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Kronik Karaciğer Hastalığı Nedeniyle Karaciğer Nakli Yapılan Çocuklarda Malnütrisyonun Değerlendirilmesinde Antropometrik Ölçümler ve Büyüme Faktörleri

Anthropometric Measurements and Growth Factors in the Evaluation of Malnutrition in Children with Liver Transplantation due to Chronic Liver Disease

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ÖZ

Amaç: Kronik karaciğer hastalığı, özellikle insülin benzeri büyüme faktörü-1 (IGF-1) ve insülin benzeri büyüme faktörü bağlayıcı protein-3 (IGF-BP3) başta olmak üzere büyüme faktörü proteinlerinin yapı ve işlevindeki değişikliklerle birlikte çocuklarda büyüme geriliğine neden olur. Bu çalışmanın amacı, antropometrik parametreler (AP) ve büyüme faktörü proteinlerini kullanarak karaciğer nakli (LT) yapılan kronik karaciğer hastalığı olan çocuklarında beslenme durumunu değerlendirmektir.

Yöntem: Karaciğer nakli uygulanan 33 hasta ve 54 sağlıklı çocuk değerlendirildi. Hastaların AP'leri karaciğer nakli öncesi ve nakilden 1, 3, 6 ve 12 ay sonra değerlendirildi. Antropometrik parametreler, IGF-1/IGFBP-3 düzeyleri ve Child-Pugh skorları arasındaki ilişki analiz edildi.

Bulgular: Kronik karaciğer hastalığı olan çocuklarda, nakil öncesi boya göre ağırlık (WFH) dışındaki tüm antropometrik ölçümler kontrol grubuna göre daha düşüktü ($p<0.05$). Child-Pugh skoru ile triseps deri kıvrım kalınlığı (TSF) ($r=-0.387$, $p=0.026$) ve orta-üst kol çevresi (MUAC) Z-skoru ($r=-0.448$, $p=0.009$) arasında negatif bir ilişki vardı. IGF-I ve IGFBP-3 düzeyleri, nakil öncesi hasta grubunda ortalama 35.24±14.68 ng/ml ve 1.31±0.9 µg/ml olup, kontrol grubundan daha düşüktü (69.88±67.45 ng/ml ve 3.2±1µg/ml) (sırası ile $p=0.001$ ve $p=0.000$). 12 ay sonra, hasta grubunun yaşa göre boy Z skoru (HFA) (-0.7±1.46) kontrol grubundan daha düşük (0.08±0.9) ($p=0.01$) iken, TSF Z skoru (0.24±0.8) ve orta kol kas alanı (MAMA) (20.67±20.28) kontrol grubundan daha yüksekti ($p=0.009$, $p=0.004$). IGF-1 ve IGFBP-3 düzeyleri nakil öncesi dönemden daha yüksekti ($p=0.000$). IGF-1 ve IGFBP-3 seviyeleri ile AP arasında ilişki saptanmadı.

Sonuç: Kronik karaciğer hastalığı nedeniyle karaciğer nakli yapılan hastalarda malnütrisyon takibinde antropometrik parametreler IGF-1 ve IGFBP-3'e göre daha güvenilirdir.

Anahtar Kelimeler: Kronik karaciğer hastalığı, Malnütrisyon, İnsülin benzeri büyüme faktörü-1, İnsülin benzeri büyüme faktörü bağlayıcı protein-3, Karaciğer nakli.

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ABSTRACT

Objective: Chronic liver disease (CLD) causes growth retardation in children, together with the changes in the structure and function of growth factor proteins, especially the insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGF-BP3). The aim of this study was to evaluate nutritional status of children with CLD undergone liver transplantation (LT) by using anthropometric parameters (AP), and growth factor proteins.

Method: Thirty-three patients undergone LT and 54 healthy children were evaluated. The AP of the patients were determined before and 1, 3, 6, and 12 months after LT. Relationship between AP, IGF-1/IGFBP-3 levels and Child-Pugh scores were analyzed.

Results: In children with CLD, all anthropometric measurements except weight for height (WFH) before transplantation were lower than the control group ($p<0.05$). There was a negative correlation between Child-Pugh score and triceps skinfold thickness (TSF) ($r=-0.387$, $p=0.026$) and mid-upper arm circumference (MUAC) Z-score ($r=-0.448$, $p=0.009$). IGF-I and IGFBP-3 levels were 35.24±14.68 ng/ml and 1.31±0.9 µg/ml in the pre-transplant patient group and were lower than the control group (69.88±67.45 ng/ml and 3.2±1 µg/ml) (respectively $p=0.001$ and $p=0.000$). After 12 months, the patient group's height-for-age (HFA) Z score (-0.7±1.46) was lower than the control group (0.08±0.9) ($p=0.01$), while TSF Z score (0.24±0.8) and mid- arm muscle area (MAMA) (20.67±20.28) was higher than the control group ($p=0.009$, $p=0.004$). IGF-1 and IGFBP-3 levels were higher than before transplantation ($p=0.000$). No correlation was found between IGF-1 and IGFBP-3 levels and AP.

Conclusion: AP are more reliable for the follow-up of malnutrition in patients undergone LT due to CLD, when compared to IGF-1 and IGFBP-3.

Key words: Chronic liver disease, Malnutrition, Insulin-like growth factor-1, Insulin-like growth factor binding protein-3, Liver transplantation.

1. INTRODUCTION

Chronic liver disease (CLD) causes malnutrition and growth retardation in children. Many factors, including lipid malabsorption, decreased intake of calorie and lack of any trace elements and increased need of energy contribute to growth retardation in CLD. Malnutrition leads to complications that affect the quality of life and survival in these patients, and also influences the success of liver transplantation (LT) (1).

The assessment of anthropometric measures is a rapid, safe, and effective method to screen for malnutrition in children. Although in most settings height and weight are sufficient anthropometric parameters to assess nutritional status, due to the fact that weight may be influenced by many factors including edema, organomegaly and ascites; height, triceps skinfold thickness (TSF) and mid-arm circumference measurements have been suggested to be more reliable in the malnutrition assessment of children with CLD (2).

Upper-arm anthropometry seems to be an important technique to determine body-composition and nutritional status especially in epidemiological, clinical diagnosis and disease prevalence (3). The measurement of mid-upper arm circumference (MUAC) has been used to identify young children with malnutrition (2). MUAC, together with TSF can be used to estimate skeletal muscle and subcutaneous fat stores (4). Mid-arm muscle area (MAMA) in the evaluation of body protein reserves and is determined by a special calculation using MUAC and TSF (3).

The liver has an important role in the growth axis. Growth hormone (GH) secreted by the anterior pituitary gland binds to its receptors in the liver and leads to insulin-like growth factor-1 (IGF-1) synthesis. IGF-1 is an anabolic hormone that mediates the effects of GH and is mainly found bound to insulin-like growth factor binding protein-3(IGFBP-3) in the circulation, that plays a role in the regulation of IGF-1(5). In CLD, malnutrition and hepatocellular dysfunction cause the rearrangement of the GH/IGF-1/IGFBP-3 axis and this

condition contributes to growth retardation in children. GH resistance is present and the serum IGF-1/IGFBP-3 level is decreased in CLD, in spite of the increased GH levels (6).

A successful LT improves the growth axis and the growth retardation in children with CLD (7). The serum IGF-1 level increases after LT while the GH decreases and reaches age-appropriate levels in children. In a few studies, it was shown that while IGF-1 levels returned to normal in children after LT, IGFBP-3 levels remained above normal for at least 1 year. The physiological cause of this condition is not completely clear (8, 9).

Our aim in this study was to evaluate the nutritional status of children with CLD undergone LT and investigate the relationship between IGF-1 and IGFBP-3 levels and anthropometric measurements after a successful LT.

2. METHOD

A total of 33 patients with biopsy-confirmed diagnosis of cirrhosis who were followed up between March 2005 and April 2009 were included in the study. Patients with co-morbidities (e.g. severe infection, hypothyroidism, severe heart disease, kidney failure and lung disease) were excluded. The control group consisted of 54 healthy children who presented to the general pediatric outpatient clinic for routine check-up. The parents of all cases were informed about the study and provided written consent.

All children with CLD underwent LT and were supported with fat-soluble vitamins (A, D, E, and K). Malnourished children were fed with medium-chain fatty acid-rich formulas. The severity of cirrhosis was determined according to the Child-Pugh scoring system. Patients with CLD were classified as Child A if the total score was between 5-6, Child B if the total score was between 7-9 and Child C if between 10 and 15 (10).

Tacrolimus, mycophenolate mofetil, and steroid therapy were administered for 3 months as a routine immunosuppressive therapy to all patients following LT. Pulse steroid therapy (10 mg/kg/day for 3-5 days) was commenced to the patients who experienced an acute rejection attack. The total steroid dose given to the patients was 152.4±87 mg/day (range 55-483). Three patients were treated with pulse steroids due to acute rejection.

Data Collection

Anthropometric Measurements

All anthropometric parameters were measured by the same physician in accordance with the standardized protocols. Weighing was performed while the child was naked, without diapers, with a sensitive baby weighing device sensitive to 10 grams (Seca sensitive baby scale) in children under two years of age, and with a weighing device sensitive to 100 grams (SECA manual weighing device with height gauge) in older children, while they were in their underwear. Height measurements were performed with a 'head and foot board' for children under two years of age and with standard stadiometer (SECA manual height measuring device) sensitive to 0.1 centimeters while standing in older children. The data obtained from the measurement of anthropometric parameters was evaluated according to the statistics program of the World Health Organization called Epi-Info™ 6 nutritional assessment (11).

MUAC was measured by a plastic measure from the midline between acromion and olecranon and TSF from the same area using a Harpender caliper (Holtan, Ltd Skinfold Crymch

UK) by applying 10 grams pressure per centimeter and the mean of three consecutive measurements was calculated.

The anthropometric measurements of children in the study and control group were determined before LT, and re-evaluated 1, 3, 6, and 12 months after LT. The anthropometric measurements control group were repeated one year after the first measurement.

The presence of malnutrition was evaluated according to weight for age (WFA), height for age (HFA), weight for height (WFH), TSF, and MUAC Z scores and TSF and MUAC percentages. Z scores below -2 standard deviation (SD) was defined as malnutrition. The formula "Z-score=Value obtained from the patient-the median value of the reference population/the standard deviation value of the reference population" was used. As for TSF, measurements regarding 80 to 90% of the normal standards were indicative of slight malnutrition, whereas measurements that corresponded to lower than 60% indicated severe malnutrition. Measurements of MUAC, showing 85 to 80% of normal standards, were suggestive of slight malnutrition, while measurements below 75% showed severe malnutrition (12).

The "National Health Statistics Reports, 2003-2006" data were used in order to calculate the TSF and MUAC measurement Z-scores (13). MAMA was calculated with the formula 3.14/4x (MUAC /3.14-TSF)^2 (14). As Z-score values for the MAMA for ages below 1 year was not available in the literature, the MAMA measurements of the patient and control groups were compared using the mean values.

Laboratory Analyses

Blood samples were taken from any peripheral vein in the morning after 12-14 hours fasting. Serum albumin, total bilirubin, IGF-1, IGFBP-3 levels and prothrombin times of the study and control group were measured at the beginning of the study. Serum total bilirubin level (Roche/Hitachi Modular ACN:101 kit) and serum albumin levels (Roche/Hitachi Modular ACN 904/911/912/9177:413 kit, Switzerland) were measured with the colorimetric method. Prothrombin time was measured with ST®A analyzers (STA-Neoplastine® Cl Pus kit, U.S.A.). IGF-1 and IGFBP-3 levels were re-analyzed on the 1st, 3rd, 6th, and 12th months after LT. Serum IGF-1 and IGFBP-3 levels were measured with the enzyme-labeled chemiluminescent immunometric method (Immulite 2000, Siemens, Germany).

Data Analysis

The data of the study were analyzed by using the SPSS 17.0 statistical package software program. Continuous variables were presented as mean±standard deviation and the categorical variables as number and percentages. In the patient group, the annual change of growth-related parameters were evaluated with the "variance analysis for repeating measurements", and the values of control group and the patient group were compared by using the "t test for independent groups". The Kruskal-Wallis test was used to compare the WFA, HFA, WFH, TSF, MUAC Z-scores of the patients according to the Child-Pugh scoring system, and the mean MAMA, IGF-1 and IGFBP-3 levels. Repeated measure analysis of variance (ANOVA) testing was used to examine pre-transplant, post-transplant 1st, 2nd, 3rd, 6th months and 1-year changes in the Z scores of WFA, HFA, WFH, TSF, MUAC and mean MAMA and IGF-1 and IGFBP-3 levels. The relationship between the Child-Pugh score and WFA, HFA, WFH, TSF, MUAC Z-scores,

mean MAMA and IGF-1 and IGFBP-3 levels, and the relationship between the rate of change of HFA Z-score and the other parameters (HFA, WFA and WFH Z-score; IGF-1 and IGFBP-3 levels; age; Child-Pugh score, steroid dose) were evaluated by Pearson correlation analysis. The statistical significance level was determined as "$p<0.05$" for all analyses.

Ethical Considerations

The ethics committee of Baskent University Faculty of Medicine approved the study (Date: 06.05.2009). Work was carried out with the project 'KA09/164'.

3. RESULTS

Of the 33 cases with cirrhosis, 20 (60.6%) were male, 13 (39.4%) female, and the mean age was 34.24±41.6 months (5 months-11 years). The control group consisted of 54 cases. In the control group, 29 (53.7%) were male, 25 (46.3%) female, and the mean age was 32.29±41.7 months (range: 5 months-11 years). There were no significant differences between the groups in terms of age and gender ($p>0.05$). Among the 33 cases with CLD, 13 were followed up with extrahepatic biliary atresia (EHBA), 7 with idiopathic neonatal cholestasis, 3 with Wilson disease, 2 with cryptogenic cirrhosis, 2 with progressive familial intrahepatic cholestasis 1 (PFIC), 2 with tyrosinemia type 1, 1 with PFIC 2, 1 with PFIC 3, 1 with autoimmune hepatitis and 1 with Alagille syndrome. The cholestatic liver disease group presented 75% of the patient group.

According to Child-Pugh scoring, three patients (9%) were classified as Child A, 13 (39.4%) as Child B, and 17 (51.5%) as group Child C. Due to the small number of patients in the Child A group, the statistics were evaluated together with the patients in the Child B group.

Anthropometric Measurements Before LT

The anthropometric measurements of the between genders were comparable within patient and control groups ($p>0.05$). Before LT, 7 (21%) patients with WFA, 10 (30%) patients with HFA, 1 (3%) patient with WFH, 10 (30%) patients with TSF, and 12 (36%) patients with MUAC had Z-scores below -2 SDS. Twenty-seven (82%) patients had TSF standard percentage below 90% and 14 (42%) patients below 60%, 16 (51%) patients had MUAC standard below 85% and 9 (27%) patients below 75% (Table 1). The mean HFA, TSF, MUAC Z scores and MAMA measurements ($p<0.0001$) and WFA Z scores ($p<0.05$) of the patients were lower than the control group. The mean WFH Z-scores of the patients and control group were comparable ($p> 0.05$).

Mean TSF Z scores of patients in the Child A+B group were found to be higher than patients in the Child C group ($p=0.05$). Other anthropometric measurements were found to be comparable between Child A+B and Child C groups ($p>0.05$). A negative relationship was found between the Child-Pugh score and the mean TSF ($r=-0.387$, $p=0.026$) and mean MUAC Z-score ($r=-0.448$, $p=0.009$). No relationship was found between the Child-Pugh score and other anthropometric measurements ($p>0.05$).

IGF-1/IGFBP-3 Levels Before LT

The mean IGF-1 and IGFBP-3 levels of the patient group before LT were 35.24±14.68 ng/ml and 1.31±0.9 µg/ml respectively and these values were lower than the mean levels of the control group (69.88±67.45 ng/ml and 3.2±1 µg/ml) ($p=0.001$ and $p=0.000$ respectively). The

growth factor levels between genders within the patient and control groups were comparable (p>0.05).

In the pre-operative period, the mean IGF-1 level was found to be 31.98±9.5 ng/ml in the Child A+B group and 38.3±18 ng/ml in the Child C group. The mean IGFBP-3 level was 1.2±0.6 µg/ml in the Child A+B group and 1.4±1.1 µg/ml in the Child C group. No relationship was found between the Child-Pugh score and mean IGF-1 (r=0.194, p=0.280) and IGFBP-3 measurements (r=-0.27, p=0.882).

Positive correlation was found between IGFBP-3 and IGF-1 levels before LT (r=0.512, p=0.002).

Table 1. Nutritional Status of Patients Before and 12 Months After Liver Transplantation.

	Before LT		**12 months after LT**	
	n	**%**	**n**	**%**
WFA Z score -2 SDS	7	21	1	3
HFA Z score< -2 SDS	10	30	7	21
WFH Z score <-2 SDS	1	3	0	0
TSF <%90	27	82	5	18
TSF <%60	14	42	1	3
TSF Z score < -2 SDS	10	30	1	3
MUAC <%85	16	51	-	-
MUAC <%75	9	27	1	3
MAMA Z score < -2 SDS	12	36	1	1

HFA: Height for age, LT: Liver transplantation, MAMA: Mid arm muscle area, MUAC: Mid-upper arm circumference, n: Number of patients, TSF: Triceps skinfold thickness, SDS: Standart deviation score, WFA: Weight for age, WFH: Weight for height.

Anthropometric Measurements After LT

Anthropometric measurements of the patient group before and after LT is shown in Table 2. During one-year follow up, the WFA, HFA, WFH Z-scores varied over time (p<0.0001, p=0.003, p=0.02). Statistically significant increases were initially detected at the sixth month following LT for all parameters mentioned above (p<0.0001, p=0.046, p=0.001) (Figure 1). The mean TSF, MUAC Z-scores and MAMA measurements also increased during the study period (p <0.0001, p<0.0001, p<0.0001), and the parameters showed incline beginning from the third month after LT (p<0.0001, p<0.0001, p<0.0001) (Figure 2,3).

Table 2. One Year Follow Up of Pre and Post Liver Transplantation Anthropometric Measurements of Patients.

	Preop	**Postop 1. month**	**Postop 3. month**	**Postop 6. month**	**Postop 1. year**
WFA Z score	-0.85±2.33	-1.41±1.2	-0.9±1.21	-0.52±1.4	-0.025±1.5
HFA Z score	-1.3±1.45	-1.23±1.5	-1.3±1.55	-0.74±1.82	**-0.7±1.46***
WFH Z score	0.26±2.69	-0.24±2.8	-0.5±2.56*	-0.59±2.67	1.15±2.57
TSF Z score	-1.23±0.75	-1.18±0.68	**0.69±0.5***	**-0.5±0.8***	**0.24±0.8***
MUAC Z score	-2.2±1.1	-2.1±1.2	**-1.3±1.2***	**-0.9±0.9***	**-0.5±1.2***
MAMA (cm2)	7.61±3.28	7.28±10.13	**12.2±7.4***	**14.7±11.25***	**20.67±20.28***

Data are given as mean ± standard deviation.
Variables with significant time effect in repeated measures ANOVA are shown in bold.
*=p<0.05 (preop- vs)
HFA: Height for age, MAMA: Mid arm muscle area, MUAC: Mid-upper arm circumference, TSF: Triceps skinfold thickness, SDS: Standart deviation score, WFA: Weight for age, WFH: Weight for height.

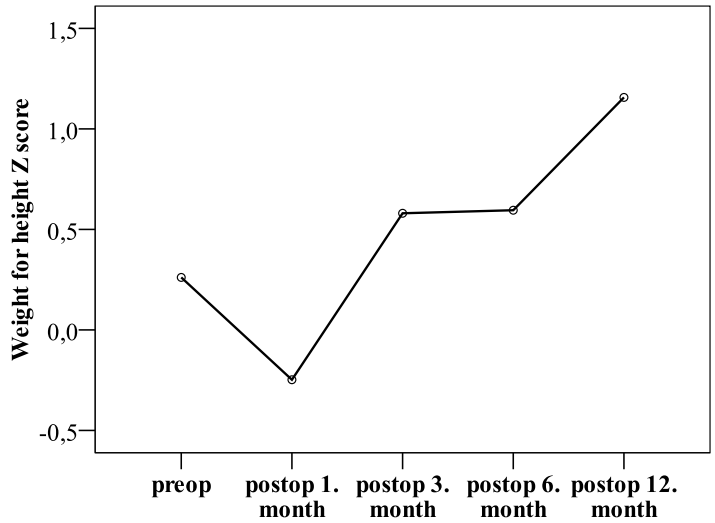

Figure 1. Weigh-For-Height Z-Score Change in a Year.

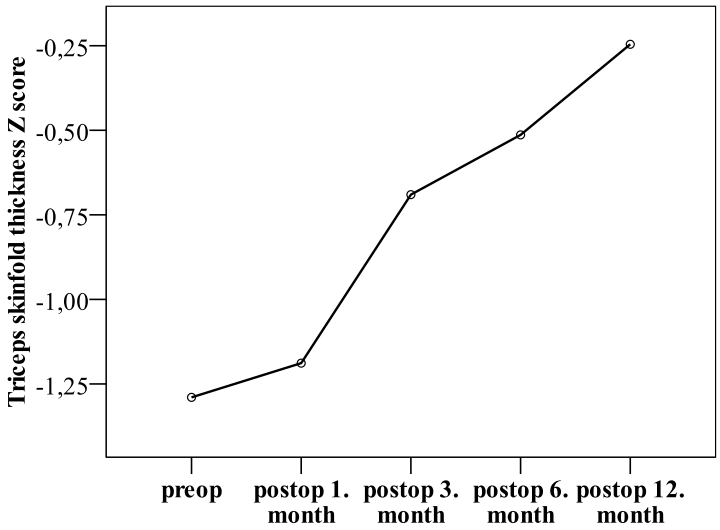

Figure 2. Triceps Skinfold Thickness Z Score Change in a Year.

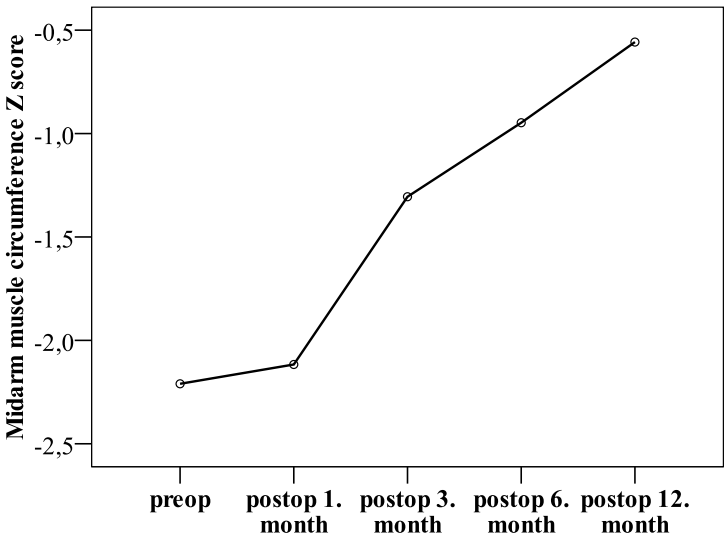

Figure 3. Midarm-Muscle Circumference Z Score Change in a Year.

IGF-1 and IGFBP-3 Levels After LT

The increase in anthropometric measurements during the one-year follow-up period after LT was not found to be associated with the increased levels in serum IGF-1 and IGFBP-3 levels (p>0.05) (Table 3).

During one-year follow-up, the mean IGF-1 and IGFBP-3 levels of the patients increased in the first month (p<0.0001, p<0.0001) after LT, reached their highest level in the third month, and start to decrease afterwards (p<0.0001, p=0.039). The mean IGFBP-3 level was observed to increase parallel to the increase in the mean IGF-1 level (r=0.634, p=0.0001) (Table 3).

Table 3. One Year Follow Up of Pre and Post Liver Transplantation IGF-1 and IGFBP-3 Measurements of Patients.

	Preoperative	**Postoperative 1. month**	**Postoperative 3. month**	**Postoperative 6. month**	**Postoperative 1. year**
IGF-1 (ng/ml)	35.24±14.68	**177.27±126***	**204.6±107.5***	**150.12±110.25***	**115.6±95.56***
IGFBP-3 (µg/ml)	1.31±0.89	**4.5±2***	**5.07±2.1***	**3.95±2.05***	**3.64±1.52***

Data are given as mean ± standard deviation.
*Variables with significant the time effect in repeated measures ANOVA are indicated in bold.
*= p<0.05 (preop- vs)
IGF-1: Insulin like growth factor-1, IGFBP-3: Insulin like growth factor binding protein – 3.

Anthropometric Measurements 1 Year After LT

Twelve months after the LT (Table 1), anthropometric parameters were as following; 1 (3%) patient had WFA Z-score under -2 SDS, 7 (21%) patients had HFA Z-score under -2 SDS, 5 (18%) patients had TSF lower than 90% of the standard, and 1 (3%) patient had lower than 60%, 1 (3%) patient had a TSF Z-score under -2 SDS, 1 (3%) patient had MUAC percentage under 75% of the standard, and 1 (3%) patient had MUAC Z score under -2 SDS (3%). Not any patients had WFH Z-score under -2 SDS.

Mean HFA Z-score of the patient group (-0.7±1.46) was lower than the mean HFA Z-score of the control group (0.08±0.9) (p=0.01). Mean TSF Z-score (0.24 ±0.8) and mean MAMA values (20.67±20.28) of the patient group were higher than the mean TSF Z-score (-0.65 ±0.21) and mean MAMA values (9.58±3.95) of the control group (p=0.009, p=0.004). WFA, HFA and MUAC Z scores were comparable between groups (p>0.05).

Patients with lower height showed a more rapid growth rate after LT (r=-0.381, p=0.02) (Table 2).

IGF-1 and IGFBP-3 Levels 1 Year After LT

No relationship was found between anthropometric measurements and mean serum IGF-1 and IGFBP-3 levels 12 months after LT (p>0.05). At the end of the first year, the mean IGF-1 (115.6±95.56 vs. 35.24±14.68 ng/ml) and IGFBP-3 levels (3.64±1.52 vs. 1.31±0.9 µg/ml) was higher than their mean pre-transplantation levels (p=0.000). The GF levels of between genders were comparable (p>0.05). IGFBP-3 level (r =0.512, p=0.002) was positively correlated with IGF-1 levels, as it was at the beginning of the study.

4. DISCUSSION

Evaluating the WFA and WFH measurements in patients with cirrhosis may result in erroneous interpretations related to presence of ascites, edema, and organomegaly. Therefore, alternative parameters have been suggested for the determination of nutritional status in these patients (15).

Sokol et al. (16) evaluated the anthropometric measurements of 56 children (aged 1 months-10 years) with CLD. They determined the mean height Z score as low, weight Z-score as near normal and WFH Z-score as normal. TSF Z score was lower than WFH Z score and the MUAC and MAMA Z-score to be moderately low. Holt et al. (17) also reported the TSF and MUAC to be more sensitive than weight and height measurement in patients with cirrhosis. Similarly, we have also detected all anthropometric measurements except the WFH Z score of chronic liver patients to be lower than the control group. The levels of HFA, TSF and MUAC Z scores in our patients were more prominently lower than the control group, when compared to WFA Z score, supporting the findings of other studies in the literature.

HFA is an indicator of chronic malnutrition, while WFH indicates acute malnutrition. At the beginning of this study, the acute malnutrition rate according to the WFA Z-score was 21% (7/33), and the chronic malnutrition rate according to the HFA Z-score was 30% (10/33). Low TSF levels were found in 82% of our patients, that is also an indicator of acute malnutrition. The TSF Z-score was below -2 SDS in 30% of our patients. Therefore, WFH Z-score in chronic liver patients has been insufficient in the determination of acute malnutrition in this study. Similarly, Sokol et al. also stated that WFH Z score was insufficient to show acute malnutrition according to TSF measurement in patients with chronic liver disease (16).

The severity of malnutrition has been reported to be proportional to the severity of CLD and liver dysfunction (18). Urgancı et al. (19) determined the TSF and MUAC Z-scores of the Child A group to be significantly higher than the Child C group in cirrhotic cases. In this study, the TSF Z-score was significantly higher in patients in the Child A+B group. In addition, a negative relationship was found between the Child-Pugh score and TSF with MUAC Z-scores of our patients. These data indicate that TSF and MUAC measurements are more valuable than height and weight measurements in CLD patients. In addition, the severity of malnutrition increases with the severity of disease, and there is therefore a need for early evaluation and support of the patients' nutritional status.

Previous studies have suggested that an increase in height following LT is achieved barely in two years (20, 21). In this study, the increase in height was significant within the first six months, earlier than the most studies reported previously in the literature. This situation may be explained with the development of patient care and follow-up in transplantation units and the advances of immunosuppressive drugs used for treatment over time. We observed the TSF and MUAC Z scores begin to improve from the third month similar to the findings of Holt et al. (17). We also have demonstrated the WFA Z score to improve later than the TSF Z score. This may be due to the significant weight loss seen within the first month with the removal of the enlarged liver, and the disappearance of edema and ascites. The TSF measurements may therefore be useful in the evaluation of the actual nutritional status of the patient during post-transplantation follow-up.

One year later after LT, the HFA Z-score of the patients (-0.7±1.46) was observed to be lower than the HFA Z-score of healthy children of same age (0.025±1.12). Studies in literature have shown negative correlations between the growth rate and the height, body weight and age at the time of transplantation and steroid use to influence height negatively (22, 23). In our study, steroid usage dose did not influence linear growth, in contrast to other studies. We think this situation may be related with short-term steroid therapy used in our patients at a lower dose.

The suggested reasons for the decrease in IGF-I of cirrhotic patients are the reduction in the functional liver parenchyma mass, changes in the effects of GH/insulin/cortisol on the liver and disease-related malnutrition (24, 25). In previous been shown that the levels of studies, it has these hormones increase due to the development of insulin, GH, and cortisol resistance in patients with CLD, and GH resistance disappears after liver transplantation (8, 26). Unfortunately, we have not evaluated insulin, GH, and cortisol levels, which stimulate IGF-1 synthesis.

A strong relationship has been found between IGF-1 and IGFBP-3 levels and liver functions in adult patients with cirrhosis (27). Most studies have demonstrated a negative relationship between the IGFBP-3 level and Child-Pugh score (28). The use of the Child-Pugh score together with IGF-1 and IGFBP-3 levels was reported to be more effective in determining the prognosis of patients with CLD (29). We saw no significant difference between the groups in terms of IGF-1/IGFBP-3 levels according to Child-Pugh score. This may be due to the small number of patients included in the study.

The IGF-1 and IGFBP-3 levels have been shown to increase after LT along with improvement of liver function (30). In this study, IGF-1 and IGFBP-3 levels have increased one month after LT, reaching their highest value in the third month and although decreasing gradually, and were still found to be higher than the control group at the end of the first year. This increase was thought to be related to the increased functional liver mass and the improvement in the GH/IGF axis, as mentioned in previous studies.

Studies in Turkey have mainly evaluated malnutrition in LT patients by APs (19, 31). Our study has evaluated the improvement in anthropometric parameters and both growth factor proteins in detail, when compared to other studies. Although IGF-1 is expected to be more sensitive in showing the nutritional status than other visceral proteins in patients with cirrhosis, since it is also synthesized by extra hepatic organs (9). There are several studies in the literature that could not find any relationship between the IGF-1/IGFBP-3 levels with nutritional status of CLD patients (32, 33). Similarly, we also could not find any relationship between IGF-1 and IGFBP-3 levels and anthropometric measurements before and after LT. Therefore, we suggest these proteins may not to be useful in the evaluation of malnutrition and its severity in CLD patients and the improvement of the nutrition parameters after LT cannot be explained with growth factors alone.

5. CONCLUSION

In conclusion, TSF has been found to be a reliable anthropometric indicator for the determination of malnutrition in patients followed up with CLD. IGF-1 and IGFBP-3 levels do not reflect the presence of malnutrition and, may not to be useful in the evaluation of the degree of malnutrition in CLD patients. The evaluation of anthropometric parameters, especially upper arm measurements at regular intervals, is needed to determine the nutritional status in children

with CLD, who have undergone LT, in addition to the height and weight measurements in follow-up.

Ethical Consideration of the Study

Ethical approval was obtained from the local ethics committee (Date: 06.05.2009).

Conflict of Interest Statement

All authors declare no conflict of interest.

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