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Histopathological studies on effect of antimalarial drug chloroquine on prostate gland of wistar rat

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ABSTRACT

Chloroquine is a medication used to prevent and to treat malaria. In the present study effect of chloroquine on prostate gland in male albino rats (*Rattus norvegicus*) was investigated. For this experimental study, 18 adult male albino rats were selected and randomly divided into 3 groups, group I, II, and III, each group with 6 animals. Group I serve as a control and group II and III were experimental and administered daily 2mg/kg body weight chloroquine orally for 30 and 45 days duration respectively and control groups received saline water for the same duration. After completion of treatment rats were sacrificed using chloroform prostate gland was dissected out and weighed, fixed in aqueous Bouin's fixative, dehydrated, embedded in paraffin wax, sections cut at 5 µm and stained with hematoxylin and eosin for histological study. Chloroquine treatment showed slight change in the body weight, whereas the weight of prostate gland decreased significantly in group II and III. Histology of prostate gland of treated group II showed degenerative changes, alveoli with degenerated epithelium, less eosinophilic secretion was present in the lumen of alveoli. These changes are more obvious in group III with more destruction of epithelium and much reduced eosinophilic secretion in lumen of alveoli. The results of present study suggest that long term administration of chloroquine has destructive effect on prostate gland which affects the fertility of male.

KEYWORDS- Body weight, chloroquine, fertility, histology, prostate gland

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INTRODUCTION

Chloroquine has been implicated as an antifertility agent[1]. Preliminary investigation has shown disruption the process of spermatogenesis following toxic administration of chloroquine[2]. A reduction in Leydig cell population and concomitant decline in plasma testosterone level has also been reported[3]. In the treatment of malaria, chloroquine is given for a short period of time, but in malaria endemic region of tropical Africa, treatment is often repeated in a period as short as 2 weeks due to repeated attack of the sickness[4]. Chloroquine therapy may last up to 12 weeks in the treatment of discoid lupus, extra intestinal amoebiasis and rheumatoid arthritis[5]. Long term treatment with chloroquine for weeks revealed derangement of the seminiferous tubules in rat. Regression of Sertoli cells may inhibit spermatogenesis since these cells are responsible for the production of androgens binding protein and fluids into the lumen of seminiferous tubules essential for normal spermatogenesis[6]. Impairment of Sertoli cells may have caused the inhibition of spermatogenesis[3].Total loss of Leydig cells would probably lead to a deficiency in testosterone which might ultimately lead to an arrest in the function of male accessory organs[7]. Loss of Leydig cells would inhibit the production of testosterone and its function, since testosterone has been shown to enhance and maintain the motility and fertility power of sperms[8]. Accessory reproductive organs need testosterone for their activity, low testosterone arrests the function of accessory reproductive organs[9]. Effect of Quinine on male rat show weight reduction in testes, epididymis and seminal vesicle and also decreases the level of serum testosterone[10].

There is very little information is available on effect of chloroquine on prostate gland particularly on histopathology. Thus the present study was performed to determine the effect of chloroquine on body weight, prostate gland weight and histopathological study of prostate gland in rat.

MATERIALS AND METHODS

Animal model

The present study was carried on healthy and sexually mature adult male albino rats (*Rattus norvegicus*) of Wistar Strain of an average body weight 180-230g. The animals were housed in a hygienic, well-ventilated room with natural light and dark cycles (12 h dark, 12 h light). They were individually housed in clean polypropylene cages with sawdust bed and covered with stainless steel wire lids.

Experimental design

The rats were randomly divided into three groups. Group I served as a control while the group II and group III received chloroquine of 2 mg/kg body weight daily for 30 days and 45 days respectively, control group received saline solution daily for same duration. The experimental protocol was approved by the Institutional Animal Ethics Committee (Registration number 478/01/a CPCSEA) of RTM Nagpur University, Nagpur, prior to commencement of study.

Body and prostate gland weights

The weight of each animal was recorded before and after treatment. After treatment rats were sacrificed using chloroform prostate gland was dissected out and weighed.

Histopathological study of prostate gland

Prostate gland of rats of all experimental groups were fixed in Bouin's fixative for at least 24 h, dehydrated in graded ethanol, cleared in xylene and embedded in paraffin wax, sections cut at 5 µm and stained with hematoxylin and eosin (HE). The photomicrographs were taken with the help of digital camera Nikon COOLPIX 8400 attached to the light microscope (Nikon Eclipse E200) and magnified to the required size.

Statistical analysis

The data obtained from the above experiments were subjected to statistical analysis. All the values were expressed in terms of mean ± SEM. The data were analyzed statistically by using Student's "t" test.

RESULTS

In the present study the chloroquine (2mg/Kg bw) treated rats showed reduction in body and prostate gland weight for 30 and 45 days duration as compared to control (table 1). Histopathological study of prostate gland of Group I animals showed normal histo-architecture (Fig. 1(a) and 1(b)). The present result revealed that histopathological study of prostate gland of group II showed significant alterations in the histological structure, various alveoli were in the process of disintegration showing degenerative epithelium (DE), lumen had reduced secretion (RS) and space between the alveoli increased (Fig. 2(a) and 2(b)). Whereas the prostate gland of group III animals showed alveoli with degenerative epithelium (DE) and lumen had much reduced secretion (RS) (Fig. 3(a) and 3(b), these destructive changes are more severe in group III as compared to Group II.

Table 1: Effect of chloroquine on body weight and weight of prostate gland

Treatment Groups	Body weight (gm)		Prostate gland wt. (mg)
	Initial wt.	Final wt.	
Group I (Control)	197.00±3.61	209.83±1.58	547±14.30
Group II (chloroquine 2mg/kg bw 30 days)	191.83±2.96	184.17±2.82*	492±7.50*
Group III (chloroquine 2mg/kg bw 45 days)	199.00±4.13	185.00±3.78*	430±8.36*

Data are expressed as mean±SEM of 6 animals, *P value <0.05 i.e. significant

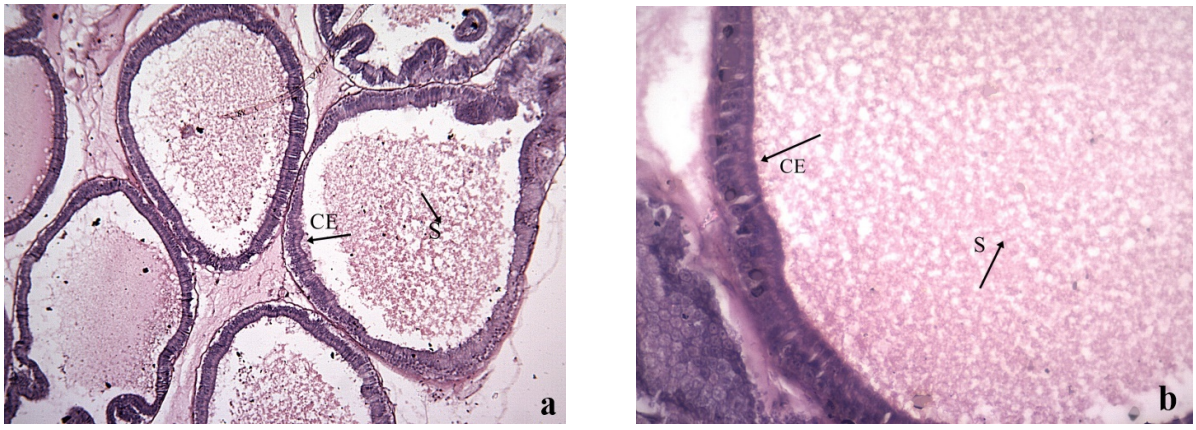

Fig. 1. Transverse section of prostate gland of Group I showing alveoli lined by cuboidal epithelium (CE) and lumen filled with secretion (S) 100X (a). b- Magnified view of (a) 400X.

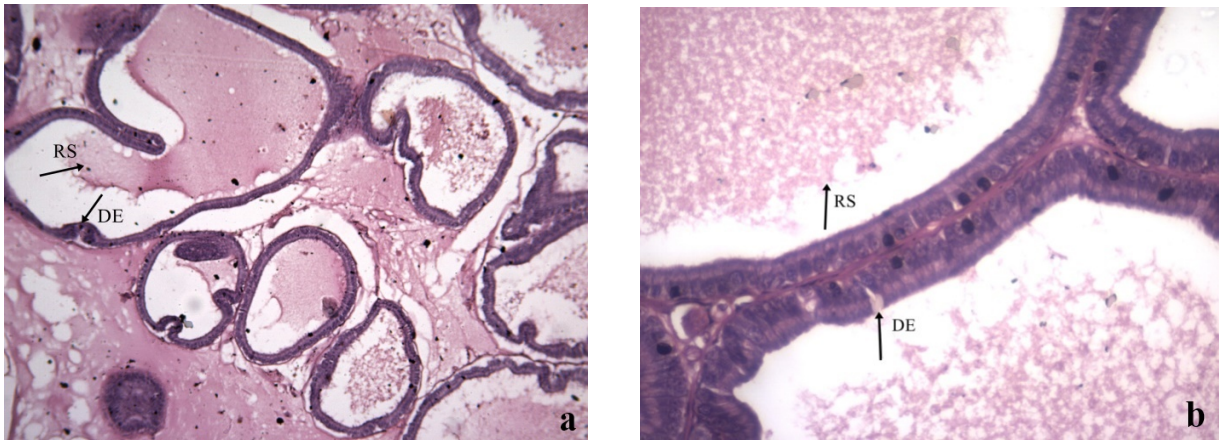

Fig. 2. Transverse section of prostate gland of Group II showing degenerative epithelium (DE) and lumen has reduced secretion (RS) 100X (a). b- Magnified view of (a) 400X.

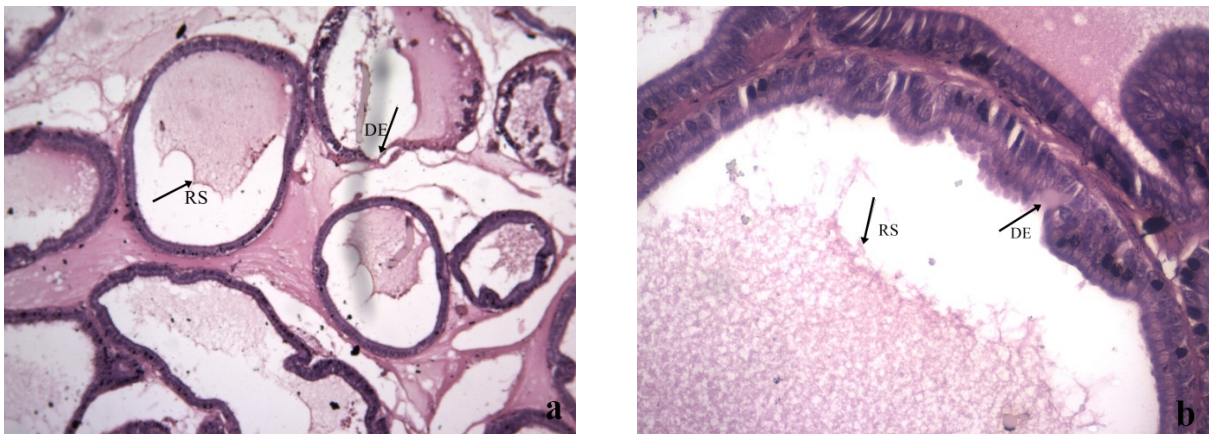

Fig. 3. Transverse section of prostate gland of Group III showing degenerative epithelium (DE) and lumen has reduced secretion (RS) 100X (a). b- Magnified view of (a) 400X.

DISCUSSION

In the present study, oral administration of chloroquine 2mg/kg bw caused reduction in body weight and prostate gland weight, high degree reduction in body weight and prostate gland weight observed in group III. The similar results are observed by, [11]in their treatment with *Tinosporea cordifolia*, [12]seed extract of *Strychnos potatorum*, and [13] ethanolic extract of *Citrullus colocynthis* schrad fruit in male rats respectively. Reduction in prostate gland weight in chloroquine treated rats clearly indicates that administration of chloroquine caused structural and functional changes in prostate gland. Prostate gland plays important role in male reproduction and its secretion is essential for the normal function of spermatozoa[14]. The result revealed that after administration of chloroquine prostate gland showed significant alterations in the histological structure, various alveoli were in the process of disintegration showing degenerative epithelium.

These results are in agreement with [15] *Citrullus colocynthis* on function of cauda epididymis and accessory reproductive organs of male rats and [16]effect of lead acetate on seminal vesicle and prostate gland. In the present study lumen of prostate gland alveoli had reduced secretion. The results are in agreement with [12]who reported the effect of methanol seed extract of *Strychnos potatorum* on accessory sex organs of albino rats, and [17]in treated of *Azadiracta indica* in rat. The destructive changes in prostate gland are more severe in group III, it indicated that if duration of treatment is increased it causes more damage to prostate gland.

CONCLUSION

In present study, administration of chloroquine (2mg/kg body weight) suggests significant alteration in weight reduction and degenerative changes in histology of prostate gland. Therefore, it can be concluded that chloroquine has potentially deleterious effect on the prostate gland**.** Prostate

gland play an important role in fertility of male hence fertility of male is suppresses after long term treatment with chloroquine.

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