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주요 개념 : 프레드니손, 신장이식, 근력, 일상생활활동

Influences of Prednisone on Muscle Strength and Instrumental Activities of Daily Living in Patients of Kidney Transplantation from Brainstem Dead Heart-beating Donors in Korea

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뇌사자로부터 공여받은 신장이식자의 근력과 일상생활활동에 프레드니손(Prednisone)이 미치는 영향

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국문초록

목적 : 본 연구의 목적은 뇌사자로부터 공여받은 신장을 이식한 대상자들이 프레드니손을 생체이식 대상자들보다 더 많이 투여받는 임상상황에서 프레드리손이 근력과 일상생활활동에 영향을 주는지 규명하기 위함이다. **방법** : 연구 대상은 뇌사자로터 신장을 응급으로 수여받은 32명이었으며 모두 혈액투석을 하고 있었다. 이식 수술 전날, 환자의 일반적인 정보, 근력, 일상생활활동에 대해 조사하였으며 이식수술 후 12주째 되는 날 외래에서 근력과 일상생활활동을 다시 조사하였다. 프레드니손 용량은 임상기록지를 통해 수집하였다. **연구결과** : 신장이식술 후 12주의 근력은 고관절 신전근력을 제외하고는 유의하게 감소되지 않았다. 그러나 신장이식 후 12주의 일상생활활동은 수술 직전보다 유의하게 감소된 것으로 나타났다. 근력은 혈액투석을 시행한 기간에 의한 영향을 더 받았으며 일상생활활동의 저하는 3개월간 활동을 제한하는 퇴원교육의 영향이 큰 것으로 볼 수 있다. **결론** : 본 연구에서 대상자의 근력과 일상생활활동은 프레드니손 투약의 영향을 받지 않았으며 오히려 혈액투석을 시행했던 기간에 따라 영향을 받은 것으로 나타났다. 따라서 혈액투석 환자들의 근력 증진을 위한 간호중재 개발이 필요하다.

Key words : IADL (Instrumental activities of daily living), Muscle strength, Prednisone, Kidney transplantation

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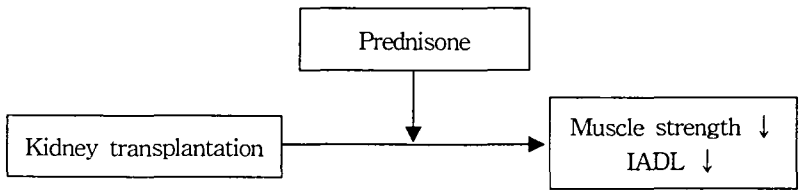
I. INTRODUCTION

Kidney transplantation has been practiced for the treatment of end stage renal disease (ESRD) all over the world. In the year 2000, the proportion of population on dialysis was 435.3 in 1,000,000 and only 10% of dialysis patients received kidney transplants in Korea (Kim, 2001). According to the 2004 report of Korean Network for Organ Sharing, kidney transplantation from brainstem dead heart-beating organ donors amounted to 124 cases in Korea. Compared with Western society, cadaveric heart-beating organ donations seldom occurred in Korea because people believe that death occurred when the heart stops beating.

Postoperative complications related to immunosuppressant are greater with cadaveric donors than with living donors (Wallace, 2003). In specific, side effects of the immunosuppressant that the kidney transplant recipients frequently experience is muscle atrophy. Prednisone among immunosuppressant was given at a dose of 20mg/day for the first three months and was then gradually reduced to a baseline dose of 10mg on alternate days after six months (Nicholson et al, 2000). However prednisone increases the activities of myofibrillar proteinase in protein metabolism and inhibits protein synthesis resulting in muscle atrophy. Long-term medication of prednisone influences mainly the fast twitch fiber which is used during lifting heavy weight, and increases the muscle size and strength. According to Mandel's report (1982), using prednisone for more than 3 months causes a decrease of muscle strength and a reduction the muscle mass and a cumulative effect of prednisone will occur as time elapses to decrease the muscle strength. This phenomenon occurred especially often in the patients aged 20~50, and it finally limits the ability to perform exercises (Mandel, 1982). Therefore it can be assumed muscle strength of kidney transplantation patient who receive prednisone will be decreased.

Instrumental activities of daily living (IADL) are a kind of regular activity related closely to daily customs — one of the methods showing functional conditions. Generally, as a kidney transplantation patient discharge from hospital, the patient is recommended to limit their activities for 2~3 months after kidney transplantation to prevent infection. In Korea, the patient is recommended to wear a mask when he goes out, to resume work or study in 3~6 months after kidney transplantation, and to avoid difficult work for 6~10 weeks (Kim, 1997). In the USA, there was no increase in the level of activities from prerenal transplantation until 6 weeks after kidney transplantation, but there was prominentincrease from 6 weeks to 16 weeks after kidney transplantation (Gallagher-Lepark, 1991). From the previous studies, IADL levels after kidney transplantation may decrease for 2~3 months but there was little study of how kidney transplantation with prednisone changes the IADL.

Based on the results of these previous studies, there seems to be a decrease in the muscle strength of kidney transplantation patients from brainstem dead heart-beating



〈Figure 1〉 Conceptual framework

donors, caused by prednisone. In addition it is assumed that weakened muscle strength will decreases IADL after kidney transplantation.

The purpose of this study is to examine the change of muscle strength and IADL by prednisone after kidney transplantation from brainstem dead heart-beating donors and to identify the related factors influencing muscle strength and IADL after kidney transplantation.

Conceptual framework

The conceptual framework of this study was depicted in Figure 1.

II. PATIENTS AND METHODS

1. Patients

Thirty-two hemodialysis patients in one medical center receiving kidney transplantation from brainstem dead heart-beating organ donors in emergency were included. Exclusion criteria for this study were episodes of acute rejection or severe current disease. Patient characteristics are given in Table 1. All patients were aged 20~50 (mean 39.75±9.91 years), and consisted of 24 male (75.0%) and 8 female (25.0%). Duration of hemodialysis was mean 19.90±16.76 months and ranged 1~72 months. The patients took more than 10mg/day of prednisone for 12 weeks and didn't do regular exercise during the period of the study. The patients received, and agreed with,the informed consent agreement, prior to their participation in the study.

2. Methods

The study was conducted using a convenient sampling method from one medical center in Seoul for 12 months. When a brainstem dead heart-beating organ donor in ICU was confirmed, the transplant coordinator prepared the recipient to receive surgery in emergency. One research assistant who worked at the transplant ward was trained in measuring muscle strength by using hand dynamometer and muscle tester. As patients admitted in the transplant ward, the research assistant measured general characteristics, muscle strength and IADL of the patients 8~12 hours before kidney transplantation. At 12 weeks after kidney transplantation, muscle strength and IADL were remeasured and prednisone dosage was identified through medical record. Measuring at 12 weeks was based on Mandel's report (1982) that prednisone for

〈Table 1〉 General characteristics of patients (N=32)

General characteristics		Number (%)
Age		
	21~30	7 (21.9)
	31~40	7 (21.9)
	41~50	17 (53.0)
	51~60	1 (3.2)
Gender		
	Male	24 (75.0)
	Femal	8 (25.0)
Marital status		
	Married	20 (62.5)
	Single	10 (31.2)
	Others	2 (6.3)
Job		
	None	18 (56.3)
	Have	11 (34.4)
	Studen	3 (9.4)
Duration of dialysis		
	1~6 months	6 (18.8)
	7~12 months	9 (28.1)
	13~24 months	8 (25.0)
	25~36 months	4 (12.5)
	≥ 37 months	5 (15.6)

more than 3 months provoke the decrease of muscle strength and the reduction the muscle mass.

2. Muscle strength

1) Grip strength.

Grip strength was measured by the hand dynamometer (Lafayette Instrument, USA). The patient was kept in an erect posture, lowered the arms, and graspedthe hand dynamometer by the hand which has no arteriovenous fistula (Bohannon, Hull, & Palmeri, 1994). Patient pressed the steel handle to the maximum. After measuring twice, higher pressure was selected as the value of grip strength.

2) Muscle strength of lower extremities.

The patient sat on the chair with the kneesat a right angle, with the feet 15~20cm above the floor. The research assistant put the muscle tester (Nicholas Manual Muscle Tester, Lafayette Instrument, USA) closely on the patient's legs and measured muscle strength by applying the muscle tester in the opposite direction against the direction of the legs moving up and down. In this way, flexor and extensor muscle strength of hip and knee joint, flexor and inversor muscle

strength of ankle joint were measured. After measuring twice, higher pressure was selected as the value of muscle strength.

3. Instrumental activities of daily living(IADL)

IADL index was developed by Deniston, Aiting, Kneisley, Hawthorne, & Port (1989) as 10 items of measuring tools to apply to the ESRD. Those items were translated and modified for this study. The index of each item ranges from 0 to 2, measuring the higher index shows more independent in the IADL. Total score of the index is from 0 to 20, score 20 shows perfect independent in the IADL. The Cronbach-alpha coefficient used for this study was .87.

4. Statistical analysis

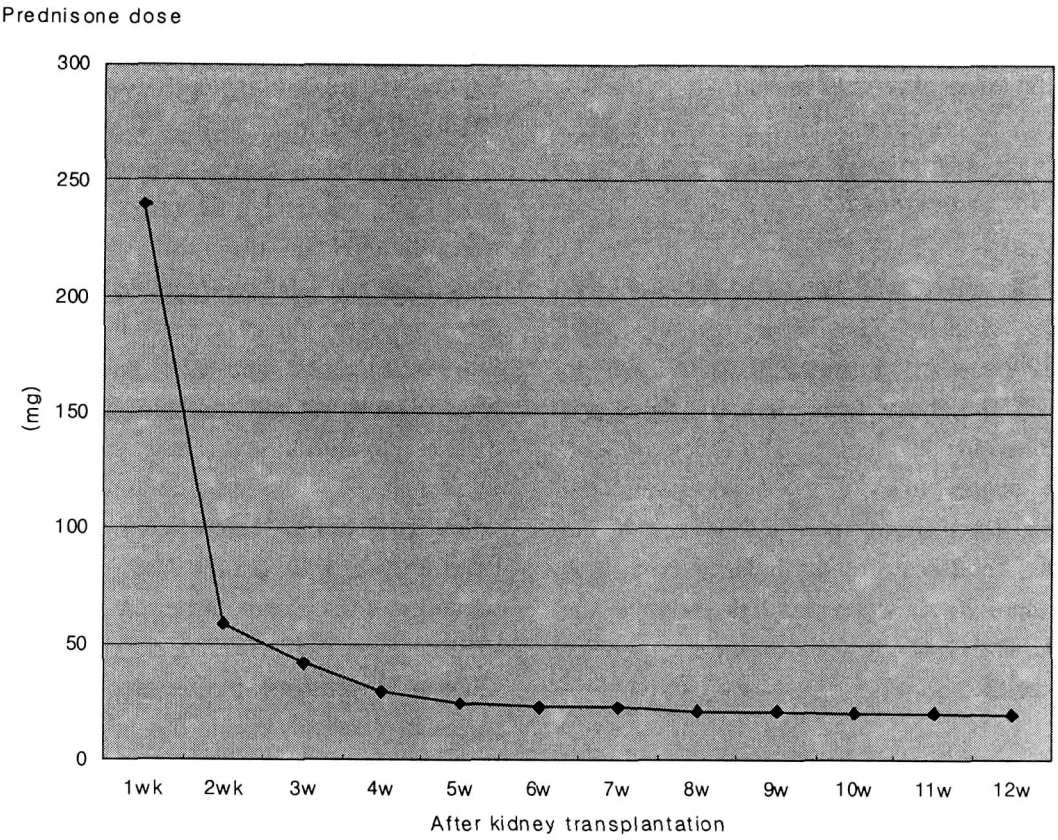
Statistical analysis was performed with SPSS-PC for Windows, version 11.0. Statistics were computed via paired t-test; all data are expressed as mean±SD. For correlation analysis, Pearson correlation coefficients were calculated. Forward stepwise multiple regression analysis was performed to explain prednisone and the other correlated parameters that influence muscle strength and IADL after kidney transplantation. For all tests, a two-tailed p value of less than 0.05 was considered to be statistically significant.

III. RESULTS

As depicted in Figure 2, the dosage of prednisone during the 1st week averaged 1680mg (240mg/day) 409.2mg (58.5mg/day) during 2nd week 310.2mg (41.3mg/day) during 3rd week and 93.2-208.1mg (13.3-29.7mg/day) from 4th to 12th week.

The changes of muscle strength from pre-renal transplantation to 12 weeks after kidney transplantation are given in Table 2. Mean muscle strength in pre-renal transplantation decreased after kidney transplantation, but it was not significant statistically except hip extensor muscle strength and IADL. Hip extensor muscle strength significantly decreased to 18.57kg at 12 weeks after kidney transplantation from 19.15kg before kidney transplantation ($t=2.543$, $df=31$, $p=.016$). After kidney transplantation, IADL score decreased significantly to 18.59 from 19.12 ($t=3.744$, $df=31$, $p=.001$).

Table 3 presents the result of multiple regression analysis about the impact of the prednisone and the correlated factors on the muscle strength and IADL after kidney transplantation. The variance of grip strength 12 weeks after kidney transplantation explained by hemodialysis period ($\beta=-.506$) and prednisone ($\beta=-.258$) was 66.9%. The variance of hip flexor strength 12 weeks after kidney transplantation explained by hemodialysis period ($\beta=-.730$) was 54.9%. The variance of hip extensor muscle strength 12 weeks after kidney transplantation explained by hemodialysis period ($\beta=-.618$) was 47%. The variance of knee flexor muscle strength 12 weeks after kidney transplantation explained by job ($\beta=-.432$), gender ($\beta=-.440$), age ($\beta=-.452$), prednisone ($\beta=-.359$) was 58.2%. The variance of knee extensor muscle strength 12 weeks after kidney transplantation explained by hemodialysis period ($\beta=-.412$) was 40.6%. But the variance of ankle flexor muscle



〈Figure 2〉 Changes of mean daily dose of prednisone by week after kidney transplantation

〈Table 2〉 Changes of muscle strength and ADL after kidney transplantation

		Before kidney transplantation	12 weeks after kidney transplantation	t	*P*
Muscle strength(kg)	Grip strength	32.09 (8.42)	31.78 (7.87)	.577	.568
	Hip flex	20.16 (2.98)	19.70 (3.01)	1.966	.058
	Hip extensor	19.15 (2.12)	18.57 (1.94)	2.543	.016*
	Knee flexor	20.15 (2.41)	19.84 (2.42)	.733	.469
	Knee extensor	18.47 (1.93)	18.40 (1.85)	.193	.848
	Ankle flexor	18.15 (2.02)	17.65 (2.10)	1.717	.096
	Ankle inversor	16.49 (2.12)	16.27 (2.11)	.781	.441
IADL		19.12 (1.31)	18.59 (1.94)	3.744	.001*

Values are mean(SD).

* $p<.05$

〈Table 3〉 Variance in muscle strength and ADL after kidney transplantation explained by dose of prednisone and the other correlated parameters.

Variable		Job	Gender	Age	Period of hemodialysis Beta(t)	Dose of Prednisone	R^2	F (*p*)
Muscle strength	Grip strength	.155 (1.083)	-.322 (-2.660)*	-.121 (-.922)	-.506 (-3.842)**	-.258 (-2.169)*	.669	10.492 (.000)**
	Hip flexor	.006 (.036)	-.050 (-.354)	.004 (.027)	-.730 (-4.745)**	-.023 (-.166)	.549	6.321 (.001)*
	Hip extensor	-.036 (-.201)	-.216 (-1.411)	-.066 (-.400)	-.618 (-3.705)**	.030 (.199)	.470	4.613 (.004)**
	Knee flexor	-.432 (-2.698)*	-.440 (-3.239)**	-.452 (-3.081)**	-.203 (-1.370)	-.359 (-2.690)*	.582	7.250 (.000)**
	Knee extensor	.071 (.371)	-.326 (-2.017)	.226 (1.290)	-.412 (-2.332)*	-.233 (-1.465)	.406	3.553 (.014)
	Ankle flexor	-.016 (-.070)	-.003 (-.018)	-.041 (-.202)	-.365 (-1.766)	-.201 (-1.082)	.187	1.200 (.337)
	Ankle inversor	-.112 (-.555)	-.101 (-.590)	-.018 (-.095)	-.494 (-2.646)*	-278 (-1.650)	.336	2.626 (.047)*
IADL		-.048 (-.337)	-.088 (-.723)	-.451 (-3.439)**	-.508 (-3.836)**	-.214 (-1.797)	.666	10.362 (.000)**

* <.05
** <.001

strength 12 weeks after kidney transplantation was not significant. The variance of knee inversor muscle strength 12 weeks after kidney transplantation explained by hemodialysis period (β=-.494) was 33.6%. The variance of IADL 12 weeks after kidney transplantation explained by age (β=-.451) and hemodialysis period (β=-.508) was 66.6%.

In specific, the number of patients who needed assistance for "travel" and "step-up exercise"before kidney transplantation was 9 (28.1%), while the number of patients after kidney transplantation was 8 (25.0%). The number of patients who needed assistance moving by public transportation or private car before kidney transplantation was 3 (9.4%), while the number of patients after kidney transplantation was 4 (12.5%).

IV. DISCUSSION

In this study, only the muscle strength of hip extensor was lower 12 weeks after kidney transplantation than before kidney transplantation. Prednisone decreased protein synthesis and reduced the density and quantity of muscle fibers, especially in the legs and thighs (Carrieri, Lindsey, & West, 1986). In this study, decreased muscle strength from prednisone of hip extensor presented first in the thigh. This result does not coincide with

the results of Kempeneers, Myburgh, Wiggins, Adams, & Noakes (1990) which reported that the oxidative capacity of quadriceps and knee muscles of the renal transplantation patients decreased, and type II muscle fibers were atrophied.

To examine the significant predictors of muscle strength and IADL after kidney transplantation, multiple regression analysis was conducted. The most significant predictor of muscle strength and IADL after kidney transplantation was the hemodialysis period. Prednisone was not predictive of muscle strength except grip strength and knee flexor. This result means that muscle atrophy probably had already occurred, according to hemodialysis period, before kidney transplantation.

In the study of Diesel et al. (1993), skeletal muscle of renal disease patient with average 5 years of dialysis occurredabnormal changes such as Z-band degeneration, myofilament loss and glycogen accumulation in the cell and type II muscle atrophy can be detected by using skeletal muscle biopsy. According to Giovenali et al. (1994)'s study, biopsy of chronic uremic patient manifested a significant degree of muscular atrophy in all types of muscle fiber. Histochemistry of muscle biopsy in 18 children with ESRD under dialysis during a ten-month period presentedmuscle atrophy, type grouping, lipidosis, glycogen depletion and mitochondrial proliferation (Prado, Prado, Oliveira, Schmidt, & Carvalhaes, 1998). In addition based on the study by Bohannon et al. (1994) that the muscle strength of ESRD with mean 22 months period of dialysis decreased for 37.9% lower than that of normal people, it is inferred that the muscle strength of patients with mean 19.9 months in this study had already decreased through long-term dialysis.

Long-term hemodialysis is a catabolic event, decreasing the circulating amino acids, accelerating proteolysis rates of whole body and muscle, stimulating the release of amino acids from muscle, so eventually the protein loss of net whole body muscle were elevated (Ikizler et al, 2002).

It is considered as a loss of amino acids and glucose to dialysate (Lofberg et al, 2000) and metabolic acidosis common in hemodialysis patients which induces negative nitrogen balance, increased muscle degradation (Bergstorm, 1995).

These results, that were not significant in the reduction of muscle strength except hip extensor, indicate that the muscle strength of patients had already decreased during hemodialysis before kidney transplantation, rather than with prednisone after kidney transplantation.

IADL index was 19.12 before kidney transplantation but decreased to 18.59 12 weeks after kidney transplantation. It is considered that the reason why the IADL index was so high, was that the patients are mean 39.75 years old with social activity, and was selected as a candidate who had no problem in IADL. According to this result, IADL level 12 weeks after kidney transplantation decreased compared with pre-renal transplantation and especially in the patients who needed assistance for moving by public transportation or private car. Also, it seems that, influenced by the discharge education of the hospital, most patients rest at home for 2~3 months

after renal transplantation except for trips to the hospital for medical treatment. In general, kidney transplantation patient receive discharge education to avoid infection and injury from the others. For example, driving is prohibited for 4 weeks, and activities are restricted for 2~3 months after renal transplantation (Nolan & Augustine, 1995). Also, returning to work or school was not recommended until 3~6 months after kidney transplantation (Kim, 1997). Most patients have rest at home except going to hospital for medical treatment for 2~3 month after kidney transplantation and as the activities of the patients increase in 2~3 months, the muscle contraction increases, which consequently results in the increase of muscle strength.

In 32 patients, 11 patients (34.4%) have a job while 18 patients (56.3%) have no job in this study. In Korea, Park et al. (1989) reported that among the 83 patients who received kidney transplantation, for more than 1 year, 65 patients (78.3%) had jobs, while 31 patients (37.3%) worked more actively, and 50 patients (62.7%) decreased their activity compared with before kidneytransplantation. The study of Han, Ha, Kim & Kim (1993) on the patients 10 years after kidney transplantation showed that 2 of 23 patients could move only with the help of their family and 21 patients could perform social activities. Thus, 11 patients recovered to normal conditions, 3 patients retired, 3 patients worked as a part-timer and 4 patients worked as a housewife. The study of Johnson, McCauley, & Copley (1980) presented that 80% of kidneytransplantation patients worked as part-timers and full-timers or housewives, while 78.3% in and Park et al. (1989) and 73.8% in worked Han et al. (1993) showed. Mabee, Tilney, Vineyard, & Wilson (1978) reported that it took an average of 12 months for the patients to work again, and Park et al. (1989) presented that it took average 13.5 months for Korean patients to resume work. In this study, 56.3% of patients have not a job, because this study has been performed after transplantation for 3 months.

Physical activity level of one month after kidney transplantation decreased compared with the level immediately before kidney transplantation, and 1 year after, it increased and reached plateau kidney transplantation (Nielens et al, 2001). However, it is recommended to increase activity progressively, since immunosuppressive drugs have a direct weakening effect on muscles and bones and excessive physical activity performed immediately after kidney transplantation might be responsible for the occurrence of epiphyseal impactions (Goffin et al., 1993).

Unfortunately, the activity level of patients in this study wasnot controlled or measured. The accurate level at which there was an increase or decrease in the activity level was unable to be determined.

This study was performed at one hospital, so these results have the limitation for generalization.

V. Conclusion

Based on the results of this study and the reviewof other literatures, it can be determinedthat the muscle atrophy occurredalready

before kidney transplantation due to hemodialysis. It means that, according to the condition of the patient before kidney transplantation, it seems necessary to advise chronic renal failure patients to receive the kidney transplantation as soon as possible in theearly stage of hemodialysis. In addition, the result of this study suggests that the development and application of an exercise program is needed to prevent the decrease of muscle strength during the period of wait as a candidate and during the period of constraining the activities after kidney transplantation. It is considered that the result of this study showed the variance of the muscle strength and IADL after kidney transplantation was affected primarily more by the duration of hemodialysis period than by prednisone, because muscle strength was already so decreased that prednisone could not affect the prominent variance in muscle strength.

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