

ROLE OF VITAMIN D IN PREVENTION OF ACUTE EXACERBATION OF BRONCHIAL ASTHMA IN ADULTS

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ABSTRACT

Objective: To determine role of vitamin D in prevention of acute exacerbation of bronchial asthma in adults when added to standard treatment.

Methodology: The study included 80 patients of either gender with age ranging from 16 to 46 years. Bronchial asthma diagnosed for at least 1 year and vitamin D levels below 30 ng/ml, no history of smoking, intake of vitamin D 6 months before trial or other chronic diseases were included in the study. They were randomly divided into two groups by using computer generated random number table, group A and group B and were given combination of standard treatment of bronchial asthma and vitamin D vs standard treatment only respectively.

Results: 25(62.5%) were male in group A while 21(52.5%) were male in group B. Mean age of study population was 29.56 ±8.06 years. Vitamin D was found more effective in prevention of exacerbations of bronchial asthma (P value 0.003).

Conclusion: Vitamin D was efficacious in bronchial asthma in terms of prevention in number of exacerbations when added to standard treatment.

Key Words: Bronchial asthma, Vitamin D, Exacerbation of bronchial asthma

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INTRODUCTION

Bronchial asthma is the chronic inflammation of the airways and their hyper responsiveness that leads to symptoms of shortness of breath, cough, wheeze and chest tightness¹. Approximately 5% of the world population is having bronchial asthma². The prevalence of asthma is increasing day by day and it has increased by more than 75% over the last two decades³.

Bronchial asthma is an ever increasing epidemic and it has been found that morbidity of asthma patients is increased by its exacerbations so early treatment of these patients is helpful in prevention of its exacerbations and complications⁴. It has been found that vitamin D supplementation is effective in prevention of exacerbations in asthmatic patients.

As of 2014, prevalence of asthma is around 334 million people worldwide⁵, and mortality rate is 2 per 100,000 patients per year⁶. 84.3% of Pakistani population is deficient in vitamin D⁷. Interest is growing in the world to see the effect of vitamin D in pulmonary disorders specially asthma. The beneficial effect of vitamin D in bronchial asthma triggered by respiratory viral

infections has been pointed out in quite a few clinical trials and a good number of observational studies^{1,3,7}. Vitamin D has significant immune modulatory effects and it is one of the essential nutrient⁸. Previously it was thought that vitamin D has role only in bone physiology and calcium metabolism but now it is also believed that vitamin D metabolism, specifically its conversion to activated form, is important for innate and adaptive immunity⁹.

Li et al¹⁰ reported the correlation of lung function with vitamin D status and they stated that a large number of asthmatic patients in China were vitamin D deficient. Studies suggest that therapeutic potential of vitamin D supplementation in asthma patients as a steroid-enhancing agent. In a study by Majak et al¹ it was found that exacerbation in bronchial asthma caused by respiratory tract infections can be prevented by vitamin D supplementation. Only 17% children who were supplemented with Vitamin D, suffered from asthma exacerbation as compared to 46% asthma exacerbation in children who were not supplemented with vitamin D¹. Asthma control may be improved by supplementation of vitamin-D through its effect on inhibition of the in-

flux of cytokines within the lungs and by increasing the secretion of interleukin 10 by dendritic and T cells. The induction of innate antimicrobial mechanism, maintenance of regulatory T-cells and inhibition of inflammation are the major roles played by vitamin D in respiratory disorders¹¹.

Emerging studies also show an association between poor clinical responsiveness to glucocorticoids and poor vitamin D status in asthmatic patients⁸. Vitamin D could dramatically reduce the need for steroids in asthma patients. Vitamin D supplementation can enhance the action of steroids on inflammatory cells taken from patients with asthma by tenfold. Vitamin D and asthma are thought to have some indirect association owing to the susceptibility to infections¹².

There is high rate of asthma exacerbations in adults in the world. It was planned to check the role of vitamin D supplement to prevent its exacerbation. This study and future studies will set a new horizon for role of novel treatments like vitamin D in the treatment of bronchial asthma.

METHODOLOGY

It was a randomized controlled trial done in Services Hospital, Lahore for a period of 6 months. Sampling technique was non-probability consecutive sampling. Patients having age ranging from 16 to 46 years and bronchial asthma diagnosed for at least 1 year with vitamin D levels less than 30 ng/ml were included in the study. While patients with intake of vitamin D 6 months before the trial, Ischemic heart disease or other chronic diseases like chronic liver disease, chronic kidney disease, chronic obstructive pulmonary disease were excluded from the study. Patients fulfilling inclusion criteria mentioned above, were assigned two groups randomly, by using computer generated random number table, group A and group B. Sample size was calculated using WHO sample size calculator for 2 sided proportions taking proportions 17% and 46%¹, power of study 80%, level of significance 5%. It turned out to be 80 (40 for each group separately).

Bronchial asthma was operationally defined as shortness of breath associated with wheezing in the chest

and improvement in forced expiratory volume in one second (FEV1) of $\geq 15\%$ following administration of 2 puffs (180 μ g) of salbutamol inhaler. Exacerbation of bronchial asthma was operationally defined as acute onset of shortness of breath in already diagnosed asthmatic patients who are having all of the following: tachycardia more than 100/min., respiratory rate more than 25/min., inability to complete a sentence in one breath and wheezing or reduce air entry on chest auscultation.

All the findings were recorded in Proforma. Group A was given vitamin D3 50,000units fortnightly for a period of three months in addition to standard treatment (Salmeterol/fluticasone inhaler preparation Salmicort® 25/250 μ g twice daily, Montelukast Montika® 10mg at night) for bronchial asthma. Group B was given standard treatment (Salmeterol/fluticasone inhaler preparation Salmicort® 25/250 μ g twice daily, Montelukast Montika® 10mg at night) of bronchial asthma treatment only. Patients had an enrollment visit and follow up was done monthly or as needed. Treatment was given to all patients depending on clinical situation and severity of asthma. Vitamin D levels were measured before treatment and after completion of treatment period of 3 months. Efficacy was measured in terms of decrease in number of exacerbations. SPSS ver. 20 was used. We calculated mean and standard deviation for variables like age and number of exacerbations (quantitative variables) and frequency and percentage for variables like gender and asthma exacerbation(qualitative variables). Chi-square test was applied to compare the number of asthma exacerbations in both groups.

RESULTS

There were total 80 cases with a mean age of 29.56 ± 8.06 . Baseline demographics were noted and presented in table 1. Prevention in asthma exacerbations were in 31(77.5%) in Group A and 19(47.5%) in Group B (p value <0.05) as shown in Table 2.

Mean serum vitamin D level before supplementation with vitamin D were 13 ± 3.45 ng/ml and Mean serum vitamin D levels after 3 months of supplementation with vitamin D were 35 ± 4.5 ng/ml.

Table 1: Demographics of the study population

Demographics		Group A (Vitamin D Supplement added)	Group B (Vitamin D Supplement Not added)
Age		29.70 \pm 7.74	29.43 \pm 8.47
Gender	Male	25(62.5%)	21(52.5%)
	Female	15(37.5%)	19(47.5%)

Table 2: Efficacy of vitamin D in prevention of asthma exacerbation

Prevention of Asthma Exacerbation	Group of treatment		P-value
	A	B	
Yes	31(77.5%)	19(47.5%)	0.003
No	9(22.5%)	21(52.5%)	

DISCUSSION

Our present study showed that vitamin D supplementation reduces exacerbation of asthma in 77.5% of patients as compared to 47.5% patients without supplementation which is quite significant. This fact has been demonstrated in several other studies¹³. A meta-analysis was conducted in 2016 including 7 studies in children and 2 studies in adults to evaluate the efficacy of supplementation with vitamin D in reducing severe exacerbation of asthma. Vitamin D supplementation decreased exacerbations rate effectively reducing systemic steroids requirement and decreased the risk of exacerbations leading to hospitalization¹³. These results support our study which also support the use of vitamin D supplementation to decrease asthma exacerbation.

Arshi et al¹⁴ conducted a study to evaluate the effects of vitamin D supplementation along with controller medications for asthma (inhaled corticosteroids or inhaled corticosteroids + long-acting β -agonist) on functions of airways. A randomized clinical controlled trial of 130 individuals 10-50 years of age in Tehran was conducted during a period of 6 months. One group received vitamin D supplementation along with controller medications for asthma. Improvement in FEV1 after 2 months was significant in two groups. The results of the study are in support of our study suggesting that vitamin D supplementation can be a valuable tool for decreasing asthma exacerbation hence asthma management¹⁴.

Studies also noted that vitamin D deficiency is associated with blunted glucocorticoid responsiveness^{10,15}. This fact supports the notion that vitamin D supplementation can decrease the need for systemic steroids for asthma exacerbation and enhance steroids response as suggested in our study.

Brehm et al^{16,17} noted that vitamin D deficiency was linked to increased eosinophil counts, IgE concentrations and airway hyper-responsiveness so leading to increase symptoms of asthma as well as its exacerbations. This also supports the results of our study. Similarly, in Italian studies, increased airway hyper responsiveness and lung functions were inversely related to serum vitamin D levels^{18,19}. This fact explains the reason of vitamin D supplementation effectiveness in decreasing asthma exacerbation as demonstrated in our study.

Searing et al²⁰ also found an increase in corticosteroid requirements and sensitivity to aeroallergens in children having low vitamin D levels. Majak P et al¹ also noticed that vitamin D deficiency is associated with increase in number of asthma exacerbations and vitamin D supplementation reduces these exacerbations.

Menon B et al²¹ demonstrated improvement in control of asthma after vitamin D supplementation and vitamin D deficiency was associated with poor asthma control in these patient. This is in keeping with the results of our study that vitamin D supplementation improves asthma control and decreases asthma exacerbations²¹. But there are more studies needed on the same pattern to confirm these results. Once a sufficient literature will be available then the related guidelines could be developed and it will put health care professional to a new way of preventing asthma related complications by adding vitamin D to the treatment of bronchial asthma.

CONCLUSION

Vitamin D was efficacious in bronchial asthma in terms of prevention in number of exacerbations when added to standard treatment.

REFERENCES

1. Majak P, Olszowiec-Chlebna M, Smejda K, Stelmach I. Vitamin D supplementation in children may prevent asthma exacerbation triggered by acute respiratory infection. *J Allergy Clin Immunol* 2011; 127:1294-6.
2. Ginde AA, Sutherland ER. Vitamin D in asthma: panacea or true promise? *J Allergy Clin Immunol* 2010; 126:59-60.
3. Shivashankar M, Mani D. A Systematic Review on Asthma. *Res J Pharm Biol Chem Sci* 2015; 6:679-87.
4. FitzGerald JM, Gibson PG. Asthma exacerbations • 4: Prevention. *BMJ Thorax* 2006; 61:992-9.
5. Global Asthma Network. The global asthma report 2014. Auckland: GAN; 2014. Available at: http://www.globalasthma-report.org/resources/Global_Asthma_Report_2014.pdf
6. Yang G, Kong L, Zhao W, Wan X, Zhai Y, Chen LC et al. Emergence of chronic non-communicable diseases in China. *Lancet* 2008; 372:1697-705.
7. Sheikh A, Saeed Z, Jafri SAD, Yazdani I, Hussain SA. Vitamin D Levels in Asymptomatic Adults-A Population Survey in Karachi, Pakistan. *Burdmann EA, ed. PLoS ONE*

- 2012; 7:e33452.
8. Mark S, Thomas J. Pulmonary disorders. In: McPhee, SJ, Papadakis MA, editors. *Current medical diagnosis and treatment*. 50th ed. New York: McGraw-Hill; 2011:239-316.
 9. Hewison M. Vitamin D and the intracrinology of innate immunity. *Mol Cell Endocrinol* 2010; 321:103-11.
 10. Li F, Peng M, Jiang L, Sun Q, Zhang K, Lian F et al. Vitamin D deficiency is associated with decreased lung function in Chinese adults with asthma. *Respiration* 2011; 81:469-75.
 11. Gupta A, Bush A, Hawrylowicz C, Saglani S. Vitamin D and asthma in children. *Paediatr Respir Rev* 2012; 13:236-43.
 12. Walker VP, Modlin RL. The vitamin D connection to pediatric infections and immune function. *Pediatr Res* 2009; 65:106R-13.
 13. Martineau AR, Cates CJ, Urashima M, Jensen M, Griffiths AP, Nurmatov U et al. Vitamin D for the management of asthma. *Cochrane Database Syst Rev* 2016; 9: CD011511.
 14. Arshi S, Fallahpour M, Nabavi M, Bemanian MH, Javad-Mousavi SA, Nojomi M et al. The effects of vitamin D supplementation on airway functions in mild to moderate persistent asthma. *Ann Allergy Asthma Immunol* 2014; 113:404-9.
 15. Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DY. Vitamin D levels, lung function, and steroid response in adult asthma. *Am J Respir Crit Care Med* 2010; 181:699-704.
 16. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS et al. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. *J Allergy Clin Immunol* 2010; 126:52-8.
 17. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med* 2009; 179:765-71.
 18. Chinellato I, Piazza M, Sandri M, Peroni DG, Cardinale F, Piacentini GL et al. Serum vitamin D levels and exercise-induced bronchoconstriction in children with asthma. *Eur Respir J* 2011; 37:1366-70.
 19. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. *J Allergy Clin Immunol* 2010; 125:995-1000.
 20. 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.
 21. Menon B, Nima G, Dogra V, Kaur C. Low level of Vitamin D is associated with poor asthma control: a randomized control trial of Vitamin D supplementation in Asthma. *Research* 2014; 1:1088.

CONTRIBUTORS

MUM conceived the idea, planned the study, and drafted the manuscript. MUM and MFR helped acquisition of data and did statistical analysis. GAS critically revised the manuscript. All authors contributed significantly to the submitted manuscript.