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Stressed experimental diabetic rats challenged with glimepiride

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Abstract

Background: This study was accomplished to evaluate the anticipated effects of glimepiride on some of the hematological parameters and antioxidant enzymes in alloxan-induced diabetic and healthy rats.

Methods: In this study, thirty-two adult albino male rats were adopted. The animals were randomly divided into four groups of eight rats each. The animals of the control group were dozed orally with 5 ml distilled water. The second was injected into intraperitoneally with 150 mg/kg of Alloxan once to induce diabetes. The third group were administered a daily oral dose of 5 mg/kg of Glimepiride. The fourth group were injected with alloxan in the same manner as the second group and then dosed orally with 5 mg/kg of glimepiride. The above-mentioned experimental protocol lasted for one month and thereafter the planned tests were done.

Results: The results showed that diabetes induced by alloxan led to significant decline in the packed cell volume (PCV), hemoglobin concentration (Hb), platelets (PLT), red blood cell counts (RBC), glutathione (GSH), alanine aminotransferase (ALT) and, alkaline phosphatase (ALP) at ($p \leqslant 0.05$) with significant elevation in the total white blood cells count (WBC), malondialdehyde (MDA), erythrocytes sedimentation rate (ESR) and aspartate aminotransferase (AST) comparing with those of the control group. The use of glimepiride alone to the healthy rats led to significant decline in RBC, PLT, GSH and AST with significant elevation in ESR and WBC without effecting PCV, Hb, MDA, ALT and ALPat ($p \leqslant 0.05$) comparing with those of the control group. Treatment of alloxan-induced diabetic rats with glimepiride led to significant decline in RBC, Hb and PCV with significant elevation in WBC, PLT, GSH, MDA and ALT at ($p \leqslant 0.05$) compared with the control group.

Conclusion: We conclude that glimepiride affects blood parameters and antioxidant enzymes.

Introduction

A large number of people are afflicted with diabetes around the globe. These people use different medications to control diabetes. One of those medications is glimepiride. Glimepiride comes with different brand names like Amaryl, Azulix, Betaglim, Daoryl, Diaglim, Dibiglim and others. We hypothesized that glimepiride may have potential side effects; therefore, this study was conducted to evaluate its safety.

The relationship between the oxidative stress and diabetes mellitus was referred to by many studies including both two main types of DM type I and type II [1]. DM is well known to cause malfunctions in different body systems including a malfunction in the antioxidant system [2]. Glimepiride is one of the second-generation sulfonylureas, a group of insulin secretagogues [3]. Glimepiride stimulates the release of insulin when it binds to specific cite of beta cells leading to closure of KATP and hence the depolarization of membrane which leads to release of insulin [4].

Methods

In this study, thirty-two adult albino male rats were adopted. They weighed 250-300 g. The conditions of the experiment were typical and unified. Then, the animals were randomly assigned into four groups of eight rats each.

1- Control group (C): a dose of 5 mL distilled water was administered orally.

2- The second group (A): animals were injected intraperitoneally with 150 mg/kg of alloxan once to induce DM.

3- The third group (GLM): animals were administered a daily oral dose of 5 mg/kg of Glimepiride.

4- The fourth group (AGLM): animals were injected with Alloxan in the same manner as the second group and then treated orally with 5 mg/kg of glimepiride. The experimental protocol lasted for one month, after which the planned tests were performed.

Results

Alloxan could cause significant decline in RBC, Hb, and PCV, on the other hand significant elevation in WBC and ESR compared with the control group at ($p \leqslant 0.05$). The same occurred when Glimepiride was dosed immediately after dosing with Alloxan. When Glimepiride was offered alone, it caused significant decline in RBC with significant elevation in WBC without affecting the Hb, PCV and ESR compared to with the control group at ($p \leqslant 0.05$). The effects of Alloxan and Glimepiride can be seen in table 1.

Focusing on some biochemical markers, Alloxan could cause a significant elevation in MDA, significant decline in AST, ALT, ALP and GSH compared with the control group at ($p \leqslant 0.05$). When Glimepiride was offered after dosing with Alloxan, it caused a significant elevation in ALT with a significant declination in GSH without affecting the AST, ALP and MDA.

Glimepiride causes significant decline in AST and GSH without affecting the ALT, ALP, and MDA compared to with those parameters of the control group at ($p \leqslant 0.05$), as can be seen in table 2.

Groups	RBC count ($X10^6$)	WBC count ($X10^3$)	ESR (mm/hr)	Hb (gm/dL)	PCV (%)
C	6.81 ±0.124^a	3.201 ±0.199^c	2.13 ± 0.147^d	12.41±0.235^a	31.30±1.03^a
A	4.32 ±0.045^d	6.231 ±0.182^a	31 ± 1.35^a	6.80±0.266^b	23.13±0.772^b
GLM	6.047 ±0.167^b	4.191 ±0.271^b	6 ± 0.430^c	12.21±0.160^a	31.46±0.25^a
AGLM	3.85 ±0.038^c	6.143 ±0.151^a	25.5 ± 1.44^b	8.04±0.012^b	26.10±0.028^b

Values represent the mean ± standard deviation. C; Control group, A; Alloxan treated group, GLM; Glimepiride treated group and AGLM; Alloxan and Glimepiride treated group.

Table 1: Glimepiride effect on blood parameters of Alloxan-induced diabetic rats.

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)	GSH (µmol/L)	MDA (µmol/L)
C	23.27±1.13^b	33.12 ±0.62^b	11.22 ± 0.126^a	5.84±0.025^a	46.33±0.722^b
A	17.13±0.81^c	37.22 ±1.22^a	9.15 ± 0.157^b	4.12±0.111^c	77.61±5.83^a
AM	23.8 ±0.341^b	19 ±1.35^c	11.137 ± 0.265^a	4.17±0.123^c	50.77±1.21^b
AMA	28.17 ±2.17^a	34.33 ±1.15^{ab}	11.5 ± 0.236^a	5.61±0.012^b	50.11±1.12^b

Values represent the mean ± standard deviation. C; Control group, A; Alloxan treated group, GLM; Glimepiride treated group, and AGLM; Alloxan and Glimepiride treated group.

Table 2: Glimepiride effect on enzymes of Alloxan-induced diabetic rats.

The effects of Alloxan can be explained by focusing on the effects of diabetes and the related sequelae. Diabetes causes an elevation in the oxidative stress status of the body and hence activates the damage to cell membranes and depletion of antioxidant enzymes of the body's defense system [5, 6]. Oxidation of sulfhydryl groups of the hemoglobin peptide chains is caused by the elevated oxidative status which leads to a decline in hemoglobin [7, 8]. The oxidative stress status also could cause an elevation in the total white blood cells as a defensive response [7- 9].

Glutathione decline might be caused as a result of a decrease in NADPH coenzyme due to oxidative stress. NADPH is a coenzyme to glutathione reductase which regenerates reduced glutathione from the oxidized form. The elevated levels of MDA might be due to the effects of diabetes [10-13]. The DM causes an increase in the free radicals and hence an increase in lipid peroxidation of cell membranes.

It can be concluded that Glimepiride could cause disturbances in hepatic enzymes, erythropoiesis, and the immune system, similar to alloxan.

Competing Interest

The authors declare that there is no conflict of interest.

Author Contributions

Wissam Sajid Hashim: The proposal of the research article, the design of the experiment, explanation of results and writing the article.
Youssef Shakuri Yasin: Preparing materials and purchasing animals and materials.
Azal Hamoody Jumaa: Information about the drugs and dosing of animals.
Emad Ayal Muter and Yousif Ahmed Khalil: Statistical analysis and taking care of animals.

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