Effects of Hemodialysis, Hemofiltration and Plasmapheresis on B2-Microglobulin in Patients With Chronic Renal Failure and Renal Transplant Recipients

KRONİKBÖBREK YETMEZIKIJ VE BÖBREK TRA NSP1A STA I TA RDA B2-MIKROC LOBUİAN DÜZEYINE HEMODFA LIZ, HEMOFIL IRASYON VIZ PIA?MA FEREZ'M ETKISI

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SUMMARY

P2-Microglobulin (#P2-M) is one of the major components of a new form of amyloid deposit found in carpal tunnel syndrome (CTS) and arthropathy of longterm hemodialysis patient. We studied serum P2-M levels in 31 patients who were dialysed with cuprophan dialyser (n:21) and hemofiltration (n:10). We also measured serum P2-M concentrations before and after plasmapheresis in 12 transplanted patients during rejection episodes. We observed that serum P2-M levels decreased during all of these procedures. There are little differences in respect to serum P2-M levels between HD and HF. But, plasmapheresis is more capable of lowering of serum P2-M levels than HD and HF.

KeyWords: P2-Microglobulin, Hemofiltration, Plasmapheresis

MATERIAL AND METHOD

Thirty one patients with chronic renal failure on maintenance hemodialysis were selected for this study. It has become evident that patients maintained by long-term dialysis may develop serious problem with joints and soft tissue (5). Recent studies have revealed that problem, especially carpal tunnel syndrome (CTS), is characterized by the deposition of amyloid in the ligaments, in the synovium of various joints and in bone (3-5). Gejyo et al demonstrated that a major component of the amyloid associated with chronic hemodialysis is a new form of amyloid fibril protein that a major component of the amyloid associated with chronic hemodialysis is a new form of amyloid fibril protein that is homologous to P2-Microglobulin (8). This observation underlined the importance of this protein for dialysis patients, since dialysis arthropathy is one of the severe and disabling complications of long term treatment with hemodialysis. We studied the blood levels of P2-M during hemodialysis, hemofiltration and plasmapheresis and compared the results.

Anlahtar Kelimeler: P2-Mikroglobulin, Hemodializ, Hemofilirasyon, Plazmaferez

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study. The determination of $P_2$-M was done in patient, treated regularly either by HD (n:21) and UF (n:10). The treatment, were done using dialysis monitors from Gambro (Gambro AK-10). Two kinds of dialysers were applied for hemodialysis; hollow fiber dialysers on 11 patients and plate dialysers on 10 patients. These dialysers had cuprophane membrane and the surface areas of plate dialysers and hollow fiber dialysers were 1.2 m$^2$ and 1 m$^2$ respectively. Hemofiltration was performed using Gambro HFM-10-1A monitors. All hemofilters (Gambro FH 7) had a polyamide membrane (surface area 1.4 m$^2$). Blood flows were maintained at about 250 ml/min during HD and 400 ml/min during HF.

Since plasmapheresis is capable of lowering the concentration of circulating antibodies and mediators of the vascular mechanism was used to treat steroid resistant rejections in renal allograft recipients. The rejections diagnosis was established on the basis of clinical signs and symptoms, laboratory investigations, radionuclide imaging technique and fine-needle aspiration biopsy. Plasmapheresis has been done on 12 renal transplant recipients with steroid resistant rejections episodes. The procedure was performed using plasma separator hollow fiber (Gambro fiber plasmafilter) which made of polypropylene. Three liters of plasma was exchanged and replaced with 1,5 mg/kg albumin and ringer’s lactate solution.

Blood samples for $P_2$-M determination were obtained before and after HD, HF and plasmapheresis sessions. All blood samples were centrifuged within one hour and the serum samples were stored at-20°C until processing. $P_2$-M in serum was measured with the "Enzygnost Beta2-Microglobulin" enzyme immunoassay (Behring AG). The principle of this procedure is as follows: if antigen exists in the sample, reaction of the antibody coated beated (solid phase) and enyme-labelled antibody with the specimen finally forms $P_2$-Microglobulin in the specimen sandwiched between complexes of the three. The complexes are then measured by photometric assay of the enzyme (using BIO-TEK INSTRUMENTS EL-307). Normal serum $P_2$-Microglobulin concentration by this method are 1,6 ±0,66 mg/dl.

The post-HD and post-HF serum $P_2$-M concentrations were corrected according to the changes in extracellular fluid volume. For this purpose, we used the formula; dividing uncorrected $P_2$ M by; 1.4-BW/0.2 BW₹ (2). BW represents the change in bodyweight during dialysis.

All results are expressed as mean ± SD. The significance was assessed by means of the student's $t$ test.

RESULTS

The serum $P_2$ M levels in different treatment groups are in Table 1. $P_2$-Microglobulin pre-treatment levels of patients with chronic renal failure were significantly elevated in all patient, to a mean of 16.74±11.24 (range: 4.4-40 mg/L). The serum concentrations at the beginning of the plate dialyscr, hollow fiber dialyser and hemofiltration were 17.82+11.72, 14.08+12.3, 16.12+10.08 mg/L respectively. The mean serum levels of $P_2$ M in renal transplant recipients with rejection crisis as 18.98 ± 11.96 mg/L before plasmapheresis.

Uncorrected mean serum levels after HF was 15.94±11.64 and after HD were 13.23 ±11.93 (plate dialyscr) and 15.67 + 10.07 (hollow fiber dialyscr) mg/L.

According to these results, posttreatment uncorrected $P_2$ M levels slightly decrease when compared with the pre-treatment levels. Correction of these serum levels for the change of the extra-cellular volume demonstrated more reduction than the before dialysis levels The decreases of approximately 26%, 19.2% and 26% were detected during hemofiltration, plate dialyscr and hollow fiber dilayser respectively (Figure 1,2,3). There are no significantly differences between these dialysis modalities. Since no change was observed in the extracellular volume during the plasmapheresis session, the post-treatment levels of $P_2$ M were not corrected. There was a significant reduction in the posttreatment levels. A decrease of 48% was detected during plasmapheresis (Figure 4).

Table 1. Scrum $P_2$ -M Levels in The Study Groups (mg/L)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Treatment</th>
<th>Posttreatment</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemofiltration (n:10)</td>
<td>17.82±11.72</td>
<td>13.26±10.42</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Plate Dialyser (n:10)</td>
<td>14.08±12.30</td>
<td>11.38 ± 11.50</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Hollow Fiber Dialyser (n:11)</td>
<td>16.12±10.08</td>
<td>12.02±7.10</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Plasmapheresis(n:12)</td>
<td>18.98±11.96</td>
<td>9.89±6.74</td>
<td>p&lt;0.05</td>
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</tbody>
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DISCUSSION

Recently, many authors have described the presence of amyloid-like deposits in synovia, bones and tendons of long-term hemodialysis patients (3-5). Gejyo et al. demonstrated that a major constituent of this material had almost a complete identity with p2 microglobulin (8). Elevated values have been found in patients with chronic renal failure (4) and it has been suggested that the high serum level of p2 -Microglobulin favours the development of amyloidosis (9). Hemodialysis with regenerated cellulose membranes (cuprophane) has been repeatedly shown to be associated with a rise in the

Figure 1. Serum concentrations of P2 M before and after III-
(n = 10)

Figure 2. Serum concentrations of P2M during plate dialyse

Figure 3. Serum concentrations of P>M during hollow fiber dialyser

Figure 4. Serum concentrations of P2 M during plas­mapheresis
p2 -Microglobulin plasma levels (7-12). However, these authors have not corrected their data for the change in distribution volume, as recently suggested by Bergstrom and Wehle (2).

Data concerning the kinetics of P2 M during hemofiltration and hemodialysis were reported by Floge and Kaiser et al (7-11). They observed a comparable decrease in the serum concentration and their data demonstrate that during HF a considerably higher amount of P2 M can be removed than during HD. But, there are still no data available which could indicate whether or not HF patients suffer to a lesser extent from amyloid like deposits than HD patients. In our study, we couldn’t demonstrate any significant differences between HD and HF treatment.

Several authors have reported a rise in serum P2 M levels in organ transplant recipients during rejection crisis (1-6). Our observation that serum P2 -Microglobulin levels increase during acute graft rejection. Since plasmapheresis is capable of lowering the concentration of circulating antibodies, it has been used as an adjunct to immunosuppressive therapy (10). We use this procedure in our center in the steroid resistant acute allograft rejections.

When we measured serum P2 M levels before and after plasmapheresis sessions, we observed that P2 M serum concentration significantly decreased (48%) after plasmapheresis.

In conclusion, our data has demonstrated that serum P2 M levels decrease during hemofiltration, hemodialysis and plasmapheresis. There are no differences between HF and HD for the eliminating of P2 M. We observed that P2 M is substantially eliminated by plasmapheresis. It is interesting to speculate if plasmapheresis could be used in the treatment of CTS, which is frequently encountered in hemodialysis patients.

Acknowledgements:

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LITERATURE


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