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Does Vitamin D supplementation benefit children with severe pneumonia? Critical appraisal of article Vitamin D supplementation for severe pneumonia - a randomized controlled trial. Nidhi C, Piyush G. Indian Pediatr. 2012;49:449–454

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ABSTRACT

Question: The primary objective was to determine the role of Vitamin D in severe pneumonia and secondarily with duration of hospitalization, time of resolution of tachypnea, chest retraction and inability to drink water.

Method: Ethical consent was obtained from institutional ethical committee and written informed consent from caregiver of the patients. It is a randomized controlled trial with double blinding. The patients aged between 2 months and 5 years with diagnosis of severe pneumonia were included. Excluded were children with severe wasting (weight for height <3SD), chronic illness, recent history of Vitamin D intake and known cases of asthma.

Randomization was done using computer generated table into interventional and placebo group. Each sachet of Vitamin D weighing 1 g containing 60,000 IU was mixed with 11 g of lactose. This total amount was divided into 60 equal doses, each weighing 200 mg and containing 1000 IU of Vitamin D. Interventional group received 1000 IU of Vitamin D for 5 days starting from the day of admission. Placebo group received lactose for same duration.

Because of safety concern, lack of safety data and absence of Vitamin D level monitoring, low dose short course Vitamin D was given in this study. Also because of above reason children <2 months were excluded.

Sample size calculation was done based on the role of Zinc for resolution of severe pneumonia taking one day as meaningful difference with standard deviation of 2.5, type I error 0.05 and power of 80%.

Initial data was collected on socio-demographic profile, feeding history (Breast feeding, exclusive breast feeding and complementary feeding), immunization status, past history of pneumonia, fuel use or smoking, socioeconomic status and anthropometry. Monitoring was done on respiratory rate, retraction, axillary temperature, feeding, mental status, oxygen saturation and laboratory variables like hemogram, blood sugar, electrolytes, calcium, phosphate and alkaline phosphatase levels.

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Main results: 283 children were diagnosed with severe pneumonia of which 200 were randomized; 100 in interventional and 100 in placebo group. The two groups were compared for all baseline characteristics. The median duration for resolution of severe pneumonia, duration of hospitalization, resolution of tachypnea, chest retraction, fever, inability to feed and lethargy were compared and found to be similar in intervention and placebo group.

Out of 200 children, 191 were discharged (97 interventional and 94 placebo group), 2 died (1 from each group), 7 left against medical advice.

No difference was observed between interventional and placebo group in resolution of severe pneumonia, duration of hospitalization or time of resolution of each symptoms.

Conclusion: No effect was observed of short term 1000 IU dose of Vitamin D on time of resolution of severe pneumonia. Further studies using higher dose of Vitamin D with long term follow up are needed to completely prove it.

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1. Commentary

Pneumonia is one of the major cause of mortality in under five children.¹ Recent studies had shown immuno-modulating action of Vitamin D.² Only one previous study done in Kabul,³ had shown direct effect of Vitamin D on recurrence of pneumonia.

In this study it is stated that children diagnosed with severe pneumonia taking WHO diagnostic criteria were included. However the criteria for defining severe pneumonia in this study were different from that used by the World Health Organization.⁴

Distinction between viral causes of pneumonia can be made by taking wheeze before enrollment in exclusion criteria. Cases of rickets, very severe pneumonia should also be excluded from the study because it will affect the treatment protocol. Other causes of increased respiratory rate can be excluded by taking chest X-ray as one of the diagnostic tool for pneumonia.

According to CONSORT guidelines, every study must define the period of work, which is not mentioned in this study. Also every study must define the baseline characteristic of population from which the sample is taken. This is also not mentioned in this study.

In this study baseline characteristics like mother's morbidity, natal history, sunlight exposure, occupation, religion and intake of calcium supplements can be compared, because above variables can effect the Vitamin D level in the child.

In the result, a difference was reported in the resolution rate of severe pneumonia, but there was no definition of resolution in the methodology section.

The authors should have included information about the quality of vitamin D used along with the name of the company and whether the company had received certificate by the Ministry of Health, Government of India, for marketing this product. The dose of Vitamin D used was very small to reach the recommended level of Vitamin D for immuno-modulating effect. For immuno-modulating effect of Vitamin D serum level should be >40 ng/ml.⁵ Heaney et al⁶

studied 67 British adults and divided them into 4 groups receiving 200, 1000, 5000, 10,000 IU/d of Vitamin D₃ for 5 months. This study showed that doses of 400, 1000, 5000 and 10,000 IU for 5 months will result in circulating concentration of 7 nmol/l (2.8 ng/ml), 17.5 nmol/l (7 ng/ml), 70 nmol/l (28 ng/ml) and 175 nmol/l (70 ng/ml) of 25(OH)D, respectively. The data also showed that for every 40 IU of Vitamin D intake, circulating 25(OH)D increases by 0.70 nmol/l (0.28 ng/ml). A steady state appears to be achieved after 90 days of each dose tested.

A better study can be triple blinded randomized controlled trial taking chest X-ray as one of diagnostic tool for pneumonia because this will exclude other causes of increased respiratory rate. WHO criteria⁴ should be properly used for diagnosis of severe pneumonia. Patient of very severe pneumonia, rickets and any wheeze before enrollment should be excluded from study. The interventional group should receive at least 10,000 IU/day Vitamin D, along with pre-interventional level of Vitamin D. One level of Vitamin D can be done at the time of discharge. The patients should be followed for recurrence of pneumonia.

This study is second of its kind which studied direct relation of Vitamin D and resolution of severe pneumonia. This study was done in resource poor population.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Bryce J, Boschi-Pinto C, Shibuya K, et al. WHO estimates of the causes of death in children. *Lancet*. 2005;365:1147–1152.
2. White HJ. Vitamin D signalling, infectious diseases and regulation of innate immunity. *Infect Immun*. 2008;76:3837–3843.

3. Manaseki HS, Masher I, Bruce J, et al. Effects of Vitamin D supplementation to children diagnosed with pneumonia in Kabul: a randomized controlled trial. *Trop Med Int Health*. 2010;15:1148–1155.
4. World Health Organization. *Management of the child with a serious infection or severe malnutrition*. Available at: http://www.who.int/maternal_child_adolescent/documents/fch_cah_00_1/en/; 2000. Accessed 19.02.13.
5. Adit AG, Jonathan MM, Carlos AC. Association between serum 25-hydroxyvitamin level and upper respiratory tract infection in the third national health and nutrition examination survey. *Arch Intern Med*. 2009;169(4):384–390.
6. Heaney RP, Davies KM, Chen TC, et al. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. *Am J Clin Nutr*. 2003;77: 204–210.