University of Mosul
College of Pharmacy

Mitochondrial Function and Biochemical Analysis of Type 2 Diabetes Patients on Metformin Therapy

A Thesis submitted

By

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Summary

Type 2 diabetes (T2D) is a multisystemic, chronic metabolic disorder that affects a large number of people. It is characterized by mitochondrial dysfunction as well as the presence of oxidative stress and low levels of ATP. Metformin is one of the most effective anti-hyperglycemic agents used as first-line oral therapy for type 2 diabetes.

This study aims to explain changes in mitochondrial copy number, glycemic index, renal and liver status in type-2 diabetic patients treated with metformin monotherapy.

A retrospective case-control study was conducted at Al- Wafaa diabetic center in Mosul, from 1st January to June 2021. Forty-seven newly diagnosed type 2 diabetes mellitus patients aged between 25-65 years (23 males, 24 females) treated with metformin for 2-6 months in the dose was between (500 mg- 1000 mg) per day, and Forty-seven (20 males, 27 females), healthy subjects with matched age as a control group.

A Questioner was filled by each subject with important basic information, then a fasting blood sample was taken, and the following tests were done (glycated hemoglobin % , blood urea (mg/dl), serum uric acid (mg/dl), serum creatinine (mg/dl), serum aspartate aminotransferase (U/L), serum Alanine aminotransferase (U/L),aspartate aminotransferase/Alanine aminotransferase ratio, serum Alkaline phosphatase (U/L), serum total protein (g/dl), serum total bilirubin (mg/dl), serum lactate (μM), serum pyruvate (μM), and serum lactate/pyruvate ratio and mt-ND1 gene).

The results of the study reveal that the mean HbA1c level in diabetic subjects was significantly higher (7.76 ± 1.94) than in the control group (5.18 ± 0.49) $p \leq 0.001$.

In diabetic subjects, the mean blood urea level was significantly higher (28.31 ± 8.24), compared to the control group (24.27 ± 5.81) $p < 0.01$.

In comparison to the control group (0.88 ± 0.08), serum creatinine was significantly higher in diabetic subjects (0.94 ± 0.20) $p < 0.05$.

There were no significant differences in serum uric acid levels between diabetic subjects (4.91 ± 0.82) and the control group (4.67 ± 1.34) $p > 0.05$.

The liver function test parameters used in this study revealed a significant increase in serum Alanine aminotransferase in diabetic subjects (20.65 ± 6.04) compared to the control group (12.95 ± 6.05) p=0.000. In diabetic subjects, serum total protein (5.80 ± 0.48) was less than in the control group (7.07 ± 0.38), p=0.000. And serum total bilirubin was significantly higher in the diabetic subjects (1.01 ± 0.44), compared to the control group (0.48 ± 0.15), p =0.000,

there was a significantly increase in serum glutamic oxaloacetic transaminase/glutamic pyruvic transaminase ratio in the diabetic subjects (1.71 ± 0.70) in comparison to the control group (0.98 ± 0.24) *p*=0.000.

There were no significant differences in serum glutamic oxaloacetic transaminase (GOT)levels in diabetic subjects (19.31 ± 5.32) compared to the control group (19.48 ± 4.32) p=0.86, and serum Alkaline Phosphatase levels in diabetic subjects (168.51 ± 51.95) compared to the control group (157.80 ± 33.19) p>0.05.

The mitochondrial function tests parameters used in this study showed that diabetic subjects had a significantly higher level of mean serum lactate (1556.02 ± 315.94) than the control group (1210.29 ± 297.09), p=0.000. In diabetic subjects, serum pyruvate levels were higher (73.68 ± 13.94) than in the control group (68.06 ± 13.80), p=0.000. and the diabetic subjects had a higher serum lactate/pyruvate ratio (21.12 ± 1.52) than the control group (17.75 ± 1.75), p=0.000.

The present study found that mitochondrial copy number significantly decreased by 32.8 fold in T2DM patients in comparison to the control group ($p < 0.01$).

Blood HbA1c and serum Uric acid, serum Uric acid and serum Creatinine, serum Alanine aminotransferase and blood HbA1c, and serum Alkaline phosphatase and serum Total bilirubin all had a significant negative correlation in the patient group.

There was a significant positive correlation between serum Uric acid and serum Urea, blood HbA1c and serum Total protein, serum lactate and blood HbA1c, and serum lactate levels and GOT/Alanine aminotransferase in our study.

In conclusion, in comparison to non-diabetic controls, diabetic patients treated with mono-metformin treatment had a lower mitochondrial copy number and moderate renal and liver impairment.

Contents

Appendix questionnaire form
Number:
Date:
Name:
Age:
Sex:
Weight:
Height:
BMI:
Type of diabetes mellitus:
Duration:
Type of treatment and Dose:
Family history:
Pregnancy:
Alcohol drinking:
Cigarette smoking:
Blood pressure:
History of disease:
History of drugs:
Chronic disease:
Dietary factor:
HbA1C previously:
Supplement Or Not:

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