EFFECT OF SPIRONOLACTONE ON ACID AND ALKALINE PHOSPHATASE IN THE TESTES OF ALBINO RAT

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ABSTRACT

The biological activity of the mineralocorticoid antagonist, spironolactone depend upon its metabolism. In this study the effect of diuretic drug compound spironolactone on the acid and alkaline phosphatase in the testes of albino rat. The drug spironolactone was administered orally daily for 7th, 14th and 21st days at the dose of 100 mg/kg body weight. Among them, the side effects of drug are that the degradation of alkaline phosphatase in the testes; while acid phosphatase increased significantly may be due to 7 α -thiospironolactone is a tissue metabolite of spironolactone and may contribute to the testicular enzymes, therapeutic actions and some other side effects. It is suggested that the decrease and increase of alkaline and acid phosphatase in the testes of albino rat are due to the side effects of spironolactone drug compound.

KEY WORDS

Drug Spironolactone, Albino rat, Acid and Alkaline Phosphatase.

INTRODUCTION

Spironolactone is an aldosterone antagonist or potassium sparing diuretic drug and is widely used in the treatment of hypertension and congestive heart failure. Various other side effects of spironolactone have been described as inhibition of adrenocortical, testicular steroideogenesis and microsomal enzymes and also increased the metabolic rate (3). It is competed with androgen, that is stimulated the drug metabolism by the decrease the concentration of plasma testosterone either by impairing the synthesis or by the stimulating metabolism of the androgen (4). Spironolactone belongs to a large group of agents which is induced the biotransformation of many compounds in mammalian hepatocytes (9). Spironolactone is decreased the testicular 17 α -hydroxylase activity and content of microsomal cytochrome p-450 in rats. The mechanism of action of spironolactone on the testes involves destruction of cytochrome p-450, resulting in decreases in the activities of steroid hydroxylases and enzymes. The metabolites of spironolactone is appeared to be an important in the biological activity of the drug and is responsible for the side effects of the drug on the

testicular cytochrome p-450 and enzymes level (8, 11, 12). The determination of both alkaline and acid phosphatase can therefore be helpful in monitoring any therapeutic response. Therefore, studies were carried out to explore further the side effects of spironolactone on the testicular alkaline and acid phosphatase in albino rat, *Rattus norvegicus*. Our results mere indicate that spironolactone interact with enzymatic activities.

MATERIALS AND METHODS

Experimental Animals

Thirty male albino rats of weight 150-200 gm (± 10 gm) were purchased from small animals breeding center JALMA Research Institute, Agra. The animals were housed in polypropylene cages maintained in controlled temperature ($27 \pm 5^\circ\text{C}$) and light cycle (12 h light and 12 h dark). They were fed with Goldmohar brand animal feed manufactured by Lipton India Limited. Food and water were provided *ad libitum*. The animals were given a week time to get acclimatized with the laboratory conditions.

Selection of Dose

In the present study, drug compound spironolactone, (Trade name Aldactone) Searle, Pharmaceuticals Company Limited, Mumbai has been used. Each dose of drug was given to the experimental group of rats at

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100mg/kg body weight for 7th, 14th and 21st day.

Experimental Procedure

Body weight of animals were recorded and then they were divided into six groups of five rats each. From which three groups were treated as experimental groups which were given compound spironolactone orally through the cathedral tube; while rest of the three groups as control groups that were given only corn oil for 7th, 14th and 21st day respectively.

Animals were fasted over night separately on 7th, 14th and 21st day. On the next day of each experimental protocol, after recorded the body weight, the animals were sacrificed by decapitation and the testes were dissected out, blotted of blood, rinsed in phosphate buffered saline (pH 7.4) and immediately proceeded for biochemical estimations.

Biochemical Estimations

The estimation of alkaline phosphatase was determined by Kind and King (5) and acid phosphatase by King method (6).

Statistical Analysis

All the data were statistically evaluated and the significance calculated using student 't' test (2). All the

results are expressed as mean $\pm$ S.Em.

RESULTS

An increase in acid phosphatase is significant ($p < 0.05$) after 7 days; while highly significant ($p < 0.01$) after 14 days and very highly significant ($p < 0.001$) after 21 days of spironolactone treated rats as compared to normal control rats (Table-1). However, the decrease testicular alkaline phosphatase is highly significant ($p < 0.01$) after 7 days; while very highly significant ($p < 0.001$) after 14 and 21 days in spironolactone treated rats when compared with controls (Table-2).

DISCUSSION

In the semen an acid phosphatase has greatest share and increase the percentage of acid phosphatase in the same cause prostatic carcinoma. In the present study, the acid phosphatase in the testes of albino rats increase due to the side effects of spironolactone treatment. Alan (1) has also been reported the marked increase acid phosphatase in the testes and distal cauda epididymis of rats; while Fujita (3) in the liver of rats due to adverse side effect of spironolactone on the hormones and membrane enzymes.

However, in the present study, the alkaline phosphatase in the testes of albino rats decrease due

Table 1. ACID PHOSPHATASE IN THE TESTES OF ALBINO RAT AFTER SPIRONOLACTONE TREATMENT

Acid Phosphatase in K.A. units					
No. of Rats	Treatment Time	Control groups		Treated groups	
		Mean	$\pm$ S.E.M	Mean	$\pm$ S.E.M
5	7 days	171.66	$\pm$ 2.09	185.00	$\pm$ 4.04*
5	14 days	182.38	$\pm$ 3.83	210.55	$\pm$ 5.29**
5	21 days	182.44	$\pm$ 3.87	232.22	$\pm$ 5.83***

Table 2. ALKALINE PHOSPHATASE IN THE TESTES OF ALBINO RAT AFTER SPIRONOLACTONE TREATMENT

Alkaline Phosphatase in K.A. units					
No. of Rats	Treatment Time	Control groups		Treated groups	
		Mean	$\pm$ S.E.M	Mean	$\pm$ S.E.M
5	7 days	35.02	$\pm$ 0.72	30.39	$\pm$ 0.85**
5	14 days	34.11	$\pm$ 0.68	21.47	$\pm$ 0.79***
5	21 days	33.13	$\pm$ 1.20	15.30	$\pm$ 0.89***
$\pm$ S.Em. = Standard Error of mean * Significant ($p < 0.05$) ** Highly Significant ($p < 0.01$) *** Very Highly Significant ($p < 0.001$)					

to the side effect of spironolactone treatment. Almost similar observations has also been reported by Setchell (10) that the activity of alkaline phosphatase in the liver of rats due to adverse side effects of spironolactone treatment; while Menard (8) and Stripp (12) due to inhibition of testicular steroideogenesis by the destruction of cytochrome p-450, which is the result from decrease steroid hydroxylases and decline lysosomal enzyme alkaline phosphatase or the activation of drug spironolactone by microsomal monooxygenase in the testes, in the presence of NADPH and oxygen which might result from decline the enzymes in the target tissue and Layne (7) in the plasma and testes of guinea pigs due to spironolactone treatment.

Studies to data indicated that the spironolactone when given in the high dose for the short period of time can have perform non specific side effects in testicular enzyme system. There action of drug are probably of significance in relation to the side effects seen clinically. Such studies should continue to a understanding of the mechanism of spironolactone particularly with respect to the role in the therapeutic action and the side effects of the drug.

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