EFFECT OF PROSTAGLANDIN E_2* ADMINISTRATION ON THE MALE REPRODUCTIVE SYSTEM: A BIOCHEMICAL AND CYTOMORPHOLOGICAL STUDY**

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ABSTRACT

Prostaglandin E_2 (PGE_2) treatment of adult male rats altered the functional integrity of testis and accessory sex organs as reflected by the changes in the estimations of the alkaline phosphatase, acid phosphatase, succinic dehydrogenase in testis, sialic acids in epididymis, citric acid in seminal vesicles and fructose in prostate. The wet weights of testis and accessory sex organs showed a slight decrease, while insignificant increase was noticed in the weight of pituitary. Histologically, prostaglandin produced marked decrease in the sperm count and increase in the number of exfoliated immature spermatozoa in epididymis. The results suggest that the changes in reproductive parameters might be a consequence of endocrinological and functional disturbances induced by PGE_2.

INTRODUCTION

PROSTAGLANDINS (PG's) play a physiological role in the hypothalamic control of gonadotropin secretion, is well established. Direct evidence has also been obtained to demonstrate the involvement of prostaglandin in the release of LRH[1,2]. Administration of PGE_2 and $PGF_{2\alpha}$ was effective to reduce LH levels[3,4]. Chronic treatment with prostaglandin produced marked decrease in spermatogenesis[4–6], *atrophy* of testis and accessory sex organs[7] and decrease in plasma testosterone level[3,7]. The goal of present research was (i) to demonstrate changes produced in biochemical constituents of testis and accessory sex organs and (ii) study of cytomorphological alteration induced by the treatment of i.m. injections of PGE_2 for 15 days.

EXPERIMENTAL

Adult male albino rats (Holtzman strain) weighing approximately 200 g were used for the present investigation. Rats were kept in well-ventilated room with standard light and dark periods and were fed with synthetic feed pellets (Hindustan Levers, Bombay) and water *ad libitum*. The rats were weighed and divided into two groups of 12 animals each. Prostaglandin E_2 (2 mg/kg b.wt.) was administered i.m. in rats, once daily, for 15 days. Control group was sham-treated with 10% ethanolic saline.

The animals were sacrificed by decapitation and testes, epididymi, seminal vesicles, prostate and pituitary glands were excised. The wet weights of the organs were taken (Table I) and small pieces of testis, epididymis and pituitary were fixed in Bouin's fixative for histological study.

Acid (ACP) and alkaline phosphatase (ALP) and succinic dehydrogenase (SDH) were determined in the testis by the techniques of Shinowara *et al.*[8] and Kun and Abood[9] respectively. The amount of sialic acids in caput and cauda was measured separately by thiobarbituric acid assay of Waran[10]. Fructose content in prostate and citric acid in seminal vesicles was determined by the methods of Mann[11] and Linder and Mann[12] respectively. The values are statistically analysed and presented in Table I. For histological study, testis, epididymis and pituitary gland were fixed in Bouin's fluid for 24–28 hours, washed with 70% alcohol, dehydrated, cleared in xylene, impregnated, the paraffin sections were cut at 7 μ and stained by Eosin-Haematoxylin stain. In order to differentiate different cells in pituitary, differential stain[24] was used.

RESULTS AND DISCUSSION

On PGE_2 administration, no change in body weight and considerable regression was seen in the wet weight of testis and seminal vesicles ($p < 0{\cdot}05$), while only slight decrease in that of epididymis and prostate. However, the weight of pituitary showed a slight increase in comparison to control (Table I). Administration of PGE_2 produced a marked change in the orientation of the seminiferous tubules (Fig. 1A, 1B). Various stages of spermatogenesis were dislocated from their site with a marked reduction in the number of spermatozoa (Fig. 1B). In some of the tubules, immature cells were migrated from the periphery to the lumen of the seminiferous tubules along with spermatozoa. Leydig cells were well developed showing normal orientation. The epididymis of PGE_2 treated animals showed an increase in the number of exfoliated immature germ cells in the lumina of ductuli of caput as well as cauda epididymis (Fig. 2B), while the number of spermatozoa significantly decreased. The epithelial linings of the ductuli of caput as well as cauda epididymi were proliferated (Figs. 2B, 3B) as compared to that of control. In pituitary, an increase in the size and number of granuleocytes (Fig. 4B) was observed.

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TABLE I

Effect of prostaglandin E_2 (PGE_2) on biochemical composition of testis and accessory reproductive organs

Values are mean ± S.E. for twelve animals in each group. Values in parentheses represent the wet weights of respective organs in mg per 100 g body weight

Animal	Testis			Epididymis		Prostate	Seminal vesicles	Pituitary mg/g
	ACP (mg of PO_4 liberated/g)	ALP (ug of PO_4 liberated/g)	SDH (μg of dye reduced/g)	Caput Sialic acids (mg/g)	Cauda	Fructose mg/g	Citric acid mg/g	
Vehicle-treated	9·3±0·7 (986±106)	6·2 ±1·2	526·0±161·0	0·0732±0·002 (333±30)	0·0617±0·001	1·72±0·42 (172±25)	0·75±0·18 (233±48)	(2·8±0·2)
PGE_2-treated (2 mg/kg b.wt. for 15 days)	9·4±1·0 (828±69)*	6·29±0·1	381·0±92·3	0·1037±0·002* (327±20)	0·105±0·001*	1·27±0·23 (166±24)	0·68±0·11 (200±40)*	(3·3±0·2)*

* $p < 0·05$ in both control and treated.

The histological observations on testis suggested that the effect of PGE_2 is both quantitative as well as qualitative. The observed decrease in spermatogenesis and such earlier reports[5] may either be due to direct action of PGE_2 on germinal epithelial cells of seminiferous tubules[14] or by inhibition of androgen secretion in leydig cells thus altering the specific receptor sites[15]. The dislocation of various spermatogenic stages may be due to testicular contraction and/or may be caused by altering testicular hemodynamics. Slight decrease in the weights of accessory sex organs was, perhaps, the manifestation of altered testicular activity[4,7].

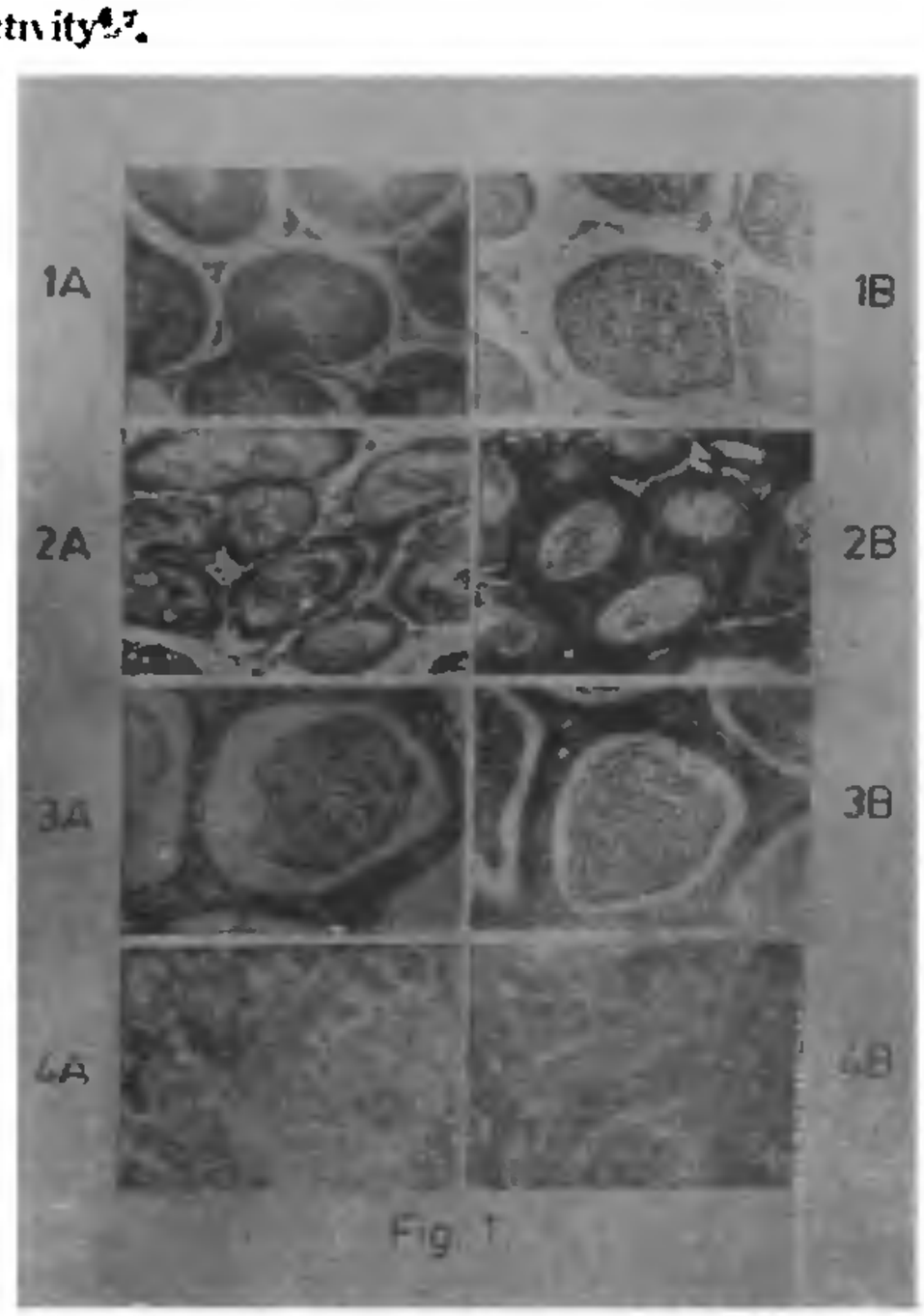

Fig. 1

FIGS. 1A–4B. Fig. 1A. Control testis showing full spermatogenesis (× 100). Fig. 1B. Treated testis with dislocated spermatogenic stages (× 100). Fig. 2A. Control caput epididymis with lumen full of sperm (× 100). Fig. 2B. Treated caput epididymis with lumen containing exfoliated immature cells (× 100). Fig. 3A. Normal cauda epididymis (× 100). Fig. 3B. Treated cauda epididymis (× 100). Fig. 4A. Control pituitary (× 400). Fig. 4B. Treated pituitary with increase in the size and number of granulocytes (× 400).

Statistical significance with PGE_2 was seen in concentrations of SDH, citric acid and fructose ($p < 0{\cdot}05$). There was marginal increase in ACP and ALP of testis and that of sialic acid in caput and cauda epididymis statistically significant ($p < 0{\cdot}05$). Increase in the activity of ALP and ACP in the present studies might be responsible for the increased phagocytotic activity of the tubules and this may be attributed to decrease in the weight of testis while the reduction in SDH might be due to severe regression and metabolic disturbance in testis[16]. Increase in sialic acid concentration in caput as well as cauda epididymis might be due to its decreased utilization required for maturation of spermatozoa. The decrease in prostatic weight and fructose level after PGE_2 administration is probably due to androgen deprivation of prostate as formation of fructose in male sex organs is hormone dependent[11]. The observed decrease in citric acid may also be attributed to insignificant decrease in testosterone level. An increase in weight of pituitary might have been due to stimulatory effect of PGE_2 on gonadotropin release as is evident from the size and number of granulocytes.

Thus, the administration of PGE_2 altered the structural and functional integrity of the testis and accessory sex organs as evident from biochemical and cytomorphological changes. These may not reflect the direct actions, but could be a consequence of other endocrinological and/or functional changes induced by PGE_2. The occurrence of higher incidence of immature spermatozoa and reduction in sperm number particularly from epididymis strongly implicates that PGE_2 caused sterility.

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