EFFECT OF THIAZIDE DRUG COMPOUND ON THE TESTICULAR PROTEIN AND CHOLESTEROL CONTENTS OF ALBINO RAT

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ABSTRACT

In this study the effect of thiazide diuretic compound on the protein and cholesterol contents in the testes of albino rats as the experimental model. The drug thiazide was administered orally daily for 10, 20 and 30 days at the dose of 100mg/kg body weight. Total protein decrease in the testes of rats were evidenced may be due to the side effects of thiazide drug compound which is linked with the hyponatremia and protein metabolism. An elevated level of cholesterol contents observed in thiazide treated rats also revealed that the side effect of drug compound thiazide and also may be due to the stimulation of catecholamine which is stimulated therefore, the biochemical estimation such as protein and cholesterol in the testes after the thiazide treatment determined the effectiveness of diuretic drug compound would provide clinical evidences of their side effects.

KEY WORDS

Drug thiazide, *Rattus norvegicus*, protein, cholesterol

INTRODUCTION

Diuretics are indispensable group of therapeutic agent. They are used to adjust the volume or composition of body fluids in a variety of clinical situations. Diuretics are widely used and generally safe, but like any therapeutic agent they may cause side effects (1). The greatest use of thiazide diuretics has been as antihypertensive agents and for the treatment of edema associated with congestive heart failure, hepatic cirrhosis and renal failure. An initial doses of thiazide compound are associated with diuresis induced and decreases the blood volume and a consequent lowering of blood pressure which activates homeostatic reflexes (2). Thiazides have many side effects including suppression of hormones and enzymes secretion (caused by their anticalciuric effect) and induction of metabolism (3).

Thiazide diuretics also cause other adverse effects that increase total cholesterol, low density lipoproteins, triglycerides and protein (4). Thiazide induce changes seem to be a dose related and may

resolve with discontinuation of therapy (5,6). Classically, the treatment with thiazide diuretic can also competes with androgens in the stimulating of drug metabolism and still seemed possible that it might act by decreasing the concentration of plasma testosterone either by impairing the synthesis of androgen (7). Keeping this idea in background the present work was taken to estimate the side effect of thiazide drug compound on the protein and cholesterol in the testes of albino rat.

MATERIALS AND METHODS

Experimental Animals

Thirty male albino rats of weight 150-200 gm (± 10 gm) were purchased from small animals breeding centre JALMA Reaserch Institute, Agra. The animals were housed in polypropylene cages maintained in controlled temperature ($27 \pm 2^\circ\text{C}$) and light cycle (12h light and 12 h dark). They were fed with Gulmohar 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 thiazide, (Trade name Esidrex) Novartis India limited, Bombay has been used. Each dose of drug was given to the

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experimental group of rats at 100mg/kg body weight for 10,20 and 30 days.

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 thiazide orally through the cathedral tube ; while rest of the three groups as control groups that were given only distilled water for 10,20 and 30 days respectively.

Animals were fasted overnight separately on 10th,20th and 30th day. On the next day of each experimental protocol, after recording 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 measurement of tissue protein was determined by Lowry's method (8) and the tissue cholesterol by Zlatkis method (9).

Statistical Analysis

All the data were statistically evaluated and the significance calculated using students 't' test. All the results are expressed as mean $\pm$ S.E.M.

RESULTS

The decline in total protein content was very highly significant ($p < 0.001$) in the testes of thiazide treated rats as compared to normal control animals. However, activity of cholesterol was very highly significant ($p < 0.001$) in thiazide treated rats when compared with controls (Table 1).

DISCUSSION

Thiazide diuretics also cause many adverse effects which is linked to potassium depletion (Ames, 1984). In the present study, the total protein content decrease in the testes of albino rats may be due to the side effects of thiazide drug compound. In the present study it has also been reported by Menard (1974). It is likely that the lipoprotein and protein contents decreases by the adverse effect of thiazide and is mainly characterized by degradation of microsomal cytochrome p-450; while Fanestil (1997) reported in the kidney the metabolic influence of drug hydrochlorothiazide. Infact, thiazide diuretics

are the most common drug inducing hyponatremia, which is linked with the degradation of protein (Friedman, 1989). Similar observations have also been made by Nishino (12) in the various endocrine glands of rats due to side effects of aldosterone antagonist drugs, while Yashida (13) observed the effects of diuretics on the energy metabolism specially with protein metabolism in humans.

All loop diuretics altered lipid metabolism to variable extent when they are used at high doses particularly in cardio vascular patients. Thiazide drug compound increase total cholesterol, low density lipoproteins and triglycerides in the blood and tissue (Ames, 1986). In the present study, the total cholesterol content in the testes increase may be due to the side effects of thiazide drug compound. In the previous study, an increase in the body and organ weight due to the side effects of thiazide drug compound can also be correlated with an increase in cholesterol content in testes of albino rats (Yadav, 2002) Almost similar observations have also been reported by Grimm (16) and Lithell (17) while Weidmann (18) and Prichard (19) explained the mechanism of cholesterol changes may be due to stimulation of catchecolamine release in response to volume depletion and which stimulated hepatic cholesterol synthesis. Fried (20) has given the clinical importance of diuretic compound thiazide which is induced hypocalcemia and served as elevation in cholesterol.

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