Original Article

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Comparison of Serum 25-Hydroxyvitamin D Levels in Children with and without Intussusception

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ABSTRACT

BACKGROUND AND OBJECTIVE: Intussusception is the most common cause of intestinal obstruction and one of the most common causes of abdominal emergencies in children, which can lead to significant mortality and morbidity if left untreated. Since vitamin D acts as a hormone in the body and plays an important role in preventing infectious and non-infectious diseases and regulating the intestinal immune response, this study was performed to investigate the relationship between vitamin D levels and the occurrence of intussusception.

METHODS: This case-control study was performed on 86 children under 6 years old and above the neonatal age referred to Amirkola Children's Hospital in 2017-2018. The diagnosis of intussusception was made by ultrasound and the control group (without intussusception) was selected from patients with elective surgery other than intussusception. Vitamin D levels of children were assessed and compared in the two groups of children with and without intussusception.

FINDINGS: In this study, 50 people were in the intussusception group and 36 people were in the control group. The mean age was 27.2±14.6 months in the intussusception group and 24.7±15.9 months in the control group (p=0.447). The mean serum 25-hydroxyvitamin D levels in children with intussusception was 36.5±14.4 ng/ml and in the control group was 32.7±13.1 ng/ml (p=0.212).

CONCLUSION: According to the results of the present study, there was no association between serum 25-hydroxyvitamin D levels in children with and without intussusception and this vitamin was not associated with the occurrence of intussusception.

KEY WORDS: *Intussusception, Vitamin D, Intestinal Obstruction, Child.*

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Introduction

Intussusception means the immersion of a part of the intestine into its distal part (1, 2). It is the most common cause of intestinal obstruction between the ages of 5 and 36 months and the most common abdominal emergency in children under 2 years of age (2-4). 60% of children with intussusception are under one year old and 80% of cases occur under 2 years of age (2). It is rare in neonates and the male to female ratio is 3 to 1 (5). About 75% of cases have idiopathic intussusception and about 25% of cases have leading points (1).

The pathogenesis of idiopathic intussusception is unclear. An imbalance between longitudinal forces that disrupts the pattern of intestinal peristalsis has been suggested as a pathogenesis (4). In the idiopathic type, the association with hyperplasia of peyer's patches been suggested, which may often be stimulated by various gastrointestinal or respiratory infections (1, 6, 7). Based on evaluations, the risk of intussusception in children increased slightly after receiving the rotavirus vaccine, but no association was reported between human rotavirus and intussusception (8).

Gastrointestinal infection or new dietary protein with swelling of peyer's patches in the terminal ileum has been suggested as a risk factor for intussusception (1). Lymphatic tissue mass leads to prolapse of the ileal mucosa into the colon and causes intussusception (9). Cystic fibrosis, celiac disease, Crohn's disease, and Henoch-Schonlein purpura are other risk factors (4, 10).

Pathologic leading points are more common in children over 2 years of age and are present in 90% of adults (1, 3). Intussusception can be associated with mucosal bleeding in idiopathic thrombocytopenic purpura, Henoch-Schonlein purpura, and hemophilia (3, 4). In typical patients, the sudden onset of symptoms is in the form of severe colic and periodic onset of pain accompanied by loud crying and bending of the legs and knees into the abdomen (11).

Infants may initially be calm and asymptomatic between attacks of pain, but if intussusception does not reduct, the child progressively becomes weaker and more drowsy (3). Eventually a shock-like condition with fever and peritonitis occurs. In the early stages following abdominal pain, vomiting occurs (3). In the prolonged stages, vomiting becomes bilious. In the early hours of the disease, the stool is normal. The stool is then reduced or cut. Occasionally there is blood in the stool (2, 3). Chronic intussusception, the symptoms of which are milder than the recurrent type, follows acute enteritis and can occur in older children (12). When clinical signs and physical findings suggest intussusception, an ultrasound should be performed to confirm the diagnosis (the presence of a target or pseudokidney appearance indicates intussusception) (9).

Successful management of intussusception includes early detection, water and electrolyte correction, and timely reduction (13). Intussusception reduction is an emergency procedure and preparation for possible surgery should be done. Non-surgical treatment involves hydrostatic placement with air, saline, or contrast enema (14). Most infants recover within the first 24 hours of reduction, but the mortality rate increases after this time (15, 16).

25-hydroxyvitamin D is known as a natural immunomodulator and regulator of various immune mediators (17). Vitamin D was initially thought to be a treatment for nutritional rickets due to calcium absorption and bone health. But later the effects outside the skeletal system, especially the effect on innate intestinal immunity, production of receptors, cytokines and antimicrobial peptides, were also considered (18, 19). There is evidence that vitamin D affects all aspects of intestinal immunity physiology and homeostasis (18, 20).

Vitamin D, a pro-steroid hormone with anti-proliferative activity, is effective in preventing many diseases (21). In recent studies, low levels of vitamin D, in addition to disorders of the skeletal system, have been implicated in the development of cancer, metabolic syndromes, infectious diseases, autoimmune disorders, type 1 diabetes, and cardiovascular disease (6, 22, 23). Vitamin D deficiency was associated with atopic diseases (5) and several studies have suggested its role in preventing leukemia and gastrointestinal lymphoma (24).

Since vitamin D has a great role in the occurrence of infectious and non-infectious diseases related to immunity in the body and also in maintaining the immune function of the intestine (20), and considering the lack of studies conducted in this area, the present study was conducted to investigate the relationship between vitamin D levels and the occurrence of intussusception.

Methods

This case-control study was approved by the ethics committee of Babol University of Medical Sciences with the code HRI.REC.1398.520 and conducted

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among 86 children under the age of 6 years and above the neonatal period referred to Amirkola Children's Hospital. After obtaining a history and initial examinations and suspicion of intussusception in all children under 6 years and above the neonatal period who were admitted to Amirkola Children's Hospital, if intussusception was diagnosed by ultrasound and also confirmed by barium enema or saline enema or confirmation of disease at laparotomy, they were included in the study.

The control group consisted of 36 children at the same age and the same gender, who were referred for routine tests for various reasons without a known history of vitamin D deficiency, or children who were hospitalized for circumcision, hernia, and hypospadias. Routine tests were performed and a questionnaire was completed for them. Nutritional history including breast milk, formula feeding and consumption of complementary foods in infancy as well as the status and place of residence were assessed in both groups. Children outside the above age range who have a history of known chronic diseases such as liver, heart, kidney, oncological and neurological diseases and the presence of a pathological leading point that has been identified during the investigation of the cause of intussusception (such as Meckel's diverticulum and polyps) and children who had a history of taking vitamin D supplements were not included in the study.

For this study, with 95% confidence and 80% test power, and according to the level of vitamin D in healthy children and sick children and also based on the central limit theorem (CLT) in the statistics, at least 30 samples were considered for each group.

The case group consisted of 50 children who were hospitalized with an initial diagnosis of intussusception. The diagnosis of intussusception was confirmed by ultrasound by a skilled radiologist and a questionnaire was completed for them. 2 cc blood clot samples were taken from the patient for examination along with other diagnostic measures during hospitalization. After centrifugation and separation of serum from blood clot, it was stored and recorded in the freezer at -70 °C at laboratory of Amirkola Children's Hospital, along with the mentioned questionnaire. The serum 25-hydroxyvitamin D level was measured by a laboratory expert in the laboratory of Amirkola Children's Hospital in two groups of control and intussusception using a photometric vitamin D kit (IDEAL Tashkhis Atieh co.) by ELISA method and then the results were compared with each other. Vitamin D levels below 12 ng/ml were defined as deficiency, between 12 and 20 ng/ml, inadequate and above 20 ng/ml were defined as adequate (13, 25).

Then the data were analyzed using SPSS 22 software and two-sample t-test and Mann-Whitney nonparametric test and $p<0.05$ was considered significant.

Results

Of 86 children referred to Amirkola Children's Hospital, 50 children were in the intussusception group and 36 children were in the control group. The mean age was 24.7±15.9 months in the control group and 27.2±14.6 months in the intussusception group. The two groups were matched in terms of age. The mean level of vitamin D in the control group was 32.7±13.1 ng/ml and in the intussusception group was 36.5±14.4 ng/ml, while the difference was not significantly different. In the control group 5.6% and in the intussusception group 2% of children were deficient in vitamin D, but this difference was not significant. The sub-normal level of vitamin D was 20 ng/ml, the frequency of which was 5 children in the intussusception group and 8 children in the control group. Vitamin D levels in the two groups of control and intussusception did not show a significant difference based on gender (Table 1).

The incidence of intussusception was not significantly different between the two groups based on gender (Table 2).

The incidence of intussusception based on the presence of the child in kindergarten, considering the increased prevalence of infection in these children and the increased risk of intussusception, showed no significant difference between the control group and intussusception group (2 patients in the control group [5.6%] and 8 patients in the intussusception group [16%]). Out of 50 patients with intussusception, 4 patients had co-infection, three of which were upper respiratory infections and one was gastroenteritis. The incidence of intussusception was not significantly different between the two groups in terms of type of nutrition (Table 3).

Furthermore, vitamin D levels in terms of gender, place of residence and nutrition were not significantly different between the two groups (Table 4).

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Table 1. Mean level of vitamin D in control and intussusception groups based on gender

Group and gender	Number	Mean±SD	P-value*
Control			
Male	17	33±12.7	0.914
Female	19	32.5±13.7	
Intussusception			
Male	27	35.2±13.4	0.477
Female	23	38.1±15.6	

T Test*

Table 2. Comparison of gender distribution in children with and without intussusception

Group	Number(%)	P-value*
Control		
Male	17(47.2)	0.535
Female	19(52.8)	
Total	36(100)	
Intussusception		
Male	27(54)	0.535
Female	23(46)	
Total	50(100)	
Total		
Male	44(51.2)	0.535
Female	42(48.8)	
Total	86(100)	

Chi Square Test*

Table 3. Comparison of the percentage of children with intussusception with the control group in terms of the history of nutrition in infancy

Group	Number(%)	P-value*
Control		
Breast milk	17(47.2)	0.5
Breast milk+formula	7(19.4)	
Breast milk+complementary foods	8(22.2)	
Breast milk+complementary food+formula	4(11.2)	
Total	36(100)	
Intussusception		
Breast milk	19(38)	0.5
Breast milk+formula	9(18)	
Breast milk+complementary foods	10(20)	
Breast milk+complementary food+formula	12(24)	
Total	50(100)	
Total		
Breast milk	36(41.9)	0.5
Breast milk+formula	36(18.6)	
Breast milk+complementary foods	16(20.9)	
Breast milk+complementary food+formula	18(18.6)	
Total	106(100)	

Chi Square Test*

Table 4. Comparison of vitamin D levels according to place of residence in the studied children

Vit D	Number	Mean±SD	P-value*
Apartment			
City	31	37.7±14.8	0.962
Village	4	32±14.49	
House with a yard			0.962
City	27	36±16.1	
Village	24	33.7±11.1	
Total	86	34.9±13.9	0.962

T Test*

Discussion

The results of the present study showed that the mean serum 25-hydroxyvitamin D level was not significantly different between the two groups and the level of this vitamin in 90% of children with intussusception and 77.8% of children in the control group was above the minimum levels and within the normal range. In our study, 5.6% of the control group and 2% of the intussusception group had vitamin D deficiency. So far, no research has been done on the relationship between vitamin D levels and the occurrence of intussusception. Studies have been conducted on the status of vitamin D levels in some gastrointestinal diseases, such as celiac disease and inflammatory bowel disease and gastroenteritis.

In a study by Ahlawat et al. on 38 children recently diagnosed with celiac disease, no significant difference was found in the serum vitamin D levels of the two groups (26). In the study of Kim et al., serum vitamin D levels were inversely related to inflammatory bowel disease activity and there were differences in patients' serum vitamin D levels in the active phase of the disease with seasonal changes (27). In a study by Thorsen et al., there was no association between serum vitamin D levels and the risk of developing inflammatory bowel disease in childhood (28). Micronutrient deficiencies were studied by Ehrlich et al. in children with inflammatory bowel disease, and the results showed that iron, zinc, and vitamin D deficiency were more common in children with inflammatory bowel disease (29).

In a study by Bittker et al. to investigate the effect of environmental variables on the incidence of celiac disease in children, ear infection before age 2, use of antibiotics before age 2, taking vitamin D drops for more than 3 months have been associated with the onset of the Crohn's disease (30). A study by Ahlawat et al. found that vitamin D levels were often low in patients with celiac disease and inflammatory bowel disease

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(31). In the present study, vitamin D levels were lower in the intussusception group, but there was no significant difference between the two groups. In a study by Hassam et al. on 188 children under the age of 5, vitamin D levels and their association with diarrhea were examined. The results of the study showed a high prevalence of vitamin D deficiency in children under 5 years of age and vitamin D levels were not associated with diarrhea in children in this age group (32).

Raftery et al. regarding the effect of vitamin D on gastrointestinal diseases found that inflammatory bowel markers were inversely associated with serum levels of vitamin D in patients with Crohn's disease who were in the recovery phase (33). Vitamin D deficiency does not appear to play a known role in some of the above studies, as in our study about intussusception. However, deficiency of this vitamin in chronic diseases such as celiac disease or inflammatory bowel disease, which started long ago and the disease has established itself, has been linked to an exacerbation of the symptoms of the disease. Perhaps in addition to the duration of these diseases, which affect the level of 25-OHD in these patients, two other issues should be noted in the difference between the results. First, depending on the geographical location of different regions, vitamin D intake will be different, and second, the intestinal microflora of individuals can also be different in different parts of the world. A study by Dimitrov et al. found that some of the intestinal microflora involved in the production of vitamin D could trigger an immune response in the intestine or cause an inflammatory condition such as inflammatory bowel disease. Vitamin D affects intestinal physiology and produces cytokines that eventually affect peyer's patches in endothelial cells (34).

Meanwhile, a study by Bittker et al. in the United States found that taking vitamin D drops for more than three months was associated with the incidence of celiac disease in the future. Although a recent study found that vitamin D levels in the intussusception group were slightly higher than the control group, it could not be concluded that high levels of this vitamin increased the incidence of intussusception (30). In this study, the prevalence of common infectious diseases before intussusception showed that most patients did not have a recent infectious disease, although some studies had previously shown the role of 25-OHD deficiency in the prevalence of common infectious diseases (35). Perhaps the justification for this difference, as in our study, is in the geographical location of the studies. In our study, it was observed that the place of residence (city / village / apartment or house with a yard) did not differ significantly between the intussusception group and the control group, which again confirms that vitamin D levels had no effect on the occurrence of intussusception. According to some studies, vitamin D levels were lower in apartment living conditions (36), but in our study, the occurrence of intussusception was not different based on living in an apartment or house. Perhaps the reason for these differences is the small number of studied cases.

Based on the results obtained in this study, the gender of the child had no effect on the occurrence of intussusception and no significant difference was observed between the control and case groups. The type of infant nutrition including breast milk, formula feeding and complementary foods did not have a significant effect in both groups. Studies had shown the protective effect of breast milk in preventing the occurrence of intussusception and the risk of intussusception was doubled in formula eaters, which is due to the difference in the presence of intestinal microbiota in breast milk compared to formula eaters, which is effective on intestinal motility (37, 38). There was also no significant difference in the relationship between vitamin D levels and place of residence in the study groups.

The limitations of this study were the small number of patients and the limited study period. It is suggested that studies be performed over a longer period of time with more patients at different seasons of the year.

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