

Role of Vitamin E on Indomethacin induced low pH of Seminal Fluid in Long Evans Rats

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Abstract

Context: Indomethacin is the most commonly and widely used nonsteroidal antiinflammatory analgesic and antipyretic drug. Though it is effective drug in various diseases, indomethacin causes inhibition of spermatogenesis by lowering the pH of seminal fluid leading to infertility. On the other hand, vitamin E enhances spermatogenesis by increasing pH of the seminal fluid. Therefore, the present study was designed to observe the protective role of vitamin E on indomethacin induced low pH of seminal fluid in testicular damage.

Objective: To observe the effects of vitamin E on indomethacin induced low pH of seminal fluid in testicular damage in Long Evans rats.

Study design: An experimental study.

Place and period of study: The study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka in the period of August, 2005 to June, 2006.

Materials and methods: Eightyfour mature Long Evans male rats were divided into four groups (I, II, III and IV). The rats of group I, II and III were treated with indomethacin at different doses and duration. Group IV rats were treated with indomethacin plus vitamin E at different doses for 49 days. The pH of seminal fluid were measured biochemically.

Results: There was significant reduction ($P < 0.001$) of pH of seminal fluid when the rats were treated with indomethacin at low (2 mg/kg body weight/day) and high (10 mg/kg body weight/day) doses for 7, 14 and 42 days, respectively. On the other hand, rats treated with indomethacin plus vitamin E for 49 days showed increase in pH of seminal fluid compared to other groups ($P < 0.001$).

Conclusion: It can be concluded from the study that vitamin E has potential role in the prevention of the antispermatogenic effects of indomethacin by increasing the pH of seminal fluid.

Key words: seminal fluid, indomethacin, vitamin E

Introduction

Indomethacin is the most commonly and widely used nonsteroidal antiinflammatory (NSAID), analgesic and antipyretic drug. It was first introduced in 1963 for the treatment of rheumatoid arthritis and related diseases^{1,2,3}. Though it is an effective drug, toxic effect to testes and accessory organs have significantly restricted its use.

Prolonged treatment with indomethacin caused decrease in prostaglandin E₂ (PGE₂) level in seminal fluid by 80-90% and reduces fertility significantly by lowering the pH of seminal fluid in human being⁴. On the other hand, vitamin E is a fat soluble vitamin. It enhances spermatogenesis by inhibition of lipid peroxidation and lowers the incidence of abnormal sperm production by increasing pH of seminal fluid^{5,6}.

Therefore, the present study was designed to observe the protective role of vitamin E on indomethacin induced low pH of seminal fluid in testicular and accessory sex organ damages.

Materials and Methods

Eightyfour mature Long Evans male rats of 2.5 to 3.5 months old, weighing 200-300 gms were included in this study.

Drugs: The following drugs were used in the present study:

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- 1) Indomethacin powder: (a) Low dose 2 mg/kg body weight/day, and (b) High dose 10 mg/kg body weight/day. Indomethacin suspensions were made in distilled water and administered intragastrically^{4,7}.
- 2) Vitamin E powder, dose 100 mg/kg body weight/day. Suspensions of vitamin E were administered intragastrically⁸.
- 3) Vehicle: Distilled water for control group, dose 2 ml/rat/day.

Methods

Eightyfour male rats were divided into four main groups (I, II, III and IV). These main groups were again divided into three subgroups 'a' (control), 'b' (indomethacin 2 mg/kg/body weight/day) and 'c' (indomethacin 10 mg/kg body weight/day). Each subgroup included 7 rats. Grouping of animals and their treatment were done on the basis of duration of treatment⁶.

Rats of group I, II and III were treated by indomethacin at low and high doses for 7, 14 and 42 days, respectively. Group IV rats were treated with indomethacin low (2 mg/kg body weight/day) and high (10 mg/kg body weight/day) dose plus vitamin E (100 mg/kg body weight/day) for 49 days.

For determination of pH of seminal fluid, the animals were sacrificed by cervical dislocation under ether anaesthesia⁷. After sacrifice, the abdomen of the rats were opened at autopsy and right seminal vesicle was taken out and used for determination of pH of the seminal vehicle. The right seminal vesicle was gently minced with a fine scissors. The PH indication paper (manufactured by Merck of Germany) was made wet with the extract of seminal vesicle. The pH was calculated by matching the colour of indicator paper with that of standard colour table⁹.

For statistical analysis, the data obtained from different groups of rats were analyzed and comparisons were made using unpaired Student's 't' test.

Results

There was significant reduction (P<0.001) in pH of seminal fluid when the rats were treated with indomethacin at low (2 mg/kg body weight/day) and high (10 mg/kg body weight/day) dose for 7, 14 and 42 days, respectively. On the other hand, rats treated with indomethacin plus vitamin E for 49 days showed significant increase (P<0.001) in pH of seminal fluid compared to control and other groups (Table I).

Table I
Effect of indomethacin/indomethacin plus vitamin E on pH of seminal fluid of different groups of rats

Groups	Duration of treatment (days)	pH of seminal fluid Mean±SD
la	7	7.59±0.13 (7.4-7.8)
lb	7	7.41±0.07 (7.3-7.5)
lc	7	7.26±0.08 (7.2-7.4)
IIa	14	7.64±0.10 (7.5-7.8)
IIb	14	7.34±0.13 (7.2-7.5)
IIc	14	7.26±0.08 (7.2-7.4)
IIIa	42	7.63±0.10 (7.5-7.8)
IIIb	42	7.30±0.08 (7.2-7.4)
IIIc	42	7.08±0.10 (7.0-7.2)
IVa	49	7.53±0.11 (7.4 7.7)
IVb	49	7.50±0.06 (7.4 7.6)
IVc	49	7.44±0.05 (7.4 7.5)
la IIa IIIa IVa	Control, 2 ml distilled water/day	
lb IIb IIIb	Indomethacin 2 mg/kg body weight/day	
lc IIc IIIc	Indomethacin 10 mg/kg body weight/day	
IVb	Indomethacin 2 mg/kg plus vitamin E 100 mg/kg body weight/day	
IVc	Indomethacin 10mg/kg plus Vitamin E 100 mg/kg body weight day	

Groups	P value
Ia vs Ib	<0.05*
Ia vs Ic	<0.001***
Ib vs Ic	<0.01**
IIa vs IIb	<0.001***
IIa vs IIc	<0.001***
IIb vs IIc	>0.10 ^{ns}
IIIa vs IIIb	<0.001***
IIIa vs IIIc	<0.001***
IIIb vs IIIc	<0.001***
IVa vs IVb	>0.50 ^{ns}
IVa vs IVc	>0.05 ^{ns}
IVb vs IVc	>0.05 ^{ns}
IIIb vs IVb	<0.001***
IIIc vs IVc	<0.001***

Figures in parentheses indicate range. Comparison between groups done by Unpaired Student's 't' test, ns = not significant, */**/*** = significant

Discussion

The pH of the seminal fluid of all indomethacin treated rats were reduced. The reduction in pH of seminal fluid were highly significant ($P < 0.001$) in the rats treated with indomethacin at low and high doses for longer duration (14 and 42 days).

Similar findings were also observed by Balasubramanian *et al.*⁷, Kumar and Chinoy⁶, and Ara¹⁰. The reduction in pH may be due to the atrophy of seminal vesicle.

The pH of seminal fluid increased markedly ($P < 0.001$) in vitamin E treated rats in comparison to control group and also to indomethacin treated group of rats. This result is similar to the results observed by Cooper and Carpenter⁸, Mishra and Acharya⁵. The increase in pH of seminal fluid may be due to inhibition of lipid peroxidation which enhances spermatogenesis and lowers the incidence of abnormal sperm production.

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