Research Article

A Clinical Study on the Effect of Telmisartan with Alpha Lipoic Acid on Microalbuminuria in Type 2 Diabetes and Hypertensive Patients

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ABSTRACT

Microalbuminuria, the clinical indicator of structural and physiological insult to kidneys, is not an uncommon presentation in chronic hypertensive patients. This six months Prospective Cohort study was conducted in the Department of General Medicine, Vivekanandha Medical Care Hospital. Totally, 272 patients with type 2 diabetes mellitus and hypertension were screened for microalbuminuria, out of which 66 patients were recruited for the study groups. Group I (Telmisartan 40 mg) included 31 patients and Group II (Telmisartan 40mg + Alpha Lipoic Acid 600mg) included 35 patients. The prevalence of microalbuminuria in patients with Type 2 Diabetes Mellitus and hypertension was 24.3%. Highest occurrence of microalbuminuria was found in the age group of 61-70 years (31.8%) and the prevalence was found to be higher in males (69.7%) when compared to females (30.3%). In patients with duration of disease more than 20 years, the prevalence of microalbuminuria was 33.33%. Compared to baseline, the urinary albumin excretion significantly decreased in Telmisartan + Alpha Lipoic Acid group (12.86 ± 0.07) than in Telmisartan group (6.19 ± 0.32). Alpha Lipoic Acid may reduce urinary albumin levels when given as an adjunct therapy with Telmisartan in microalbuminuria patients with type 2 diabetes mellitus and hypertension.

Keywords: Alpha lipoic acid, telmisartan, microalbuminuria, albumin.

INTRODUCTION

Renal injury is strongly linked to the presence of microalbuminuria (defined as urinary albumin excretion 30 - 300 mg/day, or 20-200 µg/min)[1]. Microalbuminuria is caused by glomerular capillary injury and so may be a marker for diffuse endothelial dysfunction. Microalbuminuria is a marker of poor renal outcomes in patients with type 2 diabetes and in essential hypertension. The incidence of type 2 diabetes mellitus is increasing worldwide, and is now one of the leading causes of end-stage renal disease[2]. In type 2 diabetes mellitus, microalbuminuria is quite common (20% to 25% of patients) in both newly diagnosed patients and patients with established diabetes.

The American Diabetes Association recommends the use of ARBs as the first line agents in the treatment of nephropathy in patients with type 2 diabetes. A number of studies using ACE-Is and ARBs have been conducted with primary endpoints of decreasing proteinuria, slowing kidney disease progression, and decreasing morbidity and mortality. Several studies have evaluated the effects of using an ACE-I and ARB in combination. These studies have shown that ACE-Is plus ARBs have a synergistic effect on proteinuria[3].

Alpha lipoic acid (ALA), also known as thioctic acid (TA), is a naturally occurring substance, acting as both biological antioxidants and metal chelators[4]. Apart from the antioxidant properties of ALA, it is found to increase nitric oxide synthesis through which endothelial function is probably improved. In addition, ALA reduces body weight[5] and changes other anthropometric indices by suppressing appetite and increasing metabolism. Some studies reported as there was significant reduction in FBS, body weight, BMI, waist circumference, blood pressure, carbohydrate, protein, fat, and energy intake[6].

Alpha lipoic acid when taken with drugs that lower blood sugar levels, may increase the risk of hypoglycaemia. Therefore, dose adjustment may be needed in those patients. Levothyroxine – Alpha lipoic acid may lower levels of thyroid hormone. Hence blood hormone levels and thyroid function should be monitored closely[7].

Past studies on diabetes in patients with hypertension indicate that the prevalence of microalbuminuria in hypertensive patients is common in later stages of the pathological state. Many studies have been performed on telmisartan for the reno-protective and cardio-protective effect. Latest studies on alpha lipoic acid warrants its efficacy in lipid peroxidation, insulin sensitivity, lipid metabolism, type 2 diabetes and microalbuminuria co-morbid condition, nerve conduction velocity, and progression of vascular diseases.

Microalbuminuria is a clinical hallmark of diabetic nephropathy[8]. A proper control and reduction of urine albumin can prevent further kidney damage. So identifying the drug therapy to reduce or restrict urinary albumin excretion is beneficial. This study is conducted in an attempt to reduce or restrict urinary albumin excretion in type 2 diabetes mellitus with hypertension as one of the co-morbidities.

Alpha lipoic acid is used as an adjunctive therapy with Telmisartan in the aforesaid patient groups in this study. If the results showed a reduction in urine albumin levels, Alpha lipoic acid can be recommended as an adjunct or supplement for type 2 diabetes patients with hypertension and microalbuminuria.

The study intends to assess the effect of telmisartan and alpha lipoic acid together on microalbuminuria in type 2 diabetes mellitus and hypertensive patients. Prevalence of microalbuminuria in these patient groups and urine albumin levels were measured prospectively as the core process of this cohort study.

METHODOLOGY

Study Design: Prospective Observational Study

Study Centre: Department of General Medicine, Vivekanandha medical care hospital, Tiruchengode.

Ethical Clearance: The proposed study was approved by the Institutional Ethics Committee (CDSCO APPROVAL: ECR/908/Inst/TN/2017) of Vivekanandha medical care hospital (Ref no. SVCP/IEC/JAN/2017/02, dated 24-02-2017).

Study Duration: January 2017 to June 2017

Sample Population: Total of 272 patients were screened for the study, out of which 66 patients were enrolled for the study after getting the informed patient consent. The required data were collected in a specially designed data entry form. The study population was grouped in to two, in which Group 1 had 31 patients and Group 2 had 35 patients.

Group 1 (31 patients): Telmisartan 40 mg (od, po)

Group 2 (35 patients)*:* Telmisartan 40 mg + Alpha Lipoic Acid 600 mg (od, po).

Study Criteria:

Inclusion Criteria:

- ✓ Patients with Type 2 Diabetes Mellitus and Hypertension.
- ✓ Patients on Telmisartan therapy.
- ✓ Both male and female patients.
- ✓ Patients in the age group of 20-80 years.

Exclusion Criteria:

- ✓ Patients with serum creatinine level of > 2.0 mg/dl.
- ✓ Patients with urine albumin ranging < 30 mg/L and > 300 mg /L.
- ✓ GFR below 60 ml / min
- ✓ Patients with hepatic impairment.
- ✓ Psychiatric patients
- ✓ Patients who are not willing or unable to give consent to participate in the study.
- ✓ Pregnant and lactating women

Study Method

Patients were enrolled in the study based on inclusion and exclusion criteria. The required data were collected from the patient using a data entry form which consists of the following details: name, age, sex, OP no, reason for admission, past medical history, past medication history, family history, social history, temperature, blood pressure, respiratory rate, heart rate, urine analysis, diagnosis and therapeutic chart containing dosage regimen and route of administration.

Totally, 272 patients were screened for microalbuminuria, who had type 2 diabetes mellitus and hypertension, by measuring their urine albumin level by performing Urine Dipstick test. 66 patients were diagnosed with microalbuminuria and were included in the study groups. The study population (66 patients) was grouped into two. In which Group 1 had 31 patients and Group 2 had 35 patients.

Quantitative estimation of urine albumin levels in patients with type 2 diabetes mellitus and hypertension was done by using Nycocard® during the first visit (baseline) and at the end of 4 months (endpoint). The effect of Alpha lipoic acid was measured by comparing the baseline and endpoint of the study groups.

Statistical Analysis

Statistical analysis of the collected data was done using one-tailed unpaired t test. GraphPad Instat v 3.10 was used to perform all statistical calculations. Arithmetic mean ± Standard deviation for all entries was calculated. Prevalence and mean difference were calculated using mathematical procedures. Statistical representations were given for all data to give a clear picture about the prevalence data.

RESULTS

A total of 272 patients who had type 2 diabetes mellitus and hypertension were screened for the study. Out of which, 66 patients were found to have microalbuminuria and the prevalence was found to be 24.3%. (Table 1, Figure 1). The prevalence of microalbuminuria based on the duration of disease course was found to the highest in more than 20 years (33.33%) of duration, followed by 17-20 years (31.81%) and others with lesser percentage in this study population.

Table 1: Prevalence and Distribution of Microalbuminuria in Diabetic and Hypertensive Patients

	Criterion	No. of Patients	Prevalence
Microalbuminuria	Case / Normal (nos.)	66 / 206	24.3%
	Male : Female (nos.)	46 / 20	69.7 : 30.3 %
	< 50 y : 50 y <	12 / 54	18.2 : 81.8 %
	< 60 y : 60 y <	32 / 34	48.5 : 51.5 %
	< 70 y : 70 y <	53 / 13	80.3 : 19.7 %
y – years; Total screened: 206; Total diagnosed: 66			

From the study population 31 patients were included in Group 1 (Telmisartan 40 mg) and 35 patients were included in Group 2 (Telmisartan 40 mg + Alpha Lipoic Acid 600 mg). Group 1 and Group 2 showed a baseline Urine Microalbumin of 78.67 ± 15.48 mg/L and 81.74 ± 16.14 mg/L, respectively. The endpoint in Group 1 was found to be 72.48 ± 15.80 mg/L and in Group 2 was 68.88 ± 16.21 mg/L (Table 2, Figure 2).

Table 2: Urine Microalbumin Levels in Diabetic and Hypertensive Patients

Study Groups	Urine Microalbumin levels Mean ± SD	
	Baseline (mg/L)	Endpoint (mg/L)
Group 1 - Telmisartan 40 mg	78.3 ± 10.38	72.12 ± 10.6*
Group 2 - Telmisartan 40 mg + Alpha lipoic acid 600mg	81.92 ± 13.71^{ns}	68.68 ± 13.76*
***SD** - Standard deviation*, * p < 0.05, ***ns** - not significant*		

The mean difference showed a greater reduction in urine albumin in Group 2 (12.86 ± 0.07 mg/L) when compared to Group 1 (6.19 ± 0.32 mg/L). The percentage reduction was 7.89 % in Group 1 and 16.16 % in Group 2 (Table 3, Figure 3).

Table 3: Reduction in Urine Microalbumin Levels in Diabetic and Hypertensive Patients

Study Groups	Mean Reduction of Urine Microalbumin (mg/L) Mean ± SD	% Reduction in urine microalbumin
Group 1 - Telmisartan 40 mg	6.182 ± 0.602	7.89
Group 2 - Telmisartan 40 mg + Alpha lipoic acid 600mg	13.242 ± 0.634*	16.16
***SD** - Standard deviation*, * p < 0.05		

DISCUSSION

Microalbuminuria represents the earliest clinical hallmark of diabetic nephropathy and is a marker of increased cardiovascular morbidity and mortality. Detection of microalbuminuria is important from the clinical stand point because its detection allows initiation of ACEIs and ARBs with the purpose of preventing or delaying the progression of diabetic nephropathy.

In this study the prevalence of microalbuminuria in type 2 diabetes mellitus patients having hypertension was found to be 24.3%. An earlier study reports that the prevalence was 24.2%[9]. Other studies report that the prevalence of microalbuminuria in type 2 diabetes were 27%[10] and 24%[11]. Overall, the prevalence of microalbuminuria in and around the study centre correlates well with the results of studies conducted in other parts of the world.

In the present study the prevalence of microalbuminuria was found to be higher in males (69.7%) when compared to females (30.3%). This is in accordance with an earlier study results where the prevalence of Microalbuminuria was found to be higher in male (76.9%) than in females (23.1%)[12]. The study also reported that the mean age of patients was 57.8 ± 14.7 years and average duration of diabetes was 9.2 years. Another study reported that the prevalence of microalbuminuria was found to be higher in females (58.7%) than in males (46.67%) [13].

The present study showed that for duration of diabetes <5, 6-8, 9-12, 13-16, 17- 20 and >20 years, the prevalence was found to be 0%, 3.03%, 7.57%, 24.24%, 38.81%, 33.33% respectively. According to an earlier study, the prevalence of microalbuminuria was found to be 36.3% and had increased with the duration of diabetes and also reported the prevalence of microalbuminuria in relation to duration of diabetes[14]. For duration of diabetes <5, 6-10, 11-15, 16-20 and >20 prevalence was found to be 30.4%, 38.1%, 49.7%, 50%, 46.7% respectively. This data differs considerably from that of the present study.

A previous study reported that the prevalence of 24.8% in 246 type 2 diabetes patients were the average duration of diabetes was 9 years among patients with microalbuminuria. Study also showed that hypertension, duration of diabetes, elevated blood glucose levels were found to be the risk factors[15].

The current study results showed that baseline urinary albumin excretion in telmisartan group was 78.67 ± 15.48 mg/L and the end point was 72.48 ± 15.80 mg/L. The reduction was low and statistically not significant. But in Telmisartan + Alpha lipoic acid group baseline was found to be 81.74 + 16.14 mg/L and the end point was 66.88 + 16.21 mg/L. In this group the reduction was found to be statistically significant due to antioxidant effect of alpha lipoic acid. This is in accordance with an earlier study [16], where twenty-four hour urinary protein excretion was found to be decreased in ARB + ALA group and study concluded that renal function was reserved well in ARB +

ALA group compared to others which prevents the further worsening of diabetic nephropathy. But the ARB used in the study was not mentioned.

The results of this study showed that microalbuminuria is an important factor for progression of nephropathy in type 2 diabetes mellitus and hypertensive patients. In this study the demography showed a 25 % prevalence of microalbuminuria in diabetes and hypertensive patients, which states that blood glucose and hypertension were not well controlled in those patients. So, diabetes mellitus and hypertensive patients should be monitored regularly for proper control of those two co-morbidities. The study results showed a higher occurrence of microalbuminuria in the male population. Better patient awareness on nephropathy and its outcome was necessary for better prognosis of the disease. The data said that the prevalence of microalbuminuria increases with age and disease progression. The prognosis of the disease depends upon blood pressure control, blood sugar control, and food and lifestyle modifications.

In the two study groups, there was a reduction in urine microalbumin. But the reduction was much higher in the telmisartan with alpha lipoic acid group, which shows that alpha lipoic acid has a considerable effect on microalbuminuria. Further, no ADRs and unwanted therapeutic outcomes were encountered during the study period. Hence, usage of alpha lipoic acid in diabetes and hypertensive patients can be recommended to control microalbuminuria.

CONCLUSION

Alpha lipoic acid is a powerful antioxidant currently used in many degenerative diseases[17]. Since, the current study offers support to the capacity of ALA in reducing microalbuminuria, it seems to have positive effects over other renal function parameters. Further studies on oral alpha lipoic acid therapy are necessary to confirm the indications of the same in various aspects of renal function. By this, ALA can be used to avoid further deterioration of kidney structures and function, so as to extend the life span and improve the quality of life of the patients.

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