



Retrospective Evaluation of the Relation between Serum Vitamin D Levels and Clinical Findings of Febrile Neutropenia in Childhood Cancer Patients

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Abstract

Vitamin D regulates many genes involved in cell differentiation and proliferation through its nuclear receptor. Induces differentiation of cells; inhibits proliferation, invasion, angiogenesis and metastatic potential of malignant cells. It is generally related to bone metabolism and has anti-inflammatory and immunomodulatory properties. As a result, the duration of neutropenia and the number of days with fever increased as vitamin D decreased. It can be thought that regular monitoring of serum vitamin D levels in patients and replacement in case of deficiency may alleviate the febrile neutropenia clinic and reduce morbidity, but larger and prospective studies are needed for this.

Keywords: Vitamin D; Febrile neutropenia; Childhood Cancer Patients

Introduction

Vitamin D regulates many genes involved in cell differentiation and proliferation through its nuclear receptor. Induces differentiation of cells; inhibits proliferation, invasion, angiogenesis and metastatic potential of malignant cells. It is generally related to bone metabolism and has anti-inflammatory and immunomodulatory properties. It has effects on inflammation, cancer, autoimmunity, allergy, cardiovascular system, infection, obesity and aging through cytokines [1-3]. The level of 25-hydroxy vitamin D (25OHD) required for optimal functioning of immune functions is not clear, but the risk of viral respiratory tract infections and sepsis increases in cases of deficiency [4]. Febrile neutropenic state causes 5% mortality in patients with solid tumours and 10% in patients with hematological malignancies. Therefore, febrile neutropenia is an important and treatment-limiting complication for cancer treatment [5]. In this study, it was aimed to show the relationship

between the clinical course of febrile neutropenia and vitamin D level in childhood cancers.

Material and Methods

Patients aged 0-18 years, who were hospitalized in the Oncology Clinic of our hospital between January 1, 2014 and January 1, 2018 and whose vitamin d was measured to evaluate the nutritional status at diagnosis, constitute the patient group. A total of 44 children without chronic disease and whose serum vitamin D levels were checked in our hospital were included in the control group. The files of the patients were reviewed retrospectively. A body temperature of >38 measured by the tympanic route was considered a febrile condition. Cases with an absolute neutrophil count (ANS) $<500/\text{mm}^3$ or an ANS $<1500/\text{mm}^3$ and predicted to enter neutropenia were considered as neutropenia. Neutropenia severity was evaluated according to the number of ANS. An ANS $<500/\text{mm}^3$ was considered severe neutropenia, an ANS between $500-1000/\text{mm}^3$ was considered moderate neutropenia, and an ANS between $1000-1500/\text{mm}^3$ was considered mild neutropenia.

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The vitamin D levels of the cases who did not receive vitamin D support in the first 2 months after diagnosis and who had an attack of febrile neutropenia; the effects of febrile neutropenia on

the time of occurrence (at the time of diagnosis, within the first month and after the first month), severity and duration were examined.

Table 1: Comparison of number of days with fever and duration of neutropenia according to vitamin D level.

	Vitamin D levels			p-value
	<15ng/ml	15-20 ng/ml	>20 ng/ml	
	Average ± SD	Average ± SD	Average ± SD	
Duration of neutropenia (day)	22,40 ± 16,44	18,00 ± 15,49	16,43 ± 17,15	*0,044
The number of febrile days (day)	5,14 ± 2,27	5,12 ± 3,13	3,86 ± 2,89	*0,015

Table 2: Comparison of days with fever and duration of neutropenia by diagnosis.

	Leukemia (n:42)	Others (n:35)	p-value
	Average ± SD	Average ± SD	
Duration of neutropenia (day)	26,00 ± 19,65	12,43 ± 7,15	*<0,001
The number of febrile days (day)	5,71 ± 2,91	3,40 ± 1,48	*<0,001

Time to recovery from neutropenia, number of days with fever, presence of complications (mucositis, abscess, etc.), glycopeptide use and antifungal use were evaluated. 25-oh vitamin d levels were studied by liquid chromatography method.

A 25 OH Vitamin D level of ≤15 ng/ml was considered as deficiency, between <15-20 ng/ml as insufficient, 20-100 ng/ml as sufficient, and >150 ng/ml as toxicity [6]. Ethics Committee Decision dated 09.07.2018 and file number 2018-100 was obtained from Health Sciences University Ankara Pediatrics Hematology and Oncology Training and Research Hospital. SPSS ('Statistical Package for the Social Sciences') program was used for statistical analysis. The t-test was used to compare clinical parameters between control and patient groups. One-way analysis of variance (ANOVA, Kruskal-Wallis test) was used for comparison between more than two groups. Descriptive statistics (mean, standard deviation, median, frequency, and rate) were used when evaluating the numerical study data. Mann Whitney U test was used to compare the non-normally distributed variables. Fisher's exact test was used to compare qualitative data. The results were evaluated at the 95% confidence interval and the significance level of p <0.05.

Results

There were 77 children (44 male, 33 female) in the patient group and 44 children (29 male, 15 female) in the control group. 42 patients were leukemia (54.5%), 13 patients were lymphoma (16.9%), and 22 patients were solid tumours (28.6%). The mean age of the patient group was 7.99 ± 5.1 years, and 8.36±2.48 years in the control group (p>0.05). The male/female ratio of the

patients was 1.33, and the male/female ratio of the control group was 1.93 (p>0.05). The mean Vitamin D level of the patients was 15.82 (4.30-39.50) ng/ml, and the control group was 18.08 (2.50-38.10) ng/ml (p>0.05). The mean vitamin D level was 16.59 ± 8.58 (4.3-39.5) ng/ml in male patients and 16.71 ± 9.57 (5.8-35.7) ng/ml in females (p>0.05). The vit d level was insufficient (<20ng/ml) in 63.6% of the patients and 47.7% of the control group (p>0.05). Vitamin D level was found to be insufficient (<20ng/ml) in 66.6% of patients with leukemia and 60% of patients with lymphoma and solid tumours (p>0.05).The mean WBC count of the patients was 6182 ± 10919 (103/μL), the mean ANS at the onset of febrile neutropenia was 938 ± 438 (103/μL), and the mean ANS at the exit from febrile neutropenia was 2432 ± 916 (103/μL). Mean duration of neutropenia was 19.83 ± 16.65 days, mean number of days with fever was 4.66 ± 2.62 days.

Vitamin d levels and entry times to febrile neutropenia were compared. Vitamin d level (n.29) of those who were neutropenic at the time of diagnosis was 13.81 ± 7.77 ng/ml. Vitamin d level of those (n.42) who had neutropenia in the first month after diagnosis was 16.94 ± 9.05 ng/ml. One month after the diagnosis, the vitamin d level of those with neutropenia (n.6) was 17.61 ± 9.13 ng/ml. There was no statistically significant difference between them. (p>0.05). Vitamin D levels were analyzed according to the severity of neutropenia. Mean vitamin D level was 13.45 ± 7.76 ng/ml in severe neutropenics (n.16), 15.88 ± 10.88 ng/ml in moderate neutropenics (n.19), 16.69 ± 7.81 ng/ml in mild neutropenics (n.42) (p>0.05). Patients were grouped according to their vitamin D levels. As the vitamin D level decreased, the duration of neutropenia and the number of days



with fever increased, and there was a significant difference between them ($p>0.05$) (Table 1). The duration of neutropenia and the number of days with fever were compared according to their diagnosis, and a statistically significant difference was found between them ($p<0.05$) (Table 2).

Discussion

In our study, the relationship between vitamin D levels and febrile neutropenia in childhood cancer patients was investigated. In the literature, there is a study evaluating the relationship between vitamin d levels and clinical outcomes in febrile neutropenic patients with aplastic anemia. Vineeta Gupta [7] investigated the relationship between febrile neutropenia and low vitamin D levels in patients with aplastic anemia and found that low vitamin D levels were associated with poor clinical outcomes and long disease duration. In our study, a significant correlation was found between vitamin D level and duration of febrile neutropenia and the number of febril days. Weaknesses of our study; The patient group was not homogeneous, the number of patients was insufficient, serum vitamin D levels were screened retrospectively, serum vitamin D levels were not checked at the time of febrile neutropenia, and the treatment protocols of the patients were different. Prospective studies in larger and homogeneous groups are needed to eliminate such variables. As a result, the duration of neutropenia and the number of days with

fever increased as vitamin D decreased. It can be thought that regular monitoring of serum vitamin D levels in patients and replacement in case of deficiency may alleviate the febrile neutropenia clinic and reduce morbidity, but larger and prospective studies are needed for this.

References

1. Rodrigo Mora J, Iwata M, von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. *Nat Rev Immunol.* 2008; 8: 685-698.
2. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007; 357: 266-281.
3. Garland CF, Gorham ED, Lipkin M, Newmark H, Mohr S. The role of vitamin D in cancer prevention. *Am J Public Health.* 2006; 96: 252-261.
4. Ginde AA, Mansbach JM, Camargo CA Jr. Vitamin D deficiency, respiratory infections and asthma. *Curr Allergy Asthma Rep.* 2009; 9: 81-87.
5. Marti F, Cullen MH, Roila F. Management of febrile neutropenia: ESMO clinical recommendations. *Ann Oncol.* 2009; 20: 166-169.
6. Misra M, Pacaud D, Petryk A, Collet-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. *Pediatr.* 2008; 122: 398-417.
7. Gupta V, Kumar V, Singh SK. Low vitamin D levels are associated with an adverse clinical outcome in febrile neutropenia. *J Pediatr Hematol Oncol.* 2016; 38: 202-204.