Effectiveness of Valsartan in Obese Versus Non-Obese Type 2 Diabetic patients presented with microalbuminuria

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ABSTRACT

Aim: To ascertain efficacy of Valsartan, an angiotensin receptor blocker (ARB) in reducing microalbuminuria in obese versus non obese patients.

Methods: This comparative study was done in Department of Nephrology Pakistan Institute of Medical Sciences Islamabad from July 1, 2018 to December 31, 2018. Patients fulfilling selection criteria were enrolled and categorized as two groups obese & non-obese; both groups were given valsartan. Urine ACR and serum creatinine was followed every month for 6 months.

Results: Average age of all cases as 52.06 ± 4.11 years while the mean age in obese and non-obese cases was 52.48 ± 4.25 years and 51.63 ± 3.95 years, respectively. The mean change in Urine ACR (from baseline to 6th months) in obese cases was 41.76 ± 25.81 and non-obese cases was 76.05 ± 7.63, p-value <0.001. In obese cases mean urine ACR at 1th and 2nd month was same from baseline, p-value > 0.05 while at 3th, 4th month was statistically lower as compare to baseline urine ACR, p-value < 0.05. Moreover, in non-obese cases the mean urine ACR was statistically decreased at 1st, 2nd, 3rd, 4th, 5th and 6th month when compared with baseline, p-value < 0.001. At 4th month in obese cases none of the cases achieved ACR < 30 while in non-obese cases 4(7.4%) cases achieved ACR < 30 with significantly higher frequency in non-obese cases, p-value < 0.05. At 4th month in obese cases 12(22.2%) cases achieved ACR < 30 while in non-obese cases 31(57.4%) cases achieved ACR < 30 with significantly higher frequency in non-obese cases, p-value < 0.001. Moreover, in non-obese cases the mean urine ACR was statistically decreased at 1st, 2nd, 3rd, 4th, 5th and 6th month when compared with baseline, p-value < 0.001. At 4th month in obese cases none of the cases achieved ACR < 30 while in non-obese cases 4(7.4%) cases achieved ACR < 30 with significantly higher frequency in non-obese cases, p-value < 0.05. At 4th month in obese cases 12(22.2%) cases achieved ACR < 30 while in non-obese cases 31(57.4%) cases achieved ACR < 30 with significantly higher frequency in non-obese cases, p-value < 0.001.

Conclusion: Valsartan is more effective in reducing microalbuminuria in non-obese patients as compared to obese patients.

Keywords: Diabetes mellitus, obesity, microalbuminuria, Valsartan

INTRODUCTION

Diabetes is defined as metabolic disorders with hyperglycemia due to inability of body for proper secretion of insulin, action of insulin, or can involve both. The condition of chronic hyperglycemia associated with diabetes is related to damage that is long-term dysfunction, and organs failure, involving eyes, nerves, kidneys, blood vessels, heart.1 Because of the aging population and an increase in obesity and sedentary lifestyle, the prevalence of DM2 is growing, particularly in Asia. Economically, diabetes type 2 burden related to obesity is generally underestimated involving factors like literacy and social-economic status. Asians have higher pre disposition for resistance to insulin at somewhat obesity of lesser degree and pronounces dysfunction in early insulin secretion2,3,5. According to strong evidence antihypertensive agents targeting RAS can slow down renal disease progression and give cardioprotection for Type 2 Diabetes patients and microalbuminuria5. Angiotensin II receptor blocker (ARB) can be used as an alternate of ACE inhibitor if one is not able to bear certain side effects of an ACE inhibitor, e.g., it can cause an irritating cough6,7. In ARB literature it is found that, Conversion of microalbuminuria to normoalbuminuria was 12.5-29%9,10. Microalbuminuria represents elevation of excretion of urinary albumin on subclinical level. It is associated with excretion rate for albumin as 30 to 300mg/day or ratio of albumin-creatinine (mg/gm) of 25-250 for males & 35-250 for females9. The presence of microalbuminuria leads to renal disease worsening and also diabetic nephropathy with CVDs. Almost 30% DM2 patients suffer urine albumin level as abnormally high; almost 75% among those patients suffer microalbuminuria & almost 25% suffer overt diabetic nephropathy11.

Microalbuminuria is directly related to CVD diseases and renal failure. Patients suffering with DM2 and hypertension, reduction in serum albumin level is noted2. Rationale of this study is to study the outcome of ARB (Valsartan) in obese versus non-obese diabetic type 2 patients suffering with microalbuminuria. This study evaluated the role of valsartan in obese type 2 diabetic patient in reduction of microalbuminuria compared to non obese type 2 diabetic patients and thus its long term renoprotective effects.

MATERIAL AND METHODS

After approval from Institutional Ethical Review Board this comparative study was conducted at the Department of Nephrology PIMS Islamabad from July 1, 2018 to December 31, 2018. Patients were enrolled by following selection criteria;

Inclusion Criteria: Patients of both gender with age ≥ 40 years having type 2 DM with microalbuminuria and good blood pressure control of <140/90 mmHg (with or without use of drugs), CKD upto stage 3 with HbA1c up to 7% was included.

Exclusion Criteria: Patients having CKD stage 4, above, HbA1c > 7% were excluded. Microalbuminuria was defined as Urine ACR of 30-300mg/g, with at least 2 of 3 measurments over 2-3 months. Then patients were divided into two groups depending upon BMI; obese (BMI ≥50) and non-obese(BMI<29.9). Both groups were given valtsartan. Urine Albumin creatinine ratio (ACR) and Serum creatinine was followed every month for 6 months.

The collected data was entered and analyzed through SPSS version 25. Quantitative variables like age, creatinine level was presented in form of mean ± S.D. Qualitative variables like gender, doubling of creatinine level, ESRD and mortality was presented in form of frequency and percentage. Independent sample t-test was applied to compare proteinuria between obese and non-obese patients. P-values0.05 was taken as significant.
RESULTS

The mean age of all cases was 52.06±4.11 years while the mean age in obese and non-obese cases was 52.48±4.25 years and 51.63±3.95 years respectively. In this study there was equal male to female ratio i.e. 50% male and female in either group.

eGFR in both groups: The mean eGFR at 0 day in obese cases was 81 ± 13.9 and in non-obese was 90±16.4, p-value = 0.058. At 6th month the mean eGFR in obese cases was 67 ± 10.2 and in non-obese cases was 84±15.5, p-value <0.05. The mean eGFR in non-obese cases was statistically higher as compared to obese cases after treatment, p-value < 0.05. The mean Change (from baseline to 6th months) in eGFR in obese and non-obese cases, however, was 14±20.0 and 6±30 respectively, p-value = 0.07 which was not significant.

Urine ACR in both groups: At 0 day the mean urine ACR in obese cases was 113.54 ± 13.82 and in non-obese cases was 112.33 ± 12.40, p-value = 0.635. At 1st month of treatment, the mean urine ACR in obese cases was 112.97±32.73 and in non-obese was 81.48 ± 16.75, p-value < 0.001. The mean urine ACR at 2nd month in obese cases was 105.13±33.59 and non-obese cases was 69.43±18.71, p-value <0.001. At 3rd month the mean urine ACR in obese cases was 96.34±35.45 and in non-obese cases was 57.70±19.10, p-value < 0.001. At 4th month the mean urine ACR in obese and non-obese cases was 87.56 ± 36.78 and 47.00 ± 18.74 respectively, p-value < 0.001. At 5th month the mean urine ACR in obese cases was 87.04 ± 40.27 and in non-obese cases was 36.81 ± 18.28, p-value < 0.001. At 6th month the mean urine ACR in obese cases was 76.05 ± 7.63 and in non-obese cases 54.36 ± 20.03, p-value < 0.001. The mean urine ACR in non-obese cases was significantly lower as compared to obese cases at each follow up, p-value < 0.05. The mean change in Urine ACR (from baseline to 6th months) in obese cases was 41.76 ± 25.81 and non-obese cases was 76.05 ± 7.63, p-value <0.001. Results are shown in Figure I and Table I.

Fig I: Comparison of urine ACR in both groups at each month of follow up

<table>
<thead>
<tr>
<th>ACR &lt; 30 at 6th months</th>
<th>BMI</th>
<th>Non-obese</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Obese</td>
<td>20</td>
<td>37.0%</td>
</tr>
<tr>
<td></td>
<td>Non-obese</td>
<td>41</td>
<td>75.9%</td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>63.0%</td>
<td>24.1%</td>
</tr>
</tbody>
</table>
diabetes as well as microalbuminuria. Significantly high reduction of 25% was seen in rates of albumin excretion at week 5 after 50 mg dose of losartan and up to 34% was seen in coming 5 weeks at a dosage of 100mg\textsuperscript{22}. Another study found higher percentage change in urea as found by Zandbergen et al., 2003 (cited above) as they reported UAER to be 56% after 24 weeks (95\%CI, 49.6 - 63.0) with valsartan and 92\% with amiodopine (95\%CI, 81.7 - 103.7), hence reporting a statistically significant between group effect (P<0.001), whereas, it was seen that valsartan had the same reduction in the levels of UAER among the two groups i.e. normotensive and hypertensive. Also normoalbuminuria became common after giving valsartan (29.9\% vs. 14.5\% and P=0.001)\textsuperscript{23}.

Another study concluded that for same reduction of BP and achieved levels of BP, among the patients of diabetes and microalbuminuria including normotensive patients, UAER was most effectively reduced by valsartan which lowered UAER more effectively than compared to amiodopine. Moreover, another study assessed the impact of angiotensin II receptor antagonist irbesartan among patients having hypertension as well as diabetes 2 with microalbuminuria. In their study, 10 among the 194 individuals in the 300mg category making 5.2\% and 19 individuals among the 195 individuals from 150mg category making up 9.7\% achieved primary end point, vs. 30 among 201 individuals from placebo category making up 14.9\% (p-value<0.001 and p-value=0.08 for respective groups)\textsuperscript{24}.

CONCLUSION
Valsartan is more effective in reducing microalbuminuria in non-obese patients as compared to obese patients. However, it is useful even in obese diabetic type 2 patients suffering from microalbuminuria as well as non-obese type 2 diabetics.

Conflict of interests: None

REFERENCES