Oyedeji K.O. et al /J. Pharm. Sci. & Res. Vol. 10(5), 2018, 1011-1013

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Effect of Vasodilator (Apresoline) on Haematological and Biochemical Parameters in Male Wistar Rats

Oyedeji K.O.*[1], Okeke O.E.[1], Obisesan Abiola[2], Oni James[2]

[1]*Department of Physiology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.*
[2]*Department of Pharmacology and Therapeutics, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.*

Abstract

Objective: This study was designed to evaluate the effect of vasodilator on haematological and plasma biochemical parameters in male Wistar rats.

Methods: Twelve male rats (120 – 140 g) were divided into control (distilled water) and vasodilator-treated (0.36 mg/kg) groups (6 per group) for haematological and biochemical studies. The animals were orally treated on daily basis for 50 days. Red Blood Cell (RBC) counts and Total White Blood Cell (TWBC) counts were determined using haemocytometer. Activities of plasma Alanine Amino Transferase (ALT), Aspartate Amino Transferase (AST), Alkaline Phosphatase (ALP), as well as levels of total protein, globulin, albumin, creatinine and Blood Urea Nitrogen (BUN) were determined by spectrophotometry. Data were analysed using descriptive statistics and ANOVA at p=0.05.

Results: Treatment of rats with vasodilator (0.36 mg/kg) caused significant ($p<0.05$) increments in PCV, Hb, platelet and neutrophil values, but significant ($p<0.05$) reductions in lymphocyte and globulin values relative to their respective controls.

Conclusion: It can therefore be concluded that the vasodilator probably has beneficial and harmful effects on haematological and plasma biochemical functions in male rats.

Keywords: Vasodilator, Rats, Total white blood cell counts, Red blood cell counts, Total protein.

INTRODUCTION

Vasodilators are medications that dilate blood vessels. Vasodilators act directly on the smooth muscle of arteries to relax their walls so blood can move more easily through them; they are only used in hypertensive emergencies or when other drugs have failed, and even so are rarely given alone.

Effects of vasodilators on coronary flow and simultaneous release of nitric oxide from guinea pig isolated hearts has been reported [1]. Hemodynamic effects of vasodilators and long-term response in heart failure has been reported [2]. Renal effects of vasodilators in acute heart failure [3] as well as their effects on isolated human uteroplacental arteries [4] have been reported.

However, due to dearth of information from literature on the effect of vasodilator on haematological and biochemical parameters in male rats, this study therefore aims at investigating the effect of this antihypertensive agent on these aforementioned parameters in male rats.

MATERIALS AND METHODS

Experimental Animals

Adult male rats weighing between 120 g – 140 g bred in the Pre-Clinical Animal House of the College of Medicine and Health Sciences, Afe Babalola University were used. They were housed under standard laboratory conditions and had free access to feed and water; they were acclimatized for two weeks to laboratory conditions before the commencement of the experiments. All experiments were carried out in compliance with the recommendations of Afe Babalola University Ethics Committee on guiding principles on care and use of animals.

Drug

Vasodilator (apresoline) tablets (Norvatis Pharma Ltd) were bought from Danax Pharmacy, Ibadan, Nigeria.

Vasodilator (25 mg) was dissolved in 10 ml of distilled water to give a concentration of 2.5 mg/ml.

The dosage of vasodilator used in this study was in accordance with that reported by the manufacturer.

Experimental Design

Twelve male rats (120 – 140 g) were randomly divided into two groups, with each consisting of six animals. The two groups were subjected to the following oral treatments once a day for fifty (50) days:

Group I: received 0.5 mL/100 g of distilled water as control group.

Group II: received 0.36 mg/kg of vasodilator.

Collection of blood samples

Twenty four hours (day 51) after the last dosing of all the groups, blood samples were collected from all the animals through the medial cantus with heparinized capillary tubes into EDTA bottles for hematological and plasma biochemical analysis. Before assays, the blood was centrifuged for 5 minutes using a bench top centrifuge (Centromix) and the plasma were used for the determination of the biochemical parameters.

Determination of Haematological Parameters

The red blood cells (RBC) and white blood cells (WBC) counts were determined by the Improved Neubauer haemocytometer method. The haemoglobin (Hb) concentration was determined according to [5] using the cyanomethaemoglobin method. The packed cell volume (PCV) was determined by the micro-haematocrit method according to [6]. Schilling method of differential lecukocyte count was used to determine the distribution of the various white blood cells [7]. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were computed according to [5].

Determination of Plasma Biochemical Parameters

The total protein concentration was determined using the Biuret method [8] and the albumin concentration by the method of [9]. The globulin concentration was calculated by subtracting the albumin concentration from the total protein concentration. Activities of plasma alanine transaminase (ALT) and aspartate transaminase (AST) were determined according to the method of [10]. The level of creatinine, urea and alkaline phosphatase were determined using the method of [11]. All the above biochemical parameters were determined in the plasma using the Randox kits.

Statistical Analysis

The mean and standard error of mean (S.E.M.) were calculated for all values. Comparison between the control and experimental groups was done using one-way analysis of variance (ANOVA) with Duncan's Multiple Range Test. Differences were considered statistically significant at $p<0.05$.

RESULTS

The effect of vasodilator (0.36 mg/kg) on haematological and plasma biochemical parameters after treatment of rats for 50 days is shown in Tables 1 and 2 respectively.

Treatment of rats with vasodilator (0.36 mg/kg) produced no significant ($p>0.05$) changes in RBC, TWBC, monocyte, eosinophil, MCV, MCHC and MCH values relative to their respective controls.

Treatment of rats with vasodilator (0.36 mg/kg) caused significant ($p<0.05$) increments in PCV, Hb, platelet and neutrophil values, but significant ($p<0.05$) reduction in lymphocyte value relative to their respective controls.

Table 1: Effect of 50 days treatment with vasodilator on haematological parameters in male rats

Parameters	Control	Apresoline (0.36 mg/kg)
PCV (%)	43.40 ± 0.52	45.20 ± 0.81*
Hb (g/dL)	14.38 ± 0.34	15.36 ± 0.48*
RBC ($\times10^6$/µL)	7.31 ± 0.32	7.40 ± 0.21
TWBC ($\times10^3$/µL)	3.70 ± 0.21	4.75 ± 0.33
Platelets ($\times10^5$/µL)	1.39 ± 0.05	1.72 ± 0.09*
Lymphocytes (%)	71.00 ± 0.83	58.60 ± 0.64*
Neutrophils (%)	25.40 ± 0.75	38.20 ± 0.73*
Monocytes (%)	1.60 ±0.11	1.80 ± 0.17
Eosinophils (%)	2.00 ±0.16	1.40 ± 0.15
MCV (FL)	59.36 ± 0.55	61.35 ± 0.91
MCHC (g/dL)	33.12 ± 0.41	33.88 ± 0.59
MCH (pg)	19.67 ± 0.34	20.77 ± 0.51

(n=6, *p=0.05)

Treatment of rats with vasodilator (0.36 mg/kg) produced no significant ($p>0.05$) changes in total protein, albumin, ALT, AST, ALP, BUN and creatinine values, but caused significant ($p<0.05$) reduction in globulin level relative to their respective controls.

Table 2: Effect of 50 days treatment with vasodilator on plasma biochemical parameters in male rats

Parameters	Control	Apresoline (0.36 mg/kg)
Total Protein (g %)	6.80 ± 0.13	6.90 ± 0.17
Albumin (gm %)	2.66 ± 0.13	2.96 ± 0.15
Globulin (gm %)	4.14 ±0.18	3.94 ± 0.08*
AST (µ/L)	42.20 ± 0.87	41.40 ± 0.83
ALT (µ/L)	29.60 ± 0.74	29.40 ± 0.84
ALP (IU/L)	110.00 ± 1.71	106.80 ± 1.93
BUN (mg/dL)	15.96 ± 0.28	16.56 ± 0.23
Creatinine (µmol/L)	0.74 ± 0.02	0.82 ± 0.03

(n=6, *p=0.05)

DISCUSSION

The result of the haematological study has shown that vasodilator caused significant increments in the PCV and Hb values. This could indicate that there were increments in the oxygen carrying capacity of the blood and the amount of oxygen delivered to the tissues, since RBC and haemoglobin (Hb) are very important in transferring respiratory gases [12].

Vasodilator caused no significant change in TWBC value which probably indicates that it has no effect on the ability of the body to defend against invading organisms [13]. Contrary result was reported by [14] in *Viscum album* extract treated rats.

Vasodilator caused significant increase in the platelet value which probably indicates an enhancement in the haemostatic function of the body. Similar result was reported by [15] in *Fadogia agrestis* extract treated rats.

Vasodilator caused significant reduction in lymphocyte value which probably indicates that the acquired immune response of the body has been compromised. Contrary result was reported by [16] in isolated ergosterol treated rats.

Vasodilator caused significant increase in the neutrophil count which probably indicates an enhancement in the ability of the body to attack and destroy invading bacteria, viruses and other injurious agents (phagocytosis). Similar result was reported [17] in *Dennettia tripetala* extract treated rats.

Vasodilator caused no significant change in the monocyte value which probably indicates that it has no effect in the phagocytic function of the body [18]. Contrary result was reported by [19] in *Saccharomyces cerevisiae* extract fed hens.

Vasodilator caused no significant change in eosinophil value which could indicate that it has no effect on the anti-allergic and anti-parasitic infectious responses of the body. Contrary result was reported by [20] in *Arctotis actotoides* extract treated rats and mice.

Vasodilator caused insignificant changes in the MCV and MCH values which probably indicate it has no effect on induction of macrocytic anaemia, since increased MCV and MCH valves are known to be indicative of macrocytic anaemia [21]. Similar result was reported by [22] in *Jatropha gossypifolia* extract treated rats.

The insignificant change in the MCHC value caused by lisinopril probably indicates that it has no effect on induction of hereditary spherocytosis, since MCHC values are known to be elevated in hereditary spherocytosis. Similar result was reported by [22] in *Jatropha gossypifolia* extract treated rats.

The result of the plasma biochemical study has shown that treatment of rats with vasodilator caused insignificant changes in total protein level. This might indicate that the drug has no effect on the buffering capacity of the blood as well as having no effect on colloid osmotic pressure, since plasma proteins have been reported to be responsible for 15% of buffering capacity of blood [13] and that osmotic pressure caused by the plasma proteins (called colloid osmotic pressure) tends to cause fluid movement by osmosis. Contrary result was reported by [23] in *Euphorbia heterophylla* extract treated rats.

Vasodilator caused no significant changes in albumin level which probably indicates that it has no effect in the plasma levels of metals, ions, fatty acids, amino acids, bilirubin and enzymes; since it has been reported that albumin serves as a carrier for metals, ions, fatty acids, amino acids, bilirubin, enzymes and drugs [13]. Contrary result was reported by [24] in *Enicostemma axillare* extract treated rats.

Vasodilator caused significant reduction in globulin level which probably indicates that this drug has compromised both the natural and acquired immunity of the body against invading organisms, since it has been reported that globulins are principally responsible for the body's both natural and acquired immunity against invading organisms [18]. Contrary result was reported by [25] in *Portulaca oleracea* extracts treated rats.

The insignificant change in the activity of AST caused by the drug could indicate it has no effect on induction of tissue necrosis, since it has been reported that elevation in the activity of AST can be associated with cell necrosis of many tissues, which allows leakage of large amounts of this enzyme into the blood [26]. Contrary result was reported by [27] in *Sida rhombifolia* extract treated mice and rats.

Vasodilator caused an insignificant change in the activity of ALT which probably indicates it has no effects on induction of hepatic damage, since it has been reported that ALT is present in the liver and other cells and is particularly useful in measuring hepatic necrosis, especially in small animals [28]. Contrary result was reported by [29] in *Moringa oleifera* extract treated rats.

Vasodilator caused no significant change in ALP level. This probably indicates the absence of cholestasis, since ALP has been

reported to be a marker of cholestasis [30]. Similar result was reported by [22] in *Jatropha gossypifolia* extract treated rats.

The vasodilator induced insignificant change in urea and creatinine levels. This probably indicates absence of nephrotoxicism (renal impairment), since urea and creatinine have been reported to be markers of kidney functions [31]. Contrary result was reported by [32] in *Passiflora edulis* extract treated rats.

CONCLUSION

In conclusion, this study has shown that the vasodilator has beneficial and harmful effects on the haematological and plasma biochemical functions in male rats. However, the effect of this antihypertensive agent on human haematological function and blood chemistry are unknown; nevertheless, considering these findings in animal model, it is recommended that patients should strictly comply with the dosage regimen as recommended by their physicians.

CONFLICT OF INTEREST

We vehemently declare that there is no conflict of interests in this research work.

REFERENCES

1. Fujita S, Roerig DL, Bosnjak ZJ, Stowe DF. Effects of vasodilators and perfusion pressure on coronary flow and simultaneous release of nitric oxide from guinea pig isolated hearts. Cardiovasc Res 1998; 38 (3): 655-67.
2. Franciosa JA, Dunkman WB, Leddy CL. Hemodynamic effects of vasodilators and long-term response in heart failure. JACC 1984; 3 (6): 1521-1530.
3. Valente MAE, Voors AA. Renal effects of vasodilators in acute heart failure. World Journal of Cardiovascular Diseases 2013; 3: 8-17.
4. Allen J, Skajaa K, Maigaard S, Forman A. Effects of vasodilators on isolated human uteroplacental arteries. Obstet Gynecol 1991; 77 (5): 765-771.
5. Jain NC. *Schalm's Veterinary Heamatology* 4th Ed. Lea and Fabiger, Philadelphia. 1986.
6. Dacie JV, Lewis SM. Practical haematology, 7th edition, ELBS with Churchill Livingston, England, 37-85; 1991.
7. Mitruka BM, Rawnsley H. Clinical, biochemical and haematological references values in normal experimental animals. Masson Publishing USA Inc, 53-54; 1977.
8. Reinhold JG. Manual determination of serum total protein, albumin and globulin fractions by the Biuret method *Standard Methods of Clinical Chemistry* (Academic Press, New York); 1953.
9. Doumas BT, Watson W, Biggs HC. Albumin standards and the measurement of serumalbumin with bromocresol green. Clinica Chimica Acta 1971; 31: 87-96.
10. Duncan JR, Praise KW, Mahaffey EA. Veterinary Laboratory Medicine (Clinical Pathology) 3rd ed. Iowa State University Press, U.S.A.; 1994.
11. Tietz NW, Prude EL, Sirgard – Anderson O. Textbook of clinical chemistry. Ed. Burtis C.A. and Ashwood E.R., W.B. Saunders Company, London, 1354 – 1374; 1994.
12. De Gruchy GC. Clinical haematology in Medical Practice. Blackwell Scientific Publication. Oxford, London, 33-57; 1976.
13. Ganong WF. Review of Medical Physiology (22nd). New York; Lange Medical books/Mc Graw Hill; 2005.
14. Imoru JO, Eno AE, Unoh FB, Enkanu E, Ofem OE, Ibu JO. Haematopoietic agents in the crude extracts from the leaves of *Viscum album* (mistletoe). Nigerian Journal of Health and Biomedical Sciences 2005; 4 (2): 139-145.
15. Yakubu MT, Akanji MA, Oladiji AT. Hematological evaluation in male albino rats following chronic administration of aqueous extract of *Fadogia agrestis* stem. Pharmacognosy Magazine 2007; 3: 34 - 38.
16. Oyedeji KO, Bolarinwa AF, Oladosu IA. Effect of isolated ergosterol constituent of *Portulaca oleracea* on Haematological Parameters in male albino rats. Asian journal of Pharmaceutical and Clinical research 2013; 6: 2.
17. Ikpi DE, Nku CO. Effect of ethanolic extract of *Dennettia tripetala* fruit on haematological parameters in albino wistar rats. Nigerian Journal Physiological Sciences 2008; 23 (1-2): 13-17.
18. Guyton AC, Hall JE. Textbook of Medical Physiology, 11th edition. Elsevier Inc; 2006.
19. Matur E, Erqul E, Erasian E, Inal G, Bilgic S, Demircan H. Effect of *Saccharomyces cerevisiae* extract on Haematological Parameters, Immune functions and the antioxidant defense system in breeder hens fed aflatoxin contaminated diets. British Poultry Science 2011; 52 (5): 541-550.
20. Jimoh FO, Adedapo AA, Sofidiya MO, Masika PJ, Afolayan AJ. Safety evaluation of the extract from the shoots of *Arctotis actotoides* in rats and mice. African Journal of Biotechnology 2008; 7 (18): 3173-3177.
22. Oyedeji KO, Awoyinka D, Abidoye D. Effect of ethanol extract of Jatropha gossypifolia on haematological and plasma biochemical parameters in male albino rats. Int J Pharm Sci Rev Res 2015; 35 (2): 41-45.
23. Apiamu Augustine, Evuen Uduenevwo Francis. Biochemical Assessment of the Effect of Aqueous Leaf Extract of *Euphorbia Heterophylla Linn* in Hepatocytes of Rats. IOSR Journal of Environmental Sciences, Toxicology and Food technology 2013; 3 (5): 37- 41.
24. Gite VN, Pokharkar RD, Chopade VV, Takate SB. Hepato-Protective activity of *Enicostemma Axillare* in paracetemol induced hepato-toxicity in albino rats. International Journal of Pharmacy and Life Sciences 2010; 1 (2): 50 – 53.
25. Oyedeji KO, Bolarinwa AF. Effects of Crude Extracts of *Portulaca oleracea* on Haematological Parameters in Albino Rats. African Journal of Biomedical research 2010; 15: 41-47.
26. Bush BM. Interpretations of Laboratory Results for Small Animal Clinicians. Blackwell Scientific Publications, London; 1991.
27. Ouedraogo M, Zerbo P, Konate K, Barro N, Laya L. Sawadogo, Effect of long-term use of *Sida rhombifolia L.* Extract on Haematological Parameters of Experimental Animals. British Journal of Pharmacology and Toxicology 2013; 4 (1): 18-24.
28. Duncan JR, Prasse KW, Mahaffey EA. Veterinary laboratory medicine (Clinical Pathology). Iowa State University Press: Ames, 102-107; 1994.
29. Ajibade TO, Olayemi FO, Arowolo ROA. The haematological and biochemical effects of methanol extract of the seeds of *Moringa oleifera* in rats. Journal of Medicinal Plant Research 2012; 6 (4): 615-621.
30. Vasudevan DM, Sreekumari S. Textbook for biochemistry for medical students. Jaypee Brothers Medical Publishers Ltd, New Delhi, 5th ed, 266; 2007.
31. Oduola T, Adeosun GO, Oduola TA, Avwioro GO, Oyeniyi MA. Mechanism of action of *Jatropha gossypifolia* stem latex as a haemostatic agent. European Journal of General Medicine 2005; 2 (4): 140–143.
32. Devaki K, Beulah, Akila G, Gopalakrishnan. Effect of aqueous extract of *Passiflora edulis* on biochemical and haematological parameters of wistar albino rats. Toxicology International 2012; 19 (1): 63-67.