ORIGINAL RESEARCH PAPER

Pediatrics

KEY WORDS: Vitamin D deficiency, diarrhoea, exclusively breast fed infants

EFFECT OF VITAMIN D SUPPLEMENTATION ON EPISODES OF DIARRHEA IN EXCLUSIVELY BREAST FED INFANTS

Pallavi Sharma Senior Resident, Department of Paediatrics, Govt. Medical College SMGS Hospital, Shalamar, Jammu.

Dev Raj* Lecturer in statistics cum statistician, PG Department of Community Medicine, Govt. Medical College Hospital, Jammu. *Corresponding Author

Vijay Kamale Professor, Department of Paediatrics MGM Medical College Hospital,Kamothe Navi Mumbai.

ABSTRACT

The objective is to study the effect of Vitamin D3 supplementation on Frequency of Diarrheal episodes in infants and to compare above mentioned parameter in 2 groups namely Vitamin D3 Supplemented exclusively breastfed infants and Vitamin D3 non supplemented exclusively breast fed infants. A randomized control study was conducted in 200 new born, who were exclusively breast fed. New borns were divided into two groups namely Group A- placebo, Group B- vitamin D supplemented i.e. 400 IU daily per orally for 9months . Both the groups were followed at regular intervals 1.5, 2.5, 3.5, 6, 9 months. At each visit episodes of diarrhea were recorded. Statistical analysis was done by SPSS17. Data were analyzed by unpaired-t test. The mean numbers of diarrheal episodes (2.32 vs 0.85; Median 2 vs 1) were significantly more in babies of placebo group as compared to Vitamin D group. Thusfrequency of Diarrhoeal episodes was significantly less in vitamin D supplemented group as compared to Placebo group.

INTRODUCTION:

Vitamin D is an essential nutrition component having unique metabolism and physiological effects compared to other vitamins; in fact, it is more suitable to be classified as a hormone. (1-5) In humans, vitamin D is synthesized in the skin from exposure to sunlight or can be obtained through dietary intake that functions as a steroidal hormone after conversion in the renal tubule to its active form 1-25-hydroxyvitamin D (25(OH)D) by 1-alpha-hydroxylase enzyme. It is a well-known fact that natural sources of vitamin D in foods are not adequate for normal body requirements. Therefore, formation of vitamin D through exposure to sunlight in skin is the major source of vitamin D (6,7). Vitamin D deficiency considered to be most common nutritional deficiency. It is common in all age groups and both sexes across country. Emerging evidence suggests that the consequences of vitamin D deficiency (VDD) extend beyond its well-known effects on bone metabolism and calcium homeostasis, and also include alterations of specific arms of immunity. The immunomodulatory properties of vitamin D may influence susceptibility to infection. Although appropriate levels for immunologic function have yet to be identified, vitamin D deficiency in relation to skeletal metabolism for children is defined as a serum 25(OH)D level <50nmol/(9). Recent epidemiologic studies also indicate that low plasma vitamin D concentrations are related to increased incidence of acute diarrhoeal episodes,respiratory infections, including acute lower respiratory tract infections (10-13) and respiratory syncytial virus (RSV) disease (14) in infants and children less than 5 years of age. Furthermore, vitamin D supplementation in randomized controlled trials conducted among schoolchildren resulted in reduced incidence of diarrhea(15).Abed NaveenTA et all reported recurrent acute diarrhoeal episodes were associated with decreased levels of vitamin D3 in preschool and school aged children(16). The present study was conducted with aim of studying the effect of Vitamin D3 supplementation on frequency of acute Diarrheal episodes in infants.

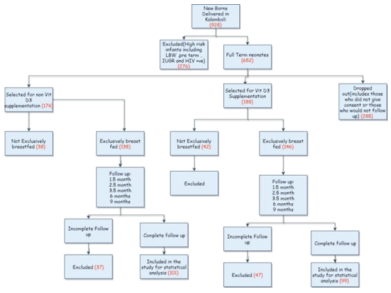
MATERIAL AND METHODS:

A randomized control study was conducted at Department of Pediatrics, MGM hospital, Navi Mumbai after ethical committee clearance during period of 6 months from 1st march 2014 to 30 September 2014 and followed up till 30 June 2015.All full term newborns delivered in hospital during study period and fulfilling eligibility criteria were included in study after taking informed consent from parents. A final sample of 200 exclusively breast fed newborns, were then randomized into two groups: Group A: Placebo group andGroup B: Vitamin D3 supplementation group (400IUOD). Both the groups were followed up at regular intervals (1.5, 2.5, 3.5, 6 and 9 months) during which episodes of diarrhea was recorded. Diarrhea: Diarrhea is defined as three or more loose or liquid stools passed per day or more frequently than in normal for the individual. WHO(17)

Exclusively breast fed is an infant who has been given exclusively breast milk and not even water for the first six months of life.

JUSTIFICATION FOR SAMPLE SIZE:

Sample size was calculated by using software PS (i.e. power and sample) version 3.1.6 and by assuming effect size 0.35, standard deviation 0.875 ,type 1 error 0.05 and type 2 error( )= 0.2 .The sample size was worked out to be 99 in each group .The recruitment of sampling units is shown asbelow:



Statistical Analysis-

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 17 for analysis. The unpaired t-test was used to test the significance of difference between the two groups. A p-value < 0.05 was taken as significant. All p-values were two tails.

RESULT:

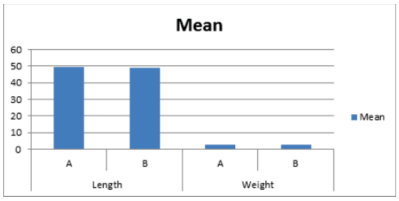
Table 1:Comparison of length and weight of infants at Birth(i.ebase line)

Parameters	GROUP	N	Mean	SD	SE	p- Value
Length	A	101	49.33	1.69	0.17	**0.82**
	B	99	49.14	1.73	0.17	
Weight	A	101	2.86	0.39	0.04	**0.77**
	B	99	2.89	0.37	0.04	

The above table shows the comparison between groups mean length and weight of two groups. The mean length and weight of group A was (49.33±1.69) cms&(2.86±0.39)kgs respectively and the mean length and weight of group B was (49.14±1.73)cms&(2.89±0.37)kgs respectively.

t-test shows that there is no statistically significant difference between the length and the weight of newborn infants of two groups (as p> 0.05) at the time of birth.

Figure 1: Showing comparison of mean length and mean weight in both groups.



It is evident from the Table: 1 and Figure: 1 that there is no significant difference between the two groups in terms height and weight at the time birth.

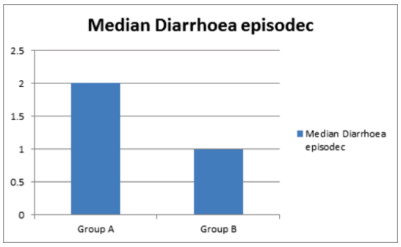
Table2: Comparison of mean number of Infection episodes of Diarrhea between two groups.

Infection Episodes	GROUP	N	Mean	Median	SE	Statistical inference	95%confidence Interval	Incidence
Diarrhea	A	101	2.32	2	0.18	t=7.46, p<0.001	(1.97 – 2.68)	0.257episodes/infant-month
	B	99	0.85	1	0.08		(0.69 – 1.01)	0.094episodes/infant-month

The above table:2 depicts the comparison of Infection episodes of diarrhea between group means. The mean Infection episodes of diarrhea in group A was (2.32 ± 0.18SE) and the mean infection episodes of diarrhea in group B was (0.85 ± 0.08SE).

t-test shows that there is significant difference between the Infection episodes of diarrhea in newborn infants of two groups (as p 0.01) . The Infection episodes of diarrhea in newborn infants in group A(ie placebo group) are more as compared to group B(ie Vitamin D supplement group).

Figure 2: Showing comparison of median Diarrhea episodes in both groups.



The above Table: 2 and Figure: 2 show that there is a significant difference between the infection Diarrhea episodes in the two groups.

DISCUSSION:

Vitamin D is well known for its role in calcium metabolism and bone health(18). In addition, vitamin D is active in the immune system(19). Low plasma levels of calcidiol, the accepted marker of vitamin D status, are associated with increased infectious disease, especially respiratory tract infections, in several populations,(20-22) including young Indian children .

A low plasma calcidiol level is widespread, even among populations at low latitude. In India, vitamin D deficiency is common among women and children(23,24). Low birth weight is also common in India and these infants are at high risk of respiratory tract infections and other morbidity.(25) Low cost interventions such as improving vitamin D status are needed to improve the health and survival of these infants.

We thus conducted this randomized control study with the hypothesis that Vitamin D3 supplementation in infant's results in reducing the offrequency ofinfectious disease like Diarrhoea. In present study, mean number diarrhoeal episodes (2.32 vs 0.85; Median 2 vs 1) were significantly more in babies of placebo group as compared to Vitamin D group. So, Vitamin D supplementation significantly increases disease resistance as shown by reduced frequency of infection episodes. These results reflect the role of vitamin D in immunity as reported by other studies. Airway epithelial cells have been found to express high levels of 1 - hydroxylase, converting 25-hydroxyvitamin D to its active form, leading to the increased production of both cathelicidin and the Toll-like receptor co receptor CD14, important in the recognition of grampositiveand negative bacteria(10). It enhances the differentiation and recruitment of macrophages, which may lead to an increased ability to fight infection(26).Several recent epidemiology studies have observed the association between inadequate vitamin D concentrations and hospitalization and/or GIT/respiratory infection among children. Mazary et al.(27)conducted a study to examine the effect of vitamin D supplementation in the first 6-months of life on the immunity and risk of infections during the first year in infants. They observed that incidence of infections were less common in infants supplemented with daily vitamin D than those not supplemented (p value = 0.01). There were significant negative correlations between the incidence of respiratory and gastrointestinal infections and maternal vitamin D levels (p value = 0.001, r= -0.65, versus p value = 0.001, r= -0.61 respectively). In the current study, the incidence of gastroenteritis was also more common in infants not supplemented with vitamin D which reflects the immune prophylactic effect against GIT infections. This immune prophylactic function of vitamin D may be due to its effect on T-helper cells. Vitamin D acts on dendritic cells, which play a central role in the activation of T-cell-mediated immune responses. As a result, a tolerogenic phenotype is induced with decreased expression of MHC class II and costimulatory ligands, decreased secretion of the immunostimulatory cytokine IL-12 and increased IL-10, an anti-inflammatory cytokine with potent inhibitory effects on Th1 and Th2 responses.20 Also, vitamin D inhibits IFN- synthesis. It also increases serum levels of TGF- 1, a complex cytokine with a role in the peripheral induction of Foxp3+ Treg immunosuppression and in wound healing and repair(26). Naveen TA et al. conducted a cross sectional study aimed to study the association between vitamin D level and recurrent acute diarrhea. They concluded that recurrent acute diarrhoea was associated with decreased serum level of vitamin D in preschool and school-age children(16).Urshima et al. have reported potential effect of vitamin D on gastrointestinal infections in children. Vitamin D supplementation in a randomized controlled trial in school-age children reduces the incidence of gastroenteritis(15).BenerA et al conducted a cross-sectional study on 458 Qatari children to determine the factors associated with low concentrations of 25-hydroxy vitamin D (vitamin D deficiency) in healthy children in Qatar. They reported a significantly higher prevalence of gastroenteritis among those who were vitamin D-deficient (p-0.02)(28). Our study supports the role of vitamin D in decreasing the susceptibility to infection-related illnesses.

CONCLUSION: vitamin D supplementation after birth should be recommended as it is associated with lower frequency of GIT infections during the first year of life. The findings support the importance of vitamin D supplementation in full term infants who are exclusively breast fed, not only for its importance for the skeletal system but also for potential immune functions.

In this study infections were studied among the control and study subjects. Other parameters have also been studied, which are not included in this paper and will be put in subsequent papers.

REFERENCES:

1. D Bringhurst FR, Demay MB, Krane SM, Kromenberg HM. Bone and mineral metabolism in health and disease. In: Kasper DL, Fauci AS, Longo DL, Braunwald E,

Hauser SL, Jameson JL, eds. Harrison's principles of internal medicine. 16th ed. New York: McGraw Hill; 2005. p.2238-48.
2. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancer, and cardiovascular disease. Am J ClinNutr. 2004;80(6):1678S-88S.
3. Marriott BM. Vitamin D supplementation: A word of caution. Ann Int Med.1997;127(3):231-3
4. Norman AW. Sunlight, season, skin pigmentation, vitamin D, and 25-Hydroxyvitamin D: Integral components of the vitamin D endocrine system. Am J ClinNutr. 1998;67:1108- 10.
5. Compston JE. Vitamin D deficiency: Time for action. BMJ. 1998;317:1466-7.
6. Fraser DR. Vitamin D. Lancet. 1995;345:104-7.
7. Raiten DJ, Piciano MF. Vitamin D and health in 21st Bone and beyond. Am J ClinNutr. 2004;80(suppl):1673S- 7S.
8. Holick MF. Vitamin D: extraskeletal health. Rheum DisClin North Am. 2012; 38:141-60.
9. Aluisio, Adam R., et al. "Vitamin D3 Supplementation and Childhood Diarrhea: A Randomized Controlled Trial." Pediatrics(2013) 132.4 : e832-e840.
10. Roth DE, Shah R, Black RE, et al. Vitamin D status and acute lower respiratory infection in early childhood in Sylhet, Bangladesh. ActaPaediatr. 2010;99:389–393.
11. Wayse V, Yousafzai A, Mogale K, et al. Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. Eur J ClinNutr. 2004;58:563–567.
12. Inamo Y, Hasegawa M, Saito K, et al. Serum vitamin D concentrations and associated severity of acute lower respiratory tract infections in Japanese hospitalized children. Pediatr Int. 2011;53:199–201.
13. Karatekin G, Kaya A, Salihoğlu O, et al. Association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection and their mothers. Eur J ClinNutr. 2009;63:473–477.
14. Belderbos ME, Houben ML, Wilbrink B, et al. Cord blood vitamin D deficiency is associated with respiratory syncytial virus bronchiolitis. Pediatrics. 2011;127:e1513–e1520
15. Urashima M, Segawa T, Okazaki M, et al. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am JClinNutr. 2010;91:1255–1260.
16. Abed, NeveenTawfik, et al. "Vitamin D status in children with recurrent acute diarrhea." Int. J. Curr. Microbiol. App. Sci(2014) 3.11 : 858-868.
17. PatwariAK,AnejaS,Integrated management of Neonatal and Childhood illness .Ghai Essential Paediatrics eighth edition (2013)758-60.
18. Holick MF, Vitamin D deficiency. N Engl J Med.2007;357:266-81
19. Van Etten E, Stoffels K, Gysemans C, Mathieu C, Overbergh L. Regulation of vitamin D homeostasis: implications for the immune system. Nutr Rev2008;66(10 suppl 2):S125-34.
20. Laaksi I, Ruohola JP, Tuohimaa P, et al. . An association of serum vitamin D concentrations < 40 nmol/L with acute respiratory tract infection in young Finnish men. Am J ClinNutr. 2007;86(3):714–717.
21. Gibney KB, MacGregor L, Leder K, Torresi J, Marshall C, Ebeling PR, et al. Vitamin D deficiency is associated with tuberculosis and latent tuberculosis infection in immigrants from sub-Saharan Africa. Clin Infect Dis2008;46:443-6.
22. Wayse V, Yousafzai A, Mogale K, FilteauS.. Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. Eur J ClinNutr. 2004;58(4):563–567.
23. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. Am J Clin Nutr2000;72:472-5.
24. Agarwal KS, Mughal MZ, Upadhyay P, Berry JL, Mawer EB, Puliyel JM. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi, India. Arch Dis Child2002;87:111-3.
25. Neonatal Mortality Formative Research Working Group. Developing community-based intervention strategies to save newborn lives: lessons learned from formative research in five countries. J Perinatol2008;28(suppl 2):S2-8.
26. Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. Science 2006;3:1770–3.
27. El-Mazary, A. A. M., et al. "Vitamin D Supplementation and the Risk of Infections in Full term Infants. Correlations with the Maternal Serum Vitamin D." Archives of Disease in Childhood 97.Suppl 2 (2012): A257-A257.
28. Bener, A., Al-Ali, M., Hoffmann, G.F. Vitamin D deficiency in healthy children in a sunny country: associated factors. Int. J. Food Sci. Nutr. 2009, 60(suppl.5): 60 70