with those obtained from studies on the effects of other chemically different PG blockers, indomethacin (a methylated indole derivative) and ibuprofen (a propionic acid derivative). It is suggested that chemically and structurally different PG inhibitors show diverse action in the same species under similar stress conditions.

Key words : prostaglandin catecholamine corticosterone stress pigeon

INTRODUCTION

There are reports that prostaglandin (PG) inhibits the release of norepinephrine (NE) from the adrenal medulla of rat, human and cat during stress conditions (1, 2). It has also been demonstrated that PGE_1 and E_2 both induce secretion of epinephrine (E) and NE from cultured bovine adrenal medullary cells (3). Regarding its action on the adrenal cortex, PGE_1 is known to significantly increase the basal secretion of corticosterone from isolated zona fasciculata cells of rats (4). In a number of species systemic administration of PGE_2 have been found to increase the circulating concentrations of ACTH and steroid production by the adrenals (5). Though extensive work in this field has been performed in various mammalian species,

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findings relating to the regulatory role of PG on the hormonal release in avian species is extremely limited. Recently Sengupta et al. (6) and Sarkar et al. (7) from our laboratory have established that chemically and structurally different PG inhibitors (indomethacin and ibuprofen) vastly differ in their mode of action on the adrenal hormonal profile during stress condition in the same avian species. Treatment with indomethacin (a methylated indole derived PG blocker) exhibited no perceptible effect on either E or NE during acute formalin stress in the pigeon; instead it caused a further rise in adrenal corticosterone content (6). On the other hand, Sarkar et al. (7) observed that administration of ibuprofen (a propionic acid derived PG inhibitor) under acute stress condition significantly reduced the adrenal NE but had no influence on E or corticosterone. In view of such diverse action of PG blockers observed earlier in our laboratory, in the present paper we aim to study the effect of other PG inhihitors differing in their chemical nature such as aspirin (acetyl salicylic acid), mefenamic acid (fenamates), diclofenac (phenylacetic acid derivative) and piroxicam (an oxicam derivative) on the avian adrenal hormonal physiology during stress.

METHODS

Young adult domestic pigeons were collected from the local bird dealer and

TABLE I : Experimental schedule.

Sl. No.	*Group*	*Number of birds in each group*	*Treatment*
1.	Control	6	None
2.	Formalin	6	0.5 ml of 10% formalin/bird was injected intramuscularly and autopsied after ½ hour.
3.	Aspirin	7	200 mg Aspirin (German Remedies, India) per kg body weight was administered orally and the birds were autopsied after 2 hours.
4.	Mefenamic acid	6	100 mg Ponstan (Parke-Davis, India) per kg body weight was fed orally and the birds were sacrificed after 2 hours.
5.	Diclofenac	6	12 mg Diclonac (Lupin Laboratory, India) per kg body weight was given orally and the birds were sacrificed after 2 hours.
6.	Piroxicam	6	6 mg Dolonex (Pfizer, India) per kg body weight was administered orally and the birds were autopsied after 2 hours.
7.	Aspirin + Formalin	7	*
8.	Mefenamic acid + Formalin	6	*
9.	Diclofenac + Formalin	6	*
10.	Piroxicam + Formalin	6	*

*PG inhibitors (Aspirin, Mefenamic acid, Diclofenac and Piroxicam) were administered according to the above schedule. After 1½ hour duration of the treatment, 0.5 ml of 10% Formalin was injected in each case and the birds were autopsied after ½ hour of the formalin treatment.

acclimatized to laboratory conditions for seven days prior to experimentation with food and water available *ad libitum*. The birds were divided into eight groups as indicated in Table I.

Experimental schedule:

The experimental protocol is detailed in the Table I. Adrenals from experimental and control birds were dissected out and immediately processed for corticosterone and catecholamine estimation. The catecholamines and corticosterone were estimated spectrofluorometrically by the methods of Laverty and Taylor (8) and Glick et al. (9) respectively. Statistical analysis was carried out by means of Student's 't' (10).

RESULTS

The data are presented in Table II. Aspirin, diclofenac and piroxicam treatments had no significant effect on the adrenal catecholamine and corticosterone contents of the pigeon, but mefenamic acid significantly reduced the epinephrine level of the adrenal gland. Formalin stress depleted the epinephrine level of the adrenal gland. Formalin stress depleted the epinephrine and increased the

TABLE II : Effect of PG inhibitors on adrenocorticomedullary responses in formalin stressed domestic pigeon (*Columba livia*).

Treatment		*Epinephrine (µg/mg tissue)*	*Norepinephrine (µg/mg tissue)*	*Corticosterone (µg/mg tissue)*
None	(6)	0.352±0.049*	0.121 ± 0.024	3.26 ±0.48
Formalin	(6)	0.227±0.029 P<0.05	0.091 ± 0.004 NS	6.221 ±0.71 P<0.005
Aspirin	(7)	0.317±0.045 NS	0.089 ± 0.005 NS	3.33 ±0.49 NS
Aspirin + Formalin	(7)	0.218±0.028 P<0.05 NS**	0.071 ± 0.004 NS NS**	6.74 ±0.90 P<0.005 NS**
Mefenamic acid	(6)	0.181±0.042 P<0.025	0.079 ± 0.012 NS	2.13 ±0.24 NS
Mefenamic acid + Formalin	(6)	0.079±0.019 P<0.001 P<0.005**	0.049 ± 0.008 P<0.001 P<0.001**	13.13 ±1.57 P<0.001 P<0.005**
Diclofenac	(6)	0.461±0.040 NS	0.140 ± 0.026 NS	3.94 ±0.49 NS
Diclofenac + Formalin	(6)	0.237±0.21 P<0.050 NS**	0.084 ± 0.006 NS NS**	5.24 ±0.92 NS NS**
Piroxicam	(6)	0.273±0.050 NS	0.124 ± 0.009 NS	2.54 ±0.82 NS
Piroxicam + Formalin	(6)	0.210±0.025 P<0.025 NS**	0.104 ± 0.005 NS NS**	4.32 ±0.72 NS NS**

* Mean ± Standard Error

** Formalin vs. PG Inhibitor + Formalin

Figures in parenthesis represent the number of specimens.

corticosterone content of the pigeon adrenal gland. Our data show that aspirin, diclofenac and piroxicam had no effect on the adrenal hormones during formalin stress whereas mefenamic acid significantly depleted the catecholamines and increased the corticosterone content during stress condition. This decreased value was less and the elevated value was more than that produced by exclusive formalin treatment in the pigeon.

DISCUSSION

Our result indicate that aspirin, diclofenac and piroxicam did not modulate catecholamine (CAM) secretion during stress condition while mefenamic acid caused a futher release of both E and NE during formalin stress. Recent findings from our laboratory reveal that ibuprofen has a regulatory role on NE during similar stress situation (7) but indomethacin practically had no perceptible influence on formalin induced CAM release (6). It would thus appear that aspirin, diclofenac, piroxicam and indomethacin are similar in their mode of action on the adrenomedullary hormones during stress while mefenamic acid somewhat resembles ibuprofen regarding its action on the adrenal CAM during conditions of stress. Mefenamic acid and ibuprofen presumably ameliorate the effect of formalin stress by releasing CAMs from the adrenal medulla in pigeon.

In the present experiments aspirin, diclofenac and piroxicam were found not to exert any significant effect on the adrenal corticosterone levels during formalin stress. These three PG blockers which fail to modulate adrenal corticosterone during stress are somewhat similar to ibuprofen regarding their action on this adrenal steroid (7). In contrast mefenamic acid increased the adrenal corticosterone content under similar condition which accounts for the synthesis/storage of this hormone. This effect is similar to the action of indomethacin on corticosterone during formalin stress studied earlier by Sengupta et al. (6). The stress physiology and the corticosterone behaviour in birds during mefenamic acid treatment cannot be accounted for and remains an area for further investigation.

From the results of the present study it appears that aspirin, piroxicam and diclofenac fail to alter the effects of formalin stress on the adrenal hormonal profile while mefenamic acid accentuates the effects of the stress. Our study reveals that chemically and structurally different PG inhibitors show diverse action in the same avian species under similar stress conditions. In this context, it seems worthwhile to explore which specific series of PG are inhibited by the prostaglandin blockers used.

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