

Original Research Article

Light Microscopic Analysis of Kidney of Sildenafil Citrate (Caverta) Treated Albino Rats

Suriya Kumari K.V.P¹, Udayakumar R², Sonia Patricia D'Souza²

¹Department of Anatomy, Sri Manakula Vinayagar Medical College & Hospital, Madagadipet, Puducherry-605107, India

²DDE Study centre, Annamalai University, Villupuram- 605602, Tamil Nadu, India

***Corresponding author**

Dr. K. V. P. Suriya kumari

Email: suriyaudhay@gmail.com

Abstract: Albino rats were chosen for the present study and the total animals were divided into eight groups (S₁-S₈), each consisting of six animals in it. The control animals (S₁) were fed with conductivity water while the experimental animals were fed with the single dosage of Sildenafil citrate (Caverta). S₂, S₃, S₄ and S₅ group of animals were sacrificed respectively after 1hour, 2.5 hours, 4 hours and 24 hours of drug administration. S₆, S₇ and S₈ group of animals were fed with the single dose of the said drug daily for 15, 30 and 45 days respectively and then, sacrificed after 4 hours of the last dosage of the drug. The kidney samples of the control and experimental animals were subjected to light microscopic analysis. From the present study, it has been found that the long-term Caverta treatment resulted in a considerable increase in periglomeruli space, destruction of glomeruli, increase in the number of vacuolated cells and the destruction of the normal architecture of the kidney. The outcome of the present study clearly depicts the fact that Sildenafil citrate (Caverta), if administrated on long-term basis, will produce adverse effects on the structure and vital function of the kidney of Albino rats.

Keywords: Albino rats, Kidney, Caverta, Light microscope, Histoarchitecture.

INTRODUCTION

Erectile dysfunction (ED) has been defined as the persistent inability of male to attain and maintain a penile erection sufficient to permit satisfactory sexual performance as a part of overall process of male sexual function [1, 2]. According to Massachusetts Male aging survey, 52% of the surveyed men aged 40-70 had some degree of ED, with dysfunction being moderate to complete in approximately half of the 70 years old men [3, 4]. Various chronic disorders such as depression, diabetes, and cardiovascular and neurological diseases were found to be associated with elevated rates of ED in men over 60 years of age [5].

Sildenafil citrate is a selective inhibitor of cGMP-specific Phosphodiesterase type 5 (PDE5). The onset and duration of action of this drug has been extensively studied by Eardley *et al.*; (1999) and Eardley *et al.*; (2002) [6, 7]. Muirhead *et al.*; (2002) have identified factors such as age and renal and hepatic impairment to affect the pharmacokinetics of the drug [8]. Though this drug has been considered to be safe, it has been found to produce mild to moderate side effects [9]. Therefore, it has been planned, in the present study, to conduct Light microscopic analysis to investigate on

the influence of Sildenafil citrate (Caverta) on the structure and functions of kidney of Albino rats.

MATERIALS AND METHODS

Healthy male Wistar Albino rats weighing about 300- 350 gm. were chosen for the present study. These animals were fed with standard pellet diet and water ad libitum. For the present study, the total animals were divided into eight groups (S₁-S₈), each consisting of six animals in it. The control animals (S₁) were fed with conductivity water while the experimental animals were fed with the single dosage of Sildenafil citrate (Caverta) [@ 1µg/g body wt.]. S₂, S₃, S₄ and S₅ group of animals were sacrificed respectively after 1 hour, 2.5 hours, 4 hours and 24 hours of drug administration. S₆, S₇ and S₈ group of animals were fed with the single dose of the said drug daily for 15, 30 and 45 days respectively and then, sacrificed after 4 hours of the last dosage of the drug.

Aseptic precaution was strictly followed in the operative procedures. Chloroform anaesthesia was used in the present investigation. A vertical ventral midline incision was made in the abdominal wall to collect both the kidney samples. Using standard procedures, each kidney sample was serially sectioned and a minimum of

100 sections per Kidney sample was stained with Eosin and Haematoxylin. These slides were studied using Stage microscope.

RESULTS

From the present study, the following observations have been made: In the case of kidney samples of Group S_1 (0 hour) animals, Glomerulus, Distal convoluted tubules, proximal convoluted tubules and the brush borders were very clear and well defined. Moreover, the histoarchitecture remains intact (Fig-1).

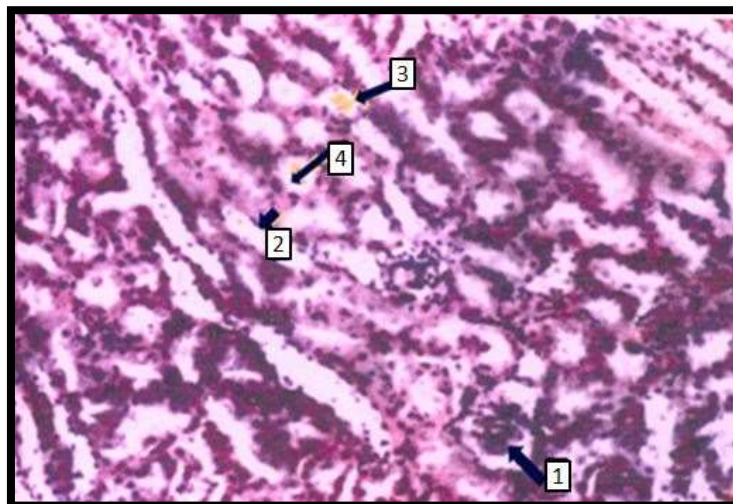


Fig-1: Section of Kidney of Albino rat [S_1 (0 hr.)] showing (1) Glomerulus, (2) Distal convoluted tubule, (3) Proximal convoluted tubule and (4) Brush border. Haematoxylin -Eosin. x100.

Increased interstitial space accompanied by marked oedema in proximal and distal convoluted tubules have been noticed for S_4 (4 hours) animals.

Moreover, extravasted blood was also noticed for the kidney samples of these animals (Fig-2).

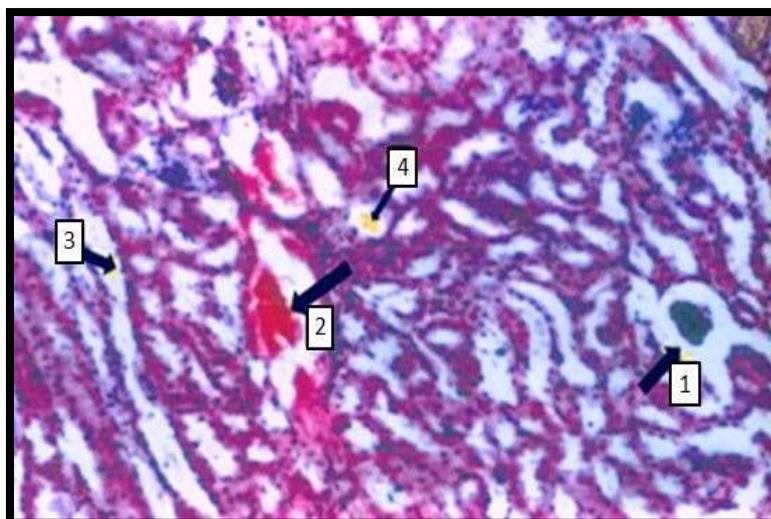


Fig-2: Section of Kidney of Albino rat [S_4 (4 hrs.)] showing (1) Glomeruli, (2) Extravasted blood, (3) Distal convoluted tubule (oedematous) and (4) Proximal convoluted tubule (oedematous). Haematoxylin- Eosin. X100.

In the case of S_5 (24 hours) samples, the histoarchitecture remains almost similar to that of control (S_1) samples.

Due to the long -term influence of the drug (Caverta), Group S_6 (15 days) samples show an increased periglomeruli space along with the distorted structure of distal convoluted tubule and proximal convoluted tubule (Fig-3).

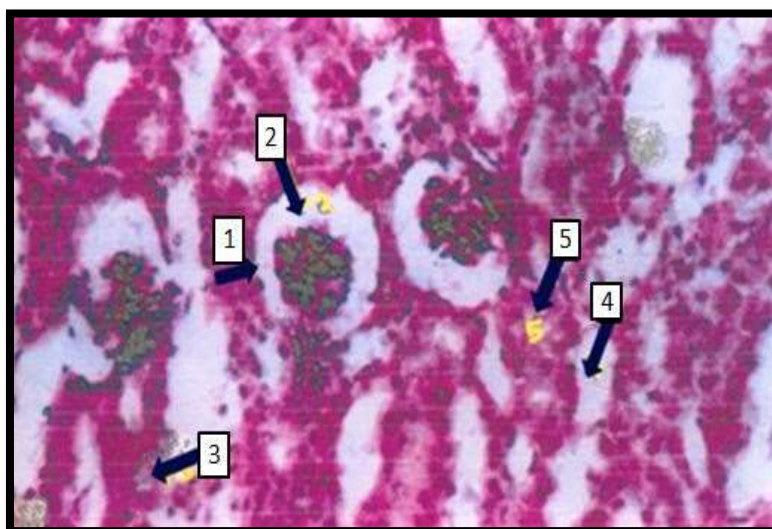


Fig-3: Section of Kidney of Albino rat [S₆ (15 days)] showing (1) Glomerulus, (2) Increased periglomeruli space, (3) Vacuolated cells, (4) Distal convoluted tubule and (5) Proximal convoluted tubule. Haematoxylin- Eosin. X100.

Similar observations have been noticed for the kidney samples of S₇ (30 days) group of Albino rats. The group S₈ (45 days) kidney samples show drastic changes in the structure of the organ. These samples

exhibit a large number of vacuolated cells, the destruction of glomeruli and hence, the destruction of normal histoarchitecture of kidney (Fig-4).

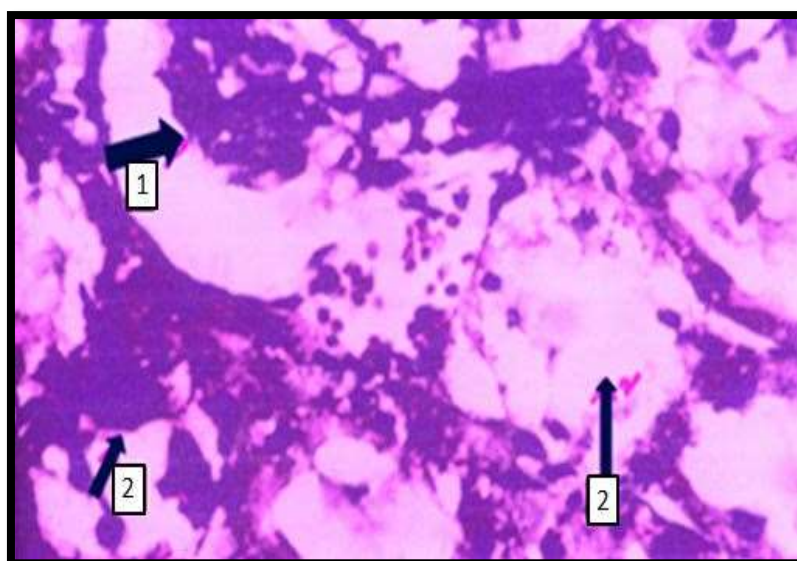


Fig-4: Section of Kidney of Albino rat [S₈ (45 days)] showing (1) Destroyed Glomerulus and (2) Destruction of normal architecture. Haematoxylin- Eosin. X100.

DISCUSSION

In the case of group S₃ and S₄ animals, it seems the defence mechanism of the animal has gradually become weak to overcome the impact of the drug (Caverta) on the structure and function of the kidney and hence, there occurred marked interstitial space oedema accompanied by extravasated blood for the samples. The observations made on S₅ (24 hours) samples point out the fact that the vigour of the drug has become almost nil after 24 hours of the drug administration and hence, the animal tried to regain its

normal conditions. The observations made on the kidney samples of S₆ (15 days), S₇ (30 days) and S₈ (45 days) crystal clearly portray the fact that even a single dose of Sildenafil citrate (Caverta) administered daily for a period of 15, 30 and 45 days resulted in the structural and functional disorder of the kidney of these animals. Structural disorders like distorted histoarchitecture of the kidney, increased number of vacuolated cells, destruction of glomeruli and increased peri glomeruli spaces have been noticed for these long-term drug treated animals.

Results obtained in the present Light microscopic study show that Sildenafil citrate (Caverta) induced many histoarchitectural changes in the kidney of Albino rats. Similar findings have been reported for kidney of Albino rat treated with Gibberellin A₃ and kidney of Albino mice with residual Maneb and Zineb [10, 11]. Sherlock and Dooley have reported cytoplasmic vacuolization to be one of the important primary responses to all forms of cell injury [12]. It implies on the increased permeability of cell membranes leading to an increase of intracellular water. As water sufficiently accumulates within the cell, it produces cytoplasmic vacuolization. The vacuolar degenerative changes have been correlated with marked disturbances which take place in lipid inclusion as a result of injurious treatment [13].

Therefore, the observations noticed in the case of kidney samples of long-term drug (Caverta) treated Albino rats such as the extravasted blood, the distorted Histoarchitecture, increased number of vacuolated cells, destruction of Glomeruli and increased peri glomerular spaces crystal clearly point out the vacuolar degenerative changes leading to the kidney dysfunction.

CONCLUSION

It is therefore concluded that Sildenafil citrate (Caverta), if administered on long-term basis, has detrimental effects on the structure and vital functions of the kidney of Albino rats.

REFERENCES

1. Morley JE; Impotence. The American Journal of Medicine, 1986; 80(5): 897-905.
2. Aytac IA, Araujo AB, Johannes CB, Kleinman KP, Mckinlay JB; Socioeconomic features and incidence of erectile dysfunction: findings of the longitudinal Massachusetts Male Aging Study. Soc. Sci. Med, 2000; 51(5): 771-8.
3. Johannes CB, Araujo AB, Feldman HA, Derby CA, Kleinman KP, McKinlay JB; Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts male aging study. J Urol, 2000; 163(2): 460-3.
4. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB; Impotence and its medical and psychological correlates: results of the Massachusetts Male Aging Study. J Urol, 1994; 151(1): 54-61.
5. Kubin M, Wagner G, Fugl- Meyer AR; Epidemiology of erectile dysfunction. International Journal of Impotence Research, 2003; 15: 63-71.
6. Eardley I, Brooks J, Yates PK, Ellis P, Boolell M; Sildenafil citrate (VIAGRA): an oral treatment for erectile dysfunction with activity

for upto four hours duration. Int J Clin Pract Suppl, 1999; 102: 32-4

7. Eardley I, Ellis P, Boolell M, Wulff M; Onset and duration of action of Sildenafil for the treatment of erectile dysfunction. British Journal of Clinical Pharmacology, 2002; 53 (suppl. 1): 61S- 65 S.
8. Muirhead GJ, Wilner K, Colburn W, Haug PG, Rouviex B; The effects of age and renal and hepatic impairment on the pharmacokinetics of sildenafil. British Journal of Clinical Pharmacology, 2002; 53 (Supplement1): 21S-30S.
9. Webb DJ, Freestone S, Allen MJ, Muirhead GJ; Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. Am J Cardiol, 1999; 83 (5A): 21 C-28C.
10. Sakr SA, Okdah YA, Sabah F El- Abd; Gibberellin A₃ Induced Histological and Histochemical Alterations in the Liver of Albino Rats. Science Asia, 2003; 29: 327-331.
11. GamzeOzbay, NurgayatBarlas, DiirdaneKolankaya; Histopathological Effects of the residual Maneb and Zineb in the Lettuces on the Liver and Kidney of Albino mice. Journal of Islamic Academy of Sciences, 1991; 4(4):336-339.
12. Sherlock S, Dooley J; In: Diseases of the Liver and Billiary system. 9th ed. Blackwell Scientific Publication, Cambridge, London, 1993; 649.
13. Zhang LY, Wang CX; Histopathological and Histochemical Studies on toxic effects of Brodifacoum in mouse Liver. Acta Acad Med Sci, 1984; 6(9): 386-388.