Original Article

The Effect of Vitamin-D Prophylaxis on Severity of Asthma

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ABSTRACT

Introduction: Asthmatic (case) children had more vitamin D deficiency compared to other (control) children and strong correlation between vitamin D level and severity of asthma symptoms.

Method: A prospective hospital based interventional study was conducted on bronchial asthmatic patients(5-17 years)to find out the role of vitamin D prophylaxis in severity and exacerbation.80 cases were included in the study. Participants were divided in 2 groups-**Intervention arm-**patients taking vitamin-D capsules **Control arm-**patients not taking vitamin-D capsules(placebo).At the end of 6 months both groups were compared to look for changes in their severity and number of exacerbation of asthma.

Results: In our study there is slight improvement in severity of asthma in both group till 3 month, at the end of 6 month there is improvement of ACTS score more in case group compared to control group. There is decrease emergency room visit more in case group compared to control group, in hospital admission in both groups and in reliever medication use more in case group compared to control group.

Conclusion: Thus, we conclude that Vitamin-D has significant improvement in severity of asthma, exacerbation of asthma and asthma control test score in case group compared to control group at the end of 6 months. So, we recommend to use vitamin D in asthmatic paediatric cases.

Key words: Vitamin D, Bronchial Asthma, Children, Deficiency

INTRODUCTION

Bronchial asthma is the most common chronic respiratory disease in childhood. Worldwide, childhood asthma prevalence appears to be increasing and in India childhood asthma ranges from 10-25%.[1,2]

Bronchial asthma is one of the leading causes for emergency room visits, hospital admissions. Lack of sleep at night due to nocturnal symptoms, it affects child's daytime concentration in school and subsequently school performance.[3]

Vitamin-D, a pro-hormone apart from its main role in calcium and bone metabolism, it reduces risk of chronic diseases like auto immune disease, malignancies, cardio vascular and other infectious disease.[4]

Numerous studies suggest the correlation between vitamin-D and bronchial asthma and asthmatic children had more vitamin-D deficiency compared to control children.[5-8] Prevalence of vitamin-D deficiency in asthmatic children range 2.04-5.69 and vitamin-D insufficiency in asthmatic children range from 0.67-2.91.[6-7]

Asthma mortality arises primarily during episodes of acute worsening of symptoms, termed exacerbations, which are commonly precipitated by viral upper respiratory infections.[9] Virus-induced asthma exacerbations are associated with increased production of pro-inflammatory cytokines such as interleukin-17A,which exacerbate allergic airway responses.[10] Vitamin-D metabolites support antiviral responses in respiratory epithelial cells and inhibit production of interleukin-17A in peripheral blood mononuclear cells.[11]

Low concentrations of major vitamin-D metabolite,25-hydroxyvitamin-D(25[OH]D),are associated with increased risk of asthma exacerbation in children.[12]

OBJECTIVES

This study was undertaken to assess effect of vitamin-D prophylaxis on severity of asthma and on exacerbation in form of number of emergency room visit, number of hospital admission and reliever medication used.

METHOD

A prospective hospital based interventional study of bronchial asthmatic patients admitted and/or came to OPD at tertiary care centre attached with medical college. Those children aged between 5-17 years presenting with bronchial asthma in pediatric outpatient department and/or admitted in pediatric ward or PICU were included in study. Children with impaired renal function, chronic liver disease, disease of calcium or bone metabolism, those on vitamin-D supplement (last 1 month) or children with loss to follow up were excluded from study.

Before study begun, it was approved by Institutional Ethical Committee. Both indoor and OPD patients with bronchial asthma were included in study. Detailed history, examination, baseline investigations were done to rule out exclusion criteria. Odd numbered patients were taken as cases and even numbered as controls.

Total 84 eligible patients of bronchial asthma were considered. Out of which, 2 have lost follow up and 2 have been excluded, because of exclusion criteria. So, 80 cases were included in final analysis. Computer generated random number list was used to allocate patients in 2 groups,I.e.40 cases in Intervention arm and 40 cases in Control arm. Single blinding was done, wherein patients weren't informed about whether they were in intervention arm or control arm. Investigator was aware of allocation of participants in 2 groups.

Intervention arm-patients with bronchial asthma who were supplemented with vitamin-D capsules (Uprise D3-60k IU) (40 patients). **Control arm-**patients with bronchial asthma who weren't supplemented with vitamin-D, and instead were given multivitamin capsules (not containing vitamin-D) as a placebo.

Baseline investigations were done. All patients were called for follow up for 6 months and vitamin-D supplement 60,000 IU was given orally every monthly to case group for 6 months. Children were observed for clinical improvement or deterioration, compliance with medications, morbidity, any toxicity of vitamin-D while follow up. All information was recorded on a record sheet. At last, both groups were compared to look for changes in their severity and number of exacerbation of asthma.

Before recruitment, parents were explained about study in local language and informed written consent was taken. In case of illiterate parents, consent was obtained in presence of literate witness. The patients were given the right to withdraw at anytime during study and were explained about confidentiality of patient's data and the results after the study.

Statistical Analysis was performed with help of Epi.Info (TM) 7.2.2.2 EPI.INFO is a trademark of the Centers for Disease Control and Prevention(CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.).Chi-square (χ^2)test was performed to find the association between 2 qualitative variables. P<0.05 was taken to be statistically significant.

RESULTS

In study, total number of males are 47, cases were 23 and remaining were controls. Chi-square) test showed that there was no significant association between gender and the patients of two groups(p=0.82).

Chi-square test showed that there was no significant association between gender and patients of two groups (p=0.82). Thus, patients of two groups were matched for their gender.

Table 1: Distribution of gender of the patients of the two groups

Gender	Case (n=40) (%)	Control (n=40) (%)	Total
Male	23 (57.5)	24 (60.0)	47 (58.8)
Female	17 (42.5)	16 (40.0)	33 (41.3)

χ^2 =0.05;p=0.82 NS-Not Significant

In our study, there is slightly improvement in severity of asthma in both groups till 3 months, however difference is statistically insignificant. At 6 months of follow up, there is improvement in asthma severity in vitamin-D group. While there is worsening in asthma severity in control group, which is statistically significant (p=0.011).

Initially cases were 29 (n=40) and 28 controls (n=40) had ACTS score≥20 (well controlled) at the end of 6 month there is improvement of ACTS score more in cases compared to controls, which is statistically significant (p=0.04)

At the beginning;6 were cases (n=40) and 8 were controls (n=40), which had no visit per month. At the end of 6-month 31 patient in case group (n=40),12 patient in control group had no visit in month. There is decreased emergency room visit, more in case group compared to control group, which is statistically significant (p<0.0001).

There were 8 were cases (n=40),7 patient were controls (n=40) had no hospitalization. At the end of 6-month 25 patient in case group (n=40),18 patient in control group (n=40) had no hospitalization in last month. There is decrease hospital admission in both groups but it is statistically insignificant (p=0.14).

At the end of 1st month 17 patients in case group (n=40) and 9 patients in control group (n=40) weren't using reliever medication. At the end of 6-month 31 patient in case group (n=40) and 18 patients in control group (n=40) weren't using reliever medication. There is a reduce reliever medication use more in case group compared to control group, which is statistically significant (p=0.0114)

DISCUSSION

In our study with 80 patients enrolled mean age of patients was 10.95 years as compared to **Yadav et al (2013) [13]**. Of 100 patients enrolled,mean age of patients admitted was 9.15 years and in **Urashima et al(2010)[14]**. In which 430 patients were enrolled in study and mean age of admission was 10 years. In **Urshima et al (2010) [14]** age of patient in range was 6-15 year. In **Yadav et al (2013) [13]** age of patient range was 5-15 year; while our study range was 5-17 years.

Our study showed higher male preponderance, similar result to **Urshima et al (2010) [14]** while **Yadav et al (2013) [13]** shows higher female preponderance.

Severity of asthma can be intermittent OR persistent (mild, moderate, severe). In our study there was slightly but statistically insignificant improvement in severity of asthma in both groups till 3 months.

In **Yadav et al (2013) [13]** there was a slight increase in the asthma severity from moderate to severe in placebo group till 5 month follow up, while there was no increase in asthma severity in vitamin group, however this difference was statistically insignificant. At 6 month follow up, improvement in asthma severity was statistically significant in favour of vitamin-D group(p=0.016). So, severity of asthma was statistically similar for both groups till 5 months of follow up but at 6+month, severity was less in vitamin-D group as compared to placebo group. A delayed beneficial effect on asthma severity was seen.

Level of control can be well controlled, not well controlled and poorly controlled according to GINA guidelines.

Table 2: Comparisons of study parameters at various intervals of study duration

Study parameters	At the end of 1st month (%)		At the end of 2nd month (%)		At the end of 3rd month (%)	
	IA	CA	IA	CA	IA	CA
Severity of asthma						
Intermittent	18 (45.0)	20 (50.0)	16 (40.0)	20 (50.0)	16 (40.0)	20 (50.0)
Mild peristent	15 (37.5)	12 (30.0)	17 (42.5)	12 (30.0)	18 (45.0)	12 (30.0)
Moderate persistent	6 (15.0)	7 (17.5)	6 (15.0)	7 (17.5)	5 (12.5)	7 (17.5)
Severe	1 (2.5)	1 (2.5)	1 (2.5)	1 (2.5)	1 (2.5)	1 (2.5)
Chi square	0.51		1.38		1.97	
P value	0.91 (NS)		0.70 (NS)		0.57 (NS)	
Asthma control test						
A. >20	29 (72.5)	28 (70.0)	29 (72.5)	28 (70.0)	29 (72.5)	30 (75.0)
B.16 to 19	6 (15.0)	8 (20.0)	6 (15.0)	8 (20.0)	6 (15.0)	7 (17.5)
C.<15	5 (12.5)	4 (10.0)	5 (12.5)	4 (10.0)	5 (12.5)	3 (7.5)
Chi square	0.41		0.41		0.59	
P value	0.81 (NS)		0.81 (NS)		0.74 (NS)	
Number of ER visits						
1 visits	6 (15.0)	820.0)	1127.5)	922.5)	1845.0)	1025.0)
2 visits	26 (65.0)	25 (62.5)	25 (62.5)	25 (62.5)	22 (55.0)	24 (60.0)
>2 visits	8 (20.0)	7 (17.5)	4 (10.0)	6 (15.0)	0 (0.0)	6 (15.0)
Chi square	0.37		0.60		8.37	
P value	0.83 (NS)		0.74 (NS)		0.015 (NS)	
No of hospitalisations						
No hospitalization	8 (20.0)	7 (17.5)	8 (20.0)	6 (15.0)	15 (37.5)	9 (22.5)
One visit	24 (60.0)	26 (65.0)	23 (57.5)	27 (67.5)	19 (47.5)	25 (62.5)
2 visits or more	8 (20.0)	7 (17.5)	9 (22.5)	7 (17.5)	6 (15.0)	6 (15.0)
Chi square	0.21		0.85		2.31	
P valve	0.89 (NS)		0.65 (NS)		0.31 (NS)	
Reliever medication used						
Not used at all	17 (42.5)	9 (22.5)	17 (42.5)	10 (25.0)	21 (52.5)	11 (27.5)
Single medication used	20 (50.0)	25 (62.5)	22 (55.0)	27 (67.5)	18 (45.0)	26 (65.0)
2 or more medications used	3 (7.5)	6 (15.0)	1 (2.5)	3 (7.5)	1 (2.5)	3 (7.5)
Chi square	4.01		3.32		7.57	
P valve	0.13 (NS)		0.18 (NS)		0.041(S)	

S-Statistically Significant; NS-Statistically not Significant

In **our study,** at the end of 6 month, there was improvement of ACTS score more in case group compared to control group, which is statistically significant(p=0.04)

In **Elango krishnan et al (2017)** [16] on 1st visit,78 children may not be under control which is indicated by ACTS score value of<19.Simultaneously, 5 children were under control, which is indicated by ACTS score range 20-27. At the end of 3 months,67 may be under control while rest 16 may not be under control. Whereas after 6 months,77 may be under control and 6 may not be under control.

There is decreased emergency room visit more in case group compared to control group, which is statistically significant(p<0.0001) In **Elango Krishnan et al (2017)** [16] at beginning of study 58 children (69.8%) had 1 visit/month and rest 25 children (30.1%) had 2 visits/month. At the end of 3 months 61 children(73.4%)haven't visited even once and 22(26.5%)children had only 1 visit/month.at last,81 children(97.6%)haven't visited even once in a month and 2 children had 1 visit/month(2.4%).The emergency room visits were gradually reduced over a period of 6 months. In **Yadav et al (2013)** [13] there was significant fall in number of emergency visits at follow up in both groups. However, fall in number of emergency visits in vitamin-D group was statistically higher than placebo group.

There is decrease hospital admission in both group but it is statistically insignificant(p=0.14). In **Elango krishnan et al (2017)** [16] on enrolment,57 children got admitted to hospital only once a month followed by 14 children with 2 admissions/month and 12 children hadn't admitted to hospital even once. From 3rd month onwards, there was no hospital admission for asthma exacerbation.

There is a reduce reliever medication use more in case group compared to control group which is statistically significant(p=0.0114). In **Schou et al (2003)** [15] there was no statistical difference found between vitamin-D and placebo group in use ofβ2-agonist/day(P=0.92) In **Elango krishnan et al (2017)** [16] at the end of 6 month there was decrease reliever medication use in patient who were supplemented with vitamin-D which is statistically significant(p<0.001)

CONCLUSIONS:

Thus, we conclude that vitamin-D has significant improvement in severity of asthma, exacerbation of asthma and ACTS (asthma control test score)in case group compared to control group(p=0.04).So, we recommend to use vitamin-D in asthmatic pediatric cases.

Limitations of study:

This was a single centred study conducted with a small sample size. A multicentric study with large sample size would provide more evidence on role of vitamin-D in control of asthma in paediatric population.

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