Study of Comparative Evaluation of Atorvastatin and Salicinol (Salacia Roxburghii) on GFR and Carotid Intima Media Thickness in Diabetic and Nondiabetic CKD Patients with Hypertension

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DOI: 10.29322/IJSRP.9.06.2019.p90131
http://dx.doi.org/10.29322/IJSRP.9.06.2019.p90131

Abstract- Background: Most of the newer concepts in Nephrology developed in the 19th and 20th century. Progression of renal failure is an area of Nephrology where our understanding has improved appreciably in the last century but still our knowledge is like a drop in ocean. We have ample of evidence that progression of renal failure can be slowed down but we still need more definite information whether established renal failure can be reversed. This pilot clinical study was planned to explore the therapeutic potential of salicinol in retardation of chronic kidney disease progression and anti-atherosclerotic property by looking for if reduction in CIMT is possible.

OBJECTIVES: To study of comparative evaluation of atorvastatin and salicinol (salacia roxburghii) on GFR and CIMT in diabetic and nondiabetic CKD patients with hypertension

METHODS: The present study was conducted in the Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Eighty patients of mild to moderate stable chronic renal failure with hypertension attending Nephrology OPD or admitted in Nephrology ward from May 2014 to June 2015 were included in the study. Patient with acute MI, congestive heart failure, unstable angina, myopathy. Subsequently patients were allocated to one of the two groups, the first group consisted of Diabetic patient treated with atorvastatin salicinol and second group was of nondiabetic treated patients.

RESULTS: Among total patients included in the study 35 were non diabetic and 45 were diabetic.

Mean serum creatinine at baseline study in diabetic & non-diabetic group were 4.3±2.0 & 5.0±1.6 & changes were statistically significant intra group. Mean CIMT in diabetic and non-diabetic at baseline were 0.92±0.07 and 0.90±0.07 and when comparing both changes were statistically significant at three month and six months suggesting CIMT regression more in diabetic group compared to non-diabetic. Mean GFR in diabetic and non-diabetic group at baseline were 23.4±15.6 and 17.8±13.7. On intergroup comparison changes were statistically significant at three month and at six month.

CONCLUSION: The male to female ratio was 2:1. Age of the patient ranged from 20yrs onward. No significant effect of the drug was seen on 24hrs urinary protein, blood pressure, hemoglobin & GFR. On comparison of non-diabetic and diabetic highly significant decrease (<0.001) in CIMT were observed at three months and at the end of study
This pilot clinical study was planned to explore the therapeutic potential of salicinol in retardation of chronic kidney disease progression and anti-atherosclerotic property by looking for if reduction in CIMT is possible.

In various experimental and clinical studies it has been demonstrated that salacia species containing salicinol has shown anti-inflammatory, Anti proteinuric and Hypolipidemic action with improvement in endothelial dysfunction. With these property the anti-inflammatory anti proteinuric and anti-atherosclerotic property of salicinol along with Adiponectin enhancing potential of salicinol has been evaluated in the present clinical trial.

The antidiabetic property of salacia species has been recognized since ancient time. The Ayurvedic practitioners of south India particularly Tamil Nadu and Kerala are using this plant for the treatment of diabetic complications like peripheral neuritis, diabetic gangrene.

The scientific evaluation on salacia species was conducted at BHU by Dubey et al (1993) and reported its antidiabetic property and its role in diabetic complications (Dubey 1994, Wani 2006, Singh 2007, Sharma 2007, Rajesh 2009).

The findings were confirmed in collaborative studies in 2005. The antidiabetic and anti-inflammatory activity of salacia was studied by Syed Ismail and Elango (1997) at the Tamil Nadu University. The aldose reductase and α-glucosidase inhibitory property were reported by Patricia et al (2005) and Yuhao Li (2004). But no worker could study the role of salacia species in the prevention and management of micro vascular complication in diabetes cases. Since it is an Indian Plant it was decided te evaluate other dimensions of salacia particularly in the management of microvascular complication including antidiabetic antiatherogenic, antioxidant and anti-inflammatory properties.

The pre-clinical and clinical studies were carried out with the view to prove the anti atherogenic hypolipedemic and anti-obesity properties of salacia species. Antioxidant properties were also determined

II. MATERIAL AND METHODS

The present study was conducted in the Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Eighty patients of mild to moderate stable chronic renal failure with hypertension attending Nephrology OPD or admitted in Nephrology ward from May 2011 to June 2012 were included in the study. Patient with acute MI, congestive heart failure, unstable angina, myopathy. Non-compliant patient & those patient taking medicines for their disease which is known to improve lipid profile (lipid lowering agent other than atorvastatin) were excluded from the study.

Initially patients were explained in detail about the experimental nature of the drugs and plan of study and only willing patient were included in the study after signing of the written consent. Before starting the drugs a through history was taken and clinical examination was done.

III. OBSERVATIONS

COMPARISON BETWEEN DIABETIC AND NON-DIABETIC (INTER GROUPS AND INTRA GROUPS)

Among total pt. included in the study 35 were non-diabetic and rest 45 were diabetic.

| TABLE 1: Comparison of Systolic Blood pressure between groups and within group on successive follow up |
|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
|                                | 0 month | 3 month | 6 month | 0 vs 3 | 0 vs 6 |
| Non Diabetic                   | 159±18  | 137±8   | 130±6   | 11.160  | 9.430  |
|                                |         |         |         | P<0.001 | P<0.001 |
| Diabetic                       | 169±19  | 140±8   | 129±5   | 15.395  | 16.375 |
|                                |         |         |         | P<0.001 | P<0.001 |
| t-value                        | -2.264  | -1.589  | 0.067   |         |         |
| p-value                        | 0.026   | 0.116   | 0.947   |         |         |

http://dx.doi.org/10.29322/IJSRP.9.06.2019.p90131
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Mean Systolic blood pressure & diastolic blood pressure in non-diabetic at baseline was 159±18 & 96±8 while in diabetic baseline SBP and DBP in 169±19 & 97±9 SBP & DBP changes on subsequent visit were statistically significant.

Table 3: Comparison of 24hr urine protein between groups and within group on successive follow up

<table>
<thead>
<tr>
<th>Group</th>
<th>24hr urine protein(Mean+SD)</th>
<th>Within the group comparison paired 't' test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 month</td>
<td>3 month</td>
</tr>
<tr>
<td>Non diabetic</td>
<td>0.954±1.101</td>
<td>0.854±0.882</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetic</td>
<td>1.776±1.446</td>
<td>0.966±0.990</td>
</tr>
<tr>
<td>t-value</td>
<td>-2.780</td>
<td>-2.231</td>
</tr>
<tr>
<td>p-value</td>
<td>0.007</td>
<td>0.029</td>
</tr>
</tbody>
</table>
Mean 24 hrs. urinary protein in non-diabetic & diabetic at baseline were 0.954±1.101 & 1.776±1.446 & were statistically significant on subsequent visit in diabetic group. On intergroup comparision, no statistically significant changes were found at the end of study.

Table 4: Comparison of Creatinine between groups and within group on successive follow up

<table>
<thead>
<tr>
<th>Group</th>
<th>Creatinine (Mean+SD)</th>
<th>Within the group comparison paired 't' test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 month</td>
<td>3 month</td>
</tr>
<tr>
<td>Non diabetic</td>
<td>5.0±1.6</td>
<td>5.6±1.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mean serum creatinine at baseline study were 5.0±1.6 & 4.4±2.0 in non-diabetic & diabetic group respectively. Changes were statistically significant at 6 months in non-diabetic group while at 3 & 6 months in diabetic group. On intergroup comparison, no statistically significant changes were found.

### Table 24: Comparison of CIMT between groups and within group on successive follow up

<table>
<thead>
<tr>
<th>Group</th>
<th>cimt (Mean+SD)</th>
<th>Within the group comparison paired 't' test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 month</td>
<td>3 month</td>
</tr>
<tr>
<td>Non-diabetic</td>
<td>0.90±0.07</td>
<td>0.77±0.06</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>diabetic</td>
<td>0.92±0.07</td>
<td>0.99±0.13</td>
</tr>
<tr>
<td></td>
<td>P=0.003</td>
<td></td>
</tr>
<tr>
<td>t-value</td>
<td>-1.044</td>
<td>-8.854</td>
</tr>
<tr>
<td>p-value</td>
<td>0.300</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean CIMT in non-diabetic & diabetic at baseline was 0.90±0.07 & 0.92±0.07 and it was statistically significant on subsequent visit in non-diabetic, while on intergroup comparison CIMT changes were statistically significant at 3 and 6 months.

### Table 25: Comparison of GFR between groups and within group on successive follow up

<table>
<thead>
<tr>
<th>Group</th>
<th>GFR (Mean+SD)</th>
<th>Within the group comparison paired 't' test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 month</td>
<td>3 month</td>
</tr>
<tr>
<td>Non-diabetic</td>
<td>17.8±13.7</td>
<td>14.6±7.9</td>
</tr>
<tr>
<td></td>
<td>P=0.191</td>
<td>P=0.093</td>
</tr>
<tr>
<td>diabetic</td>
<td>23.4±15.6</td>
<td>19.3±11.4</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>t-value</td>
<td>-1.657</td>
<td>-2.059</td>
</tr>
<tr>
<td>p-value</td>
<td>0.102</td>
<td>0.043</td>
</tr>
</tbody>
</table>
Mean GFR at baseline in non-diabetic & diabetic were 17.8±13.7 & 23.4±15.6 & was statistically significant at 3 and 6 months in diabetic and on intergroup comparison statistically significant changes found at three and six months.

**Discussion**

Due to rapid urbanization and industrialization, the incidence of diseases particularly Diabetes mellitus, Hypertension and CHD are increasing worldwide at an alarming rate. Due to remarkable risk profile of modern synthetic agents there is an urgent need to develop eco-friendly and bio-friendly plant-based products to replace synthetic chemicals since chronic disease is a lifelong process. India has a rich national heritage in the form of plant based remedies. These plants have shown pharmacological therapeutic potentials in the prevention and managements of various mental and physical diseases. It is pertinent to mention here that we have extensive experience based knowledge but we are lacking with evidence based scientific documentation required for global acceptance of these natural products. Recently World Health Organization has provided guidelines for validation of these plant origin products for its global acceptance.

There is an urgent need to focus new concepts and targets for the managements of chronic diseases. As in the present investigation, we are concentrating on the treatment modalities for
chronic kidney disease with hypertension with abnormal lipid profile.

Among 95 patients of chronic renal failure taken for study, Eighty patient of chronic renal failure with hypertension completed the six months follow-up and were finally included in the study. Group-I consisted of forty patients treated with Salicinol and Atorvastatin, Group-II consisted of forty patients treated with Atorvastatin only.

Age of patient ranged from 20 years onwards. Mean age of patient in various group were well matched & there was no significant statistical differences. Mean age of group-I was 53.9 yrs & Mean age of Group-II was 51.75. There was male preponderance in our patient. Overall 65% patients were male & 35% were female. In Group-I 62.3% patient were male while in Group-II 67.5% were male. The male predominance in our patient is probably a reflection of male dominance in the social structure of our society. We have a society where male children are more cared for and adult male is the bread earner of the family. So, probably male patient are brought for the treatment to the hospital more frequently.

On comparison of SBP & DBP in non-diabetic & diabetic group changes were not significant at the end of study.

on comparison of 24hrs urinary protein value changes In diabetic & non-diabetic were found to be insignificant at the end of study. Mean serum creatinine at baseline study in diabetic & non-diabetic group were 4.3±2.0 & 5.0±1.6 & changes were statistically significant intra group, but on intergroup comparison changes were insignificant suggesting probably no specific role of salicinol in diabetic group as for as renal impairment progression is related.

Mean CIMT in diabetic and non-diabetic at baseline were 0.92±0.07 and 0.90±0.07 and when comparing both changes were statistically significant at three month and six months suggesting CIMT regression more in diabetic group compared to non-diabetic.

Mean GFR in diabetic and non-diabetic group at baseline were 23.4±15.6 and 17.8±13.7. On intergroup comparison changes were statistically significant at three month and at six month.

Thus the beneficial effect of salicinol was observed and for further substantiating the finding by prospective study is recommended.

IV. SUMMARY AND CONCLUSION

Present study entitled "Study of Comparative evaluation of atorvastatin and salicinol (salacia Roxburghii) on GFR and carotid intima media thickness in patient of chronic kidney disease with hypertension" was conducted at the Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi between the period of May 2011 to June 2012.

Eighty patient of mild to moderate chronic renal failure were included in the study. Forty patient, each were randomized to two groups. Group-I were on Atorvastatin & Salicinol while Group-II were kept on Atorvastatin only. The salient features of this study are:

1. The male patients dominated over the female patients with a male to female ratio of 2:1.
2. Age of the patient ranged from 20yrs onward. Majority of the patient were above 40yrs of age.
3. Commonest symptom was weakness in all the groups followed by anorexia, swelling over body, pallor & sleep disorders.
4. No significant effect of the drug was seen on 24hrs urinary protein, blood pressure, hemoglobin & GFR.
10. On comparison of non-diabetic and diabetic significant decrease (<0.05) in GFR were observed at the end of study.
11. On comparison of non-diabetic and diabetic highly significant decrease (<0.001) in CIMT were observed at three months and at the end of study.

Thus on overall favorable effect of salicinol was seen with respect to decrease in serum creatinine & carotid intima media thickness. However in this study the follow-up period was only six months which is relatively a short period to assess the effect of salicinol on GFR & CIMT which has a natural course running into years. A large prospective study is recommended to further establish the findings of this study.

REFERENCES


AUTHORS
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