UTTAR PRADESH JOURNAL OF ZOOLOGY

42(24): 10-14, 2021
ISSN: 0256-971X (P)

CO-ENZYME QlO ADMINISTRATION AND ITS EFFECT ON LONG TERM GLYCEMIC CONTROL IN PATIENTS WITH TYPE-2 DIABETES MELLITUS

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Ana Cláudia Correia Coelho, University of Trás-os-Montes and Alto Douro, Portugal.
Reviewers:
(1) Mohamed Abdel-Raheem Ali Abdel-Raheem, National Research Centre, Egypt.
(2) Mirna Dwirastina, Indonesia.

Received: 11 September 2021
Accepted: 23 November 2021
Published: 30 November 2021

Original Research Article

ABSTRACT

Diabetic becomes a severe health concern and a pan disease worldwide. Type 2 diabetic (T2D) is majorly seen in the people and its population growth is ever increasing. The glycemic control is a major way in controlling T2D. The prevention and the optimal diagnosis are two major steps for reducing disease burden in the present life style. This study aimed at the effect of coenzyme q 10 supplementation on long term glycemic control (HbA 1 c level) in Type 2 diabetes mellitus (DM2). This study was carried out in Department of Pharmacology and Department of Medicine Bharath Institute of Higher Education and Research, Chennai, Tamilnadu during the period of August 2015 - February 2016 (6months). These results showed that a close relationship is existing between the DM2 and deficient coenzyme Q10 (CoQ10) level. Further, it showed the supplementation of oral hypoglycemic (Biguanide Metformin) could improve glycemic control and blood coenzyme Q10 level positively.

Keywords: Type 2 diabetes mellitus; coenzyme Q10; mitochondrial dysfunction; oxidative stress; antioxidant; adenosine triphosphate.

1. INTRODUCTION

The Diabetes mellitus (DM) is one of the oldest disease known to human and classified as type I and Type II based on its physiological variations [1]. It becomes a epidemic worldwide fue to aging and elder population in many countries. The under developed and developing countries are predominately affected by DM and prone for disease outbreak [2-3]. It was estimated that nearly 366 million people were affected by it as on 2011 and the number could be doubled on 2030 (up to 552 million). The changes and seductive

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life style are the important causes for it higher prevalence. The decreased physical activity, overweight, oil packed food and further physiological variations were increase the chances for DM among the population [3-4]. DM2 is a slow and chronic disorder raised due to the defects in secretion and enzymatic activity of the insulin. The metformin was approved before 40 years since then, it is being used against the diabetic. It increases the insulin sensitivity of both hepatic and peripheral tissues. It also inhibited the hepatic gluconeogenesis ai *in vitro* and *in vivo* level through enhancing tyrosine kinase activity, GLU4 activity and efficient glycogen synthesis [5-6]. Coenzyme Q10 (CoQ10) is a naturally found every cell of the human body and act as an anti oxidant during mitochondrial energy transportation. Thus it is an important factor for the cellular transportation and the ATP production [7]. It is a primary scavenger of the free radicals and predominately found as in reduced form. Meanwhile, the dta related to its role in glycemic control is scarce [8-10]. Hence this study was undertaken to evaluate · and observe the safety, effect of Coenzyme Q10 supplementation on long term glycaemic control (HbA 1c) in patients already diagnosed with Type 2 Diabetes Mellitus.

2. MATERIALS AND METHODS

Randomised, parallel assignment, open label, longitudinal intervention study of administrating Coenzyme Q10 to patients already having Type 2 Diabetes Mellitus who are already on Biguanides (Metformin) find observing the efficacy and safety of the drug under study. Department of Pharmacology and General Medicine, Bharath Institute of Higher Education and Research, Chennai. The study duration was between August 2015 and February 2016 (6 months). The total sample size consisted of 40 patients. The patients were separated in to two groups, Study group A (COENZYME QIO 100mg bid along with METFORMIN (20 patients) and Study group B: METFORMIN prescribed dose according to blood glucose level (20 patients). The inclusion criteria were patients with higher than 18 years of age, both sexes, newly diagnosed type 2 diabetic patients (1yr or less), (BMI -29.9), patients on treatment with only biguanides- metformin, HbAlc level <8 %, Patient with borderline dyslipidemia and not on treatment (according to guidelines from the NCEP Adult Treatment Panel III to evaluate lipid levels and CVD risk). The exclusion criteria included Patient with known cardiac disease- hypertension, dyslipidaemic on treatment, heart failure, myocardial ischemia, 2. Women who are pregnant or breast-feeding, who are on oral or injectable contraception or who are likely to get pregnant, Patient on treatment for type 2 diabetes mellitus with a different class of drug. Patients who have insulin-dependent or uncontrolled Diabetes, Mellitus or biguanides with insulin dependent, Patients with type 1 diabetes mellitus, Patients with clinical cardiovascular disease that includes unstable myocardial infarction angrnapectoris, previous or CV A in the last 1yr, congestive heart failure, transient ischemic attack, (TIA), significant aortic or mitral valve disease. Patients with significant renal or hepatic disease, Patients who have peripheral vascular disease, Patient with BMI 30 or aboveand Patients with HbAlc level more than 8.1% [9-11].

The study was approved by the Institution Ethics Committee of Bharath Institute of Higher Education and Research. Informed written consent was obtained from the patients, who were inducted into the study. Details of the study were explained to the participants and the informed consent was obtained in their own language. The primary efficacy end-point was percent change from baseline fastingblood glucose, HbA 1c and blood coenzyme QlO levels at the end of 24 weeks. [Time Frame: Baseline to 24 weeks [11-12]. The results were presented based on the Percent change from baseline in Total Cholesterol, Triglycerides, LDL, and HDL till the end of 24 weeks. [Time Frame: Baseline to 24 weeks]. Percent change from baseline in BMI till the end of 24 weeks. [Time Frame: Baseline to 24 weeks].

Data analysis was performed by means of the SPSS statistical software package for Windows (version 10.0; SPSS Inc. Chicago, USA); results were expressed as the mean±SD.

3. RESULTS AND DISCUSSION

The two groups were matched in respect of their Age, fasting blood-glucose level, HbAlc, profile of the lipid types (TC, LDL, HDL and TG), Blood Coenzyme Q10 level and BMI before starting the study. The number of males and females of the two groups were matched in the above table. The improvements in the fasting blood glucose, long term glycaemic control (HbA 1c), blood coenzyme Q10 levels, lipid profile and BMI parameters from baseline, 3months to 6months were compared between the groups to identify the superiority of the combination of coenzyme Ql0 to the standard Oral Hypoglycaemic Drug (metformin). Metformin with Coenzyme Q10 on fasting blood-glucose at 3 month treatment period reduced to 96.15±6.49, compared to baseline value 103.55±4.55, which is significant. At the end of 6month treatment period it reduced to 91.85±6.11, which is very highly significant according to the pValue. The value of Metformin alone on fasting blood glucose at baseline was 100.75±5.82. At the end of 3month reduced

minimally 100.05±4.78, which is not significant statistically. On sixth month visit, it reduced to 99.07±5.28, which also not significant according to the p Value (Fig. 1).

Table 1. Age distribution

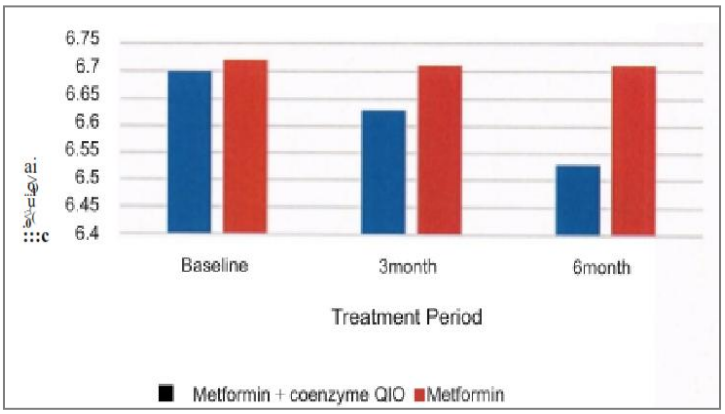
Variable	Group A (Metformin + Coenzyme QlO) n= 20	Group B (Metformin) n=20
	Mean± SD	Mean± SD
Age(years)	50 .15 ±6.57	46.90±6.18
FBS	103. ±4.55	100.75±5.82
HbAlc	6.7L1r_., J.24	6.72 ±0. 27
TG	115.7±10.33	112±10.91
LDL	105.79±23.33	108.52±21.32
HDL	41.75±5.94	42.05±7.98
TC	170.68±24.56	173.38±21.78
Blood		
CoQl0	1.02±0.24	1.03±0.21
BMI	24.23±1.70	23.84±1.43

The Value in Metformin and Coenzyme Ql0 on long term glycaemic control (HbAlc) at baseline was 6.70 ±0 .24. At 3month HbAlc level reduced to 6.63±0.2, which is not significant. At the end of 6month treatment period HbAlc level reduced further to 6.53±0.21, significant according to p Value.

The value of Metformin alone on long term glycaemic control (HbAlc) at baseline was 6. 72±0.27. At 3month HbAlc level minimally reduced to 6.71±0.29, which is not significant. At the end of 6month treatment period HbAlc level being same 6.71 ±0.29, which is also not significant according to pValue.

3.1 Effect on Lipid Profile between the Two Groups

Triglycerides level at baseline 123.70±10.84 in the combination group of metformin and coenzyme Q10. At 6month of the treatment period there was minimal reduction to 121.75±9.43 (Table. 6). In the metformin group the triglycerides level reduced from 125.10±10.91 to 123.60±8.53. [Time Frame: baseline to 6month]. LDL level in metformin and coenzyme Q10 group from baseline (127.31 ±23 .33), it has increased at the end of treatment period (6month),. 129 .15±21.64, which is not significant according to pValue (Table. 7). In metformin group, baseline level of 127.73±21.32 has minimally reduced to 123.88±20.52, which is also not significant according to p Value. A study conducted in UK (UKPDS 35) showed that the reduction in intensive blood glucose control was similar to the reduction found in the epidemiological study. The study also adds there is a direct relation between the risk of complications of diabetes and glycaemia over time, of which microvascular complication is greater than macrovascular complication. [12].



.Fig. 1. Effect on HbAl c between the two groups

Table 2. Gender distribution

Gender	Group				Total	
	Metformin +Coenzyme QlO		Metformin			
	No.	%	No.	%	No.	%
Male	8	40%	10	50%	18	45%
Female	12	60%	10	50%	22	55%
Total	20	100%	20	100%	40	100%

Table 3. Effect on Fasting Blood Glucose between the two groups

	Initial visit (Mean ± SD)	Third month (Mean ± SD)	Sixth Month (Mean ± SD)
Metformin + Coenzyme Ql0	103.55±45 ,5	96.15±6.49*	91.85±6.11**
Metformin	100.75±5.82	100.05±4. 78ns	99.0 7±5 .2 8n s

**p<0.05 vs. baseline. **p<0.01 vhs. Baseline, ns P>0.05- not significant.*

Table 4. Triglycerides

	Initial visit (Mean ± SD)	Third month (Mean ± SD)	Sixth Month (Mean ± SD)
Metformin +Coenzyme QLO	115.7±10.84	115 .6± 6.67 11	114.7± 9.4311
Metformin	112±10.91	114. 05± 5.62 11	113 .05± 8.53 11

Table 5. LDL

	Initial visit (Mean ± SD)	Third month (Mean ± SD)	Sixth Month (Mean ± SD)
Metformin +Coenzyme QL0	105 .79 ± 23 .33	105 .56 ± 25 .31n s	107.49±21. 64n s
Metformin	108.93±21.32	108.52± 22 .32n s	10 8 . 8 8 ± 20 .52n s

Table 6. HDL

	Initial visit (Mean± SD)	3 Mo n t hs (Mean± SD)	6 Mo nth s (Mean ± SD)
Metformin + Coenzyme Q10	41. 75 ± 5 .94	4 1. 20 ±5 .19n s	4 1. 30 ±5 .4 3n s
Metformin	42.05±7.98	40.70 ±6 .6 1n s	4 0.95 ±6 .5 3n s

Table 7. Total cholesterol

	B ase line (Mean ± SD)	3 Mo n th s (Mean ± SD)	6 Mon th s (Mean ± SD)
Metformin + Coenzyme QI0	170.68±24.56	16 9.8 8 ± 24 . 19n s	1 71. 73 ± 25 .4 3"5
Metformin	173.3 8 ± 21. 78	172.03±21.61n s	172.4 4± 21.5 3" 5

4. CONCLUSION

The study showed that the Metformin with Coenzyme QIO reducuced the blood glucose along with HbAlc level. It could be used for the social welfare.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

CONSENT

Informed written consent was obtained from the patients, who were inducted into the study. Details of the study were explained to the participants and the informed consent was obtained in their own language.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Abdulfatai B. Olokoba, Olusegun A et al. Type 2 Diabetes Mellitus: A review of current trends. 2012;27(4):269-273.
2. Christopher Weidner, Prevention and therapy of type 2 diabetes by selective modulation of the human peroxisome proliferator activated receptor gamma (PPARy); 2011, June; PhD Thesis Freie University, Berlin.
3. Jaakko Tuomilehto, Jaana Lindstrom, Johan G. Eriksson, et al., Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;May 3, 344:1343-1350
4. Ralph A. DeFronzo. Pharmacologic therapy for type 2 diabetes mellitus. 1999 Aug 17;131(4):281-303.
5. Bailey CJ, Turner RC. Metformin. N Engl J Med. 1996;334:574 -9.
6. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with noninsulin-dependent diabetes mellitus. The Multicenter Metformin Study Group. N Engl J Med. 1995;333:541-9.
7. DeFronzo RA, Barzilai N, Simonson DC. Mechanism of metformin action in obese . ,id lean noninsulin-dependent diabetic subjects. J Clin Endocrinol Metab. 1991;73:1294-301.
8. Stumvoll N, Nurjhan N, Perriello G, et al. Metabolic effects of metformin in non-insulin-dependent diabetes mellitus. N Engl J Med. 1995;333:550-4.
9. JohnsonAB, Webster JM, Sum CF, et al. The impact of metformin therapy on hepatic glucose production and skeletal muscle glycogen synthase activity in overweight ty pe II diabetic patients. Metabolism. 1993;42: 1217-22
10. Wollen N, Bailey CJ. Inhibition of hepatic gluconeogenesis by metformin. Synergism with insulin. Biochem Pharmacol. 1988;37:4353-8.
11. Cusi K, Consoli A, DeFronzo RA. Metabolic effects of metformin on glucose and lactate metabolism in noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab. 1996;81: 4059-67.
12. Klip A, Leiter LA. Cellular mechanism of action of metformin. Diabetes Care. 1990;13:696- 70 4.
13. Overvad K, Diamant B, Holm L, et al. Review Coenzyme QJO in health and disease. 1999 Oct; 53(10):764-70.
14. Shobha Prakash J. Sunitha, and Mayank Hans, Role of coenzyme Q10 as an antioxidant and bio energizer in Periodontal Diseases. 2010 Dec;42(6):334-337.
15. Alternative Medicine Review ,Coenzyme QJ0, 2007; 12(2)
16. Robert Alan Bonakdar, Erminia Guarneri, Coenzyme QJ0, 2005 Sep 15;72(6):1065 - 1070.
17. Robert C. Turner, FRCP; Carole A. Cull, PhD et al., Glycemic Control With Diet, Sulfonylurea, Metformin, or Insulin in Patients With Type 2 Diabetes Mellitus, Progressive Requirement for Multiple Therapies (UKPDS 49), Lancet, 1998; 352:837-853.
18. Hoda Zahedi, Shahryar Eghtesadi, Soroush Seifirad et al. Effects of CoQJ0 Supplementation on Lipid Profiles and Glycemic Control in Patients with Type 2 Diabetes: a randomized, double blind, placebo - Controlled Trial. 2014;13: 81
19. Eriksson JG, Forsen TJ, Mortensen SA, Rohde MCA. The effect of coenzyme QJ0 administration on metabolic control in patients with type 2 diabetes mellitus. 1999; 9(2-4):315-318.
20. Saurabh RamBihariLalShrivastava, Prateek Saurabh Shrivastava et al., Role of self-care in management of diabetes , mellitus, Journal of Dia be l'-, . & Metabolic Disorders. 2013;12:14.
21. Dawn E. DeWitt, MD, MSc; Irl B. Hirsch, MD, Outpatient Insulin Therapy in Type 1 and T ype 2 Diabetes Mellitus, Scientific Review JAMA. 2003; 289(17):2254-2264.