https://muthmj.mu.edu.iq

Muthanna Medical Journal
2024; **11**(1):21-26

http://dx.doi.org/10.52113/1/1/2024-1-26

Physiological appraisal of glipizide in rabbits

Wissam Sajid Hashim *[1], Nadia Abdullatif Ali Hassan [2], Jala Amir Salman Alahmed [3]

Abstract

Forty adult male rabbits were adopted to evaluate the squelae of the use of Glipizide. The results have revealed that streptozotocin causes significant declination in red blood cell count RBC, hemoglobin HB, packed cells volume PCV, alanine aminotransferase ALT, alkaline phosphatase ALP, glutathione GSH, triacylglycerols TAGs, and high-density lipoprotein HDL besides a significant elevation in total white blood cells count WBC, erythrocyte sedimentation rate ESR, malondialdehyde MDA, and low-density lipoprotein LDL. Glipizide alone causes significant declination in RBC, Alanine aminotransferase AST, GSH, TAGs, and VLDL besides a significant elevation in WBC, ESR, total cholesterol TC, and LDL. Considering the use of Glipizide plus streptozotocin, it causes a significant declination in RBC, HB, PCV, GSH, and HDL besides a significant elevation in WBC, ESR, LDL, TAGs, and VLDL.

Keywords: Glipizide, Streptozotocin, Diabetes, Rabbits

* Correspondence author: dr.w80@mu.edu.iq, dr.wissam2013@gmail.com
[1] *Department of Physiology and Medical Physics, College of Medicine, Al-Muthanna University.
[2] Bilad Alrafidain University College
[3] Department of Physiology, Pharmacology and Biochemistry, College of Veterinary Medicine, University of Basra
Received 03 November 2023; revised 02 March 2024; accepted 30 March 2024, available online 7 April 2024.

Introduction

The incidence of diabetes in the modern world is horrible in fact; making a jump like records throughout the years, for instance, it was recorded as about one hundred millions of people inflicted with diabetes in 1980 and this number was drastically elevated to about four hundred and twenty-two million in 2014; taking into our minds all the correlated dysfunctions and diseases which are caused by or related to diabetes such as blindness, limbs amputations, renal failures, and cardiac attacks [1]. Diabetes mellitus, of its two types; type one and type two, has been proven and documented to be correlated with oxidative stress, and this relation is very hard coming as concomitant with alterations in the metabolic pathways of glucose, damage, and alterations in the beta cells of the pancreas, change in the lipid peroxidation status and the antioxidant milieu systems of the body [2-4]. Many medicaments are used nowadays to treat or control diabetes including our drug of choice in this study; Glipizide or Glipizide. We have chosen glipizide to elucidate its anticipated side effects on some body functions. Glipizide belongs to the family of insulin secretagogues which is known as sulfonylurea; the family that compromises many others [5]. Release of insulin as a consequence of depolarization of cellular membrane which is induced by KATP inhibition is initially triggered by the binding of Glipizide to beta cells specific sites [6].

Materials and methods

In this study, forty adult albino male rabbits were adopted. They weighed 1.5 - 1.7 kilograms in range. The conditions of the experiment were typical and unified. Then, the animals were set randomly into four groups of ten rabbits each.

1. Control group (C): animals were injected intraperitoneally with 1 ml of normal saline.
2. The second group (SZ): animals were injected intraperitoneally with 65 mg/kg of Streptozotocin one time to induce diabetes [7].
3. The third group (G): animals were administered a daily oral dose of 5 mg/kg of Glipizide [8].
4. The fourth group (SZG): animals were injected with streptozotocin in the same manner as the second group and then dosed orally with 5mg/kg of Glipizide. The above-mentioned experimental protocol was extended for one month and thereafter the planned tests were done.

Results and Discussion

The effects of Glipizide, streptozotocin, and streptozotocin plus Glipizide were apparent on different functional parameters. Table 1 reveals these effects on the blood aspects where the red blood cell count RBC declined significantly in all the groups, the total white blood cells WBC elevated significantly in all groups, the hemoglobin concentration HB and the packed cells volume PCV declined significantly in streptozotocin and streptozotocin plus Glipizide groups comparing with those of the control group at ($p \leq 0.05$). The antioxidant enzymes were also afflicted, the streptozotocin caused significant declination in alanine aminotransferase ALT with significant elevation in ALT in the streptozotocin plus Glipizide group. The aspartate aminotransferase AST was significantly elevated in the Glipizide group only with significant declination in the alkaline phosphatase ALP of the streptozotocin group only. The glutathione GSH has declined significantly in all groups with significant elevation in the malondialdehyde MDA of the streptozotocin group, comparing all these with the control group at ($p \leq 0.05$); Table 2. The total serum cholesterol TC and the low-density lipoprotein LDL were significantly elevated in the Glipizide group, with significant elevation in the triacylglycerols of the streptozotocin plus Glipizide group. The high-density lipoprotein HDL significantly declined in all groups while the very low-density lipoprotein VLDL significantly declined in the Glipizide group and significantly elevated in the streptozotocin plus Glipizide group, comparing all these with the control group at ($p \leq 0.05$); Table 3**.**

The above-mentioned effects of streptozotocin can be explained by focusing on the effects of diabetes and the related sequelae. Diabetes causes elevation in the oxidative stress status of the body hence activating the damage to the cell membranes besides depletion of the antioxidant enzymes of the defense body system [9-10]. Oxidation of sulfhydryl groups of the hemoglobin peptide chains is caused by the elevated oxidative status which leads to the declination of hemoglobin [11-12]. The oxidative stress status also could cause elevation in the total white blood cells as a defensive body response [11-13].

Glutathione declination might be caused as a result of a decrease in NADPH coenzyme due to oxidative stress. NADPH is a coenzyme to glutathione reductase which renders the reduced form of glutathione from the oxidized one. The elevated levels of MDA might be due to the effects of diabetes [14-17]. The latter causes an increase in the free radicals and hence an increase in the peroxidation of lipids of the cell membranes [18]. The results in this study come under the study of [19].

Table 1.

Glipizide effect on blood parameters of Streptozotocin induced diabetic rabbits

Groups	**RBC count ($X10^6$)**	**WBC count ($X10^3$)**	**ESR (mm/hr)**	**HB (gm/dl)**	**PCV (%)**
C	7.22 ± 0.11^a	4.81 ± 0.22^c	2.52 ± 0.12^d	12.37 ± 0.45^a	45.20 ± 1.11^a
SZ	5.30 ± 0.81^d	8.44 ± 0.43^a	31 ± 2.3^a	9.22 ± 0.34^b	30.24 ± 0.91^b
G	6.14 ± 0.31^b	6.41 ± 0.51^b	7 ± 1.7^c	12.41 ± 0.26^a	45.33 ± 0.62^a
SZG	4.61 ± 0.28^c	8.38 ± 0.37^a	29 ± 1.44^b	9.36 ± 0.41^b	29.84 ± 0.88^b

Values represent the mean ± standard deviation. C; Control group, SZ; Streptozotocin treated group, G; Glipizide treated group, and SZG; Streptozotocin and Glipizide treated group.

Table 2.

Glipizide effect on enzymes of Streptozotocin-induced diabetic rabbits

Groups	ALT (U/L)	AST (U/L)	ALP (KAU)	GSH (μmol/L)	MDA (μmol/L)
C	25.33±1.12[b]	30.11 ±0.82[b]	12.22 ± 0.23[a]	7.72±0.71[a]	61.41±0.88[b]
SZ	17.22±0.71[c]	34.13 ±1.22[a]	9.12 ± 0.33[b]	5.35±0.21[c]	93.4±5.23[a]
G	25.26 ±0.92[b]	15 ±1.16[c]	12.42 ± 0.42[a]	5.27±0.32[c]	58.92±1.71[b]
SZG	29.23 ±1.41[a]	33.17 ±1.11[ab]	12.32 ± 0.35[a]	6.41±0.51[b]	59.27±1.58[b]

Values represent the mean ± standard deviation. C; Control group, SZ; Streptozotocin treated group, G; Glipizide treated group, and SZG; Streptozotocin and Glipizide treated group.

Table 3.

Glipizide effect on lipid profile of Streptozotocin induced diabetic rabbits

Groups	TC (mg/dl)	TAGs (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
C	98.37±1.22[b]	99.16 ±2.44[b]	27.43 ± 0.44[a]	61.7±2.55[b]	20.13±0.26[b]
SZ	100.27±1.72[b]	97.3 ±3.13[b]	21.22 ± 1.11[b]	64.93±2.88[b]	20.11±0.53[b]
G	125.31 ±2.29[a]	92.77 ±3.66[b]	20.83 ± 1.93[b]	88.13±1.62[a]	18.33±0.49[c]
SZG	97.22 ±2.09[b]	125.4 ±4.38[a]	21.73 ± 2.51[b]	67.93±2.91[b]	25.23±1.12[a]

Values represent the mean ± standard deviation. C; Control group, SZ; Streptozotocin treated group, G; Glipizide treated group, and SZG; Streptozotocin and Glipizide treated group.

Abbreviations

Not applicable

Declarations

Ethics approval and consent to participate

Funding

No funds from any institute

Competing Interests

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. World Health Organization. Diabetes; (2022). https://www.who.int/news-room/fact-sheets/detail/diabetes.
2. Moussa SA. Oxidative stress in diabetes mellitus. Romanian .J. Biophys. 2008;18(3):225-236.
3. A. Darenskaya, L. I. Kolesnikova, and S. I. Kolesnikov. Oxidative Stress: Pathogenetic Role in Diabetes Mellitus and Its Complications and Therapeutic Approaches to Correction. Bulletin of Experimental Biology and Medicine. 2021;171(2): 179-189.
4. Whitney EN, Cataldo CB, Roltes SR. Understanding normal and Clinical Nutrition. Sixth edition, Wadsworth, Thomson Learning. 2002.
5. Kalra S, et al. Place of sulfonylureas in the management of type 2 diabetes mellitus in South Asia: a consensus statement. Indian J Endocrinol Metab. 2015;19(5):577.
6. Brunton LL, Dandan RH, Knollmann BC. Goodman & Gilman`s, The Pharmacological Basis of Therapeutics. Thirteenth edition, USA. 2018;2:874-875.
7. Mir M, Darzi M, Baba O, Khan H, Kamil S, Sofi A, Wani S. Streptozotocin Induced Acute Clinical Effects in Rabbits (Oryctolagus cuniculus). Iranian Journal of Pathology. 2015;10(3), 206-213.
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539772/pdf/ijp-10-206.pdf
9. Peng Z, Yuan S, Shu-xia Z, Ai-xiao X, Sai-zhen C, You-gong D. Pharmacokinetic study of glipizide effected by roxithromycin in rabbits. Chinese Journal of Clinical Pharmacology and Therapeutics. 2012; 17(2): 181-184. http://manu41.magtech.com.cn/Jweb_clyl/EN/abstract/abstract8651.shtml.
10. Abou-seif MA, Youssef AA. Oxidative stress and male IGF-1, gonadotropin and related hormones in diabetic patients. Clin-Chem. Lab. Med. 2001;39 (7): 618-623.
11. Desnoyers M (2000). Anemias associated with Heinz bodies. Schalm`s Veterinary Hematology, 5th ed. Feldman B. F., Zinkl J. G., Jain N. C. Baltimore, Lippincott Williams and Wilkins, PP: 178 – 180.
12. Barrett KE, Boitano S, Barman SM, Brooks H. Ganong`s Review of medical physiology. 25th ed .Mc-Graw Hill. U.S.A. Sanfrancisco. 2016.
13. Murray RK, Granner, DK, Mayes PA, Rodwell VW. Harper's Biochemistry 25th ed. Appleton and Lange, USA. 2000.
14. Neil OMJ. The Merck Index: An Encyclopedia of chemicals, drug, and biological .14th edition. Merck & Co., INC. USA. 2006.
15. Salis A, Petrson R, Stecker M, Patal N, Willis L, Galley P, Eclavea A, Dreesen R. Suprarenal Intraarterial infusion of alloxan and streptozotocin during Balloon occlusion of the Juxtrarenal abdominal aorta: A simple technique for inducing Diabetes Mellitus in Canines with reduced mortality. Academic Radiology. 2001; 8:473 – 477.
16. Siemianowicz K, Gminski J, Telega A, Wojcik A, Psielezna B, Bochenek R, Francus T. Blood antioxidant parameters in diabetic retinopathy .Interr. J.Mol.Med. 2004;14 (3):433-437.
17. Whitney EN, Cataldo CB, Roltes SR.Understanding normal and Clinical Nutrition. Sixth edition, WADSWORTH, Thomson Learning 2002.
18. Yilidirim O. The effect of vitamin C and cobalt supplementation on antioxidant status in healthy and diabetic rabbits. African .J. Biotechnology. 2009;8(19):5053-50.

19. Kromhauser C, Garcia R, Wrobel JR. Serum SE and GPx concentration in type 2 diabetes mellitus patients .Prim Care Diabetes. 20008; 2(2)81-85.
20. Yasin YS, Hashim WS, Qader SM. Evaluation of metformin performance on alloxan-induced diabetic rabbits. Journal of Medicine and Life. 2022;15(3):405-407.