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Research Article

EVALUATION OF PROTECTIVE EFFECT OF ANTIOXIDANT VITAMINS IN PATIENTS WITH DIABETIC NEPHROPATHY

V. G. KUCHAKE[1], DR. C. D. UPASANI[2]

[1]R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule, [2]Shriman Sureshdada Jain College of Pharmacy, Neminagar, Chandwad, Nashik. Email: cdupasani@rediffmail.com

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ABSTRACT

Background: Diabetes mellitus has been a cause of concern for developed and developing countries. The progression of disorder cause prolonged exposure of vascular tissues to hyperglycemia resulting in long-term microvascular/macrovascular complications in the health; and nephropathy is one of them.

Objective: The main aim of study was to evaluate the combine effect of antioxidant vitamins E and C on microalbuminurea and HbA1c level in patients with diabetic nephropathy.

Method: A randomized, open controlled clinical trial was conducted at Indira Gandhi Memorial Hospital, Shirpur (Maharashtra) on 108 diabetic nephropathy patients (100 men and 8 women) aged between 35–60 years who have had diabetes for at least 5 years.

Result: During the study period a total 108 patients with diabetic nephropathy were selected for the study as per WHO based guidelines as well as inclusion and exclusion criteria of the study. These 108 patients divided in to two groups such as positive control and vitamin group. Each group contains 54 patients for evaluation of the parameters for four months follow-up for both control as well as vitamins group, after 4 months of supplementation of antioxidant vitamin E and C, it was found that the difference between initial and final values of microalbuminurea in control group patients there was not significant decline in microalbuminurea level. While in vitamins group there was significant difference ($p<0.05$) decline in microalbuminurea level from 34.1±0.08 to 31.8±0.45. Similarly in HbA1c (Glycosylated hemoglobin) group, the difference between initial and final values of HbA1c in control group patients there was not significant decline in HbA1c level. While in vitamins group there was significant difference ($p<0.05$) decline in HbA1c level from 8.7±0.04 to 5.8±0.3.

Conclusion: Diabetes is a chronic illness that requires a combine effect of treatment regimen for better glycemic control as well as to prevent its complications. Patient adherence to medication and lifestyle modifications plays an important role in diabetes management. This study concludes that, the combine effect of antioxidant vitamin E and C significantly lowers urinary albumin excretion rate (UAER) and glycosylated hemoglobin (HbA1c) in patients with diabetic nephropathy.

Keywords: Antioxidant vitamins, Diabetic nephropathy.

INTRODUCTION

Over the years, diabetes mellitus has been a cause of concern for developed and developing countries[1]. The disorder is ever increasing and is looming large as an epidemic. If the number of patients in the developed and developing worlds with diabetes is combined, it is currently 100 million, and is ever increasing. It is predicted that this increase will amount up to 200-225 million within the next 25 years[2]. The manifestations of the disorder cause considerable human sufferings and massive economic cost, despite of the enormous facilities available to control its growth rate.

The progression of disorder cause prolonged exposure of vascular tissues to hyperglycemia resulting in long-term microvascular/macrovascular complications as cardiovascular diseases, renal disease, cerebro-vascular diseases, etc.; these are the prime causes of morbidity, disability and premature death[3]. Apart from managing diabetes mellitus alone, it becomes imperative to correct any risk factor for associated disorders. Managing the disorder and controlling its associated complications require correct diagnosis, self-care, exercise and sticking to the strict drug-dose-food-intake regimen. Any irregularities in dosage regimen can definitely invite severe complications in the health; and nephropathy is one of them. Management of diabetes required tight glycemic control because blood glucose control reduces Hb1Ac levels. The Hb1Ac of less than 7% indicates decreased risk for clinical and structural manifestations of diabetic nephropathy in type 1 and type 2 diabetic patients. Intensive treatment of diabetes reduces the incidence of microalbuminurea. Intensive treatment of glycemia aiming at Hb1Ac less than 7% should be pursued as early as possible to prevent the development of microalbuminurea.

Diabetic nephropathy (DN) is a clinical syndrome characterized by persistent albuminuria (>300 mg/24 hours), on at least two occasions separated by 3–6 months. Patients invariably develop associated hypertension, such that it may be considered part of the syndrome[4].It is a common complication of diabetes characterized by the development of proteinuria, culminating in end-stage renal disease with a particular high risk of cardiovascular morbidity and mortality in diabetic patients[5]. It is leading cause of chronic kidney disease and is associated with increased cardiovascular mortality affects 40 % of type 1 and type 2 diabetic patients. It increases the risk of death[6]. It affects more than one-third of patients with type 1 diabetes and an ever increasing proportion of patients with type 2 diabetes[7]. Traditionally, nephropathy is divided into two types based on the urinary albumin excretion rate (UAER): incipient and overt. Incipient nephropathy is manifest as microalbuminurea (UAER 20–200 mg/24 hours) and usually occurs after 6–15 years of diabetes. Although hypertension is not a manifestation at this stage, a loss of nocturnal 'dipping' of blood pressure has been noted in this patient group and is suggested to precede and predict the development of microalbuminurea. Although microalbuminurea is a marker of incipient nephropathy, not all patients will progress to overt nephropathy. Roughly 25% of patients will revert to normal albumin excretion, and 40% will remain microalbuminuric. The development of proteinuria (UAER >200 mg/24 hours) with established hypertension defines the onset of overt nephropathy. Subsequently the rate of decline in renal function correlates with blood pressure levels, with the development of end-stage renal failure occurring within a median of 7 years from the onset of overt nephropathy[8].

Based on the literature it was observed that, Levels of plasma ascorbic acid were found to be significantly lower in diabetic patients compared with nondiabetic control subjects in most studies. Based on various study, the researchers observed that individuals with diabetes have significant defects of antioxidant protection, which may enhance their susceptibility to oxidative

stress[9,10,11]. Oxidative stress is imbalance between ROS generation and antioxidant system that scavenges or reduces ROS concentration. Redox imbalance caused by increased ROS production and / or reduced antioxidant reserve, leads to pathological consequences including damage to proteins, lipids and DNA. It is hypothesized to play an important part in the development of late diabetes complications. Chronic hyperglycemia increases oxidative stress and considerably modifies the structure and function of proteins and lipids due to glycoxidation and peroxidation[12]. These modified products could contribute to the morphological and functional abnormalities seen in the kidney of patients with diabetes[13]. For these reasons, there has been interest in the use of dietary antioxidants as an intervention to attenuate diabetic nephropathy.

Jeanette Schultz Johansen, et al. observed that the role of antioxidant vitamins in experimental models as well as observational studies strongly suggest that antioxidants should confer beneficial effects in reducing cardiovascular complications in diabetes. It should be emphasized that clinical trials with antioxidants in diabetes are limited and majority of these trials focused on the use of vitamin E and C. Small trials with vitamin E demonstrated beneficial cardiovascular effects. Beckman, et al. reported that administration of vitamin E and C combination for six months had a positive effect on endothelium dependent vasorelaxation in type 1 diabetic patients as well as improved renal function in type 2 diabetic patients[14].

A further important question is whether a combination of antioxidant vitamins provides better protection; the purpose of the study was to determine the combine effect of antioxidant vitamin E and C in patients with diabetic nephropathy.

MATERIAL

This study was done to substantiate the effects of externally administered antioxidant vitamins on the renal function of the patients with diabetes. In this study estimate bioavailability and therapeutic utility of orally administered Vitamin 'E', Vitamin 'C' was done in patient with Diabetic Nephropathy.

METHOD

A randomized, open controlled clinical trial where the diabetic patients were selected by sex and randomly assigned to two treatment groups using the randomization procedure. Depending upon the treatment, patients were divided into two groups, first group considered as positive control group, second group considered as vitamin group in which patients received combination of antioxidant vitamin E plus vitamin C. This entire two group received treatment of diabetes and hypertension. Each subject received one tablet of a combination of vitamin E and C per day for a period of 4 months. Patients were instructed to take the tablets with breakfast or dinner meals. Each tablet contained one of the following preparations and hence determined the corresponding groups: group 2 vitamins, vitamin E (400mg) and vitamin C (500mg). During study period urine and serum sample of patient's measurements were done at the start of the run-in phase, at randomization, and at the end of each treatment period.

Study site and setting

The study was carried out in outpatients department (OPD) of Indira Gandhi Memorial Hospital, Shirpur; patients were currently following the treatment of diabetic nephropathy.

Source of data

All neccesary & relavant information were collected from outpatient department cards, laboratory data report, treatment chart and verbal communication with patient.

Collection of data

The format for the collection of the data is prepared as per WHO based guidelines and the study was approved by Institutional Human Ethical Committee of R.C.Patel Institute of Pharmaceutical Education & Research, Shirpur which involved patient as well as medication information such as name, dose, frequency, route etc. and Patient information such name, age, sex, socioeconomic parameter, past medical history, & duration of treatment.

Statistical analysis

Results are expressed as mean with SD or 95% confidence intervals by using paired Student's t-test to compare differences between the initial and final values. Statistical significance level was $P < 0.05$.

Measurements

Measurements were done at the start of the run-in phase, at randomization, and at the end of each treatment period of the open controlled phase. All the Urine and Serum sample were measured by Automated Biochemistry Analyzer VITROS Fusion 5 FS1 (JHONSON and JHONSON company), and the average of these measurements was used.

RESULTS

A total 108 patients with diabetic nephropathy were selected for the study as per WHO based guidelines as well as inclusion and exclusion criteria of the study. These 108 patients divided in to two groups such as positive control and vitamin group. Each group contains 54 patients for evaluation of the parameters for four months follow-up for both control as well as vitamins group, after 4 months of supplementation of antioxidant vitamin E and C; it was found that the difference between initial and final values of microalbuminurea in control group patients there was not significant decline in microalbuminurea level. While in vitamin group there was significant difference ($P < 0.05$) decline in microalbuminurea level from 34.1±0.08 to 31.8±0.45 (Figure No: 1). Similarly results of HbA1c (glycosylated hemoglobin), the difference between initial and final values of HbA1c in control group patients there was not significant decline in HbA1c level. While in vitamins group there was significant difference ($P < 0.05$) decline in HbA1c level from 8.7±0.04 to 5.8±0.3 (Figure No: 2).

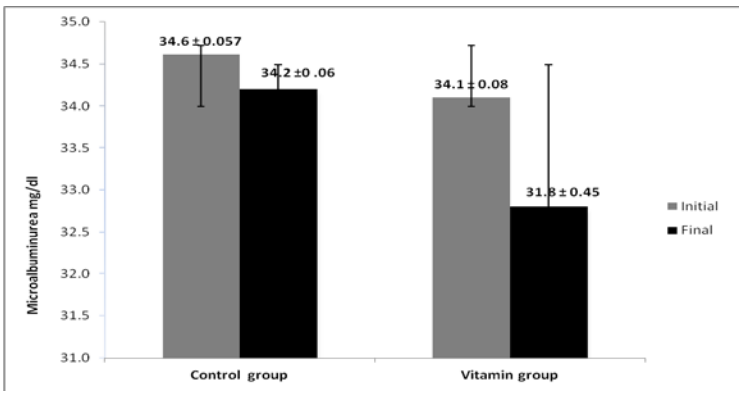

Fig. 1: Effect of antioxidant vitamin E plus C on microalbuminurea in patients with diabetic nephropathy

Significance of difference in the means was determined by Paired t- Test. * $p < 0.05$

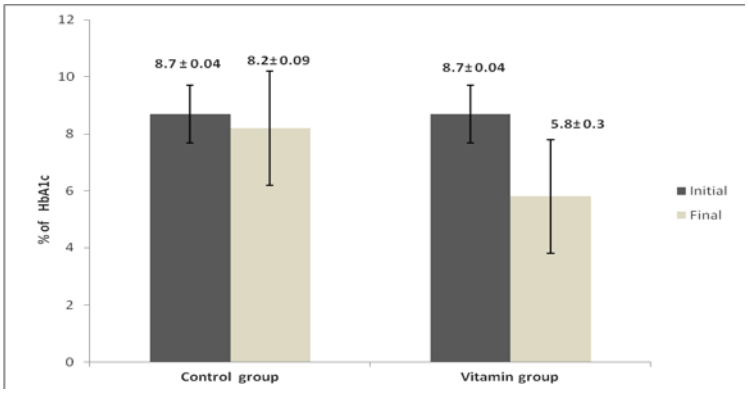

Fig. 2: Effect of antioxidant vitamin E plus C on HbA1c in patients with diabetic nephropathy

Significance of difference in the means was determined by Paired t- Test. * $p < 0.05$.

CONCLUSION

The worsen condition of sufferers is mostly due to poor control of complications associated with diabetes mellitus. Thus, apart from managing diabetes mellitus alone, it becomes imperative to control its associated complications such as nephropathy. Management of diabetes nephropathy is extremely expensive and frustrating. Therefore, prevention is better by supplementation of antioxidants, especially antioxidant vitamins. Treating diabetes complications require correct diagnosis, self-care, exercise and sticking to the strict drug-dose-food-intake regimen. There has been a dearth of clinical data which would support the therapy in treating diabetic patients, throw light on its pros & cons. Data demonstrate that treatment with combination of vitamins E plus vitamin C, significantly lowers the urinary albumin excretion rate (UAER) and glycosylated hemoglobin (HbA1c) level in patients with diabetic nephropathy. This clinical study could support for treating diabetes better than other therapies, it would also excel in assorting confidence in the diabetic population regarding the therapy because supplementation of antioxidants especially vitamins when it comes to treat patients with diabetes and its complications which is claimed to be devoid of side-effects.

REFERENCE

1. Colin Berry, Jean-Tardif, martial G, Bourassa: Coronary heart disease in patients with Diabetes. Journal of American College of Cardiology 2007; 49(6):631-42.
2. Lars Ryden. Managing cardiovascular risk in patients with diabetes: Heart 2000; 84 (suppl I):123-25.
3. Amy Stancoven, Darren K. McGuire. Preventing Macrovascular Complications in Type 2 diabetes Mellitus: Glucose control and beyond: The American Journal Cardiology 2007 June 4; 99 (IIA):5-11.
4. D J Fraser, A O Phillips: MEDICINE 35:9 Diabetic nephropathy.
5. Roya Babaei-Jadidi, Nikolaos Karachalias: Prevention of Incipient Diabetic Nephropathy by High-Dose Thiamine and Benfotiamine. Diabetes, VOL. 52, AUGUST 2003.
6. Gorge I. Gross, Mirela j. de Azevedo, sandra P. Silveiro. Diabetic Nephropathy: Diagnosis, Prevention, and Treatment:Diabetes care, January 2005. Volume 28, number 1.
7. D. J Fraser, A. O Phillips. Diabetic nephropathy: medicine 35:9.2007.
8. Ruggenenti P, Fassi A, Ilieva AP, et al. Preventing microalbuminuria in type 2 diabetes: *N Engl J Med* 2004; **351:** 1941–51.
9. Pecoraro RE, Chen MS: Ascorbic acid metabolism in diabetes mellitus: *Ann N Y Acad Sci* 498:248–258, 1987.
10. Cunningham JJ, Ellis SL, McVeigh KL, Levine RE, Calles-Escandon J: Reduced mononuclear leukocyte ascorbic acid content in adults with insulin-dependent diabetes mellitus consuming adequate dietary vitamin C. *Metabolism* 40:146 – 149, 1991.
11. Maxwell SR, Thomason H, Sandler D, Leguen C, Baxter MA, Thorpe GH, Jones AF, Barnett AH: Antioxidant status in patients with uncomplicated insulin-dependent and non-insulin-dependent diabetes mellitus. *Eur J Clin Invest* 27:484–490, 1997.
12. Sundaram RK, Bhaskar A, Vijayalingam S, Viswanathan M, Mohan R, Shanmugasundaram KR: Antioxidant status and lipid peroxidation in type II diabetes mellitus with and without complications. *Clin Sci* (*Lond*) 90:255–260, 1996.
13. Kakkar R, Mantha SV, Radhi J, Prasad K, Kalra J: Antioxidant defense system in diabetic kidney: a time course study. *Life Sci* 60:667– 679, 1997.
14. Joshua A. Beckman, Allison B. Goldfine, Mary Beth Gordon, Leslie A. Garrett, John F. Keaney, Jr., and Mark A. Creager. Oral antioxidant therapy improves endothelial function in Type 1 but not Type 2 diabetes mellitus.