Histopathological Effects of Prazosin Drug on Lung of Rats

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ABSTRACT

*This study was conducted at the laboratory of histology and anatomy, Faculty of Medical and Health Techniques/Kufa, and laboratory of post Graduate/ Department of biology, Faculty of Science/University of Kufa, The present study was conducted to investigate the effect of Prazosin hydrochloride on some organs in male rats (*Rattus norvegicus*), about 25 mature male rats with the average body weight of 210-290gram and three months age were randomly divided into four groups (5rats / group). The first group was given orally with distilled water as a control group and the other groups (second, third, and fourth) were also given orally with three doses of Prazosin (25, 50, 75 mg /kg. b.wt.) daily for a period of eight weeks. At the end of the treatment period (eight weeks), rats were sacrificed, blood samples obtained, and organs lung, and spleen. The histopathological changes of lungs in the rats treated with prazosin at dose 25 mg/kg.b.wt for 8-weeks showed emphysema and dilation in some of the alveoli, hemorrhage distributed inside the tissue of the lung, polymorphic nuclear infiltration due to pneumonia, the pulmonary artery revealed degenerative changes in the tunica media structure (smooth muscle) and hyperplasia in the connective tissue around pulmonary artery and alveoli. These symptoms which occur in rats treated with prazosin at dose 50 and 75 mg/kg b.wt. as well as the histopathological changes of rat lung demonstrate severe hemorrhage, emphysema, thickening in the wall of some alveoli, pneumocyte necrosis (pneumocyte type 1 and pneumocyte type 2), and showed exudate among lung tissue. Histopathological changes of Spleen in the rats treated with prazosin at doses (50 and 75)mg/kg b.w. for 8-weeks revealed histopathological changes, which represented by proliferation in the white pulp lead to fused white pulp together and destruction of some components of red pulp, stenosis in many splenic venous sinuses, the germinal artery show thickening in the tunica media and stenosis occurs, degenerative change in many nuclei of lymphocytes, and proliferation in the component of the white pulp.*

Keywords: Prazosin, Lung, *Rattus norvegicus*

Article Information

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INTRODUCTION

Adrenogenic receptors were originally classified into beta and alpha subtypes, with α -further classification in to α_1 and α_2 receptors. Currently there are three subtypes in the alpha sub family 1a, 1b, and 1d, difference in receptors amino acid sequence among these subtype alter the binding properties of specific agonist and antagonist, in human prostatic cell the α_1 receptor type is the most prevalent type, making the targeting of this subtype therapeutically useful (1).

The current genetic studies offered that the α_1 receptors subtype represents as (70%) of the α_1 receptors in the prostate gland (Chen, *et al.*, 2000). The second subtype of α -adrenergic antagonist have greater attraction for alpha 1-

receptors than α_2 -receptors, leading to enhanced side effects profile, these second generation agents include prazosin, terazocin, doxazocin and alfazocin (2). Prazosin hydrochloride are indicated in the treatment of high blood pressure, can be used alone or in combination with other antihypertensive groups such as diuretics or beta-adrenergic blocking agents (3). Trazocin, Doxazocin, and Prazosin are a selective α_1 receptor blockers that all have similar three α_1 receptors subtypes. It is distinguished from other blocker Tamsulosin. A study has presented that alpha (α_1 AR) relieve bladder based irritability symptoms, in contrast to blockade of the α_1 and β -adrenergic receptors

which leads to orthostatic hypotension; a side effect associated with non-select alpha blockers (4).

Prazosin is orally active and has a slight effect on cardiac function due to its alpha-1 receptor selectivity. However, when prazosin is happening, heart rate and contractility go up in order to maintain the pre-treatment blood pressures because the body has stretched homeostasis at its unusually high blood pressure. The blood pressure dropping effect becomes seeming when prazosin is taken for longer periods of time. The antihypertensive appearances of prazosin make it a second-line choice for the treatment of high blood pressure (5). Prazosin clamps promise as a pharmacologic treatment for alcohol dependence after a 2009 pilot trial was accomplished. A larger controlled Phase II "Clinical Trial of the Adrenergic Alpha-1 Antagonist Prazosin for Alcohol Dependence" is presently started (6).

METHODS

Preparation of Prazosin Hydrochloride (Miniperss) solution:

The Prazosin was obtained from (pfizerlab, Germany) at concentration (5mg/kg), and prepared different con. That given via oral administration to rats as Four groups, first is control, and other groups second, third, and fourth were treated respectively with (0.5 ml) of volume dose from prazosin at doses 25, 50, and 75mg/kg for 8-weeks, given orally.

Histological Study

Serial sections were prepared from 25 of adult rats were used serial section of lung, to determine the disorder of these tissues when they were compared with control.

Harris Hematoxylin and Eosin Stain

It is routine stain that used to demonstrate the general histology structures (7).

Verhoeff's Van Gieson Stain

That was used for detecting the collagen fibers in the lung we used as well as the section in general (8).

RESULTS

The histopathological change of lung in the rats that treated with prazosin at low dose (fig.2&5) showed, destruction in the wall of aveoli and dilation in some of alveoli, hemorrhage inside tissue of lung, polymorphic nuclear and vacuolation of nuclei mainly lymphocyte. at intermediate dose (fig.3&6) demonstrated, fibrosis, sever blood hemorrhage, emphysema, thickening in the interstitail pulmonary wall, necrotic cells, and show sloughing of the oxudate inside tissue.

Degenerative changes of pulmonary artery and the tunica media was changed in the structure, and hyperplasia in the connective tissue arround pulmonary artery and alveoli. The histopathological change of lung in the rats treated with prazosin at high dose (fig.4&7) demonstrated, emphysema accumulation of edematous fluid inside the tissue, the alveoli were dilated and some, and the cell sloughing

inside the alveoli, we saw sever blood hemorrhage. And necrotic cells when compared with fig.1.

Fig. 1: control Normal histological section of the lung of rats. Demonstrated: 1- alveoli and normal pneumocyte type 12- Inter alveolar wall (septum). (H&E stain 400x).

Fig.2: Histopathological change of lung in the rats treated by prazosin at dose 25mg/kg. demonstrated: polymorphic nuclear leucocytic filtration mainly (lymphocytes) Degenerative changes of pulmonary artery. Thickening in the wall of inter alveolar septum. Hyperplasia in the interstitial connective tissue around the pulmonary artery. Hemorrhage. (H&E stain 400x).

Fig.3 Histopathological change of lung in the rats treated by prazosin at dose at dose 50 mg/kg. demonstrated: thickening in the interstitial pulmonary wall of alveoli. sever hemorrhage . (H&E stain 400x).

Fig.4: Histopathological change of lung in the rats treated by prazosin at dose at dose 75mg/kg. demonstrated- :odematous oxudate (hyperplasia around pulmonary artery and respiratory bronchiole) ,pumonary artery 3-sever hemorrhage inside pulmonary artery.respiratory bronchiole (hypertrophic of the epithelial lining simple columnar) .sloughing of epithelial lining in the lumen of respiratory bronchiole . (H&E stain 400x).

Fig.5: Histopathological change of lung in the rats treated with prazosin at 25mg/kg. demonstrated: degeneration of the muscle of pulmonary artery. interstitial pneumonia ,changes in the shape of pneumocytes type1, sloughing of epithelial lining the alveoli . , and some of alveoli was shrinkage and pathological changes of connective tissue fibers (elastic fibers) (Verhoeff'sVan-Gieson stain 400x

Fig.6: Histopathological change of lung in the rats treated with prazosin at 50mg/kg. demonstrated: dilation of some alveoli , shrinkage of some alveoli , interstitial pneumonia , and destruction of alveolar wall. (Verhoeff'sVan-Gieson stain 400x).

Fig. 7:Histopathological change of lung in the rats treated with prazosin at 75mg/kg. demonstrated: degeneration of pneumocytes type 1 and sloughing epithelial lining of alveoli , degeneration occur in pneumocytes type 2 and dilatation of alveoli, and pathological changes of connective tissue fibers. (Verhoeff'sVan-Gieson stain 400x)

DISCUSSION

Histopathological changes study

The results in this study showed significant increase in the diameter of alveoli of lung , due to prazosin hydrochloride led to dilation in the

structure of organs, caused of cells were hypertrophied, may be attributed to the toxicity effects of prazosin on the organ .It's due to inflammation of lung tissue (infiltration of polymorph nuclear), the present study agree with pervious study on alfuzosin induced liver toxicity that obtained by Seok, et al., (9).

The lung section of rats that treated with prazosin at low dose revealed dilation of alveoli ,destruction in the inter alveolar wall, hypertrophied in some of pneumocystis type and hemorrhage, , and at moderate and high doses of prazosin showed more polymorphic nuclear leucocyte filtration mainly (lymphocytes).Emphysema, hyperplasia in the interstitial connective tissue around the pulmonary artery and some alveoli were dilated . also the tissue revealed sever hemorrhage inside pulmonary artery, hypertrophic of lining simple columnar of respiratory bronchiole and slaving of epithelial lining in the lumen of respiratory bronchiole, admiration of prazosin leading to acute lung injury by inflammation that developed rapidly the vascular surface of the lung, cellular apoptosis can mediate death of cells in a variety of the lung and heart diseases Izabella, et al.,(10) revealed that doxazosin at high dose induced renal fibrosis, through inhibition of α -1-beta-adrenoreceptor in mesangial cells exerts an anti-fibrotic

CONCLUSIONS

From the current study, it can be concluded that

1. Prazosin has ability to cause hyperthyroidism when it is give at high dose for eight-weeks, that is causes loss weight retardation, and hair lost.

REFERENCES

- Blanchad, N. R. ;** and Abu Baker, A. M. (2010) The treatment of benign prostate hyperplasia. Retrevid from [http://www.uspharmacist. Com /continuing education /ceviewtest//essonid/ 105803](http://www.uspharmacist.Com /continuing education /ceviewtest//essonid/ 105803).
- Debruyne, F. M.** (2000) Alpha blockers: are all creater equal .Urology .,PP: 56(5 suppl 1) :3-6.
- Moffat, A.C.;** Osselton, M.D.; and Widdop, B. (2005).Clarkès Analysis of Drugs and Poisons, Pharmaceutical press.
- Zeilefsky, J.R. ;** and Stephen, A.O. (2010). Garact and Glaucoma In: The Glaucoma book: apractical; evidence basal approach to patient care schav know, P.N. and John, R. (ed.) . 1st (ed.) Springer Sceince and Business media. LLc., Newyork, PP: 889-892.
- Shen, Howard.** (2008). Illustrated Pharmacology Memory Cards:Phar Mnemonics. Minireview. p. 13.

2. Prazosin at high dose has led to increase the free radicals, reduction liver, kidney and cholestasis biomarkers, imperfect hepatic marker enzymes, increase fibrosis severity and dilation the thyroid, hepatic, lung, and kidney cells design.
3. Prazosin at high doses causes primary hyperthyroidism. The use of antihypertensive medication has been implicated in a variety of important alterations in endocrine functions .This drug induced endocrine alterations which can cause new clinical problems for the patient and present diagnostic and management challenges to the physician
4. Lung: emphysema and intestinal pneumonia

RECOMMENDATION

The following suggestions may be recommended for further studies

1. Avoid give prazosin at high doses .
2. 2Studying the effect of prazosin hydrochloride on accessory gland of male reproductive system such as prostate gland ,testis, epididymis and seminal vesicle.
3. Studying of other types of alpha blockers used in benign prostate hyperplasia therapy and make a comparisons between them.
4. Conduct electron microscope study to clarify the exact effects caused by the drug which block the growth of sperm in the seminiferous tubule and vitality in the epididymis, and ovum in ovary in female reproductive system.

Bawaskar, H.S. ;and Bawaskar, P.H. (2008). "Scorpion sting: A study of clinical manifestations and treatment regimes" .Current Science 95, (9): 1337–1341

Bancroft, J. D. ; and Stevens, A. (1999). Theory and Practice of Histological Techniques. Fourth edition. New York: Churchill Livingstone. pp 312.

Linda, L.; Vacca, (1985). Laboratory Manual of Histochemistry. Raven Press. New York.

Seok, Y.K.; Byung, HO.; Seok, Ho. Dong; Hyo. J.; oung, Woon, C.; Kim, C. ; and Yoon, W.C. (2007). Alfuzosin Induced Acute Liver Injury. The Korean Journal of hepatology: 13. 414-418.

Izabella, Z.A.; Pawlaczyk.; Samita, R.; Patel; Kevin, P.G. ; and Harris (2009). The role of the α -1-adrenoreceptor in modulating human mesangial cell matrix production. Nephrology Daly Transplantation.