RESEARCH ARTICLE

Effect of Vincristine on some biochemical parameters in male Albino Rat

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ABSTRACT

Vincristine ((C_{46} H_{56} N_4 O_{10})) is one of the most widely used effective oncostatic drug. It is an indole-indolin alkaloid from periwinkle plant vincarosea. The drug was administered intravenously to six adult male rats at dose levels of 0.06 and 0.12 mg/KgBW/day respectively. The object of the present work is to study the Vincristine effect on the reproductive accessory gland and testes. Vincristine prevents metastatic growth by preventing the formation of spindle fibers, thereby arresting mitosis without affecting replication of DNA. Vincristine affect on biochemical parameters. The total protein, citric acid and fructose decreased significantly in low dose and high dose treatment as compare to control ($P < 0.001$)). The body weight and organ weight also significantly decreased in low and high dose regimen as compare to vehicle treated control. From the foregoing mono-therapeutic study, it is concluded that this chemotherapy schedule belongs to the category of anti-gonadotropic and anti-androgenic.

Key words: Vincristine, Biochemical, Albino rat

INTRODUCTION

The vinca alkaloids are cell-cycle specific agents and, in common with other drugs such as colchicine, podophyllotoxin and taxanes, block cells mitosis (George *et al*., 1965; Bensch and Malawista, 1968; Dustin, 1984). The biological activities of these drugs can be explained by their ability to bind specifically to tubulin and to block the ability of the protein to polymerize into microtubules. Through disruption of the microtubules of the mitotic apparatus, cell division is arrested in metaphase. In the absence of an intact mitotic spindle, the chromosomes may disperse throughout the cytoplasm (exploded mitosis) or may clump in unusual groupings, such as balls or stars. The inability to segregate chromosomes correctly during mitosis presumably leads to cell death.

MATERAILS AND METHOD

The six adult male Rats weighing between 284 to 360 gms were selected for the present study collected from R.C. Patel Pharmacy College Shirpur.

Table 1: Experimental Design for Vincristine Treatment

Number of animals and sex	Treatment	Dose (mg/Kg BW)	Route	Duration
6 males (Experimental)	Vincristine	0.06 mg daily	I.V.	10 days
6 males (Experimental)	Vincristine	0.12 mg daily	I.V..	10 days
6 males (Control)	Saline	E.V.	I.V.	10 days

(Abbreviations: - E.V. = Equal Volume, I.V. = Intra Venous, BW=Body weight)

Even though the order Rodentia is highly exploited for the experimental purposes are easily available and can undergo all the laboratory tests without any difficulty, hence is suitable for experimental work. For the present study adult male rat weighing between 284 to 360gms were collected in wire mesh cages. The animals were kept in captivity in the wire mesh cages experiencing natural daylight and temperature. After a week of acclimatization to laboratory conditions, the animals were used for different sets of experiments.

Biochemical Assay

The concentration of proteins, fructose and citric acid in the testis and accessory reproductive organs were carried out.

Preparation of homogenate

Dry weights of the reproductive organs were taken before proceeding for the bio-chemical analysis so that the estimated value of enzymes and substrates can be calculated / gram dry weights of the reproductive tissue. The homogenate was prepared in 10 ml of distilled water as well as 10ml of saline. The tissue was ground with mortar and pestle. Clear supernatant obtained after centrifugation at 3000 r.p.m. was used for various biochemical assays.

a) Estimation of Protein

Biochemically protein was estimated by the method of Lowry *et al*., (1951).

b) Estimation of Citric Acid

Biochemically citric acid was estimated by the method of Ettinger *et al*., (1952).

c) Estimation of Fructose

Biochemically fructose was estimated by the method of Foreman *et al*., (1973).

RESULT AND DISCUSSION

For the present work anti cancer drugs, Vincristine (VCR) was studied.

Vehicle treated control

Body Weight :

The body weight varies from 284 gms to 360 gms in a mature adult.

Organ Weight:

During active breeding period, the weight of testis was 1.385 to 1.390 gms., seminal vesicle was varied from 0.210 to 0.240 gms . and prostate was 0.320 to 340 gms.

Biochemical study

Protein

The value of protein in control animal was found to be 2.370 (range 2.360 – 2.380 mg/gm, Table-4 & bar diagram) was recorded (P<0.001).

Citric acid

In vehicle treated control the value of citric acid was 0.545 mg/gm (range 0.535-0.555) Table-4 & bar diagram) (P<0.001).

Fructose

Significant decrease (range 1.118-1.138.920 mg/gm, Table-4 & bar diagram) in the fructose content was noticed (P<0.001).

Low dose treatment

Body weight

The total body weights of all the animals treated with 0.06 mg/kg BW/day showed significant decrease (P<0.05) as compared to control animals (Table-2 & bar diagram).

Organ weight

0.06 mg/kg BW/day for 10 days registered a decrease in the testis, prostate and seminal vesicle as compared to control animals (Table-3 & bar diagram).

Biochemical study

Protein

A significant decrease in the protein concentration (range 1.910 – 0.930 mg/gm, Table-4 & bar diagram) was recorded (P<0.001).

Citric acid

This treatment resulted into significant decrease (range 0.420-0.440 mg/gm, Table-4 & bar diagram) in its citric acid content (P<0.001).

Fructose

Significant decrease (range 1.097-1.117 mg/gm, Table-4 & bar diagram) in the fructose content was noticed (P<0.001).

High dose treatment

Body weight

The total body weight of all the animals treated with 0.12mg/kgBW/day for 10 days showed significant decrease (P < 0.01) in their body weight as compared to low regimen treated group (Table-2 & bar diagram).

Organ weight

In high dose treatment of Vincristine with 0.12mg/kgBW/day for 10 days registered a decrease in testes, seminal vesicle and prostate weights (P<0.05)) as compared to low dose treated animals. (Table-3 & bar diagram).

Biochemical study

Protein

The total protein content after treatment dropped significantly (range 0.620-0.640 mg/gm, Table-4 & bar diagram) (P<0.001).

Citric acid

The concentration of citric acid showed significant decline (range 0.230-0.250, Table-4 & bar diagram) (P<0.001).

Fructose

The concentration of fructose after administration of VCR registered an increase (range 0.965-0.985 mg/gm, Table-4 & bar diagram) (P<0.001).

Table 2 & Fig. 1: Effect of 0.06 mg and 0.12 mg Vincristine daily for 10 days on initial and final body weights of male albino rats (values are mean ± SE, figures in parenthesis are number of animals used)

Treatment	Total body weight	
	Initial	Final
Control (6)	324±6.4	330 ± 14
0.06mg/kg BW daily 10 days (6)	310 ± 6.4	303 ±14
0.12mg / Kg BW daily 10 days (6)	340 ± 7.6	320± 12*

P value < 0.05

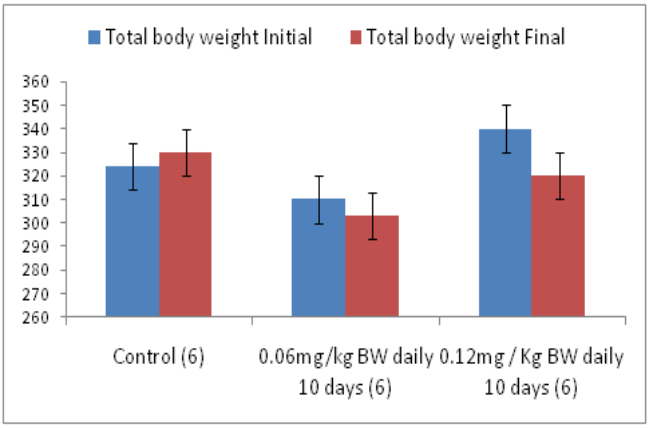

Table 3: Effect of 0.06 mg and 0.12 mg/kg BW Vincristine daily treatment for 10 days on organs weight of male albino rats (values are mean ± SE, figures in parenthesis are number of animals used).P value < 0.05

Treatment	Total Organ weight		
	Testes	Seminal vesicle	Prostate
Control (6) Control	1.385±0.33	0.210±0.028	0.320±0.0081
0.06mg/kg BW daily 10 days (6)	1.373±0.034	0.206±0.027	0.315±0.0081*
0.12mg / Kg BW daily 10 days (6)	1.360±0.32	0.202±0.020	0.308±0.0081

Table 4: Effect of 0.06 mg and 0.12 mg/kg BW Vincristine daily treatment for 10 days on biochemical parameters of male Albino rats (values are mean ± SE, figures in parenthesis are number of animals used).

Treatment	Protein	Citric acid	Fructose
Control (6)	2.370±0.02	0.545±0.04	1.128±0.02
0.06mg/kg BW daily 10 days (6)	0.920 ±0.03	0.430±0.03	1.107±0.02
0.12mg / Kg BW daily 10 days (6)	0.630 ±0.02	0.240±0.03	0.975±0.02

P value – P < 0.001

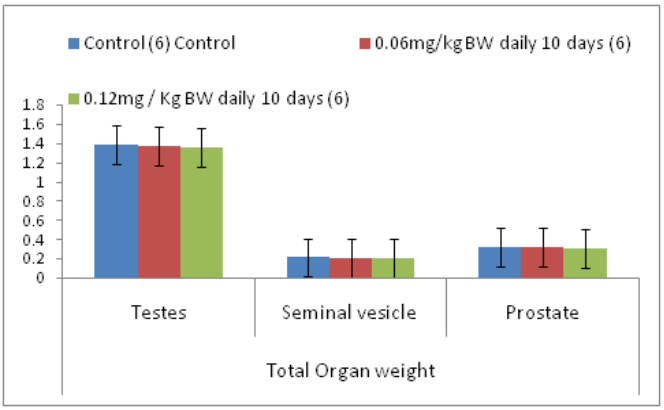

Fig. 2: Effect of 0.06 mg and 0.12 mg/kg BW Vincristine daily treatment for 10 days on organs weight of male albino rats (values are mean ± SE, figures in parenthesis are number of animals used).P value < 0.05

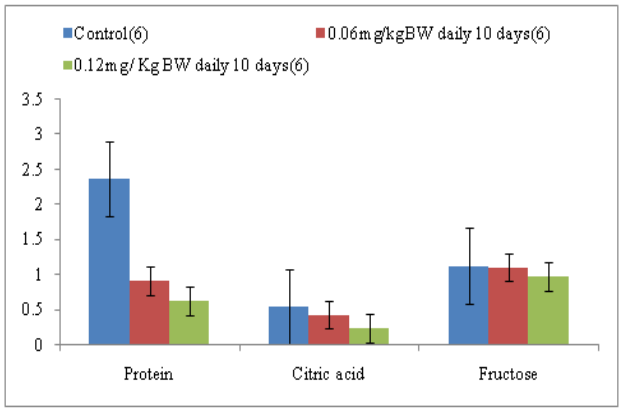

Fig. 3: Effect of 0.06 mg and 0.12 mg/kg BW Vincristine daily treatment for 10 days on biochemical parameters of male Albino rats (values are mean ± SE, figures in parenthesis are number of animals used).

DISCUSSION

Body weight

It may be suggested that a reduction in the total body weight with these chemotherapeutic drugs (VCR) treatment may be due to decline in the circulating blood serum androgen since androgen are a potent stimulant of nitrogen retention and their administration readily leads to an increase in body weight in both men and women (Kochakian, 1950; Forbes, 1985; Bhasin *et al*., 1997).

Organ weight

A reduction in the weights of testis and the accessory organs or glands of the Vincristine treated rats (both the low and high dose treated groups) points to reduced androgen levels of androgen binding protein (ABP) in the testis and a reduction in the circulating androgen. This is because the biosynthesis and secretion of ABP appears to be regulated by both FSH and androgens (Tindall and Means, 1976; Buchanan and Riches, 1986).

Proteins

Proteins are major constituent of animal tissues and show considerable variation during different metabolic states and play important role in reproductive physiology. It also acts as a source of plastic material and carriers of enzymes, antigens, hormones and other essential substances also play important physiological role for the tissue development. Proteins are involved in a number of important cellular activities (Brachet, 1940; Caspersson, 1941). Vincristine resulted in to decreased in protein content in male squirrel (Chaudhari and Sastry, 2014).

In the present study treatment with vincristine, the significant decrease ($P < 0.001$) in the total protein content with low dose treatment (0.06 mg / Kg BW/day) and with high dose Vincristine (0.12 mg/Kg BW/day) was observed. VCR treatment studies manifested antiandrogenic and antifertility effects in intact male albino rats.

Citric Acid

Citric acid is a tri-carboxylic acid and like dicarboxylic acids, it is not metabolized by sperm since it is unable to cross the plasma membrane. Even though it is frequently included as a buffer in diluents used for sperm storage, its normal role in seminal biochemistry is not at all clear. Citric acid is a well known chelating agent of divalent cations and may protect sperm from heavy metal poisoning, to which sperms are particularly susceptible (White and Holland, 1977). In view of the importance of calcium in uptake for the acrosome reaction seminal citrate may, due to its chelating role, prevent the acrosome reaction from occurring prematurely as studied by Yanagimachi and Usai (1974) in bull.

A significant decline in citric acid ($P < 0.001$) content with low dose and high dose VCR resulted. Decrease in the citric acid concentration is associated with the degenerative changes of spermatogenic elements (Dixit *et al*., 1979).

Fructose

Estimation of fructose values in very important during the study in male reproduction because fructose concentrations have been assumed to be good and easily accessable indices of androgenic activity and Leydig cell function (Phadke *et al*., 1973). Beside this seminal fructose provides an indication of size, storage and secretory activity of seminal vesicle (Mann and Lutwak – Mann, 1951).

In the present study treatment with vincristine, the significant decrease ($P < 0.001$) in the fructose content with low dose treatment (0.06 mg / Kg BW/day) but significant increase ($P < 0.001$) with high dose Vincristine (0.12 mg/Kg BW/day) was observed.

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