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Enteral feed based gradual improvement of body mass index and normalization of micronutrients in children with malnutrition

Malnutrisyonlu çocuklarda enteral beslemeye dayalı vücut kitle indeksi'nin kademeli iyileştirilmesi ve mikrobesinlerin normalleşmesi

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Abstract

Aim: Malnutrition is a serious and frequently encountered condition affecting more than 900 million individuals worldwide. Its relationship with negative clinical outcome, bad prognosis and susceptibility to diseases has been demonstrated in numerous studies alongside with the importance of early nutritional intervention. The aim of this study was to define the beneficial influence of a hypercaloric enteral supplement on body mass index (BMI) z-score as well as ferritin, vitamin B12 and vitamin D micronutrients.

Methods: This study is a retrospective observational study. Records of patients who were diagnosed with malnutrition via a physician by having height and weight scores below -2 standard deviation were collected from Gaziosmanpaşa Training and Resource Hospital, Istanbul, Turkey. A comparative statistical analysis was performed on 205 pediatric malnutrition patients (ages 1 to 16) by gathering their BMI, ferritin, b12 and vitamin D at baseline with their measurements at 2 follow-up visits after the administration of hypercaloric (1.5kcal/mL) enteral supplement over 6 months.

Results: There was a significant inverse correlation between BMI z-scores and the duration of enteral supplement administration, reflected by a 33.2% reduction of the mean BMI z-scores from -2.11 to -0.7 over 6 months ($Z=-12.4$, $P<0.001$). Additionally, there was a reduction in the number of patients with excessive or insufficient amounts of ferritin, b12 and vitamin D concentrations with 80%, 41.7% and 39.3% respectively over six months.

Conclusions: Hypercaloric enteral supplementation is a short-acting and highly beneficial nutritional intervention in pediatric patients diagnosed with malnutrition, which provides a robust improvement in the BMI z-scores as well as a 2-tailed improvement of aforementioned micronutrients after six months of supplementation.

Keywords: Pediatrics, Malnutrition, Gastroenterology, Therapeutics

Öz

Amaç: Malnutrisyon, dünya çapında 900 milyondan fazla insanı etkileyen ciddi ve sık karşılaşılan bir durumdur. Malnutrisyon; olumsuz klinik sonuç, kötü prognoz ve hastalıklara yatkınlık ile yakından ilişkilidir, bu yüzden erken müdahalenin öneminin altını çizen çok sayıda çalışma yapılmıştır. Bu çalışmanın amacı, hiperkalorik enteral beslenme tedavisinin vücut kitle indeksi (VKİ) z-skorunun yanı sıra ferritin, B12 vitamini ve D vitamini mikro-besinlerinin üzerindeki yararlı etkilerini tanımlamaktır.

Yöntemler: Bu çalışma geriye dönük gözlemsel bir çalışmadır. Doktor tarafından boy ve kilo ölçümleri -2 standart deviasyonun altında olarak malnütrisyon tanısı almış hastaların kayıtları, Türkiye'nin İstanbul ilinde bulunan Gaziosmanpaşa Eğitim ve Araştırma Hastanesinden toplanmıştır. Toplamda 205 pediatrik malnutrisyon hastasının (1-16 yaş) ilk ziyaretine ait VKİ, ferritin, B12 vitamini ve D vitamini kayıtları, hiperkalorik (1,5 kcal/mL) müdahaleye başlandıktan 6 ay sonrasına kadar yapılan 2 vizite ölçümleri ile karşılaştırılarak istatistiksel olarak analiz edilmiştir.

Bulgular: VKİ z-skorları ile enteral beslenme tedavisi uygulama süresi arasında görsel ve istatistiksel olarak ek hastalık durumları farketmeksizin anlamlı bir ters korelasyon görülmüştür ($Z=-12,4$, $P<0,001$). Ortalama VKİ z-skoru %33,2'lik bir düzelme ile 6 aylık müdahale sonrası -2,11'den -0,7'ye yükselmiştir. Ek olarak, altı ay boyunca ferritin, B12 vitamini ve D vitamini konsantrasyonları gereğinden fazla veya yetersiz olan hasta sayısında sırasıyla %80, %41,7 ve %39,3 oranında azalma görülmüştür.

Sonuçlar: Hiperkalorik beslenme tedavisi, malnutrisyon teşhisi konan pediyatrik hastalarda hızlı, etkili ve oldukça faydalı bir beslenme müdahalesi olup, altı aylık takviye sonrası BMI z-skorlarında anlamlı düzelme ve yukarıda bahsedilen mikro besinlerde 2-taraflı iyileşme sağlamıştır.

Anahtar kelimeler: Pediatri, Malnutrisyon, Gastroenteroloji, Tedavi

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Introduction

Malnourishment negatively affects the therapeutic outcome from infectious and malignant diseases and delays wound healing because it weakens the bodily functions and affects >900 million individuals worldwide [1]. Thus, malnutrition is a sign of poor outcome and is not always reversible after recovering from the malnourishment state, especially in cancer patients with disturbed energy metabolism [2]. Protein energy malnutrition (PEM) is an undernourishment state that increases susceptibility to various infectious diseases [3]. Undernourishment is a worldwide health problem that affects all age groups and is caused by various factors related to underdevelopment and poor nutrition in developed countries [4]. Malnutrition in childhood is a significant problem and during early childhood, it has a significantly negative effect on all aspects of development.

Despite the importance of a healthy diet for positive treatment outcomes and maintaining resistance to numerous diseases, congenital and acquired conditions, such as allergies, type I diabetes mellitus, inflammatory bowel disease (IBD), and congenital heart disease (CHD), can alter the dietary requirements or results in an immune reaction to food [5]. Especially in patients with accompanying diseases such as patients with Ulcerative colitis (UC) or celiac disease (CD), food allergy is a common consequence, among which 64% and 66% of the patients, respectively, have been reported to have food intolerance [6]. Moreover, the prevalence of CD increases in patients with diabetes mellitus and other autoimmune disorders, which highlights the importance of timely intervention [7].

The present study aimed to determine the effects of a novel prescription enteral nutritional supplement in pediatric patients with such underlying diseases as primary and secondary malnutrition. Study parameters were measured at baseline and then at two follow-ups during 6 months of enteral nutritional supplementation.

Materials and methods

Sample

The study included 205 pediatric patients (ages 1 to 16) diagnosed with malnutrition after presenting to the gastroenterology outpatient clinic of Gaziosmanpaşa Training and Resource Hospital due to inability to gain weight. Patients with height and weight below -2 standard deviation scores (SDS) and who were prescribed with nutritionally complete, dietary fiber-containing hypercaloric (1.5 kcal mL^{-1}) enteral supplement were included in the study. Patients' chronic diseases, biochemical scores, and nutrient requirements were recorded. Laboratory values, height and weight, and BMI were measured at baseline, and compared with measurements obtained after 3 and 6 months of the administration of aforementioned enteral supplement. Weight, height, and BMI z-scores were compared between time points to evaluate clinical improvement.

Observation

The results were obtained via comparing the vitamin D, B12, and ferritin levels, and BMI over the course of 6 months of enteral supplementation, according to posology calculations, which were dependent on the calculated energy requirements in each patient. Baseline measurements were obtained, and then measured again after 3 and 6 months of enteral supplementation. The patients were grouped according to age, as follows: 0-2 years; 3-5 years; 6-8 years; 9-12 years; 13-16 years. Additionally, as primary malnutrition was the most common condition (77%) in the cohort, followed by CD, UC, Familial Mediterranean Fever (FMF), food allergy, Crohn's disease, CHD, and asthma, these diseases were divided into 2 groups—primary malnutrition and secondary malnutrition.

Standardization and reference ranges

Optimal micronutrient reference ranges were obtained from Gaziosmanpaşa Training and Resource Hospital, as follows: Ferritin: 20-200 ng m L^{-1}, B12: 126.5-505 pg mL^{-1}, vitamin D: 30-100 ng mL^{-1}. Vitamin D values <20 ng mL^{-1} were considered as deficient, 20-30 ng mL^{-1} insufficient, and >100 ng mL^{-1}, excessive. Standardization of BMI values was maintained according to lambda (L), mu (M), and sigma (S) parameters, which refer to power in the Box-Cox transformation for skewness, median, and generalized coefficient of variation, respectively [8]. LMS parameters for each age group and gender were obtained from Centers for Disease Control and Prevention website [9]. To calculate each BMI z-score (BMIz) according to LMS parameters, the following formula [10] was used:

$$BMIz = \left[\left(\frac{BMI}{M}\right)^{L} - 1\right] \div (L \times S)$$

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY, US). Descriptive statistical range values are indicated, and Friedman's test was used for all statistical calculations due to non-normally distributed datasets. In order to determine the significance of the non-parametric subgroup trends, the Wilcoxon test was used separately for each relationship. The level of statistical significance was set at $P<0.05$.

Ethical approval

The authors state that they have obtained the ethical approval from the ethics committee of Taksim Eğitim ve Araştırma Hastanesi on 02/10/2019 with session number 141. In addition, all patients signed the informed consent forms prior to inclusion in the study.

Results

The improvement in BMIz over the course of 6 months of enteral supplementation can be seen in Figure 1. This improvement was based on the difference in BMIz between baseline and the 6^{th}-month values (–2.11 and –0.7, respectively), which indicated a mean 1.41 (33.2%) improvement. The greatest improvement in BMIz was in the 1-2 years age group, followed by 3-5 years, 6-8 years, 9-12 years, and 13-16 years. There was a significant improvement in BMIz during the first 3 months of enteral supplementation, but very little from 3-6 months in the 13-16 years age group (Figure 1). Overall, the BMIz improved significantly over the course of 6 months of enteral supplementation ($P<0.001$). The comparative improvement in BMIz between each measurement time point was also significant ($P<0.001$) (Table 1). Both patient groups (primary malnutrition and secondary malnutrition) had a significant decrease in BMIz

during the 6 months of enteral supplement use based on Friedman's test (P<0.001) (Figure 2).

Ferritin values increased significantly over the course of 6 months of enteral supplementation (Figure 3a and Table 1). Moreover, the mean baseline ferritin level was 22.60 ng mL^{-1}, which is close to the minimum required level, but increased to 28.71 ng mL^{-1} after 6 months after enteral supplement usage. Baseline ferritin values showed that 40 patients had a level below the required minimum of 20 ng mL^{-1}, whereas 24 patients at 3 months and 8 patients at 6 months had a level below the required minimum level.

Table 1: Significance of the improvement in the study parameters after 3 and 6 months of enteral supplement use, as compared to baseline values given as descriptive statistics

	Mean (SD)	Median (Min-Max)	*P*-value
BMIz (baseline)	–2.12 (1.88)	-1.67 (–11.32-0.97)	<0.001*
BMIz (3rd month)	–1.29 (1.55)	-0.98 (–9.74-2.12)	
BMIz (6th month)	–0.71 (1.34)	-0.51 (–6.52-2.99)	
BMIz (3rd month)-BMIz (baseline)			<0.001**
BMIz (6the month)-BMIz (baseline)			<0.001**
BMIz (6th month)-BMIz (3rd month)			<0.001**
Ferritin (baseline) ng mL^{-1}	22.60 (19.44)	17.00 (2-190)	<0.001*
Ferritin (3rd month) ng mL^{-1}	24.88 (13.45)	21.00 (8-118)	
Ferritin (6th month) ng mL^{-1}	28.71 (12.53)	26.00 (13-124)	
Ferritin (3rd month)-ferritin (baseline)			<0.001**
Ferritin (6th month)-ferritin (baseline)			<0.001**
Ferritin (6th month)-ferritin (3rd month)			<0.001**
B12 (baseline) pg/ml	340.64 (194.75)	290.00 (126-1500)	0.447*
B12 (3rd month) pg/ml	320.39 (129.46)	284.00 (140-872)	
B12 (6th month) pg/ml	312.20 (99.54)	291.00 (149-670)	
Vitamin D (baseline) ng/mL	24.34 (17.14)	22.00 (8-213)	<0.001*
Vitamin D (3rd month) ng/mL	26.39 (7.56)	26.00 (13-62)	
Vitamin D (6th month) ng/mL	29.37 (7.1)	28.00 (14-49)	
Vitamin D (3rd month)-vitamin D (baseline)			<0.001**
Vitamin D (6th month)-vitamin D (baseline)			<0.001**
Vitamin D (6th month)-vitamin D (3rd month)			<0.001**

* Friedman's test, ** Wilcoxon signed-rank test, SD: Standard deviation

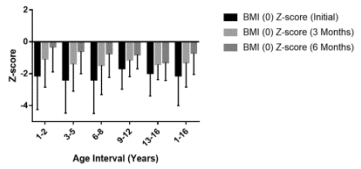

Figure 1: BMIz values at baseline, and after 3 and 6 months of enteral supplement use. Standard deviations for each age group, as well as all patients are indicated over each column.

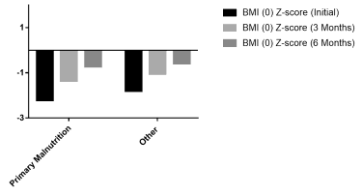

Figure 2: BMIz values in the patients with primary malnutrition and secondary malnutrition at baseline, and after 3 and 6 months of enteral supplementation.

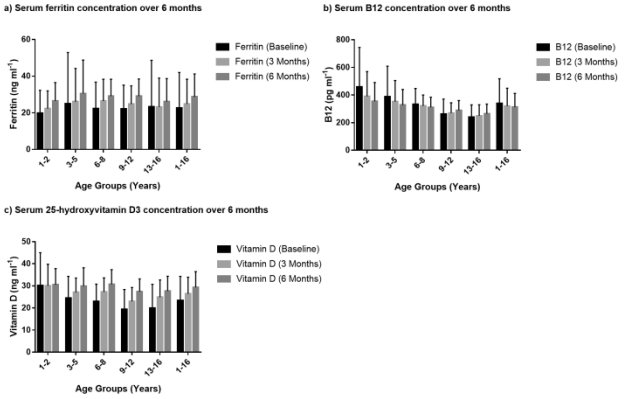

Figure 3: Ferritin, B12 and 25-hydroxyvitamin D3 values at baseline, and after 3 and 6 months of enteral supplementation. Standard deviations for each age group are indicated over each column.

There was not a significant change in the vitamin B12 level (Figure 3b and Table); however, the number of patients with a high B12 level decreased significantly over the course of 6 months. At baseline, 12 patients had a high B12 level (>505 pg mL^{-1}), versus 10 and 7 patients at 3 and 6 months, respectively. The highest B12 levels were 1500 pg mL^{-1}at baseline, 872 pg mL^{-1}at 3 months, and 670 pg mL^{-1} at 6 months, which indicated enteral supplementation stabilized the B12 level.

There was a significant increase in the vitamin D level over the course of 6 months of enteral supplement use (Figure 3c and Table 1); however, the increase in the 1-2 years age group was lower than in the other age groups (Figure 3c). Baseline values indicate that 56 patients had an insufficient vitamin D level (<30 ng mL^{-1}), but after 3 months of enteral supplementation 53 patients had an insufficient level, and after 6 months only 34 patients had an insufficient level, indicating that there was on overall improvement in the vitamin D level over the course of 6 months of enteral supplementation.

Discussion

Malnutrition and undernourishment occur due to multiple causes in all countries. In developing countries and underdeveloped countries, undernourishment is the primary cause of nutritional disorders [11], whereas in developed countries malnutrition is the primary cause of nutritional disorders, including DM and obesity [12]. The spectrum of nutritional disorders occur in all age groups [13].

It was reported that malnutrition negatively affects the immune system, wound healing, and drug metabolism, which have serious negative effects on the prognosis of such diseases as cancer, cardiovascular diseases and infectious diseases [14]. Pediatric malnutrition and undernourishment can have very serious consequences, negatively affecting development, as well as long-term negative effects via epigenetic modifications [1,13]. These serious consequences include poor quality of life, high healthcare costs, and poor response to cancer treatments and treatments for infectious diseases [14,15]. In developed countries, the prevalence of malnutrition can be as high as 50% of the population and even higher in developing or underdeveloped countries [16].

Timely treatment is very important for all diseases, including malnutrition due to the above-mentioned negative cascade of reactions that develop over time. Most importantly, cachexia, which is a syndrome that causes continuous consumption of energy combined with metabolic disorders such as anorexia during a chronic inflammatory condition or cancer [17], should be diagnosed and treated as early as possible [18]. Diagnosis should signal the initiation of nutritional intervention due to the fact that the longer the body is exposed to the stress of inadequate nutrition, the higher the probability of long-term negative effects [18, 19]. Early nutritional intervention aims to support normal growth and eating behavior, which ameliorate malnutrition and/or prevent the risk of having malnutrition in the future, enhancing patient quality of life [20].

The Quetelet index, also known as BVMI, is used to evaluate the nutritional status of patients and is based on the relationship between weight and height [21]. In addition to BMI, ideal body weight (IBW) and weight-for-height (WFH) can be used to evaluate nutritional status [22]; however, WHO accepts BMI as the measurement of nutritional status [23]. Despite some

controversies about BMI [24], alongside with the insufficiencies of BMI upon informing the analyzer about specific localizations of fat around the body [25], in overall measures, BMI maintains its clinical significance on tracing obesity and it's as valuable as more expensive methods for adiposity calculations. In the present study, BMI was the measurement used to determine the effectiveness of enteral nutritional supplementation.

There was an insignificant decrease in BMIz values after 3 months of enteral supplementation usage in the present study's 13-16 years age group, which might have been because this age group included only 23 patients, whereas the other age groups included in the study comprised 35-51 patients. Similarly, the significant decrease in BMIz values in the 1-2 years age group, which included 35 patients, might have been due to the same reason; however, there was an overall significant decrease in BMIz values. Both the patients with primary malnutrition and secondary malnutrition had a significant decrease in BMIz over the course of 6 months of enteral supplementation, which may indicate the benefits of hypercaloric supplement are not dependent on the type of malnutrition. Additionally, the baseline BMIz in the patients with primary malnutrition was worse (–2.21) than in the patients with secondary malnutrition (–1.80), which improved to –0.73 and –0.61, respectively at 6th month. The patients with primary malnutrition might have had greater improvement in the BMIz because their baseline BMIz values were worse.

The overall decrease in the percentage of the patients in the present study with excessive or insufficient ferritin, B12, and vitamin D levels with observed improvement of 80%, 41.7%, and 39.3%, respectively, is an indication of the beneficial effect of the enteral supplement. Enteral supplementation clearly improved the ferritin and vitamin D levels in the patients during the course of 6 months, except in the 1-2 years group in the case of vitamin D, whereas there wasn't a significant overall increase or decrease in B12 levels.

Vitamin D is a crucial micronutrient, and an inhibitory stimulant in tumor cells via activation of an apoptotic cascade in malignant cells. It decreases the rate of tumor progression by preventing their uncontrolled proliferation, and limiting angiogenesis and migration [26, 27]. Vitamin D insufficiency is a signal of tumor progression, but it is also inversely correlated with obesity due to limited adipose tissue formation [28]. Additionally, low ferritin and B12 levels of 46.6% and 21.1, respectively, was reported in a cohort of 1252 pediatric and adult patients with morbid obesity [29]. An inverse correlation between the B12 level and BMI has also been reported [30]. As such, in addition to the improvement in BMIz observed in the present study, the increase in the number of patients within the reference range for ferritin, B12, and vitamin D after 6 months of enteral supplementation is another clear indication of the effectiveness of the nutritional intervention described herein.

Limitations

A cohort of patients more than 200 for each primary and secondary malnutrition should be observed to indicate no difference between effectiveness of hypercaloric supplement more confidently. Additionally, more follow-ups covering more than a year should be added to this kind of analysis to observe the long-term effectiveness of our nutritional intervention.

Conclusions

Enteral nutritional supplementation is an effective nutritional intervention that significantly improves BMIz values and yields a 2-tailed improvement in micronutrient levels after 6 months of administration, regardless of diagnosed disease.

References

1. Martins VJB, Toledo Florêncio TMM, Grillo LP, do Carmo P Franco M, Martins PA, Clemente APG, et al. Long-lasting effects of undernutrition. Int J Environ Res Public Health. 2011;8(6):1817-46. Epub 05/26. doi: 10.3390/ijerph8061817. PubMed PMID: 21776204.
2. Kim DH. Nutritional issues in patients with cancer. Intestinal research. 2019;17(4):455-62. Epub 10/14. doi: 10.5217/ir.2019.00076. PubMed PMID: 31597414.
3. Schaible UE, Kaufmann SH. Malnutrition and infection: complex mechanisms and global impacts. PLoS medicine. 2007;4(5):e115. Epub 2007/05/03. doi: 10.1371/journal.pmed.0040115. PubMed PMID: 17472433; PubMed Central PMCID: PMCPmc1858706.
4. Amoroso L. The Second International Conference on Nutrition: Implications for Hidden Hunger. World Rev Nutr Diet. 2016;115:142-52. Epub 2016/05/21. doi: 10.1159/000442100. PubMed PMID: 27197665.
5. Fakhoury M, Negrulj R, Mooranian A, Al-Salami H. Inflammatory bowel disease: clinical aspects and treatments. J Inflamm Res. 2014;7:113-20. doi: 10.2147/JIR.S65979. PubMed PMID: 25075198.
6. Kotlyar DS, Shum M, Hsieh J, Blonski W, Greenwald DA. Non-pulmonary allergic diseases and inflammatory bowel disease: a qualitative review. World J Gastroenterol. 2014;20(32):11023-32. doi: 10.3748/wjg.v20.i32.11023. PubMed PMID: 25170192.
7. Ludvigsson JF, Ludvigsson J, Ekbom A, Montgomery SM. Celiac Disease and Risk of Subsequent Type 1 Diabetes. A general population cohort study of children and adolescents. 2006;29(11):2483-8. doi: 10.2337/dc06-0794.
8. Cole TJ. The LMS method for constructing normalized growth standards. Eur J Clin Nutr. 1990;44(1):45-60. Epub 1990/01/01. PubMed PMID: 2354692.
9. Statistics NCfH. Percentile Data Files with LMS Values August 4, 2009 [cited 2019 July 3]. Available from: https://www.cdc.gov/growthcharts/percentile_data_files.htm.
10. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj. 2000;320(7244):1240-3. doi: 10.1136/bmj.320.7244.1240. PubMed PMID: 10797032.
11. Barr RD, Gomez-Almaguer D, Jaime-Perez JC, Ruiz-Argüelles GJ. Importance of Nutrition in the Treatment of Leukemia in Children and Adolescents. Arch Med Res. 2016;47(8):585-92. doi: 10.1016/j.arcmed.2016.11.013. PubMed PMID: 28476186.
12. Mathers CD, Lopez AD, Murray CJL. The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001. In: Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL, editors. Global Burden of Disease and Risk Factors. Washington (DC): World Bank, The International Bank for Reconstruction and Development/The World Bank Group.; 2006.
13. Bundy DAP, de Silva N, Horton S, Patton GC, Schultz L, Jamison DT. Investment in child and adolescent health and development: key messages from Disease Control Priorities, 3rd Edition. Lancet (London, England). 2018;391(10121):687-99. Epub 2017/11/21. doi: 10.1016/s0140-6736(17)32417-0. PubMed PMID: 29153316.
14. Bauer J, Jürgens H, Frühwald MC. Important aspects of nutrition in children with cancer. Adv Nutr. 2011;2(2):67-77. Epub 03/10. doi: 10.3945/an.110.000141. PubMed PMID: 22332035.
15. van Eys J. Effect of nutritional status on responses to therapy. Cancer Res. 1982;42(2 Suppl):747s-53s. Epub 1982/01/01. PubMed PMID: 6799193.
16. Sala A, Pencharz P, Barr RD. Children, cancer, and nutrition—A dynamic triangle in review. Cancer. 2004;100(4):677-87. doi: 10.1002/cncr.11833.
17. Dhanapal R, Saraswathi T, Govind RN. Cancer cachexia. J Oral Maxillofac Pathol. 2011;15(3):257-60. doi: 10.4103/0973-029X.86670. PubMed PMID: 22144825.
18. Nursing RCo, Fellow FGRCN. Nutrition in Children and Young People with Cancer: RCN Guidance: RCN; 2014.
19. Schoeman J, Dannhauser A, Kruger M. Malnutrition in paediatric oncology patients2010.
20. Nieuwoudt CH. Nutrition and the child with cancer: Where do we stand and where do we need to go? South Afr J Clin Nutr. 2011;24. doi: 10.1080/16070658.2011.11734376.
21. Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. J Chronic Dis. 1972;25(6):329-43. Epub 1972/07/01. PubMed PMID: 4650929.
22. Brinksma A, Huizinga G, Sulkers E, Kamps W, Roodbol P, Tissing W. Malnutrition in childhood cancer patients: a review on its prevalence and possible causes. Crit Rev Oncol/Hematol. 2012;83(2):249-75. Epub 2012/01/24. doi: 10.1016/j.critrevonc.2011.12.003. PubMed PMID: 22264939.
23. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organization technical report series. 1995;854:1-452. Epub 1995/01/01. PubMed PMID: 8594834.
24. Rahman M, Berenson AB. Accuracy of current body mass index obesity classification for white, black, and Hispanic reproductive-age women. Obstet Gynecol. 2010;115(5):982-8. doi: 10.1097/AOG.0b013e3181da9423. PubMed PMID: 20410772.
25. Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutr Today. 2015;50(3):117-28. Epub 04/07. doi: 10.1097/NT.0000000000000092. PubMed PMID: 27340299.
26. Krishnan AV, Trump DL, Johnson CS, Feldman D. The role of vitamin D in cancer prevention and treatment. Endocrinol Metab Clin North Am. 2010;39(2):401-18, table of contents. Epub 2010/06/01. doi: 10.1016/j.ecl.2010.02.011. PubMed PMID: 20511060; PubMed Central PMCID: PMCPmc5788175.
27. Fleet JC. Molecular actions of vitamin D contributing to cancer prevention. Mol Aspects Med. 2008;29(6):388-96. Epub 2008/08/30. doi: 10.1016/j.mam.2008.07.003. PubMed PMID: 18755215; PubMed Central PMCID: PMCPmc2613446.
28. Kong J, Li YC. Molecular mechanism of 1,25-dihydroxyvitamin D3 inhibition of adipogenesis in 3T3-L1 cells. Am J Physiol Endocrinol Metabol. 2006;290(5):E916-24. Epub 2005/12/22. doi: 10.1152/ajpendo.00410.2005. PubMed PMID: 16368784.
29. Arshad M, Rezvandoost N, Pazouki A, Riazi S, Aghababa Rangraz M, Mokhber S. Assessment of the Serum Levels of Hemoglobin, Ferritin, and Vitamin B12 in a Sample of Iranian Population with Morbid Obesity. J Minim Invasive Surg Sci. 2016;Inpress. doi: 10.17795/minsurgery-37637.
30. Baltaci D, Kutlucan A, Turker Y, Yilmaz A, Karacam S, Deler H, et al. Association of vitamin B12 with obesity, overweight, insulin resistance and metabolic syndrome, and body fat composition; primary care-based study. Medicinski glasnik : official publication of the Medical Association of Zenica-Doboj Canton, Bosnia and Herzegovina. 2013;10(2):203-10. Epub 2013/07/31. PubMed PMID: 23892832.

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