THE EFFECTS OF ACE-I AND ARB ON PERITONEAL ALBUMIN LOSS AND SERUM ALBUMIN LEVELS IN PERITONEAL DIALYSIS PATIENTS

Betül Öğütmen, M.D. / Serhan Tuğlular, M.D.
Emel Akoğlu, M.D. / Çetin Özener, M.D.

Sub-Department of Nephrology, Department of Internal Medicine, School of Medicine, Marmara University, Istanbul, Turkey.

ABSTRACT

Objective: Anti-proteinuric effects of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) have been established in various renal diseases. However, the effects of ACE-I and ARB on the permeability of peritoneal membrane are unknown and the effect of ACE-I and ARB use on peritoneal permeability in patients undergoing continuous ambulatory peritoneal dialysis has not been studied.

Methods: Fifty non-diabetic patients with high peritoneal permeability, who had been on a regular peritoneal dialysis (PD) treatment for at least one year, were included in the study. The patients were prospectively randomized either fosinopril 10 mg/day p.o (n=25) (group 1) or valsartan 80 mg/day p.o (n=25) (group 2) for 12 months. All patients received standard 35-cal/kg/day diets with 1.2-g/kg/day protein intake and strict salt restriction. All patients were on standard PD program (2 L; 1.36%, 4 exchanges/day). Annual mean serum albumin level, calculated from the monthly serum albumin level and peritoneal albumin values obtained from the dialysate after 8 hours, dwell on two occasions 6 months apart were measured twice yearly.

Results: A significant increase in the serum albumin values, (3.68±0.56 g/dl vs. 3.94±0.46 g/dl, p<0.0001) a significant decrease in peritoneal fluid albumin values (9.06±2.65 g/dl vs. 7.08±1.43 g/dl, p<0.01) were observed in the ACE-I group following the treatment. While no significant change (3.75±0.48 g/dl vs. 3.87±0.37 g/dl, p>0.05) was observed in the serum albumin values, a significant decrease (8.62±3.87 g/dl vs. 5.84±2.94 g/dl, p<0.01) was obtained in peritoneal fluid albumin values for the ARB group.

Conclusion: At the end of the study a significant decrease was observed in the peritoneal protein values for patients on ACE-I and ARB.

Key Words: Peritoneal dialysis, Angiotensin converting enzyme inhibitor, Angiotensin receptor blocker and albumin

INTRODUCTION

Abnormal excretion of protein in the urine has long been recognized as a marker of glomerular injury (1-3). Peritoneal protein leakage is the most common cause of functional transport abnormality from continuous ambulatory peritoneal dialysis (CAPD) in long-term
Betül Ögütmen, et al.

peritoneal dialysis. During CAPD, various morphological changes take place in the peritoneum, including mesothelial denudation, interstitial fibrosis, neovascularization, and vascular alterations. Angiotensin-II (ANG-II) plays a role in stimulating macrophages and fibroblast-like cells to secrete TGFβ-1. A perivascular/interstitial fibrosis, for instance, accompanies chronic elevation in either circulating ANG-II or aldosterone (4) and, in case of ANG II, occurs in response to abnormal vascular permeability and the escape of macromolecules (5). These effects of ANG II in CAPD patients can be prevented by the same method described above for clinical studies, and peritoneal protein loss may be reduced.

MATERIALS AND METHODS

High and high-average transporter patients who have been on regular CAPD treatment for at least one year, who have not used any non-diabetic, essential amino acid and whose level of blood pressure was between 140-160/90-100 mmHg and daily urinary output between 50-300 cc were included in this study. Patients were selected by an open randomized method. Twenty-five patients were selected for fosinopril 10 mg, and 25 for valsartan 80 mg treatment. Before treatment, annual mean peritoneal albumin values were obtained for those patients on a diet of 35 cl/kg/day; (45% carbohydrate, 20% fat, 30% protein) and Standard PD program (2 L; 4 exchanges/day). Among the patients who used their medications for one year, who had an infection with a CRP level above 5 mg/l, who were identified to have additional volume during the visits and who could not comply with their medication and diet, and those who had to leave the standard dialysis program were excluded from the study. At the end of a year, while 23 of the patients on fosinopril completed the study, only 13 of the patients on valsartan did so. Serum and peritoneal albumin values were obtained by the method of spectrophotometry.

Statistical analysis: GraphPad was prepared by the Prisma V.3 packet program. Besides, the descriptive statistical methods (means, standard deviations) used in analysing data, a separate t test was used for comparisons between groups, and a paired t test was used for repeating measures of the groups. The results were evaluated for the significance level of p<0.05 with a confidence interval of 95%.

RESULTS

Twenty-two patients from the ACE-I group and 13 patients from ARB group completed the study. Three patients from the ACE-I group were excluded from the study, two for lack of compliance and one because of a peritonitis attack. In ARB group, 12 patients were excluded from the study, 6 for lack of compliance, 1 for active pulmonery tuberculosis, 2 for peritonitis, 1 for dental infection, 1 for insufficient dialysis due to leakage and for instrumental peritoneal dialysis, 1 for continuing additional volume. Table I demonstrates age and Body Mass Index (BMI) for the remaining patients.

Table I: Age and BMI comparison of each group.

<table>
<thead>
<tr>
<th></th>
<th>ARB (n=13)</th>
<th>ACE (n=22)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.38±13.65</td>
<td>47.59±14.47</td>
<td>-</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>25.08±4.96</td>
<td>23.64±3.85</td>
<td>0.96</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

BMI: Body Mass index

While no significant changes (3.75±0.48 g/dl vs. 3.87±0.37 g/dl, p>0.05) were observed in the serum albumin values, a significant decrease (8.62±3.87 g/dl vs. 5.84±2.94 g/dl, p<0.01) was obtained in peritoneal albumin values in the ARB group. After treatment, a significant increase (3.68±0.56 g/dl vs. 3.94±0.46 g/dl, p<0.0001) in the serum albumin values and a significant decrease in the peritoneal albumin levels (9.06±2.65 g/dl vs. 7.08±1.43 g/dl, p<0.01) were observed in the ACE-I group. (Figs 1-2)

Fig. 1: Comparative values of serum albumin in both treatment groups before and after treatment.
Fig. 2: Comparative values of peritoneal albumin in both
treatment groups before and after treatment.

The rate of exchange between pre and post-
treatment serum albumin values in the ACE-I
group was significantly higher than in that of the
ARB group. In contrast, the rate of exchange
between pre and post-treatment peritoneal
albumin values in the ACE-I group was not
significantly different than that of the ARB group
(Table II).

Table II: Serum and peritoneal albumin exchange rates in
both treatment groups

<table>
<thead>
<tr>
<th></th>
<th>ARB (n=13)</th>
<th>ACE-I (n=22)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Albumin</td>
<td>3.13±6.33</td>
<td>7.34±5.31</td>
<td>-2.08</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Peritoneal Albumin</td>
<td>26.92±26.06</td>
<td>16.64±28.18</td>
<td>0.98</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

DISCUSSION

Remarkable antiproteinuric effects of ACE-I and
ARBs, leading agents in antihypertensive
treatment for the last century have been
demonstrated in various clinical and
experimental studies regardless of their blood
pressure lowering effects (3,6-10). These agents
have been used to prevent the vasoactive,
Proliferative, pro-oxidative, and permeative
pathophysiological effects of ANGII treatment
such as vasoconstriction, aldosteron release,
sodium retention, hypertrophy in renal mesengial
and tubulointerstitial cells, collagen
accumulation, cardiac hypertrophy in
Cardiomyocytes and fibroblast and cardiac
collagen accumulation, increased secretion by
endothelium, increased release of vasopressin,
facilitated sympathetic-adrenergic activation,
facilitated superoxide formation, increased level
of plasminogen activator inhibitor-1, and
accelerated gene expression (11,12).

A variety of morphological changes in the
peritoneal membrane develop by similar
mechanisms in patients undergoing peritoneal
dialysis and lead to increased membrane
permeability and thus to increased protein
leakage into the peritoneal fluid. This is an
unwanted situation for patients undergoing
CAPD. The present study was conducted based
on the idea that protein leakage of the peritoneal
membrane could be decreased by use of ACEI
and ARB regardless of their antihypertensive
effects. At the end of the study a significant
decreased was observe in the values for
peritoneal protein.

At the end of the study, a significant decrease
was observed in the peritoneal protein values in
patients on ACE-I and ARB. While there was a
significant increase in serum albumin values in
the ACE-I group, a respective increase in the
ARB group was not found to be significant. The
large numbers of dropouts in ARB group and
relatively smaller number of patients compared to
the ACE-I group were considered to be
responsible for this result.

In conclusion, ACE-I and ARB use in CAPD
patients led to decreased loss of albumin into
peritoneal fluid. The increase observed in the
values of serum albumin in the ARB group failed
to reach a significant level due to the decreased
number of patients in this group. These results
need to be supported by clinical and experimental
studies involving a large number of patients.

REFERENCES

pressure control, proteinuria, and the
progression of renal disease: the Modification
of Diet in Renal Disease Study. Ann Intern
Med 1995;123:754-762

2. Bidani AK, Griffin HA, Picken N, Lansky DM:
Continuous telemetric blood pressure
monitoring and glomerular injury in the rat
265:F391-F398

3. Gruppo Italiano Di Studi Epidemiologici in
Neurologia (GISEN): Randomized placebo-
controlled trial of effect of ramipril on decline


