Association between Plasma Level of Vitamin D and Tonsillar Hypertrophy in Children Undergoing Tonsillectomy

Akbar Pirzadeh¹, Afshan Sharghi² and Mehrdad Nikmanesh³

¹Department of Otorhinolaryngology, Fatemi Hospital, Ardabil University of Medical Sciences, Ardabil, Iran ²Department of Community Medicine, Faculty of Medicine, Ardabil University of Medical Science, Ardabil, Iran; a.sharghi@arums.ac.ir ³Faculty of Medicine, Ardabil University of Medical Science, Ardabil, Iran

Abstract

Background and Objects: Vitamin D effects on body immune system. Tonsils as a part of immune system have active role in transferring foreign material into lymphoid cells and diagnosis of antigens. Tonsil hypertrophy with difficulty in breathing or ingestion is one of the indications of tonsillectomy. The purpose of this study is to evaluate association between plasma level of vitamin D and tonsil hypertrophy. Method: This case control study was done on 200 children that admitted to Ear, Nose, Throat (ENT) clinic, divided into 2 groups. Case group included 100 patients that had tonsil hypertrophy (grade 3 or 4)which accompanied with signs such as snoring. These patients were candidate for tonsillectomy. Control group didn't have any related disease and didn't take any drugs. In addition to completing questionnaire, plasma level of 25(OH) vitamin D was measured by Electro Chemi Luminescence (ECL) and all data were analyzed by statistical methods in SPSS version 16. **Results**: Plasma level of vitamin D in males was significantly higher than females. In people with tonsil hypertrophy, plasma level of vitamin D was significantly lower than control group but there was no relationship between plasma level of vitamin D and tonsil size. 95 of people (47.5%) had vitamin D deficiency. Vitamin D deficiency had no difference in both groups' but was more prevalent in case group (65% in case group versus 35% in control group) and was significantly higher in males than females. **Conclusion:** results showed that plasma level of vitamin D in females and patients with tonsil hypertrophy is lower and vitamin D deficiency is more prevalent in children with tonsil hypertrophy. Thus, another study should be designed to confirm correlation between vitamin D and tonsil diseases and after confirmation, use of vitamin D supplements should be considered in patients with tonsil diseases.

Keywords: Tonsil Disease, Tonsil Hypertrophy, Tonsillectomy, Vitamin D

1. Introduction

Adenotonsillectomy is a common surgery in infants and indices such as tonsil hypertrophy that deal to problem in breathing and swallowing defined for it. Acute tonsillopharyngitis accounts for 1-2% among adult people who referred to emergency departments of all hospitals. The association between vitamin D deficiency and the susceptibility to infections of the respiratory tract has been suggested for many years $\frac{1-5}{2}$.

Local and systemic infections play a role in the pathophysiology of tonsil diseases and inflammation, and their control is effective in reducing the number of surgical procedures. Recent studies today focus on the effects of non-classic vitamin D, which involves various aspects of the immune response. According to recent studies,

*Author for correspondence

the low level of Vitamin D In addition to being associated with infectious and autoimmune diseases, the high prevalence of infectious and inflammatory diseases is associated with upper and lower airways including influenza, pneumonia, otitis and rhinosinusitis¹.

In a study showed that 60% of referred patients to ENT clinic, had vitamin D deficiency. Some studies found significant relation between vitamin D deficiency and tonsil diseases⁶⁻⁸ and some studies dose not found^{1.9}.

Many studies showed the efficiency of the immune system could be improved by using vitamin D^{10} .

Considering to the controversy about the relationship between vitamin D and tonsil diseases and, on the other hand, due to the lack of a study in this topic, the aim of this study was to assessment the Association between plasma level of vitamin D and Tonsillar Hypertrophy in children undergoing tonsillectomy.

2. Methods and Materials

This case-control study was done on 200 patients referred to ENT clinic. Patients divided randomly in two groups. The case group included 100 patients with tonsil hypertrophy in grade 3 or 4 which candidate for tonsillectomy and control group including healthy patients without any especial diseases and history of surgery and tonsil hypertrophy. All of patients in two groups were visited by an ENT specialty. Data collected by a checklist including characteristics such as age, sex, residence place, history of drug use and also clinical symptoms. All patients completed the consent form.

2.1 Inclusion and Exclusion Criteria

All patients with age in range 3-15 years suffered to hypertrophy in grade 3 or 4 as a case group and other patients without immunological disorders and Malabsorption disorders as a control group entered in the study.

Patients with using special drugs such as corticosteroids or Multivitamins containing vitamin D or Patients who did not require routine blood tests excluded from the study.

2.2 Laboratory Methods

We obtained blood samples from all patients to measure the Serum Vitamin D level and we used ELISA method for measure the Vitamin D level. We divided the Vitamin D levels in three categories such as:

Vitamin D deficiency (<10 ng/ml|), insufficient (>=10 and < 20) and Normal value (>=20 and <=100) and toxic level (>100 mg/nl) (20).

2.3 Statistical Analyses

Collected data were analyzed by descriptive and analytical methods in SPSS version 22. We used t-test for compare mean between two variables. The p<0.05 was considered as significant.

3. Results

Of all patients, 128 (64%) were male and rest of them were female and gender distribution was similar between two groups. The mean age of all patients was 7.12 ± 3.18 in age range 3-15 years and the difference between two groups wasn't significant. Of all patients, 95 (47.5%) had vitamin D deficiency and 74 (37%) had vitamin D insufficiency. The mean of vitamin D level in all patients was 21.83 ± 12.48 ng/mL. The mean of vitamin D level in case group was 19.21 ± 9.8 ng/mL which was significantly lower than control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in case group was 19.21 ± 9.8 ng/mL which was significantly lower than control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in Control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in case group was 19.21\pm9.8 ng/mL which was significantly lower than control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in Control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in case group was 19.21\pm9.8 ng/mL which was significantly lower than control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in Control group with 24.45 ± 14.25 ng/mL. The mean of vitamin D level in male patients: 23.22 ± 11.95 ng/mL significantly higher than female patients with 19.36 ± 13.09 ng/mL (Figure 1). Snoring during sleep in colds with 70% was the most common symptoms in patients (Table 1).

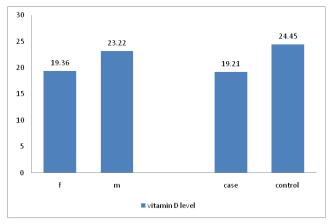


Figure 1. The level of vitamin D by sex and groups.

In case group, 68% had tonsil hypertrophy with grade 3 and 32% had tonsil hypertrophy with grade 4. The mean of vitamin D level in group with tonsil hypertrophy with

Groups Problem	Case		Control		Total			OR
	n	%	n	%	n	%	p-value	OK
Breathing	90	45	12	6	102	51	0.001	66
Snoring during sleep	88	44	21	10.5	109	54.5	0.001	27.6
Snoring during sleep in colds	99	49.5	41	20.5	140	70	0.001	142
Sleep apnea	79	39.5	11	5.5	90	45	0.001	30

 Table 1. Frequency of symptoms among patients in two groups

grade 3 was similar to group with tonsil hypertrophy with grade 4 (19.79±8.58 ng/mLv.s 17.97±12.02 ng/mL).

62% in case group and 33% in control group had vitamin D deficiency (under 20 ng/dl) and the rate of vitamin deficiency in case group more common than control group (about 2 time).

Of all patients with vitamin D deficiency in two groups, 57.9% were male and 42.1% were female. Of all 62 patients with low vitamin D level in case group, 39 (62.9%) had tonsil hypertrophy in grade 3 and 23 (37.1%) in grade 4. The mean of vitamin D level in patients with vitamin D deficiency was 13.18±4.51 ng/mL. The mean of vitamin D level in case group was 13.38±3.9 ng/mL and control group was 12.79±5.52 ng/mL and the difference wasn't significant. The mean of vitamin D level in male patients with vitamin D deficiency were 14.53±4.32 ng/mL and female patients with vitamin D deficiency were 11.31±4.12 ng/mL and the difference was significant. Of all patients with insufficiency in vitamin D, 67.5% were male and 32.4% were female. 33.8% were in case group and 66.2% in control group. Of all patients with insufficiency in vitamin D in case group, 80% had hypertrophy in grade 3 and 20% in grade 4 and there weren't significant relation between vitamin D level and gender and size of tonsil.

4. Discussion

In this study 200 infants between 3-15 age groups entered in the study and divided randomly in two equal size groups. In Reid et al., study, 33 infants in range 4-16 years participated in the study but this study had not control group⁶.

In study¹, 47 infants under tonsillectomy and 15 infants go under elective procedures without tonsillectomy participated in the study.

In other study the age range of infants who participated in the study was 2-12 years which was similar to our study cases^{7.9}.

In our study the mean level of vitamin D in cases with tonsil hypertrophy was significantly lower than control group and in cases with vitamin D insufficiency, the mean of vitamin D in case group wasn't difference with control group. In Reid et al., study, 15.6% of patients had vitamin D deficiency (25(OH)D<50 nmol/L) and in 78% the level of vitamin D was lower than 75 nmol/L⁶.

In studies^{1.9}, there wasn't significant difference between two groups.

In study², in case group 18% of infants had vitamin D level lower 80 nmol/L and based on the vitamin D deficiency in infants with tonsillitis was more common.

In study^Z, there was significant difference between two groups in level of vitamin D (p=0.01). In case group 4.7% of infants had vitamin D level lower 50 nmol/L. The vitamin D deficiency in infants with tonsillitis was common than other infants.

In study¹¹, Mean serum levels of 25(OH) vitamin D among subjects with recurrent GAS tonsillopharyngitis were significantly lower from the controls (11.5 ng/mL \pm 4.7 vs. 26 ng/mL \pm 7; p = 0.001).

Vitamin D insufficiency was more prevalent in children with recurrent tonsillitis than in healthy children¹². Two double-blind randomized controlled trials of vitamin D supplementation have shown that vitamin D reduces the incidence of URT infection^{13,14}.

In functioning of the immune system in various infectious and autoimmune conditions vitamin D could have a main role. In a study¹⁰ showed that the concentration of vitamin D in all participants was 11.96+/-5.85 ng/ml and the difference between two groups with otitis media and control was statistically significant.

In study^{1.6.7.9} the total vitamin D level in male was significantly higher than female but in infants with vitamin D deficiency (95 cases), the mean level of vitamin D in female was significantly higher than female. In infants with vitamin D insufficiency (74 cases), there wasn't significant relation between the mean level of vitamin D and gender which was similar to other studies in other places.

In study⁶, there wasn't significant relation between vitamin D level and size of tonsil which wasn't similar to Reid et al study. The increase in the size of tonsil lead to lower level of vitamin D is not discussed^{1,7,9} on this relation in studies.

The role of vitamin D in adenotonsillar hypertrophy were studied in many studies¹⁵⁻¹⁷ and the results of studies showed that level of vitamin D could be correlated to ton-sillar size and also could prevent the mitogenic- induced proliferation of tonsillar tissue.

5. Conclusion

Results showed that the mean level of vitamin D and its deficiency in patients with tonsil hypertrophy significantly lower than control group. Also the results showed that the mean of vitamin D in male significantly was more than female, but in this study there wasn't significant relation between the level of vitamin D with tonsil size (grade 3 or 4).

6. Limitation

The serum vitamin D level in infants could be affected by nutrition and exposure to sun. Also the check for study polymorphism receptor gene of vitamin D (VDRD) doesn't do in this study.

Conflict of interest: none-declared

7. References

- Esteitie R, Naclerio RM, Baroody FM. Vitamin D levels in children undergoing adenotonsillectomies. Int. J. Pediatr. Otorhinolaryngol. 2010; 74(9):1075-77. https://doi.org/10.1016/j.ijporl.2010.06.009. PMid: 20638140.
- Adams S John, Hewison M. Update in vitamin D. J. Clin. Endocrinol. Metab. 2010; 95(2):471-83. PMCID: PMC2840860. https://doi.org/10.1210/jc.2009-1773. PMid: 20133466, PMCid: PMC2840860.
- 3. Moore R. Atlas of head and neck surgery-otolaryngology, by Byron J. Bailey and Karen H. Calhoun, Lippincott Williams & Wilkins, Philadelphia; 2001. p. 1018.
- Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1996. Vital Health Stat. 1998; 13(134):1-37.

- Najada AS, Habashneh MS, Khader M. The frequency of nutritional rickets among hospitalized infants and its relation to respiratory diseases. J. Trop. Pediatr. 2004; 50:364-8.
- Reid D, Morton R, Salkeld L, Bartley J. Vitamin D and tonsil disease--preliminary observations. Int. J. Pediatr. Otorhinolaryngol. 2011 Feb; 75(2):261-4. doi: 10.1016/j. ijporl.2010.11.012, https://doi.org/10.1016/j.ijporl. 2010.11.012. PMid: 21131064.
- Yildiz I, Unuvar E, Zeybek U, Toptas B, Cacina C, Toprak S, Kilic A, et al. The role of vitamin D in children with recurrent tonsillopharyngitis. Ital. J. Pediatr. 2012; 38:25. https://doi.org/10.1186/1824-7288-38-25. PMid:22682426, PMCid:.PMC3453523.
- Bartley J, Reid D, Morton RP. Prevalence of vitamin D deficiency among patients attending a general otolaryngology clinic in South Auckland. Ann. Otol. Rhinol. Laryngol 2009; 118(5):326-8. DOI: 10.1177/000348940911800502. https://doi.org/10.1177/000348940911800502. PMid: 19548380.
- Aydın S, Aslan I, Yıldız I, Ağaçhan B, Toptas B, Toprak S, et al. Vitamin D levels in children with recurrent tonsillitis. Int. J. Pediatr. Otorhinolaryngol. 2011; 75(3):364-67. doi: 10.1016/j.ijporl.2010.12.006. https://doi.org/10.1016/j. ijporl.2010.12.006. PMid: 21215466.
- Asghari A, Bagheri Z, Jalessi M, Mahdi Salem M, Amini E, Ghaleh Baghi S, et al. Vitamin D levels in children with adenotonsillar hypertrophy and otitis media with effusion. Iranian Journal of Otorhinolaryngology. 2017; 29(1):29-33.
- Nseir W, Mograbi J, Abu-Rahmeh Z, Mahamid M, Abu-Elheja O, Shalata A. The association between vitamin D levels and recurrent group: A streptococcal tonsillopharyngitis in adults. International Journal of Infectious Diseases. 2012; 16:e735-38. https://doi.org/10.1016/j. ijid.2012.05.1036. PMid: 22841558.
- Aydin S, Aslan I, Yildiz I, Agachan B, Toptas B, Toprak S, et al. Vitamin D levels in children with recurrent tonsillitis. Int. J. Pediatr. Otorhinolaryngol. 2011; 75:364-67. https:// doi.org/10.1016/j.ijporl.2010.12.006. PMid: 21215466.
- Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza: A in schoolchildren. Am. J. Clin. Nutr. 2010; 91:1255-60. https://doi.org/10.3945/ ajcn.2009.29094. PMid: 20219962.
- Laaksi I, Ruohola JP, Mattila V, Auvinen A, Ylikomi T, Pihlajamaki H. Vitamin D supplementation for the prevention of acute respiratory tract infection: A randomized doubleblinded trial amongst young Finnish men. J. Infect. Dis. 2010; 202:809-14. https://doi.org/10.1086/654881. PMid: 20632889.
- Mc Carty DE, Chesson Jr AL, Jain SK, Marino AA. The link between vitamin D metabolism and sleep medicine. Sleep Medicine Reviews. 2013; 18(4):311-19. https://doi. org/10.1016/j.smrv.2013.07.001. PMid: 24075129.

- Reid D, Morton R, Salkeld L, Bartley J. Vitamin D and tonsil disease preliminary observations. Int. J. Pediatr. Otorhinolaryngol. 2011; 75(2):261-64. https://doi. org/10.1016/j.ijporl.2010.11.012. PMid: 21131064.
- 17. Nunn JD, Katz DR, Barker S, Fraher LJ, Hewison M, Hendy GN, et al. Regulation of human tonsillar T-cell proliferation by the active metabolite of vitamin D3. Immunology. 1986; 59(4):479-84.