

SHORT COMMUNICATION

EFFECT OF INDOMETHACIN ON FERTILITY IN MALE RATS

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Summary: The antifertility effects of indomethacin were studied in male rats. A dose of 3 mg/rat/day for 7 days was found to induce 'functional' sterility through some action on extragonadal sperms.

Key words : Indomethacin fertility male rats

INTRODUCTION

Prostaglandins have been shown to play an important role in male reproduction (8). A direct effect on sperm physiology has also been reported (12). Thus PGF₂ when present in larger than physiological concentrations significantly affects sperm motility (2). In contrast PGE probably improves the quality of the sperm motility (3,10). Any impairment in their normal physiological levels may be related to the testicular physiology and to sperm motility. In fact, some clinical infertility conditions are attributed to prostaglandin levels (7). The discovery that indomethacin and many other non-steroidal antiinflammatory drugs inhibit prostaglandin synthesis (9), has served as a tool in assessing the role of prostaglandins in male reproduction.

The present communication reports our findings on effects of indomethacin on extragonadal sperms and fertility of male rats.

MATERIALS AND METHODS

Colony bred adult albino rats (180-200 gm) of good collective fertility record were used in this investigation. They were maintained in air conditioned (25°±2°C) quarters under uniform husbandry conditions throughout the experimental period. Standard

rodent pellet diet of Hindustan Lever Ltd., India and water *ad libitum* were also provided to these animals. Two days prior to castration, the animals were given testosterone propionate (TP) therapy (1 mg in 0.2 ml of sterile olive oil, intramuscular) which was continued for seven days post-operatively (total regime 9 days) to maintain their mating potential. Three groups of rats received 1 mg, 2 mg, and 3 mg/rat of indomethacin in aqueous gum acacia suspension orally for 7 days beginning on the day of castration. Control rats similarly received the vehicle alone.

During the treatment period the rats were individually allowed to mate with coeval females of proven fertility and their fertility patterns i.e. numbers of corpora lutea, implantation sites and litters were recorded in each group on day 10 of pregnancy. At the termination of experiments the treated rats were sacrificed by cervical dislocation and spermatozoa were collected from the epididymis (caput, corpus and cauda) and vas deferens for phase contrast microscopic assessment of number motility and morphology.

RESULTS

The results of the fertility performance of female rats with male rats treated with different doses of indomethacin are presented in Table I. As is evident, the female rats mated with male rats receiving 1 and 2 mg of indomethacin showed a normal fertility performance; their litter size was comparable to control rats. There was not much of post implantation foetal resorption nor any foetal abnormality noticed. In contrast the rats given 3 mg of indomethacin daily failed to induce pregnancy in the female although the population of corpora lutea was normal.

TABLE I : Effect of indomethacin on fertility in male rats.

Treatment	Number of male animals	Total number of corpora lutea	Total number of implantations	Total number of litters	Percentage inhibition
NONE	6	66 (6)*	53	50	24.24
INDOMETHACIN 1 mg	6	62 (6)	49	46	25.80
INDOMETHACIN 2 mg	6	58 (6)	48	44	24.13
INDOMETHACIN 3 mg	5	59 (5)	3	2	96.61

*Number of females mated in parentheses.

The number, motility and morphology of the sperms collected from the different portions of the epididymis and vas remained unaffected in the rats receiving 1 and 2 mg doses of indomethacin. No signs of general sluggishness were noticed indicating that the libido remained normal. Rats administered 3 mg of indomethacin daily for 7 days showed some signs of sedation; however, this did not affect their mating behaviour. At autopsy there was a general impairment of spermatozoal motility in all the regions of genital tract, although morphologically they appeared normal.

DISCUSSION

The results of the present study show that indomethacin 3 mg/rat/day for 7 days produced sterility through some action on spermatozoa. Doses lower than this were ineffective. No toxic symptoms were noted in rats administered 3 mg indomethacin except that of some animals showed mild sedative effects which did not alter their mating potential.

The antifertility effect observed are difficult to explain; however, many possibilities merit consideration. It has been known that indomethacin and many other non-steroidal antiinflammatory drugs including aspirin, inhibit prostaglandin synthesis. Since prostaglandins appear to be ubiquitous in the male reproductive tract, a role for endogenous prostaglandins on the spontaneous activity of the epididymis and also on sudden contraction produced during ejaculation is possible. In fact, the effects of prostaglandins on the contractile activity have been studied in isolated organs e.g. epididymis (5,6), vas deferens (1,11,13) and seminal vesicle (13,15). The prostaglandin content of the seminal plasma may be altered. A 7-day course of aspirin, another prostaglandin synthetase inhibitor has been shown to reduce prostaglandin content of human seminal plasma (4). Alternatively, the treatment may alter the transport of sperms in epididymis and vas deferens so as to affect the maturation (14) and metabolism prior to ejaculation. It seems likely that prostaglandin synthetase inhibitory activity might play a role in the antifertility effects observed although the possibility of indomethacin molecule *per se* exerting an anti-spermatozoal effects cannot be ruled out.

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