



Evaluation of Serum Vitamin D Level in Babies Followed with the Diagnosis of Laryngomalacia

Serdar Ferit Toprak¹, Muhammed Aryal² and Serkan Dedeoglu^{3*}

¹Department of Audiology, Artuklu University, Mardin, Turkey

²Department of Otorhinolaryngology, Dicle University, Diyarbakır, Turkey

³Department of Otorhinolaryngology, University of Health Sciences Gazi Yasargil Training and Research Hospital, Turkey

*Corresponding Author: Serkan Dedeoglu, Department of Otorhinolaryngology, Diyarbakır, University of Health Sciences Gazi Yasargil Training and Research Hospital, Turkey

Received: 📅 November 11, 2022

Published: 📅 November 25, 2022

Summary

Objectives: The relationship between vitamin D and laryngomalacia is not fully known. Our study aimed to investigate whether there is any relationship between laryngomalacia and vitamin D.

Materials and Methods: Thirty-two patients under one year of age with a diagnosis of laryngomalacia without any other disease were included in our study. Anamnesis, physical examination, and examination with a flexible endoscope were performed. Serum levels of calcium, parathormone (PTH), and vitamin D were analyzed as laboratory tests and compared between the two groups.

Results: There was a significant decrease in serum vitamin D levels compared with the control group infants ($p = 0.002$). There was no significant difference in serum calcium and parathormone levels (Calcium $p = 0.089$, PTH $p = 0.689$).

Conclusions: In our study, Vitamin D levels of infants in the control group were found to be higher than those of infants with laryngomalacia. However, there was no difference in parathormone and calcium serum levels. We suggest that vitamin D deficiency may cause the etiology of laryngomalacia, which has not been entirely determined.

Keywords: Stridor; Parathormone; Calcium; Laryngomalacia

Abbreviations: PTH: Parathormone; 25-OH D: 25-Hydroxy Vitamin D; SD: Standard Deviation; SPSS: Statistical Package for Social Sciences

Introduction

Laryngomalacia can be defined as the inward collapse of the supraglottic region during respiratory intake [1]. It is the most common congenital laryngeal anomaly in infants, causing 45% to 75% of stridor symptoms in infants under one year of age [2]. The

most important symptom is a loud breathing problem that increases with breathing. Difficulty breathing is worse with crying, breast-feeding, and lying down. Symptoms begin after birth and usually disappear after the age of two years [1,3]. Although laryngomalacia

is seen as a disease with mild symptoms in the first 24 months of life in children followed up with a diagnosis of laryngomalacia, respiratory distress requiring surgery may occur in a very small number of children [2]. The diagnosis is made by observation of supraglottic collapse on flexible laryngoscopic examination [4]. Although surgery is not considered in many babies with laryngomalacia, this intervention may be necessary if the baby is not developing and has a severe respiratory failure [4,5]. The exact cause and pathophysiology of laryngomalacia are still unknown.

Different theories are considered in the etiology of laryngomalacia. Incomplete cartilage development, muscular and nervous system disorders, reflux are the most common causes [5-7]. Since these theories cannot fully explain the reason and pathophysiology of laryngomalacia, studies in this field continue. There is much research on vitamin D. Although vitamin D is an important cellular vitamin, its deficiency can cause many diseases [8-10]. There are articles in the literature that try to find the effect of vitamin D [11,12]. It was observed that most of these studies were on extremity diseases, and there were very few studies on vitamin D related to the larynx and trachea. Although vitamin D deficiency is known to be associated with congenital stridor [13,14], an etiological link of vitamin D with laryngomalacia has not yet been found. Another issue is that publications have investigated the relationship between chondromalacia and vitamin D serum levels [15,16]. By analyzing these studies, we thought it was essential to investigate the link between vitamin D and laryngomalacia. In our study, we aimed to find the relationship between the amount of vitamin D in the blood and patients with laryngomalacia. This study aimed to examine whether vitamin D serum levels are low in infants with laryngomalacia.

Materials and Methods

This study was conducted by the principles of Good Clinical Practice and the Declaration of Helsinki. This case-controlled, non-randomized study was performed on patients consulted or admitted to the otorhinolaryngology outpatient clinic from pediatric outpatient clinics. The study group included 32 infants (21 boys, 11 girls) who were less than one year old, born at a typical birth week, had no congenital disease and were diagnosed with laryngomalacia by endoscopy. Other genetic respiratory tract diseases (such as hemangioma in the vocal cord region, tracheal obstruction), wheezing after birth (history of croup and mechanical ventilator dependence), infectious or nervous system diseases, and babies thought to have genetic diseases were determined as exclusion criteria. As a control group, 38 healthy infants (28 boys, 10 girls)

younger than one year of age without signs of laryngomalacia were included. Detailed anamnesis, systemic physical examination, flexible laryngoscopic examination, and laboratory tests (25-Hydroxy vitamin D (25-OH D), calcium (Ca), and parathormone (PTH)) were performed. In the detailed anamnesis, it was questioned whether wheezing was present with breathing and whether respiratory distress increased with breastfeeding or lying down.

On physical examination, the presence of suprasternal retraction was examined. A laryngoscopic exam was performed with a flexible laryngoscope in the otorhinolaryngology outpatient clinic. The babies were placed on their mothers' laps, and the laryngeal region was observed by entering the nostrils with the endoscope and advancing the nasal cavity nasopharynx oropharynx. This examination revealed laryngomalacia when the supraglottic collapse was observed during inspiration. None of the infants required operation. All sick and healthy infants were given 400 units of vitamin D daily by mouth from birth within the scope of the vitamin D supplementation and administration program of the Ministry of Health. Vitamin D serum levels were measured after informed consent was obtained from the parents of patients with laryngomalacia and healthy individuals selected as the control group. Ca, PTH, and 25-OH D levels were measured in the serum obtained by centrifuging the blood. Patients were divided into standard (≥ 30 ng/ml), deficiency (29-20 ng/ml), deficiency (19-10 ng/ml), and severe deficiency groups according to vitamin D levels (≤ 9 ng/ml and below) [17,18]. The ethics committee approved this study of Dicle University Faculty of Medicine at its meeting dated 10.11.2021 with ethics committee number 445.

Statistical Analysis

IBM SPSS Statistics 20 (Statistical Package for Social Sciences v.21, IBM, Chicago, IL) program was used to calculate statistical data. Data were expressed as mean and standard deviation (SD). Student's t-test was used to compare the means between cases and controls, with a p-value of $< .05$ considered statistically significant. 25-Hydroxy vitamin D, calcium, and parathormone were analyzed using the Kolmogorov-Smirnov test. Of the 70 infants in our study, 49 were boys, and 21 were girls. The mean age was 4.83 ± 1.23 months. It was found that there was no significant difference between healthy infants and those diagnosed with laryngomalacia. Table 2 shows a substantial decrease in serum 25-hydroxy vitamin D levels compared to the control group infants ($p = 0.002$). There was no significant difference in serum calcium and parathormone levels ($p = 0.089$ for calcium and $p = 0.689$ for PTH).

Table 1: Serum Vitamin D levels in the groups.

	≥ 30 ng/ml (normal)	20-29 ng/ml (insufficiency)	10-19 ng/ml (deficiency)	≤ 9 ng/ml (Severe deficiency)
Laryngomalacia	8 (%25)	16 (%50)	6 (%19)	2 (%6)
Control	33 (%86)	4 (%11)	1 (%3)	0 (%0)

Table 2: Comparison of blood values between groups.

	Laryngomalacia	Control	p
25-Hydroxy Vitamin D(ng/ml)	24.8±10.3	34.2±11.6.	0.002
Calcium (mg/dl)	10.8 (9.4-11.9)	10.9 (9.7-12.1)	0.089
PTH (pg/ml)	39.7±18.9	43.7±21.6	0.689

Discussion

Laryngomalacia is an anomaly of the larynx that occurs from birth. It is the most common cause of stridor in the neonatal period. It has an appearance characterized by supraglottic collapse. The etiopathogenesis is still unexplained [1-3]. In the literature, very few publications investigate vitamin D and laryngomalacia in infants. In our study, the relationship between vitamin D and children with laryngomalacia was tried to be found. Vitamin D levels of infants in the control group were found to be higher than those of infants with laryngomalacia. Many research articles have also shown that serum vitamin D levels of healthy infants are higher than those of infants with laryngomalacia. [3,19]. In our study, higher serum vitamin D levels were found in the control group infants compared to the infants followed up with a diagnosis of laryngomalacia.

There was no significant difference in serum calcium and PTH levels. Typically, PTH serum levels should be elevated in infants with laryngomalacia who had low serum vitamin D levels, but no elevation was observed. The function of vitamin D in the body is to increase the absorption of Ca from the intestines and to prevent the excretion of Ca through the urine in renal function, and PTH contributes to the increase in serum vitamin D levels. PTH receptors are involved in the maturation of cartilage tissues [20, 21]. Numerous articles investigate the relationship between vitamin D and chondromalacia [15,16,22]. Osteoarthritis and vitamin D deficiency have been associated with disease progression [23].

Immature chondrocytes in the larynx may be thought to cause laryngomalacia. Studies in the literature suggest that vitamin D influences brain and nerve formation in the intrauterine period [24,25]. Because of this data, vitamin D deficiency may be considered a cause of laryngomalacia. However, normal PTH serum levels, instead of PTH serum levels expected to increase in response to vitamin D deficiency, raise questions such as whether there is any problem with PTH receptors and whether these receptors have not completed their proliferation or maturation. Therefore, further studies with PTH may provide insight into the cause of laryngomalacia. During pregnancy, vitamin D of the fetus comes from the mother through the placenta. A mother's vitamin D deficiency may cause the baby's vitamin D deficiency. It may be necessary to examine vitamin D serum levels in mothers. In future studies, maternal serum vitamin D levels may provide valuable information for the etiology of laryngomalacia.

Conclusion

In this study, we suggest that vitamin D deficiency may cause the etiology of laryngomalacia, which has not been entirely determined. In addition, investigating serum vitamin D deficiency in pregnant women may help explain the etiopathogenesis of laryngomalacia with low vitamin D deficiency in newborn babies.

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DOI: [10.32474/SJO.2022.09.000313](https://doi.org/10.32474/SJO.2022.09.000313)



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