Bone loss in pediatric renal transplant recipients

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SUMMARY

The factors that affect bone mineral density (BMD) and the long term progress of BMD after transplantation in children is still unknown.

Therefore we performed a cross-sectional study to determine BMD in 83 recipients who received living renal allotransplants in Mansoura Urology & Nephrology Center between 1981 and 2001 (mean age at transplantation 13.2 ± 3.1 years) by dual energy x-ray absorptiometry at various time intervals up to 16 years after transplantation (mean duration after transplantation was 48 ± 34 months, range 6-192 months). The Z-score for lumbar spine was -2.28 ± 2.06 and -1.44 ± 1,44 for the total body. Osteopenia/osteoporosis were present in about two thirds of our kidney transplant recipients.

The significant predictors for osteopenia/osteoporosis by univariate analysis were cyclosporine based immunosuppression, the cumulative steroid dose/m^2 surface area, graft dysfunction and the urinary deoxypyridinoline.

Using logistic regression analysis the cumulative steroid dose/m^2 surface area and the urinary deoxypyridinoline were the major significant predictors for bone loss.

Key words: ***Bone loss. Children. Renal transplant.***

PÉRDIDA ÓSEA EN RECEPTORES PEDIÁTRICOS DE TRASPLANTE RENAL

RESUMEN

Los factores que afectan a la Densidad mineral ósea (BMD) y lo que ocurre a largo plazo con la BMD después del trasplante en niños es todavía desconocido. Por ello realizamos un estudio transversal para determinar la BMD en 83 receptores que recibieron un allotrasplante renal de vivo en Mansoura Urology and Nephology Center entre 1981 y 2001 (media de edad al trasplante 13,2 ± 3,1 años) por densitometría radiológica de doble energía, en varios intervalos de tiempo hasta 16 años después del trasplante (media de duración después del trasplante fue 48 ± 34 meses, rango de 6-192 meses). El valor de Z-score en columna lumbar fue de –2,28 ± 2,06 y de -1,44 ± 1,44 en cuerpo total. Osteopenia/osteoporosis estuvo presente en dos tercios de nuestros receptores de trasplante renal.

Los predictores significativos para osteopenia/osteoporosis por análisis univariante fueron la inmunosupresión basada en ciclosporina, la dosis de esteroides acumulativa por m^2 de área de superficie, disfunción del injerto y la deoxypyridinolina urinaria.

Usando análisis de regresión logística la dosis acumulativa de esteroides por m^2 de área de superficie y la deoxypyridinolina urinaria fueron los mayores predictores para pérdida de masa ósea.

Palabras clave: ***Pérdida ósea. Niños. Trasplante renal.***

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MATERIAL AND METHODS

A total of 83 pediatric renal graft recipients presented for routine transplant examination at various time intervals after transplantation were evaluated by bone densitometry between 2000 and 2001. The selection criteria were patients with functioning graft at least 6 months post renal transplantation. Patients with a prior history of parathyroidectomy or treatment with fluoride, calcitonin or bisphosphonates were excluded.

All patients received living renal allotransplants at Mansoura Urology & Nephrology Center between 1981 and 2001.

All subjects underwent bone mineral densitometry and a biochemical evaluation of their renal allograft function, calcium metabolism and bone turnover.

Measurement of BMD was performed by DEXA using lunar DFXMD 7517 machine, US. The BMD results were expressed as Z-score. The BMD was measured on the lumbar spine at L2-L4 and for the total body.

RESULTS

Our study included 83 renal transplant patients who underwent renal transplantation at the age of 17 years or less. All patients received live donor transplant, fifty three were males while thirty were females. At the time of the study the mean age of our cases was 16.3 ± 3.2 years, the mean serum creatinine was 1.9 ± 3.8 mg / dl, the mean corrected creatinine clearance was 62 ± 25.9 ml/min.

Bone loss was common in the study population at both lumbar spine and the total body. About 2/3 of our cases had osteopenia/osteoporosis.

The significant risk factors for osteopenia/osteoporosis by univariate analysis were the cyclosporine based immunosuppressive regimen, cumulative dose of steroids/m^2 surface area, the graft dysfunction and the urinary deoxypyridinoline.

A multiple regression model was performed using the logistic regression analysis. Only the cumulative steroid dose/m^2 surface area and the urinary de-

Table I. Effects of pre and post-transplant parameters on whole boy BMD of 83 pediatric transplants

	Number	BMD < -1	P. value
Age			
13 years or less	40	22 (55.00%)	
More than 13 years	43	32 (74.82%)	0.064
Sex			
Male	53	38 (71.70%)	
Female	30	16 (53.33%)	0.092
Original kidney disease			
Hypoplastic kidney	22	4 (63.64%)	
Glomerular disease	22	17 (77.27%)	
Tubulointerstitial disease	20	12 (60.00 %)	
Hereditary nephritis	10	5 (50.00%)	
Unknown	9	6 (66.67%)	0.609
Pretransplant dialysis			
No	22	11 (50.00%)	
Yes	61	43 (70.49%)	0.084
Immunosuppressive regimen			
Cyclosporine based	63	45 (71.43%)	
Tacrolimus based	8	7 (38.89%)	0.022
Acute rejection episode			
No	51	31 (60.78%)	
Yes	32	23 (71.19%)	0.302
Chronic rejection			
No	67	41 (61.19%)	
Yes	16	13 (81.25%)	0.130
Alternate-day steroid			
No	62	42 (67.74%)	
Yes	21	12 (57.14%)	0.379
Cumulative steroid dose			
16 g/m^2 or less	47	28 (59.57%)	
More than 16 g/m^2	36	26 (72.22%)	0.231
Cumulative steroid index			
10 g/m^2 or less	42	23 (54.76%)	
More than 10 g/m^2	41	31 (75.61%)	0.046

oxypyridinoline were significant predictors for bone loss.

Table 1 shows that all of the pre-transplant variables were not significant as risk factors for osteopenia /osteoporosis. Only the cyclosporine based therapy and cumulative steroid dose more than 10 g/m surface area were significant post-transplant risk factors for osteopenia/osteoporosis.

Table 2 shows that the graft function and the urinary deoxypyridinoline were significant post-transplant risk factors for BMD.

DISCUSSION

Post-transplant bone disease seems to be a universal finding in adult transplant recipients, and is most probably related to steroids. Reports on bone mineral density in children after renal transplantation are not uniform[1].

There was a decreased in BMD in both lumbar spine and the total body BMD with more affection of the lumbar spine (Z-score= -2.28 ± 2.06 *versus* -1,44 ± 1,44). Feber et al, explain the greater spinal bone loss by the high metabolic activity of the vertebral trabecular bone, which is also more prone to the side effects of steroids[2].

Two thirds of our cases had decreased bone density. Feber et al, found significant demineralization in 62% of children[2]. Moderate to severe osteopenia in children following transplantation was also reported by other authors[3,4].

The significant risk factors for osteopenia/osteoporosis were use of cyclosporine based therapy, cumulative steroid dose/m^2 surface area, renal dysfunction and urinary deoxypyridinoline.

Both cyclosporine and tacrolimus have been demonstrated to cause high-turnover bone loss in animal studies[5] but, not yet proven to occur in human[6].

Although it is well established that pharmacological doses of steroids have a powerful inhibitory effect on bone formation, they probably do not directly stimulate bone resorption[7]. In most studies bone mineral density was related to cumulative dose of steroids[8,9]. However, in some no correlation between BMD loss and steroids was found[10,2].

Although osteopenia has been reported in some studies in patients with renal insufficiency in renal transplant patients[7,11], others have reported no diminution in bone density with renal dysfunction[12].

In conclusion, osteopenia and osteoporosis are common in pediatric and adolescent renal transplant patients. The cumulative steroid dose/m^2 surface area and the urinary deoxypyridinoline were the major predictors for bone loss.

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Table 2. Effects of posttransplant laboratory parameters on whole body BMD of 83 pediatric transplants

	Normal BMD (number = 29)	Reduced BMD (number = 54)	P. Value
S.cr (mg/dl)	1.68 ± 1.78	2.48 ± 2.74	0.030
Cr.cl. (ml/min)	73.83 ± 21.88	52.46 ± 20.99	0.040
S. Calcium (mg/dL)	9.59 ± 0.76	9.29 ± 0.74	0.606
S. phosphorus (mg/dL)	3.66 ± 1.00	3.94 ± 1.05	0.693
S. Albumin (g/dL)	3.87 ± 0.48	3.87 ± 0.42	0.928
Alkaline phosphatase (IU/L)	140.76 ± 85.32	141.77 ± 66.89	0.253
Intact PTH (pg/ml)	7.66 ± 8.63	10.67 ± 12.65	0.328
Osteocalcin (ng/ml)	44.80 ± 20.65	46.83 ± 23.52	0.662
Urine deoxypyridinoline	71.32 ± 64.30	123.86 ± 61.20	0.002
Urine Ca/cr	0.05 ± 0.07	0.04 ± 0.06	0.657

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