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Original scientific paper

Laboratory and Sonographic Findings in Dialyzed Patients with Bilateral Chronic Knee Pain versus Dialyzed Asymptomatic Patients

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A B S T R A C T

The aim of this study is to evaluate connection of plasma level of β2-microglobulin, C-reactive protein and uric acid as well as sonographic parameters like thickness of synovial membrane, thickness of femoral condylar cartilage and presence of joint effusion and Baker's cysts with bilateral knee pain in dialyzed patients, comparing them with parameters in asymptomatic dialyzed patients. Plasma levels of β2-microglobulin and C-reactive protein were significantly higher in symptomatic patients while uric acid level showed no difference among the groups. In symptomatic patients synovial membrane was thicker and in those patients there were more knee effusions and Baker's cysts. Thickness of femoral condylar cartilage showed no difference between groups. That suggests that inflammatory mechanisms developing from β2-microglobulin accumulation could be important factor in bilateral knee pain in dialyzed patients even in shorter duration dialysis.

***Key words**: β2-microglobulin, sonographic parameters, bilateral knee pain, dialysis*

Introduction

Dialysis related arthropathy with stiffness and motion reduction in shoulders and knees are associated with long term hemodialysis, over 10 years. Shoulders are predominantly involved[1,2], but important changes may be occurred in hip and knee, as well as in small carpal joints and spine. Presumptive changes are commonly associated with accumulation of fibrils of β2-microglobuline in bones and joints due to insufficient elimination during hemodialysis[2,3].

The knee joint changes are described as hypertrophy of synovial membrane, joint effusions and consecutive presence of Baker's cysts. That implicate the strong inflammatory component which can bee associated with goat and pseudogoat[4,5] and β2-microglobuline modified with advanced glycation and products as a major component in amyloid deposits around which monocytes and macrophages increase the secretion of interleukins as inflammatory mediators[6,7]. That would lead to cartilage and bone destructions as well as involvement of synovial membrane[8,9].

Patients with knee pain after dialysis duration shorter then 10 years and even asymptomatic patients may have some analogous morphologic joint changes[3].

The aim of this study is to evaluate connection of plasma level of β2-microglobulin, CRP and uric acid with bilateral knee pain in dialyzed patients. The morphologic parameters presumptively associated with previous laboratory findings will be evaluated in symptomatic and asymptomatic dialyzed patients.

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Materials and methods

Patients and variables

Real-time sonography of 76 knees of 38 patients receiving chronic haemodialysis was performed. Sixteen patients were suffering of bilateral chronic knee pain (5 females and 11 males, mean age 61,3) and twenty two were asymptomatic (8 females and 14 mails, mean age 52,6) without previous history of rheumatic disease. The 10 MHz transducer (Shimatzu SDU 1200) was used.

Thickness of synovial membrane in suprapatellar recess was measured.

Thickness of femoral condilar cartilage (medial, central and lateral) was measured according to Aisen's technique[10].

In each knee in flexion six measurements were taken just above of superior margin of patella (two medially, two centrally and two laterally). The mean value of each couple of results was calculated and the same procedure was repeated 2 cm above the patella. The mean values of measurements of those two main positions were calculated.

The presence of joint effusion and presence of Baker's cysts were evaluated.

Laboratory parameters (plasma level of β2-microglobulin, C-reactive protein (CRP) and uric acid) were performed.

Data analysis

The software package Statistica 6. was used.

To estimate statistical significant difference between numeric parameters t-test and Mann-Whitney test were used. Corelation between categoric variables between groups was estimated by χ^2 test.

Results

The mean duration of dialysis in symptomatic patients was 87.6 months and asymptomatic 73.4 months. There was no significant difference among groups (Table 1).

Plasma level of β2-microglobulin and CRP is significantly higher then in asymptomatic dialyzed. There was no significant difference between groups in plasma level of uric acid (Table 2).

The thickness of synovial membrane in suprapatellar recess in symptomatic patients was significantly higher then in asymptomatic patients (Table 3).

There was no significant difference between symptomatic and asymptomatic dialyzed patients in thickness of femoral cartilage (Figure 1) in all three positions (medial, central and lateral) (Table 4).

Joint effusion is found in significantly more knees in symptomatic then in asymptomatic dialyzed patients (χ^2=14.49, p≤0.001, Figure 2 and 3), as well as Baker's cysts (χ^2=13.69, p≤0.001, Figure 4 and 5).

TABLE 1
DURATION OF HEMODIALYSIS IN SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

		Sympthomatic N=16	Asymptomatic N=22	p
Hemodialysis duration (months)	X±SD	87.6±59.0	73.4±50.5	0.43
	median	65.5	54.0	
	in-max	24.1–195.0	17.0–124.0	

Mann Whitney

TABLE 2
PLASMA LEVEL OF β2-MICROGLOBULINE, CRP AND URIC ACID IN SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

		Sympthomatic N=16	Asymptomatic N=22	p
Arβ2-microglobuline (mg/L)	X±SD	32.4±13.0	22.7±8.07	<0.01
	median	32.5	20.1	
	min-max	14.1–68.2	8.1–41.6	
CRP (mg/L)	X±SD	27.7±17.9	13.9±7.37	<0.01
	median	22.5	11.5	
	min-max	7.0–76.0	4.0–35.0	
Uric acid (μmol/L)	X±SD	417.0±83.1	416.0±60.0	0.99
	median	429.0	404.0	
	min-max	250.0–540.0	308.0–508.0	

Mann Whitney

TABLE 3
THICKNESS OF SYNOVIAL MEMBRANE IN BOTH KNEES IN SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

		Symptomatic N=16	Asymptomatic N=22	p
Thickness of synovial membrane (left knee) (mm)	X±SD	4.20±0.64	3.57±0.28	<0.001
	median	4.0	3.6	
	min-max	3.30–5.30	3.0–4.20	
Thickness of synovial membrane right knee) (mm)	X±SD	4.35±0.76	3.65±0.36	<0.001
	median	4.10	3.60	
	min-max	3.40–5.70	3.10–4.80	

t-test

Discussion

There was no significant difference among symptomatic in asymptomatic patients concerning duration of hemodialysis. Asymptomatic patients had also important joint changes.

Connection of plasma level of the β2-microglobulin showed controversial results in previous reports. In the investigations of the dialysis arthropaty affecting shoulder Nagi and associates had found no connection between plasmatic level of β2-microglobuline and joint effusion, one of the important parameter of the painful shoulder in dialyzed patients[11].

Baldrati and associated found no connection between plasmatic level of β2-microglobuline in patients with dialyzed related amyloidosis and dialyzed patients without it. They even found no correlation between plasmatic level of β2-microglobulin and dialysis duration[12].

Sethi and associates had investigated different joints affected by dialysis arthropathy in patients receiving

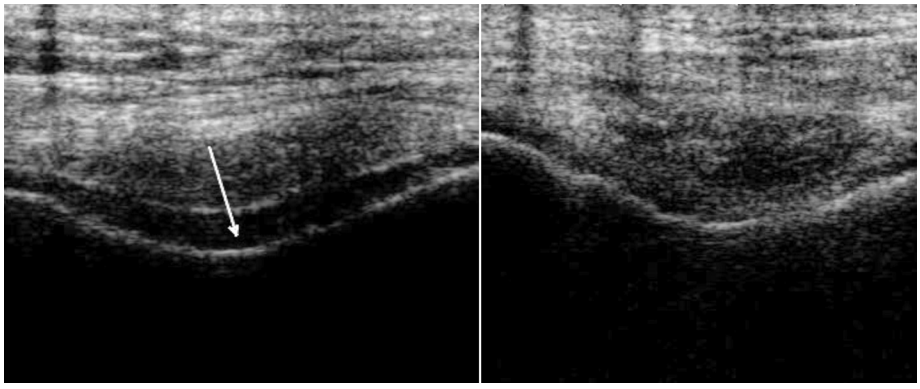

Fig. 1. Femoral condylar cartilage (white arrow). a) normal thickness, b) thin cartilage with irregular margins.

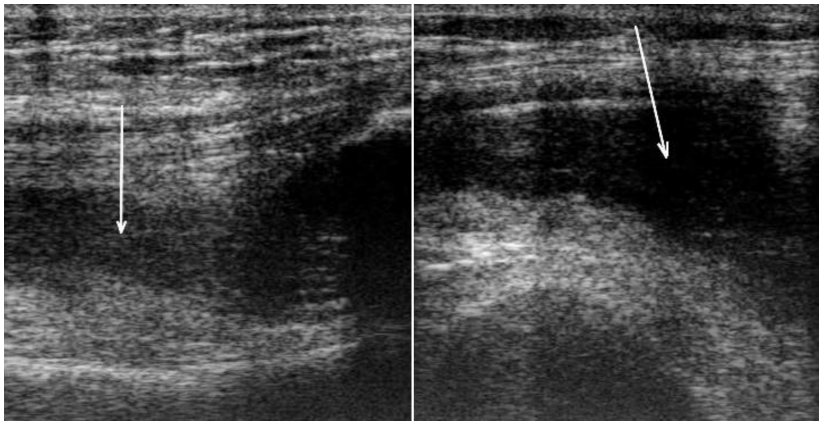

Fig. 2. Suprapatellar bursa effusion (white arrow). a) longitudinal view, b) transverse view.

TABLE 4
THICKNESS OF FEMORAL CONDYLAR CARTILAGE IN BOTH KNEES IN SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

		Symptomatic N=16	Asymptomatic N=22	p
Thickness of femoral condilar cartilage (lateral) (left knee)(mm)	X±SD	2.17±0.64	2.29±0.48	0.53
	median	2.0	2.3	
	min-max	1.4–3..5	1.5–3.3	
Thickness of femoral condylar cartilage (central) (left knee)(mm)	X±SD	2.26±0.63	2.46±0.41	0.24
	median	2.0	1.9	
	min-max	1.5–3.5	1.9–3.3	
Thickness of femoral condylar cartilage (medial) (left knee)(mm)	X±SD	2.17±0.55	2.15±0.26	0.88
	median	2.0	2.1	
	min-max	1.3–3.4	1.8–2.8	
Thickness of femoral condylar cartilage (lateral) (right knee)(mm)	X±SD	2.06±0.55	2.26±0.49	0.24
	median	2.0	2.0	
	min-max	1.2–3.0	1.5–3.6	
Thickness of femoral condylar cartilage (central) (right knee)(mm)	X±SD	2.33±0.46	2.52±0.40	0.17
	median	2.25	2.45	
	min-max	1.7–3.1	1.8–3.2	
Thickness of femoral condylar cartilage (medial) (right knee)(mm)	X±SD	2.09±0.52	2.21±0.34	0.41
	median	1.9	2.15	
	min-max	1.2–3.0	1.7–2.8	

t-test

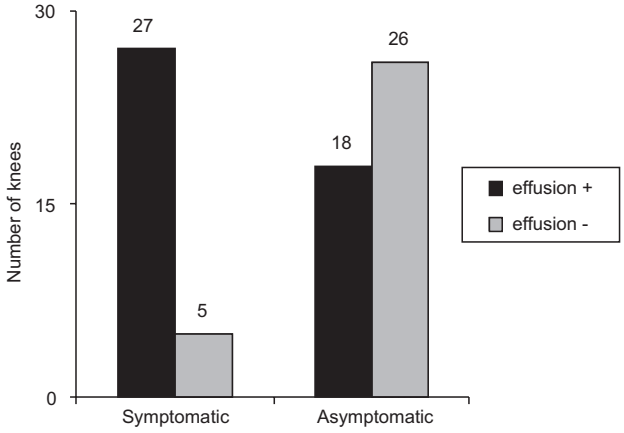

Fig. 3. Presence of knee effusions in symptomatic and asymptomatic dialyzed patients.

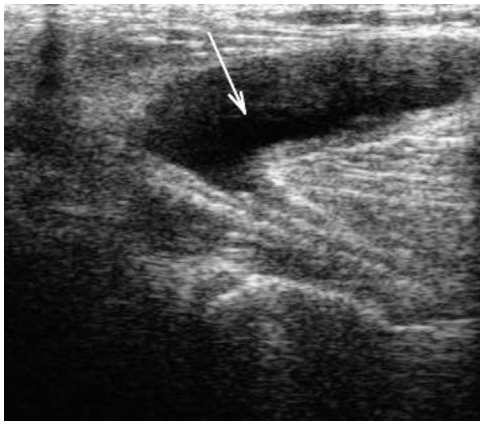

Fig. 4. Baker's cyst (white arrow).

long term dialysis and reported that plasma level of β2-microglobulin was higher in patients with arthropaty then dialyzed patients without it[13].

Kazama and associated point out that plasma level of β2-microglobulin decreases after renal transplantation, influencing the diminishing the joint symptoms[14].

Joint deposits don't disappear but inflammation around them does[15].

In our previous investigations we found higher level of β2-microglobulin in dialyzed patients with painful shoulder using machine learning algorithm[16].

We didn't found in literature special report about knee simptoms and plasma level of β2-microglobulin.

In our investigation we found significant higher plasma level of β2-microglobuline in patients with bilateral joint pain what confirms its connection with painful shoulder in dialyzed patients.

C reactive protein (CRP) is also associated with dialyzed arthropathy and its higher level in symptomatic confirm the inflammatory component of the syndrome[13].

In our patients CRP plasma level was statistically significant higher in symptomatic patients.

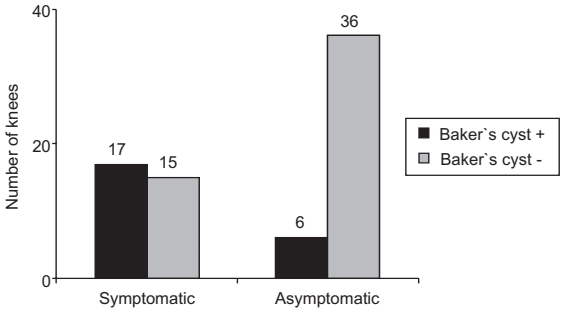

Fig. 5. Baker's cyst in symptomatic and asymptomatic dialyzed patients.

There was no significance in plasma level of uric acid among groups. However goat as possible cause of knee pain and inflammation should always be considered.

Thickness of synovial membrane, joint effusion and thinning and destruction of articular cartilage are associated with inflammatory reaction in long term dialysis and imaging technique are used to prove them although they can be sensitive but not specific[17,18]. That can also be found in the various conditions such as goat and pseudogoat, rheumatoid arthritis[19,20] and osteoarthritis[21].

Baker's cyst, also called a popliteal cyst, is swelling caused by knee joint fluid protruding to the popliteal area of the knee. When an excess of knee joint fluid is compressed by the body weight between the bones of the knee joint, it can become trapped and separate from the joint to form a fluid-filled sac.

Baker's cysts are not uncommon and can be caused by virtually any cause of joint swelling (arthritis). The most common form of arthritis associated with Baker cysts is osteoarthritis. Baker cysts also can result from cartilage tears (such as a torn meniscus), rheumatoid arthritis and other knee problems. Due to increasing amount of synovial fluid, it can be faund also in dialyses patients with and without symptoms[2].

In our investigations there were significantly thicker sinovial membrane, more knees with joint effusion and Baker's cysts in symptomatic patients.

The thickness of femoral condilar articular cartilage showed no difference between groups, but it was thin and modified and showed decrease thickness considering normal subjects[2]. Small difference in age among groups and previous history without rheumatic disease are another contribution of the statement that important joint changes occur early in dialyzed patients even in asymptomatic.

Conclusion

Plasmatic level of β2-microglobulin is strongly connected with chronic bilateral knee pain in dialyzed patients, as well as CRP as sign of acute inflammation, while uric acid level showed no difference among the groups. That is supported by morphologic parameters associated with histological proved amyloidosis in patients on long term dialysis, more then 10 years, such as higher thickness of synovial membrane and more joint effusions and Baker's cysts in symptomatic patients. Thickness of femoral condylar cartilage, however, showed no difference between groups, but it was thin and modified. It is obvious that important joint changes occur even in patients on shorter term dialysis and that inflammatory mechanisms developing from β2-microglobulin accumulation could be important factor in bilateral knee pain. Therefore, procedures that diminish plasmatic level of β2-microglobulin should take important part in joint lesions prevention.

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LABORATORIJSKI I ULTRAZVUČNI NALAZI DIJALIZIRANIH BOLESNIKA S OBOSTRANOM KRONIČNOM BOLI KOLJENA U ODNOSU NA ASIMPTOMATSKE DIJALIZIRANE

S A Ž E T A K

Svrha istraživanja je ustanoviti povezanost plazmatske razine β2-mikroglobulina, C-reaktivnog proteina i urata kao i ultrazvučne čimbenike kao što su debljina sinovijalne membrane, debljina hrskavice kondila femura i prisutnost zglobnog izljeva i Baker-ovih cista s obostranom koljenskom boli dijaliziranih bolesika, uspoređujući ih s ultrazvučnim čimbenicima u asimptomatskih dijaliziranih bolesnika. Plazmatska razina β2-mikroglobulina i C-reaktivnog proteina bile su značajno više u simptomatskih bolesnika, dok razina urata nije pokazala razlika među skupinama. U simptomatskih bolesnika sinovijalna je membrana bila deblja i u tih je bolesnika bilo više koljenskih izljeva i Baker-ovih cista. Debljina femoralne hrskavice nije pokazala razlika među skupinama. To ukazuje da upalni mehanizmi nastali zbog nakupljanja β2-mikroglobulina mogu biti značajan faktir u nastanku koljenske boli kod bolesnika čak i na kratkotrajnijoj dijalizi.