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Clinical Manifestations of Pediatric Pneumonia Aged 3 Months to 12 years; Evaluation of Effect of Vitamin A

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Abstract

Background: The effect of vitamin A on clinical manifestations of pediatric pneumonia was evaluated.

Method: In this randomized double-blinded clinical trial, ninety children between 3 months and 12 years of age with pneumonia admitted to Qaem and Dr. Sheikh Hospital children's ward were assessed. They were randomly divided into two groups: one receiving vitamin A (or retinol) and the other receiving a placebo. Clinical features such as tachypnea, fever, cough, rales, wheezing, and intercostal retraction were recorded and compared between the groups every 12 hours for 120 hours. The significance level was set at less than 0.05.

Results: Of the participants, 42 patients (46.7%) were female and 48 (53.3%) were male. The mean age of all children was 18.37±9.23 months. There were no significant differences between the groups in terms of age and sex (P-values > 0.05). In the group receiving vitamin A, fever was significantly reduced after 60 hours, (P-values < 0.05) and cough was significantly reduced at 24 hours (P-value: 0.025) and 36 hours (P-value: 0.049). However, vitamin A had no effects on other clinical manifestations of pediatric pneumonia (all P-values > 0.05).

Conclusion: The prescription of vitamin A was effective in reducing fever and cough in pediatric pneumonia.

Key Words: Pediatric, Pneumonia, Retinol, Vitamin A.

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1- INTRODUCTION

Pneumonia can be caused mainly by viruses and bacteria. Among the types of pneumonia, community-acquired pneumonia (CAP) is the most common and responsible for about 80% of deaths in children affected by respiratory tract infections (1-4). It is estimated that 7%-13% of all pneumonia cases require hospitalization, and in severe cases especially in young children (5, 6). It can let to death. Vitamin A has various physiological effects related to vision, growth, cell differentiation, hematopoiesis, and immune system reactivity (7, 8) However, there is still no consensus in the literature regarding the effectiveness of this supplementation in respiratory disorders (9, 10).

Several studies have investigated the effectiveness of nutritional and dietary interventions, such as vitamins, minerals, and probiotics for the treatment of acute respiratory infections in children (11). While some studies have reported beneficial effects, including reductions in symptom severity or hospitalization duration, particularly in relation to zinc supplementation for pneumonia, the overall evidence remains inconclusive. Meta-analyses indicate that no specific dietary supplement can currently be recommended for the routine treatment of these infections. Limited studies have investigated the effect of vitamin A on pediatric pneumonia (12).

Therefore, this study aimed to investigate the potential therapeutic effects of vitamin A supplementation on clinical outcomes in pediatric patients diagnosed with pneumonia. Specifically, we focused on evaluating its impact on the severity of clinical manifestations and the duration of hospitalization, given the existing but inconclusive evidence regarding its efficacy in respiratory infections.

2- METHOD

This study was conducted as a double-blind clinical trial on children aged 3 months to 12 years hospitalized for pneumonia in the pediatric wards of Ghaem and Dr. Sheikh Hospital.

The inclusion criteria included children aged 3 months to 12 years with a diagnosis of pneumonia based on clinical and radiological assessment. The exclusion criteria were any chronic disease, diabetes mellitus, asthma, acute bronchiolitis, and recent vitamin A intake within the last 72 hours, and a history of hospitalization within the last three weeks.

A total of 45 children were used as controls, and 45 children as cases. Pneumonia was diagnosed based on history, physical examination, chest radiography, and a radiologist’s written report confirming the presence of pneumonia. The children were randomly divided into two groups. The control group received a placebo that was identical in in shape, color, and taste to the drug, while the second group received vitamin A syrup (10,000 units for children under one year and 15,000 units for children over one year) daily during hospitalization (syrup ordered from Dr. Rakhshandeh's pharmacy). Blood samples were taken at the beginning of hospitalization to determine serum retinol levels. Patient symptoms, such as tachypnea, fever, cough, retraction, rales, and wheezing, were evaluated every twelve hours and recorded in a questionnaire during hospitalization.

2-1. Statistical Analysis

After coding, the data were analyzed using SPSS software on a computer. Appropriate central and dispersion indices, tables, and charts were utilized for description. The t-test was employed to analyze and compare quantitative and normally distributed variables, while the Mann-Whitney test

was used for quantitative and non-normally distributed variables.

2-2. Ethical Considerations

This study was approved by the ethical committee of Mashhad University of Medical Science (IR.MUMSREC.1391.93).

3- RESULTS

In this study, 45 children were assessed as intervention group and 45 children were assessed as control group. The demographic data of both groups can be seen in Table 1.

We assessed respiratory signs and symptoms in the groups, and the related data can be found in Table 2. Based on our findings, only cough was significantly reduced in the intervention (retinol) group at 24 and 36 hours post-medication (P-value: 0.025 and P-value: 0.049, respectively). Other measures showed no significant differences between the two groups.

Table-1. The demographic data of participants based on groups.

	Group					
	Retinol		Control		Total	
	Number	Percent	Number	Percent	Number	Percent
Girl	20	44/4	22	48.9	42	46.7
Boy	25	55/6	23	51/1	48	53/3
Total	45	100	45	100	90	100
P-value*	0.456					

	Group			
Age (Month)		Retinol	Control	Total
	Mean	15.8	20.94	18.37
	Standard deviation	7.6	8.8	9.23
	P-value**	0.989		

* P-value based on Chi-square test

**P-value based on Mann-U- Whitney test

Fever was assessed in the groups at different times, and the related results are shown in Table 3. Based on our findings, there was no difference between the groups during the first 48 hours. However, the retinol group had significantly lower fever than the control group after 48 hours (P-values < 0.05), and retinol administration significantly reduced the fever on days 3 and 4.

Retinol levels were also measured in the case and control groups. Serum retinol levels in the control group were less than 0.2 mg/L in 22 patients (49%) and higher than 0.2 mg/L in 23 patients (51%). In the case group, these numbers were 25 (56%) and 20 patients (44%), respectively, and this difference was not significant (P=0.526) as shown in Table 4.

Table-2. Respiratory sign and symptoms in different time of assessment in the groups.

Tachypnea			
Time of assessment	Control (number/percent)	Retinol (number/percent)	P-value
12 hours	45 (100)	45 (100)	-
24 hours	45 (100)	45 (100)	-
36 hours	45 (100)	45 (100)	-
48 hours	45 (100)	45 (100)	1
60 hours	35 (77/7)	34 (75/5)	0.723
72 hours	26 (57/7)	21 (46/6)	0.231
84 hours	16 (35/5)	12 (26/6)	0.412
96 hours	10 (22/2)	8 (17/7)	0.605

108 hours	7 (15/5)	6 (13/3)	0.654
120 hours	1 (2/2)	1 (2/2)	0.497
Cough			
Time of assessment	**Control (number/percent)**	**Retinol (number/percent)**	**P-value**
12 hours	45 (100)	45 (100)	0.97
24 hours	45 (100)	37 (80.4)	0.025
36 hours	45 (100)	37 (80.4)	0.049
48 hours	44 (97.7)	37 (80.4)	0.089
60 hours	39 (86.6)	33 (73.3)	0.241
72 hours	26 (57.7)	21 (46.6)	0.321
84 hours	13(50)	12 (26.6)	0.761
96 hours	7 (15.5)	8 (17.7)	0.650
108 hours	6 (13.3)	5 (11.1)	0.651
120 hours	4 (8.8)	1 (2.2)	0.290
Retraction			
Time of assessment	**Control (number/percent)**	**Retinol (number/percent)**	**P-value**
12 hours	21(46/6)	18 (36)	0.712
24 hours	20 (44/4)	18 (36)	0.421
36 hours	20 (44/4)	18 (36)	0.421
48 hours	19 (42/2)	15 (33/3)	0.458
60 hours	13 (28/8)	11 (24/4)	0.312
72 hours	7 (15/5)	7 (15/5)	1
84 hours	4 (8/8)	4 (8/8)	1
96 hours	1(2/2)	1(2/2)	1
108 hours	0	1(2/2)	1
120 hours	0	0	-
Wheezing			
Time of assessment	**Control (number/percent)**	**Retinol (number/percent)**	**P-value**
12 hours	17 (36.9)	11 (24.4)	0.245
24 hours	17 (36.9)	11 (24.4)	0.189
36 hours	15 (33.3)	11 (24.4)	0.165
48 hours	11 (24.4)	7 (15.5)	0.245
60 hours	6 (13.3)	7 (15.5)	0.567
72 hours	5 (11.1)	6 (13.3)	0.134
84 hours	2 (4.4)	2 (4.4)	1
96 hours	2 (4.4)	2 (4.4)	1
108 hours	1 (2.2)	1 (2.2)	1
120 hours	1 (2.2)	1 (2.2)	1
Rales			
Time of assessment	**Control (number/percent)**	**Retinol (number/percent)**	**P-value**
12 hours	42 (93.3)	40 (88.8)	0.603
24 hours	40 (88.8)	40 (88.8)	1
36 hours	40 (88.8)	40 (88.8)	1
48 hours	37 (80.4)	36 (80)	0.989
60 hours	29 (63)	29 (63)	1
72 hours	21 (46.6)	21 (46.6)	1
84 hours	16 (35.5)	12 (26.6)	0.239
96 hours	8 (17.7)	9 (20)	0.432
108 hours	7 (15.5)	4 (8.8)	0.743
120 hours	4 (8.8)	3 (6.6)	1

P-value based on Chi-square test

Table-3. Comparison of fever in both groups.

	Control (number/percent)	Retinol (number/percent)	P-value
12 hours	45 (100)	45 (100)	-
24 hours	45 (100)	45 (100)	-
36 hours	45 (100)	45 (100)	1
48 hours	44 (97.7)	41 (91.1)	0.345
60 hours	36(80)	19(42.2)	0.002
72 hours	21(46.6)	7(15.5)	0.004
84 hours	10(22.2)	3(6.6)	0.024
96 hours	6(13.3)	0	0.027
108 hours	2(4.4)	0	0.614
120 hours	1(2.2)	0	1

P-value based in Chi-square

Table-4. Comparison of serum retinol levels in control and retinol groups.

		Group	
		Control (number/percent)	Retinol (number/percentage)
Retinol levels	Less than or equal to 0.2 mg/L	22 (49%)	25 (56%)
	More than 0.2 mg/L	23 (51%)	20 (44%)
P-value		0.526	

P-value based in Chi-square

The number of hospitalization days was compared between both groups. According to Table 5, the mean hospitalization days in the retinol group were 4.34±1.15 days and in the control group, they were 4.19±1.21 days. This difference was not significant (P=0.528).

Table-5. Average days of hospitalization in the retinol and control groups.

	Mean ± SD
Average days of hospitalization in the retinol group	1.15± 4.34
Average days of hospitalization in the control group	1.21±4.19
P-value	0.528

4- DISCUSSION

In the current study, we assessed the effect of vitamin A on clinical manifestations of pneumonia in pediatrics. We found that vitamin A significantly reduced fever (after 60 hours) and cough (at 24 hours and 36 hours) of medication but had no effects on other clinical manifestations of pediatric pneumonia.

Hu et al. evaluated the effect of vitamin A supplementation as an adjuvant therapy in pediatric pneumonia. They found that vitamin A administration significantly reduced the duration of fever and cough and length of hospital stay without inducing adverse effects (13) .In our study, we also found that vitamin A supplementation decreased fever and cough. While these studies were similar in this respect, there was no difference in the length of hospital stay between the two groups, This was one of the differences between the two studies, but both studies highlighted the beneficial effects of vitamin A supplementation in pediatrics with pneumonia.

Vitamin A is essential for immune function and healing after infections. Research shows that children in low- and middle-income countries often have inadequate levels of these nutrients (14,

15). Vitamin A deficiency can severely affect pediatric health, contributing to increased morbidity and mortality. It weakens immune function and the respiratory epithelium, potentially causing scaly metaplasia, which reduces defenses against infections and heightens bronchial reactivity (16, 17). An integrative review illustrated that subclinical vitamin A deficiency is prevalent in pediatric pneumonia (18). These issues highlight that hypovitaminosis of vitamin A has a remarkable effect on the occurrence of worsening pneumonia.

A study assessed vitamin A's effects on pneumonia immunologically. They showed that serum vitamin A levels in neonatal pneumonia from S. pneumoniae in mice were below 0.7 µmol/L from days 2 to 7 post-infection, and pulmonary vitamin A production remained significantly lower than in control mice from days 7 to 28. Vitamin A supplementation after infection increased Foxp3+ regulatory T cells and Th1 cells while decreasing Th2 and Th17 cells. This treatment also alleviated airway hyperresponsiveness and reduced inflammatory cell infiltration in allergic airway disease (19). There are limited studies as clinical trials in this respect, and performing the current clinical trial was one of the advantages of our study. Based on the mentioned study, vitamin A administration can improve the immunologic response against common causes of bacterial pneumonia. Our study did not assess laboratory response, but we showed that administration of this vitamin can improve patients' fever and cough.

Although in our study the length of hospital stay in our patients had no differences between two groups, in the study of Atta et al. they found that the supplementation significantly reduced the length of the hospital stay (20), similar to Hu et al.'s study (13). It should be noted that Atta et al. assessed the effect of the combination of vitamin A and zinc.

Although in a systematic review and meta-analysis study a few number of clinical trials conducted, continuous vitamin A administration did not show any positive clinical effects on acute respiratory tract infections (12).

Previous studies have shown that vitamin A administration, whether preventive or therapeutic, is not recommended as an effective intervention in the management of childhood pneumonia, except in specific cases of documented severe vitamin A deficiency (21). However, the results of the present study demonstrated that in our patients, vitamin A supplementation significantly reduced the severity of symptoms such as cough and fever.

So, it seems that administering vitamin A in pediatric pneumonia maybe favorable. However, because of the lack of studies in this respect, more studies should be done to evaluate the clinical and laboratory effects of the prescription of vitamin A in pediatrics who suffer from pneumonia. Our limitations in this study are the sample size. Increasing the number of samples and the multicenter nature of the study would have a great impact on the results. Further studies should also evaluate the effects of this supplementation on different types of infections.

5- CONCLUSION

Vitamin A supplementation may be a helpful additional to the treatment of pediatric pneumonia. However, more well-designed clinical trials are needed to confirm its effectiveness and establish standardized treatment protocols.

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