International Journal of Anatomy and Research,
Int J Anat Res 2016, Vol 4(1):1977-80. ISSN 2321-4287
DOI: http://dx.doi.org/10.16965/ijar.2016.124

Original Research Article

HISTOLOGICAL INVESTIGATIONS ON KIDNEY OF SILDENAFIL CITRATE (EDEGRA) TREATED ALBINO MICE

K. V. P. Suriyakumari *[1], R. Udayakumar [2], T. Ruba [2].

[*1] Department of Anatomy, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Puducherry, India.

[2] DDE Study Centre, Annamalai University, Villupuram, Tamil Nadu, India.

ABSTRACT

Background: Edegra (Sildenafil citrate), an effective oral therapy for Erectile Dysfunction, being the citrate salt of Sildenafil is a selective inhibitor of cGMP- specific phosphodiesterase type 5 (PDE 5).

Aim: To study the long- term impact of Sildenafil citrate on the histological components of kidney of Albino mice.

Materials and Methods: Thirty six healthy male Wistar Albino mice were selected on weight basis and divided into six groups (S_1, S_2, S_3, S_4, S_5 and S_6), each consisting of six animals in it. Here, Group S_1 and S_5 served as the control while the rest of the four groups (i.e. S_2, S_3, S_4 and S_6) served as the experimental ones. Group S_1 animals were treated with a single dosage of conductivity water while the experimental animals, namely, S_2, S_3 and S_4 were treated with a single dosage of the chosen drug (@ 1µg/g body wt.) and sacrificed after 1 hr., 4 hrs. and 24 hrs. of the last dosage. Group S_5 animals were treated daily with a single dosage of conductivity water while the group S_6 animals were treated daily with a single dosage of the chosen drug (@ 1µg/g body wt.) for all the 15 days and then sacrificed after 4 hrs. of the last dosage. Vertical ventral midline incision was made in the abdominal wall to collect both the kidney samples. The organs were preserved in 10% formalin saline, processed and stained with Eosin and Haematoxylin stains.

Results: Histopathological observations have been made on the collected kidney samples of Albino mice treated with Sildenafil citrate (Edegra). Increase in the periglomerular spaces, shrinkage of Glomeruli, increased number of vacuolated cells and reduced number of Glomeruli in cortical area due to destruction of Glomeruli have been strikingly noticed for long- term drug treated samples.

Conclusion: Sildenafil citrate (Edegra), if administered for a long- term, will produce drastic impacts on the histoarchitecture and vital functions of kidney of Albino mice.

KEY WORDS: Albino mice, Kidney, Edegra, Histology, Vacuolated cells.

Address for Correspondence: Dr. K. V. P. Suriyakumari, Professor and Head, Department of Anatomy, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Puducherry- 605107, India, **E-Mail:** suriyaudhay@gmail.com

Access this Article online

Quick Response code

DOI: 10.16965/ijar.2016.124

Web site: International Journal of Anatomy and Research
ISSN 2321-4287
www.ijmhr.org/ijar.htm

Received: 30 Jan 2016 Accepted: 12 Feb 2016
Peer Review: 31 Jan 2016 Published (O): 29 Feb 2016
Revised: None Published (P): 29 Feb 2016

INTRODUCTION

Erectile dysfunction (ED) is a common and multifactorial disease that strongly impairs the quality of life in man [1-4]. Increasing age, duration of diabetes, poor glycemic control, cigarette smoking, hypertension, dyslipidemia and cardiovascular disease were identified to be the potential risk factors [5- 8].

Edegra (Sildenafil citrate), an effective oral therapy for ED, being the citrate salt of Sildenafil is a selective inhibitor of cGMP- specific phosphodiesterase type 5 (PDE 5). The time

course of effect of this drug was examined in a study showing an effect for up to four hours [9, 10]. Though this drug has been reported to be well tolerated, Sildenafil citrate has mild to moderate side effects. Therefore, the present investigation was carried out to study the long term impact of Sildenafil citrate on the histological components of kidney of Albino mice.

MATERIALS AND METHODS

Permission for the present study was obtained from the Institutional Ethics Committee and all etiquettes were adhered to.

Thirty six healthy male Wistar Albino mice were selected on weight basis and acclimatized for a period of seven days before starting the investigations. Standard experimental conditions such as temperature (24±2 °C), humidity (60- 70%) and 12 hrs. of light / dark cycle were maintained. Feed and water were allowed *ad libitum* under strict hygienic conditions.

These animals were divided into six groups (S_1, S_2, S_3, S_4, S_5 and S_6), each consisting of six animals in it. Here, Group S_1 and S_5 served as the control while the rest of the four groups (i.e. S_2, S_3, S_4 and S_6) served as the experimental ones. Group S_1 animals were treated with a single dosage of conductivity water while the experimental animals, namely S_2, S_3 and S_4 were treated with a single dosage of the chosen drug (@ 1µg/g body wt.) and sacrificed after 1 hr., 4 hrs. and 24 hrs. of the last dosage. Group S_5 animals were treated daily with a single dosage of conductivity water while the group S_6 animals were treated daily with a single dosage of the chosen drug (@ 1µg/g body wt.) for all the 15 days and then sacrificed after 4 hrs. of the last dosage.

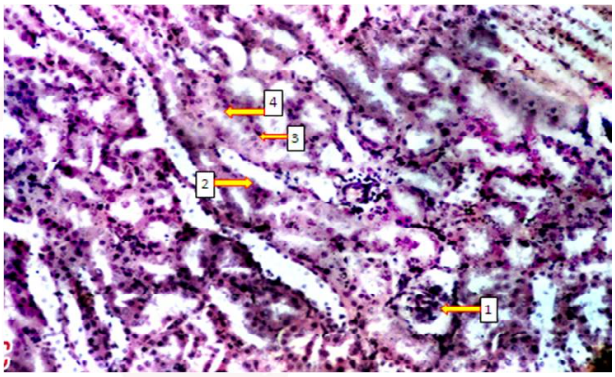
'Drug' here refers to Sildenafil citrate (Edegra from M/s Sun Pharma, India) purchased from the market. Chloroform anesthesia was used and a vertical ventral midline incision was made in the abdominal wall to collect both the kidney samples. The organs were preserved in 10% formalin saline, processed and stained with Eosin and Haematoxylin stains.

RESULTS AND DISCUSSION

Histopathological observations have been made on the collected kidney samples of Albino mice treated with Sildenafil citrate (Edegra) and the outcome of the present investigation clearly portrays the following facts:

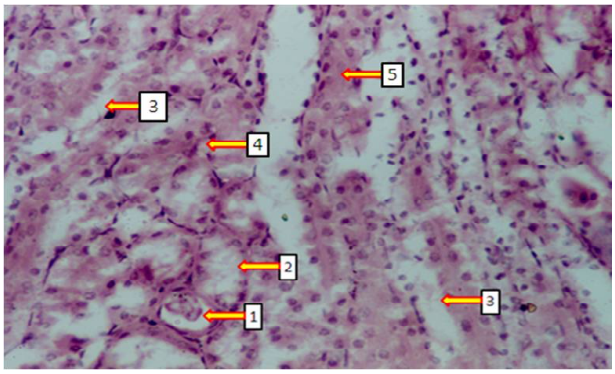
In the case of S_1 (0 hr.) samples, the cortex and the medullary regions of the kidney appear to be normal. The internal structure of the nephron involving the Glomeruli, the proximal convoluted tubules and the distal convoluted tubules is found to be normal. Moreover, the interstitial spaces are uniform [Fig. 1].

Fig. 1: Section of Kidney of Control (0 hr.) samples of Albino mice showing (1) Glomerulus, (2) Distal Convoluted tubules, (3) Proximal Convoluted tubules and (4) Brush borders. Haematoxylin - Eosin. x 100.



Slight dilation of the brush borders of the proximal convoluted tubules accompanied by a mild increase in the interstitial spaces occurs after one hour of drug (Edegra) administration (S_2) [Fig. 2].

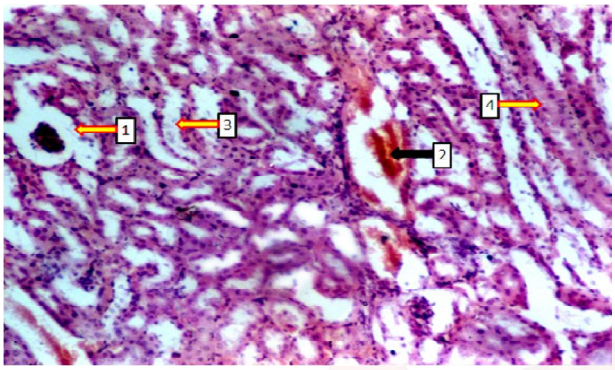
Fig. 2: Section of Kidney of drug treated (1 hr.) Albino mice showing (1) Glomerulus, (2) slightly dilated Proximal Convoluted tubules, (3) slightly dilated Distal Convoluted tubules, (4) mildly increased interstitial space and (5) dilated brush borders. Haematoxylin - Eosin. x 200.



The situation gets further aggravated for S_3 (4 hrs.) samples with prominent dilation of the brush borders of the proximal convoluted tubules accompanied by a marked increase in the interstitial spaces. Besides, extravasted blood has

been noticed for these kidney samples [Fig. 3]. After 24 hours of drug (Edegra) treatment (S_4 samples) the situation tends to regain its normal conditions.

Fig. 3: Section of Kidney of drug treated (4 hrs.) Albino mice showing (1) Glomerulus, (2) Extravasted blood, (3) dilated Distal Convoluted tubules and (4) dilated Proximal Convoluted tubules. Haematoxylin - Eosin. x100.



The impact of this drug on the histoarchitecture of kidney is well pronounced in the case of S_6 (15 days experimental animals). Increase in the periglomerular spaces, shrinkage of Glomeruli,

Fig. 4: Section of Kidney of drug treated (15 days experimental) Albino mice showing (1) Shrinkage of Glomerulus, (2) increased periglomerular space, (3) destruction of Glomerulus, (4) distorted Distal Convoluted tubules and (5) distorted Proximal Convoluted tubules. Haematoxylin- Eosin. x 200

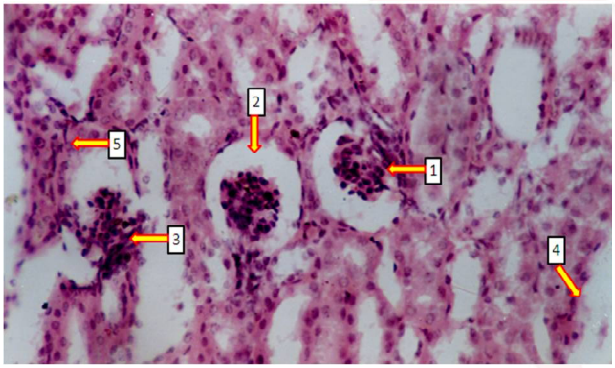
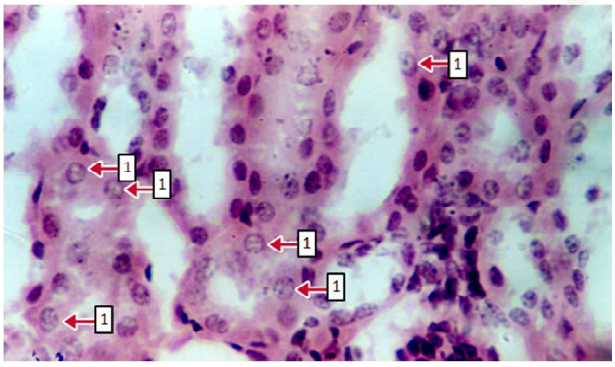


Fig. 5: Section of Kidney of drug treated (15 days experimental) Albino mice showing (1) more number of vacuolated cells. Haematoxylin- Eosin. x 400



increased number of vacuolated cells and reduced number of Glomeruli in cortical area due to destruction of Glomeruli have been strikingly noticed for long- term drug treated samples [Fig. 4 and 5].

The present Light microscopic observations indicate many interesting changes in the histoarchitecture of the kidney of the drug (Edegra) treated Albino mice. Similar findings depicting various histological and histochemical changes induced by Gibberellin A_3 on kidney of Albino rats [11], by residual Meneb and Zineb in the lettuces in kidney of Albino mice [12], by Gibberellic acids on chromosomes of mice [13] and by Fenvelerate Insecticides on various organs of Albino mice [14] have been reported.

The results of the present histopathological study can be discussed as follows:

Under normal conditions, there is a subtle balance between the free radical generation and the antioxidant defense system [15]. The drug induced changes in the structure of the kidney of Albino mice have been well managed by antioxidant defense mechanism and hence, the observed symptoms were found to be mild for S_2 (1 hr.) samples. In the case of S_3 (4 hrs.) samples, it seems the defense mechanism has been overcome by the influence of the drug resulting in the explicit changes in the structure such as the prominent dilation of the brush borders of the proximal convoluted tubules and the increased interstitial spaces. Extravasated blood has also been detected for these kidney samples. As the animals could not tolerate the vigour of the drug (Edegra), it results in the Glomerular hypertension and hence, the internal bleeding. As the onset and duration of action of this drug is from 30 minutes to 4 hours [9, 10], the vigour of this drug is almost nil after 24 hours of drug administration. Hence, the animals tried to regain almost its normal conditions for S_4 (24 hrs.) samples.

The increase in periglomerular spaces accompanied by the shrinkage of the Glomeruli, as noticed in the case of S_6 (15 days experimental) samples, may be due to oedema. Cytoplasmic vacuolization has been reported to be one of the important primary responses to all forms of cell injury and found to occur due to

increased permeability of cell membranes resulting in an increase of intracellular water [16]. As water sufficiently accumulates within the cell, it produces cytoplasmic vacuolization. Zhang and Wang (1984) correlated the vacuolar degenerative changes with the marked disturbances which take place in lipid inclusions as a result of injurious treatments [17]. Therefore, the increased number of vacuolated cells in the case of long- term drug (Edegra) treated kidney samples (S_6 group) may be indicative of cell injury.

As the Glomerlus is mainly responsible for ultrafiltration, the histological changes such as shrinkage of the Glomeruli and the reduced number of Glomerulus in the cortical area, as observed in the case of S_6 (15 days experimental) group of animals, stress the fact that the vital functions of the kidney get altered and may culminate in the electrolytic and water imbalance in the body. The occurrence of oedema and the alterations in the structure and functions of the nephron units, as noticed for the long- term drug (Edegra) treated animals, may be the precursor of the syndrome, namely, Nephrosis.

CONCLUSION

Based on the outcome of the present histological analyses, it is concluded that Sildenafil citrate (Edegra), if administered for a long- term, will produce drastic impacts on the histoarchitecture and vital functions of kidney of Albino mice.

ACKNOWLEDGEMENTS

The authors express their sincere thanks to the authorities of Annamalai University, Tamil Nadu (INDIA) and Sri Manakula Vinayagar Medical College and Hospital, Puducherry (INDIA) for their timely help and support in the execution of the present investigations.

Conflicts of Interests: None

REFERENCES

[1]. Gauv AI. Erectile dysfunction- Are you prepared to discuss it? Postgraduate Medicine, 1995; 97: 127-143.

[2]. Burnett A L. Erectile dysfunction: a practical approach for the primary care. Geriatrics, 1998; 53(2): 46-48.

[3]. Korenman S G. New insights into erectile dysfunction: a practical approach. American Journal of Medicine, 1998; 105(2): 135-144.

[4]. Benet AE, Melman A. The epidemiology of erectile dysfunction. Urologic Clinics of North America, 1995; 22(4): 699-709.

[5]. 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.

[6]. McCulloch DK, Young RJ, Prescott RJ, Campbell IW, Clarke BF. The natural history of impotence in diabetic men. Diabetologia. 1984; 26(6): 437-440.

[7]. De Berardis G, Pellegrint F, Francioso M, Belfiglio M, Di Nardo B, Greenfield S et al. Identifying patients with type 2 diabetes with a higher likelihood of erectile dysfunction: the role of the interaction between clinical and psychological factors. J. Urol., 2003; 169(4): 1422-1428.

[8]. Naliboff BD, Rosenthal M. Effects of Age on Complications in Adult Onset Diabetes. Journal of the American Geriatrics Society, 1989; 37(9): 838-842.

[9]. 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. International Journal of Clinical Practice, 1999 Suppl June; 102: 32-34.

[10]. Eardley I, Ellis P, Boolell M, Wulff M. Onset and duration of Sildenafil citrate for the treatment of Erectile dysfunction. British Journal of Clinical Pharmacology, 2002; 53 (Suppl 1): 615-655.

[11]. Sakr SA, El-Messedy FA and Abdel-Samei HA. Histopathological and histochemical effects of gibberellin A_3 on the kidney of albino rats. J Egypt Germ Soc Zool, 2002; 38: 1- 10.

[12]. Gamze Ozbay, Nurgayat Barlas, Diirdane Kolankaya. Histopathological effects of the residual Meneb and Zineb in the lettuces on the liver and kidney of Albino mice. Journal of Islamic Academy of Sciences, 1991; 4(4): 336-339.

[13]. Bakr SM, Moussa EM, Khater Esh. Cytotoxic evaluation of Gibberellins A_3 in swiss Albino mice. J. Union Arab. Biol., 1999; 11: 345-351.

[14]. Abdeen AM, Amer TA, El- Habibi EM, Kamal EM. Histological and histochemical studies on the effect of the fenvalerate insecticide on some organs of the Albino mice. J. Union Arab Biol., 1994; 2A: 129-166.

[15]. Bhuvarahamurthy V, Balasubramanian N, Govindasamy S. Effect of Radiotherapy and Chemotherapy on circulating antioxidant system of human uterine cervical carcinoma. Mol Cell Biochem, 1996; 158: 17-23.

[16]. Sherlock S, Dooley J. In: Disease of the liver and biliary system. 9th edition. Blackwell Scientific Publication, Cambridge, London, 1993, 649.

[17]. 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.

How to cite this article: K. V. P. Suriyakumari, R. Udayakumar, T. Ruba. HISTOLOGICAL INVESTIGATIONS ON KIDNEY OF SILDENAFIL CITRATE (EDEGRA) TREATED ALBINO MICE. Int J Anat Res 2016;4(1):1977-1980. **DOI:** 10.16965/ijar.2016.124