

Effects of Hemodialysis, Hemofiltration and Plasmapheresis on P₂-Microglobulin in Patients With Chronic Renal Failure and Renal Transplant Recipients

KRONİKBÖBREK YETMEZLİKİ VE BÖBREK TRA NSPIA NTLİ İİA STA İA RDA B2-MİKROGLOBULİN DÜZEYİNE HEMODİALİZ, HEMOFİLTRASYON VE PLAZMAFEREZİN ETKİSİ

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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 cuprophane 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

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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

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ÖZET

P₂-Mikroglobulin, uzun süre hemodializ tedavisi uygulanan hastalarda görülen kar/ml tünel sendromu ve artropatilerde toplanan amiloid özelliğindeki maddenin en önemli komponentidir. Biz hastanemizde cuprophan dializer ile hemodializ uygulanan 21 ve hemofiltrasyon uygulanan 10 hastamızın, ayrıca rejeksiyon episodü sırasında plazmaferez uyguladığımız 12 renal transplantlı hastamızın tedavi öncesi ve sonrası P₂-M düzeylerini ölçtük. Tüm bu işlemler sonrasında P₂-M düzeyinin azaldığını gözlemledik. Ancak bu azalmanın plazmaferez tedavisi sırasında, hemodializ ve hemofiltrasyona göre fazla olduğunu saptadık.

Anahtar Kelimeler: P₂-Mikroglobulin, Hemodializ, Hemofiltrasyon, Plazmaferez

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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.

MATERIAL AND METHOD

Thirty one patients with chronic renal failure on maintenance hemodialysis were selected for this

study. The determination of P₂ -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 m² and 1 m² respectively. Hemofiltration was performed using Gambro HFM-10-1A monitors. All hemofilters (Gambro FH 7) had a polyamide membrane (surface area 1,4 m²). Blood flows were maintained at about 250 ml/min during HD and 400 ml/min durin 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, radionuclerde 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 seperator 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 p₂ -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. p₂ -M in serum was measured with the "Enzygnost Beta₂-Microglobulin" enzyme immunoassay (Bchring AG). The principle of this procedure is as follows: if antigen exists in the sample, reaction of the antibody coated beated (solid phase) and ensymc-labelled antibody with the specimen finally forms (β₂-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 β₂-Microglobulin concentration by this method are 1,6 ± 0,66 mg/dl.

The post-HD and post-HF serum P₂ -M concentrations were corccted according to the changes in extracellular fluid volume. For this purpose, we

used the formula; dividing uncorrected P₂ M by; $1 - \frac{\Delta BW}{BW}$ (2). BW represents the change in bodyweight during dialysis.

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

RESULTS

The serum P₂ M levels in different treatment groups ae in Table 1. P₂ -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 dialyser, 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 p₂ 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 dialyser) and 15.67 ± 10.07 (hollow fiber dialyser) mg/L.

According to these results, posttreatment uncorrected p₂ 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 dialyser 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 P₂ 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. Serum P₂ -M Levels in The Study Groups (mg/L)

	Pre-Treatment	Posttreatment	P value
Hemofiltration (n:10)	17.82 ± 11.72	13.26 ± 10.42	p < 0.05
Plate Dialyser (n:10)	14.08 ± 12.30	11.38 ± 11.50	p < 0.05
Hollow Fiber Dialyser (n:11)	16.12 ± 10.08	12.02 ± 7.10	p < 0.05
Plasmapheresis (n:12)	18.98 ± 11.96	9.89 ± 6.74	p < 0.05

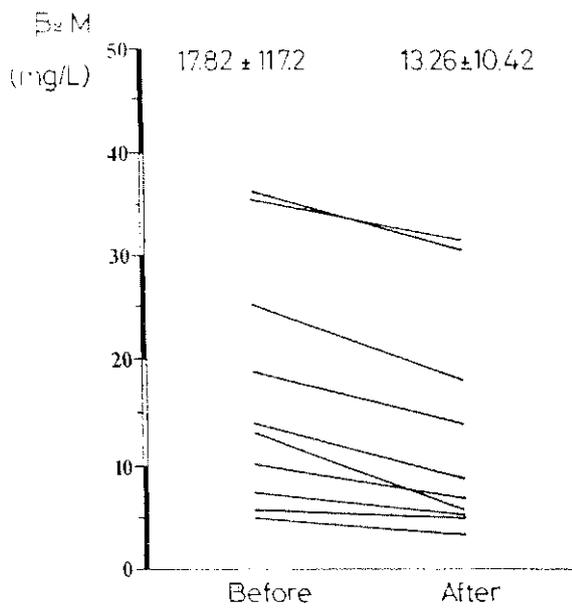


Figure 1. Serum concentrations of P₂ M before and after III- (n = 10)

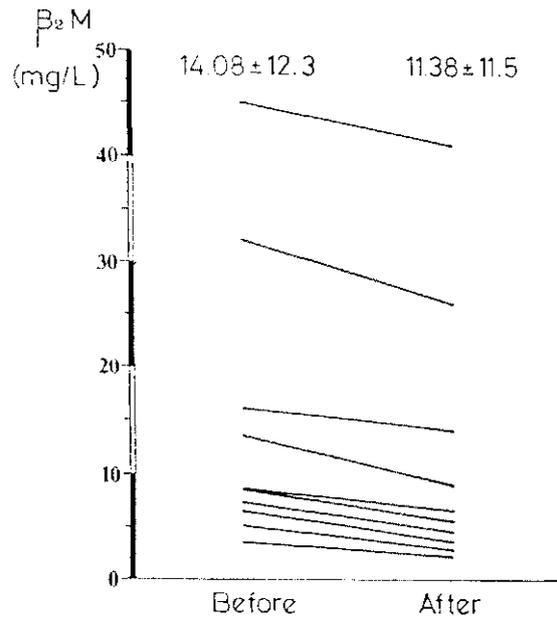


Figure 2. Serum concentrations of P₂M during plate dialyse

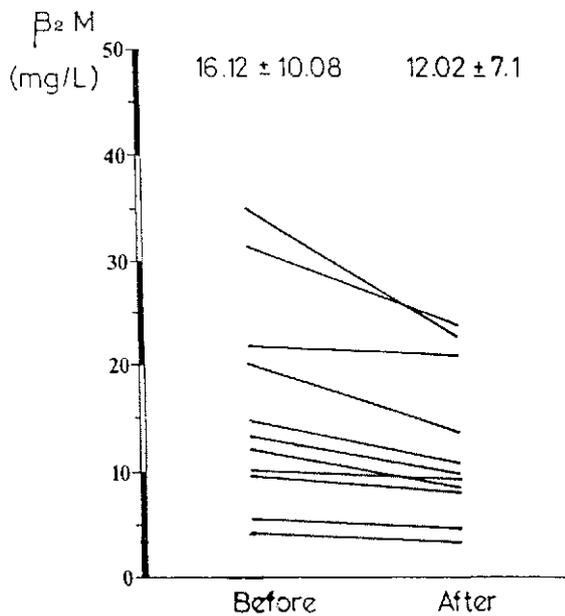


Figure 3. Serum concentrations of P₂ M during hollow fiber dialyser

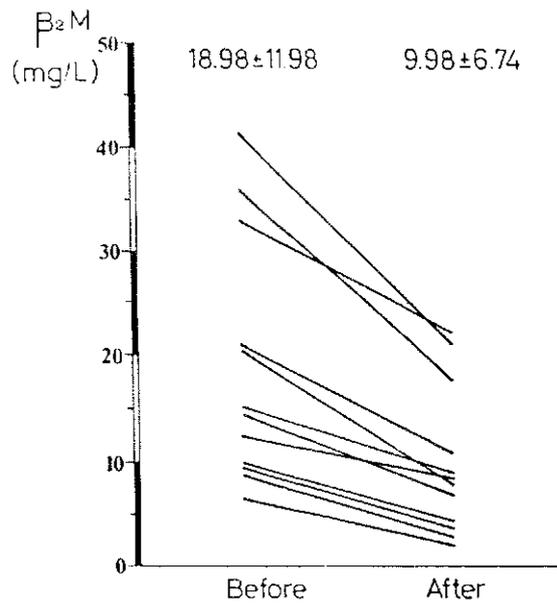


Figure 4. Serum concentrations of P₂ M during plasmapheresis

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 iden-

lity 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 cellululosic membranes (cuprophane) has been repeatedly shown to be associated with a rise in the

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 Flocq 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 depositions 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 elimination 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.

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