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Research Article

Vitamin D Levels in Children With Otitis Media With Effusion: A Case-Control Study

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Abstract

Background: Otitis media with effusion (OME) is one of the main sources of hearing impairment in children. One of the possible causes of middle ear infection and OME is immune system disorders. Based on previous studies, vitamin D deficiency plays an important role in the incidence of middle ear infections.

Objectives: This study aimed to determine blood levels of vitamin D in children with OME (as an inflammation of the middle ear) in comparison to a control group of patients admitted to Loghman-Hakim hospital in Tehran.

Patients and Methods: In this case-control study, one hundred twenty children with OME who were admitted to Loghman-Hakim hospital between April 2013 and March 2014 and who were candidates for adenotonsillectomy were studied. They were divided into two groups based on tympanometry. The first group contained patients with OME and hearing loss of Type B or Type C2, and the second group (control) contained patients without OME and tympanometry of Type A or Type C2. On the day of surgery, blood samples were obtained for measurement and comparing of serum levels of vitamin D in the two groups.

Results: In this study, 120 children (40 cases and 80 controls) that were candidates for tonsillectomy were studied. The largest number of cases was males (60%). The mean age of patients with otitis media was 5.7 ± 2.6 years-old and in the control group was 7.2 ± 2.2 years-old. The mean levels of vitamin D in children with OME was 26.1 ± 14.6 ng/mL and in children in the control group was 29.5 ± 17.9 ng/mL (P=0.27). **Conclusions:** Although there was not a significant relation shown between vitamin D levels between the two groups in our study, the vitamin D level in OME patients was less than in the control group. Therefore, it seems that measuring the level of vitamin D in these patients is necessary, and a deficiency of vitamin D must be treated. In order to achieve certain results with more detail we suggest more studies with larger sample sizes and covering a longer time period are needed on this topic.

Keywords: Otitis Media Effusion, Vitamin D, Deficiency, Insufficiency, Hearing Impairment

1. Background

Otitis media (OM) is one of the most prevalent diseases in childhood and is the main reason for visiting a doctor, in children under three years of age. Almost 80% of children up to the age of seven are infected once, but some are infected frequently (1). OM is seen as acute otitis media (AOM), recurrent otitis media, chronic otitis media and otitis media with effusion (OME)(2). The pathophysiology of OME is associated with eustachian tube dysfunction (3). The most common causes of this obstruction are adenoid hypertrophy, sub mucosal cleft palate, allergies, upper respiratory tract infection, tumors, sinusitis, AOM and radiation. Obstruction of the eustachian tube causes accumulation of fluid in the middle ear (4). The risk factors of OME are male gender, bottle-feeding (though controversial), early occurrence of otitis in childhood, populated places, low socioeconomic status, smoking at home, parental history of otitis media, young age and race, where it is common in whites (5). One of the possible causes of middle ear infections and OME is immune system disorders (6). In recent years, several studies have been conducted on the risk factors associated with the weakening of the immune system, in which the role of vitamin D can be pointed out. Vitamin D reduces inflammation by decreasing the production of interleukins and interferon gamma (7).

Cayir et al. studied the role of vitamin D in the treatment of children with recurrent otitis media and concluded that administration of vitamin D, in addition to common treatments, is a good option in the treatment of upper respiratory tract infections such as otitis media (8). In another study by these authors, they studied the vitamin D levels in children with acute otitis media and concluded that vitamin D deficiency plays an important role in the incidence of middle ear infections (7). Marchisio et al. investigated the role of vitamin D in reducing the risk of recurrent middle ear infections. They suggested that serum levels of vitamin D in children with acute recurrent otitis media should be tested, and in children with low levels of

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vitamin D supplementation, in addition to conventional treatment methods, might be effective in improving the disease (9). Mulligan et al. studied the relation between vitamin D deficiency and chronic sinusitis; they concluded that low levels of vitamin D could be one of the risk factors for chronic or fungal sinus infections (10).

2. Objectives

Based on the results of studies of systemic inflammatory diseases and its association with vitamin D levels, this study assumes that OME, as an inflammatory process, may be associated with vitamin D deficiency. Thus, the aim of this study was to determine blood levels of vitamin D in children with OME compared to a control group.

3. Patients and Methods

3.1. Study Type and Population

This hospital-based cross-sectional study was conducted between April 2013 and March 2014 at Loghman-Hakim hospital. One hundred twenty children who were candidates for adenotonsillectomy based on inclusion criteria were enrolled in the study during the mentioned time period. The sample size was calculated using a Raosoft sample size calculator, using a 5% margin of error, confidence level of 95%, and response distribution of 5%. Patients were randomly divided into study (patients with OME) and control (patients without OME) groups and matched for age and gender.

3.2. Inclusion Criteria

3.2.1. Study Group

Included in the study group were children aged between 3 to 10 years-old with OME and who were candidates for adenotonsillectomy based on the drainage of the middle ear (glue) during myringotomy and who experienced hearing loss (type B) or (type C2) based on tympanometry.

3.2.2. Control Group

The control group included children between 3 to 10 years-old without OME and who were not candidates for adenotonsillectomy based on normal physical exam and tympanometry (type A) and (type C1).

3.3. Exclusion Criteria

1) Tympanometry (type B) and lack of the drainage of the middle ear.

2) Tympanometry (type B) and response to antibiotic therapy.

3) Factors affecting blood levels of vitamin D, such as malignancies, renal failure, liver failure, and vitamin D consumption during the last week.

3.4. Blood Sampling and Vitamin D Levels

Blood samples were taken from all patients to evaluate serum levels of 25(OH) D3 measured by enzyme-linked immunosorbent assay (ELISA). A vitamin D level < 15 ng/mL was considered as deficiency, 15-30 ng/mL was considered as vitamin D insufficiency, 31-60 ng/mL was regarded as normal and levels > 60 ng/mL were considered as toxic.

3.5. Ethics

This study was approved by the Shahid Beheshti University of Medical Sciences ethics committee. Each patient signed an informed consent form when enrolled in the study and patients' medical records and personal information were kept confidential.

3.6. Data Analysis

The Statistical package for social sciences (SPSS) version 21 (SPSS Inc., Chicago, IL) was used for data analysis. Quantitative variables were expressed as Mean \pm SD and qualitative variables were expressed as number and percentage. To compare the results between the two groups, a paired sample independent t-test was used, and qualitative variables were compared by Chi-square and Fisher's exact tests. A P < 0.05 was considered as significant.

4. Results

4.1. Demographic Data

One hundred twenty children with and without OME were studied in two groups: a study group (40 individuals, 24 males (60%) and 16 females (40%)) and a control group (80 individuals, 47 males (58.8%) and 33 females (41.2%)) (P > 0.999). Mean age of the study group was 5.7 ± 2.6 years-old and of the control group was 7.2 ± 2.2 years-old (P = 0.002).

4.2. Tympanometry Results

Of 80 children in the control group, 70 (87.5%) were Type A and 10 individuals (12.5%) were Type C1. of 40 children in the OME group two patients (5%) were type C2 and 38 individuals (95%) were type B.

4.3. Blood Levels of Vitamin D

The mean vitamin D level in the OME group was 26.1 ± 14.6 ng/mL with a minimum of 6 ng/mL and a maximum of 67.6 ng/mL. In the control group, the mean was 29.5 ± 17.9 ng/mL with a minimum of 8.1 ng/mL and a maximum of 139 ng/mL. Vitamin D levels were not significantly different between the two groups (P = 0.27). The number of patients in each level of vitamin D is shown in Table 1, where there was no significant difference between the two groups (P = 0.49).

Variables	OME Group	Control Group	P Value
Vitamin D levels ,ng/mL			0.49
<15	8(20)	11 (13.8)	
1-30	22 (55)	42 (52.5)	
31 - 60	8 (20)	25 (31.2)	
>60	2(5)	2 (2.5)	

^aValues are expressed as No. (%).

5. Discussion

OME in children may lead to speech delay and learning problems, and in the case of chronicity, serious complications, such as hearing loss, adherence or rupture of the tympanic membrane, ear ossicular problems and even behavioral problems, are to be expected (11). Despite the considerable role of vitamin D in human health, its deficiency is a major health problem worldwide (12). Unfortunately, the amount of vitamin D from food sources is not enough and vitamin D-rich food sources are limited and unable to provide the required amounts. This is the most important cause of the outbreak of vitamin D deficiency even in European and American countries. In fact, the production of Vitamin D in the presence of ultraviolet solar radiation in the skin is the main source (13). Vitamin D has anti-inflammatory effects and has a modulation role in the immune system. The effect of the immune modulating effects of vitamin D applies from its receptors on the majority immune cells (14). Vitamin D reduces the activity of nuclease factor, interleukin and IFN γ , which results in lowering of the inflammation process (15). In several studies, the role of vitamin D deficiency has been proven in respiratory and middle ear infections (7, 9). Sabetta et al. (16) stated that a vitamin D level of more than 30 ng/mL significantly (P < 0.0001) reduces the risk of respiratory infections.

In this study, 120 children who were candidates for adenotonsillectomy were studied in two groups; an OME and a control group. In the OME group, most patients were boys (60%), and according to recent studies, male gender is one of the risk factors for OME (17). Twenty percent of patients with OME had vitamin D deficiency (< 15 ng/mL), compared to 13.8% in the control group. Vitamin D insufficiencies (15-30 ng/mL) were 55% and 52.5% in the OME and control group, respectively. In a study by Linday et al. (18), in eiht patients (50%) the level of Vitamin D was under 20 ng/mL, which was considered as deficiency, and in 31% of the patients the level was insufficient (21-29 ng/ mL). Cayir et al. (19) reported the mean level of Vitamin D in 58 (69%) individuals was under 20 ng/mL (deficiency), compared to 32 (30%) in the control group. In our study the mean level of vitamin D in OME children was less than the control group, however, the difference between the two groups was not significant.

In a study conducted in Tehran in 2004 (20), the different levels of vitamin D deficiency, severe, moderate and mild were reported as 9.5%, 57.6% and 14.2%, respectively.

According to the results of the mentioned studies, a significant correlation was indicated between vitamin D deficiency and different infections such as middle ear infections. Although in our study there was not a significant relation between vitamin D levels in the two groups, the vitamin D level in OME patients was less than the control group. Thus, it seems that measuring the level of vitamin D in these patients is necessary and, in the case of deficiency, it should be treated. Administration of vitamin D supplements, in addition to conventional treatments, can be useful in treating OME.

In order to achieve certain results and more detail it is recommended that the sample size should be larger and that future studies be conducted over a longer time period.

References

- Erdivanli OC, Coskun ZO, Kazikdas KC, Demirci M. Prevalence of Otitis Media with Effusion among Primary School Children in Eastern Black Sea, in Turkey and the Effect of Smoking in the Development of Otitis Media with Effusion. *Indian J Otolaryngol Head Neck Surg.* 2012;64(1):17–21. doi: 10.1007/s12070-011-0131-z. [PubMed: 23449553]
- Bluestone CD, Stephenson JS, Martin LM. Ten-year review of otitis media pathogens. *Pediatr Infect Dis J.* 1992;11(8 Suppl):S7-11. [PubMed: 1513611]
- Poe DS, Abou-Halawa A, Abdel-Razek O. Analysis of the Dysfunctional Eustachian Tube by Video Endoscopy. Otol Neurotol J. 2001;22(5):590–5. doi:10.1097/00129492-200109000-00005.
- Bhat V, Bhandary SK, Shenoy V. Otitis media with effusion in relation to socio economic status: a community based study. *Indian J Otolaryngol Head Neck Surg.* 2012;64(1):56–8. doi: 10.1007/s12070-011-0163-4. [PubMed: 23449688]
- Kubba H, Pearson JP, Birchall JP. The aetiology of otitis media with effusion: a review. *Clin Otolaryngol Allied Sci.* 2000;25(3):181– 94. [PubMed: 10944048]
- Pichichero ME, Reiner SA, Brook I, Gooch 3rd WM, Yamauchi T, Jenkins SG, et al. Controversies in the medical management of persistent and recurrent acute otitis media. Recommendations of a clinical advisory committee. *Ann Otol Rhinol Laryngol Suppl.* 2000;183:1–12. [PubMed: 10963616]
- Ashhurst-Smith C, Hall ST, Burns CJ, Stuart J, Blackwell CC. In vitro inflammatory responses elicited by isolates of Alloiococcus otitidis obtained from children with otitis media with effusion. *Innate Immun.* 2014;**20**(3):320–6. doi: 10.1177/1753425913492181. [PubMed: 23812253]

- Cayir A, Turan MI, Ozkan O, Cayir Y, Kaya A, Davutoglu S, et al. Serum vitamin D levels in children with recurrent otitis media. *Eur Arch Otorhinolaryngol.* 2014;**271**(4):689–93. doi: 10.1007/s00405-013-2455-7. [PubMed: 23543299]
- Marchisio P, Consonni D, Baggi E, Zampiero A, Bianchini S, Terranova L, et al. Vitamin D supplementation reduces the risk of acute otitis media in otitis-prone children. *Pediatr Infect Dis J.* 2013;32(10):1055–60. doi: 10.1097/INF.0b013e31829be0b0. [PubMed: 23694840]
- Mulligan JK, White DR, Wang EW, Sansoni SR, Moses H, Yawn RJ, et al. Vitamin D3 deficiency increases sinus mucosa dendritic cells in pediatric chronic rhinosinusitis with nasal polyps. *Otolaryngol Head Neck Surg*. 2012;**147**(4):773–81. doi: 10.1177/0194599812448852. [PubMed: 22627120]
- Rovers M, Haggard M, Gannon M, Koeppen-Schomerus G, Plomin R. Heritability of symptom domains in otitis media: a longitudinal study of 1,373 twin pairs. *Am J Epidemiol.* 2002;**155**(10):958–64. [PubMed: 11994236]
- Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int*. 2009;**20**(11):1807–20. doi: 10.1007/s00198-009-0954-6. [PubMed: 19543765]
- Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87(4):1080S-6S. [PubMed: 18400738]
- 14. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and

markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutr J.* 2008;**7**:4. doi: 10.1186/1475-2891-7-4. [PubMed: 18226257]

- Timms PM, Mannan N, Hitman GA, Noonan K, Mills PG, Syndercombe-Court D, et al. Circulating MMP9, vitamin D and variation in the TIMP-1 response with VDR genotype: mechanisms for inflammatory damage in chronic disorders? *QJM*. 2002;**95**(12):787– 96. [PubMed: 12454321]
- Sabetta JR, DePetrillo P, Cipriani RJ, Smardin J, Burns LA, Landry ML. Serum 25-hydroxyvitamin d and the incidence of acute viral respiratory tract infections in healthy adults. *PLoS One.* 2010;5(6):e11088. doi: 10.1371/journal.pone.0011088. [PubMed: 20559424]
- Androw F, Inglis JR, Gates A. Acute otitis media and otitis media with effusion. In: Cummings CW. Cummings otolaryngology head and neck surgery. Philadelphia: Mosby Company; 2005. pp. 4445-68.
- Linday LA, Shindledecker RD, Dolitsky JN, Chen TC, Holick MF. Plasma 25-Hydroxyvitamin D Levels in Young Children Undergoing Placement of Tympanostomy Tubes. *Rhinol Laryngol J.* 2008;**117**(10):740-4. doi:10.1177/000348940811701006.
- Cayir A, Turan MI, Ozkan O, Cayir Y. Vitamin D levels in children diagnosed with acute otitis media. J Pak Med Assoc. 2014;64(11):1274-7. [PubMed: 25831645]
- 20. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M, et al. Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public Health*. 2004;**4**:38. doi: 10.1186/1471-2458-4-38. [PubMed: 15327695]