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Gentamicin and Ofloxacin Effect in Plasma Testosterone Levels of Rats with Freund's Adjuvant Arthritis

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INTRODUCTION-AIM

Gentamicin (G) an aminoglycoside antibiotic besides its well known side effects, nephrotoxicity, ototoxicity and neuromuscular blockade is considered as a calcium channels antagonist. This action may cause inhibition of various neurotransmetters and autacoids release and problems in neurotransmission (1,2) because Ca^{++} is a very important mediator of different cellular events including muscle contraction, excitation – secretion coupling, enjymic activity and membrane excitability (3,4). Recently it has been reported that G affects the steroidogenic enzymes of testes and accessory sex organs and provoques a decline in the sperm count of rats (5,6). The fluoroquinolone ofloxacin (Ofl) is another antimicrobial agent acting in a different way. In high doses it concentrates in the joints and induces arthropathies in experimental animals and inhibits the development of cartilage in children (5). On the other hand Freund's adjuvant arthritis (FAA) has been connected with reduced testosterone levels in rats (8,9,10). Reduced testosterone levels were also reported in males with rheumatoid arthritis (11). The present study was undertaken in order to investigate the influence of G and Ofl on plasma testosterone levels of rats with FAA.

METHODS

Adult male Wistar rats of 300-350 g BW were used. Animals were maintained in well ventilated room with 12 hrs light/dark cycle and access to food and water ad libitum. They were divided into groups of 6 animals each. Group 1 served as control and received 0.1ml NaCl 0.9% I.M. injection in the paw of the right back foot (day 0). Group 2 received G sulphate 17.5mg/kg/12hrs. for 4 consecutive days between 20-24th day of the experiment. Group 3 received an injection of 0.1ml complete Freund's adjuvant (CFA) (M. butiricum in paraffin oil 5mg/ml) in the paw of the right back foot and the same treatment of G as group 2. Group 4 received a sc injection of 25mg Ofl. for 4 consecutive days between 20-24th day of the experiment. Group 5 treated as group 4 plus CFA (day 0). Group 6 received 20mg/kg IM (G) 14,5 and 2.5hrs before the sacrifice of the rats. Group 7 was treated as group 6 plus CFA (day 0). FAA was provoqued by the injection of CFA in the paw of the right back foot of the rats. The immune response was started to manifest 24-48hrs after the FAA injection (day 0). First in the form of topic inflammation in the extremity of the treated foot and secondly the inflammation was extended in the other foot and at the end of the 2nd week all the extremities were involved. In most of the rats the inflammation was extended to the testes and the base of the tail. Clinically the inflammatory disease reached its peak at the end of the 3rd week (acute phase of FFA) where signs of hyperalgesia, lack of mobility and decreased body weight were observed. During the acute phase (W 2-4), hind paw and fore paw joint diameters were increased. Rats were weighed for the last time few min before sacrifice by decapitation. Blood was collected and the seminal vesicles weight was also measured. Testosterone (T)

leterminations were performed by specific RIA Serono Diagnostic S.A). All results were expressed as means ± SEM and were statistically analyzed using student's t test P<0.05 was taken o be statistically significant (Table 1).

RESULTS

G administration induced a statistically significant decrease of T in comparison with the control group p<0.025. Decreased T levels were also observed in the group (3) with G and FAA p<0.025 in the acute stage of the inflammatory disease. Ofl. does not seem to influence T levels n the 4th group while in the 5th group of Ofl plus FAA reduced T levels were observed P<0.001, in comparison with group 1. In the group 6 the two doses of G did not significantly alter the T levels P>0.1 although there is a tendency to decrease. T levels reached again normal values in the regression phase of FAA (group 7). Reduced body and seminal vesicles weight observed only in the groups with FAA.

Table 1

GROUP	BW g	T levels ng/ml	SVW mgs/SEM
1	364.1±31	4.50±0.75	1445.7±78.3
2	364.5±5.3	1.42±0.42	1450.5±81.0
3	283.0±5.3	1.51±0.26	778.2±67.9
4	359.2±6.1	3.42±0.74	1410.9±105.1
5	271.2±10.8	1.22±0.31	713.7±91.9
6	328.9±7.9	2.86±1.07	1400.1±85.6
7	243.0±6.9	4.14±1.42	1360.0±95.0

DISCUSSION AND CONCLUSIONS

Our data indicate that G reduces T levels when was administered twice a day for 4 consecutive days, but the decrease in T levels was not statistically significant when G was administered only wice. Ghosh and Dasgupta reported recently that reatment of rats with 40-100mg/kg of G for 7 days lowers the activities of 2 steroidogenic enzymes in a dose dependent fashion, and that hese alterations are reversible 15 days after stopping the G treatment [5,6]. These results actually confirm and support our data providing that 17-β and 3-β hydroxysteroid dehydrogenases are ndispensable for T biosynthesis from pregnenolone. We speculate that the reduction of T levels by G is due to the inhibition of Ca^{++} channels in some stage of the steroidogenesis process. This effect is reversible and dose dependent. G does not influences body or seminal vesicles weight. Ofl has no effect either on T levels or body and seminal vesicles weight. On the other hand our study indicates that chronic inflammatory process of FAA in the rat is accompanied by a significant decrease of T levels in plasma being in accordance of those reports by Barbier et al (7) and Bruot – Clemens (8). The fact that there is a parallel reduction of T levels and seminal vesicles weight only in the FAA rats in the acute phase of the inflammation suggests that the inflammatory process is responsible for both reductions. The above is supported by the recovery of T levels in the regression phase of the FAA followed by an increase of the seminal vesicles weight.

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