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EFFICACY OF VITAMIN A AS AN ADJUVANT THERAPY VERSUS PLACEBO IN YOUNG CHILDREN WITH ACUTE LOWER RESPIRATORY TRACT INFECTION

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Abstract

Background:
Acute lower respiratory tract infection causes significant illness in young children. Standard management often yields limited improvement. As Vitamin A shows potential immune benefits but lacks sufficient evidence, this study was conducted to evaluate its adjuvant therapeutic efficacy.

Objective:
To compare the efficacy of vitamin A as an adjuvant therapy versus placebo in addition to standard treatment in young children with acute lower respiratory tract infection.

Duration:
Three months w.e.f 22-01-2025 to 21-04-2025

Methodology:
After ethical approval, 236 children with ALRTI admitted to the Pediatric Ward of Children's Hospital Lahore were enrolled after informed consent. Using the lottery method, Group A received routine treatment plus Vitamin A, and Group B received placebo. All underwent standard management, monitored bi-daily, and data were analyzed using SPSS version 27.

Results:
A total of 236 children (mean age 6.95±1.93 years) were included, with equal BMI distribution and slight female predominance. Pneumonia was most common (50.4%). Group A (Vitamin A) showed significantly higher improvement (81.4%) than Group B (placebo, 61.0%) (p=0.001), consistent across age, BMI, gender, and ALRTI subgroups.

Conclusion:
Vitamin A supplementation as an adjuvant therapy demonstrated significantly higher efficacy in young children with acute lower respiratory tract infections compared to placebo. This enhanced efficacy was consistent across various age, gender, and BMI groups, particularly among those with pneumonia and bronchiolitis, supporting its beneficial role in improving recovery outcomes.

INTRODUCTION

The incidence of acute respiratory infections (ARI) among children under five years in Pakistan remains significant. Nationally, about 14% of children under five suffer from ARIs, making it a leading cause of

childhood illness and death.[1,2] Lower respiratory tract infections (LRTIs), which include pneumonia, bronchitis, and bronchiolitis, are among the most serious forms of ARIs. Globally, around 150 million new cases of pneumonia are reported every year, with over 90% occurring in developing countries.[3,4] According to the Global Burden of Disease Study 2017, LRTIs caused about 808,920 deaths in children under five years of age.[5]

Several lifestyle and environmental factors contribute towards higher rate of LRTIs among children. Exposure to indoor air pollution, frequent contact with other children, living in overcrowded households, and being underweight are recognized risk factors.[6] Even in developed nations, LRTIs remain a public health concern. For instance, in Belgium, while most LRTIs in adults are mild and self-limiting, they still result in an average of 3.5 days of sick leave per person each year, adding to the socioeconomic burden.[7] Common treatments for ALRTIs include macrolides, fluoroquinolones, beta-lactam antibiotics and nebulization. Among these, macrolides such as clarithromycin are widely used and have proven effective in managing ALRTIs.[8]

Keeping in view continuing global impact of respiratory infections, there is growing interest in supportive treatments for boosting recovery. Vitamin A has shown an important role in growth and repair of body tissues, supports production of red and white blood cells, enhances antibody formation, and maintains epithelial integrity. Its proven benefit in treating measles-related pneumonia has led researchers to explore its possible role in reducing the duration and severity of ALRTIs.[9]

Riaz et al. at Shaikh Zayed Medical Complex Lahore, Pakistan reported efficacy of vitamin A supplementation (VAS) to be 85.0% vs. 69.0%; p-value<0.05 than placebo in children with acute lower respiratory tract infection. Though promising, yet this evidence was limited and involving children aged 2–60 months.[9] Therefore, further research was necessitated to confirm these findings and clarify the concerns raised by Zhang et al., who reported that excessive VAS may increase respiratory infection risk in well-nourished children.[10]

Therefore, this study was planned to further evaluate the efficacy of vitamin A supplementation as an adjuvant therapy in young children with acute lower respiratory tract infection, aiming to provide stronger local evidence for its safe and effective use in clinical practice.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Pediatrics, Children's Hospital Lahore. The study duration was three months following the approval of the synopsis. A total of 236 patients (118 in each group) were included in the study. The sample size was calculated with a 95% confidence level and 5% margin of error, assuming an expected efficacy of Vitamin A supplementation to be 85.0% compared to 69.0% in the placebo group.[9] A non-probability consecutive sampling technique was used for sample selection. Children of both genders aged 4–10 years presenting with acute lower respiratory tract infection (ALRTI) as per operational definitions were included. Patients who had previously received Vitamin A supplementation, had Vitamin A deficiency, severe bronchial asthma, congenital heart disease, or a history of chest infection within the last six months were excluded. The study was based on the hypothesis that there is a difference in the efficacy of Vitamin A as an adjuvant therapy versus placebo in addition to standard treatment in young children with ALRTI.

Acute Lower Respiratory Tract Infection (ALRTI) was diagnosed when any one of the following conditions was present: Pneumonia was defined as fever ≥100°F and respiratory rate >40/min for ≥24 hours, confirmed on chest X-ray showing consolidation involving one or more lobes. Bronchitis was identified by the presence of runny nose, low-grade fever (37.2–38.0°C), chest congestion (wet cough), and wheezing. Bronchiolitis was diagnosed when respiratory rate was >40/min for ≥24 hours with hyperinflated lungs and prominent markings on chest X-ray (PA view). Efficacy was defined as complete resolution of ALRTI symptoms by the fifth day of treatment.

After approval from ethical review comittee, 236 eligible children admitted with ALRTI were enrolled after informed written consent from parents or guardians and divided into two groups using the lottery method where Group A received routine treatment plus Vitamin A supplementation (n=118), and Group B received routine treatment plus

placebo (n=118). All patients received oxygen, intravenous antibiotics, and nebulization as per hospital protocol. Group A was given Vitamin A syrup at a dose of 1500 IU once daily for five days, while Group B received one drop of olive oil daily for the same duration. The temperature, respiratory rate, recessions of the chest, and tolerance to feeding were observed in patients twice a day. Treatment and monitoring were performed by the same staff and findings were recorded by the principal researcher under the supervision of a senior consultant in order to reduce bias. The confounding variables were controlled with the help of exclusion criteria.

All data was entered and analyzed using SPSS version 27. Numerical variables such as age and BMI were expressed as mean ± SD. Categorical variables such as gender, type of ALRTI, and treatment efficacy were presented as frequencies and percentages. Efficacy between the groups was compared using Chi square test, considering a p-value ≤0.05 as statistically significant. For addressing effect modifiers, data was stratified for age, gender, BMI, and type of ALRTI and post-stratification Chi-square tests were applied using the same level of significance.

RESULTS

A total of 236 children were included in the study, with a mean age of 6.95±1.93 years. Among them, 143 (60.6%) were between 4–7 years of age, while 93 (39.4%) were between 8–10 years. The mean body mass index (BMI) was 25.86±3.98 kg/m², with an equal distribution of 118 (50.0%) children in both the normal-weight and overweight/obese categories. There was a slight female predominance, with 125 (53.0%) females compared to 111 (47.0%) males. Regarding the type of acute lower respiratory tract infection (ALRTI), pneumonia was the most common presentation, observed in 119 (50.4%) children, followed by bronchiolitis in 80 (33.9%) and bronchitis in 37 (15.7%) cases. Data is given in Table 1. Both groups were statistically comparable at baseline, with no significant differences observed in demographic or clinical characteristics (p-value > 0.05), as presented in Table 2. Table 3 shows the comparison of treatment efficacy between the two study groups. In Group A (routine standard treatment plus Vitamin A supplementation), 96 (81.4%) children showed improvement, whereas in Group B (routine standard treatment plus placebo), efficacy was observed in 72 (61.0%) children. The difference between the two groups was found to be statistically significant (p = 0.001) using the Chi-square test, taking p ≤ 0.05 as the level of significance.

Table 4 shows subgroup comparisons of efficacy between Group A (Vitamin A supplementation) and Group B (placebo). Across all subgroups, Group A demonstrated higher improvement rates. Significant differences were observed by age (4–7 years: 82.4% vs 62.3%, p=0.007; 8–10 years: 79.5% vs 59.2%, p=0.034), BMI (normal weight: 76.6% vs 57.4%, p=0.027; overweight/obese: 87.0% vs 64.1%, p=0.004), and gender (male: 79.2% vs 56.9%, p=0.012; female: 83.1% vs 65.0%, p=0.021). Among ALRTI types, Vitamin A showed significantly higher efficacy in pneumonia (85.2% vs 65.5%, p=0.012) and bronchiolitis (76.3% vs 54.8%, p=0.044), while the difference in bronchitis (78.9% vs 61.6%, p=0.235) was not significant which may however be associated with small sample size in this particular subgroup.

Table 1: Demographic Characteristics of Patients Included in the Study

Characteristics	Total (236)
Age (years)	6.95±1.93
• 4-7 years	143 (60.6%)
• 8-10 years	93 (39.4%)
BMI (kg/m²)	25.86±3.98
• Normal Weight	118 (50.0%)
• Overweight/Obese	118 (50.0%)
Gender	

• **Male**	111 (47.0%)
• **Female**	125 (53.0%)
Type of ALRTI	
• Pneumonia	119 (50.4%)
• Bronchitis	37 (15.7%)
• Bronchiolitis	80 (33.9%)

Table 2: Comparison of Baseline Characteristics between the Study Groups

Characteristics	Group A (n=118)	Group B (n=118)	p-value
Age (years)	6.87±1.94	7.03±1.93	0.523
• 4-7 years	74 (62.7%)	69 (58.5%)	0.505
• 8-10 years	44 (37.3%)	49 (41.5%)	
BMI (kg/m^2)	25.62±4.01	25.11±3.96	0.343
• Normal Weight	64 (54.2%)	54 (45.8%)	0.193
• Overweight/Obese	54 (45.8%)	64 (54.2%)	
Gender			
• Male	53 (44.9%)	58 (49.2%)	0.514
• Female	65 (55.1%)	60 (50.8%)	
Type of ALRTI			
• Pneumonia	61 (51.7%)	58 (49.2%)	0.860
• Bronchitis	19 (16.1%)	18 (15.3%)	
• Bronchiolitis	38 (32.2%)	42 (35.6%)	

Chi Square test/ Independent sample t test, taking p-value≤0.05 as significant.

Table 3: Comparison of Efficacy between the Groups

Characteristics	Group A (n=118)	Group B (n=118)	p-value
Efficacy			
• **Yes**	96 (81.4%)	72 (61.0%)	0.001
• **No**	22 (18.6%)	46 (39.0%)	

Chi Square test, taking p-value≤0.05 as significant.

Table 4: Comparison of Efficacy between the Groups Stratified for Subgroups

Group	Sub Group	Group A (n=118)	Group B (n=118)	p-value
Age	4-7 years	61/74 (82.4%)	43/69 (62.3%)	0.007
	8-10 years	35/44 (79.5%)	29/49 (59.2%)	0.034
BMI	Normal Weight	49/64 (76.6%)	31/54 (57.4%)	0.027
	Overweight/Obese	47/54 (87.0%)	41/64 (64.1%)	0.004
Gender	Male	42/53 (79.2%)	33/58 (56.9%)	0.012
	Female	54/65 (83.1%)	39/60 (65.0%)	0.021
Type of ALRTI	Pneumonia	52/61 (85.2%)	38/58 (65.5%)	0.012
	Bronchitis	15/19 (78.9%)	11/18 (61.6%)	0.235 *
	Bronchiolitis	29/38 (76.3%)	23/42 (54.8%)	0.044

*** Chi Square test, taking p-value>0.05 as insignificant.**

DISCUSSION

Acute lower respiratory tract infection (ALRTI) is a leading cause of illness and death among young children, particularly in developing countries.[11,12] Despite the use of standard treatments such as antibiotics, oxygen therapy, and supportive care, morbidity remains high.[12] Recently, Vitamin A has gained attention for its potential immune-enhancing and antioxidant properties that may aid in recovery from respiratory infections.[13,14] However, evidence regarding its efficacy as an adjuvant therapy in ALRTI remains limited, controversial and with different variables in each study.[9,10] Therefore, this study was planned to evaluate the efficacy of Vitamin A supplementation compared with placebo in young children with acute lower respiratory tract infection.

Comparison of the findings of this study with previously published research shows both consistent and contrasting results regarding the efficacy of Vitamin A supplementation in children. Pakistani researchers Riaz et al. reported that Vitamin A supplementation was significantly more effective in children with acute lower respiratory tract infections with 85% of patients receiving Vitamin A supplementing in the Vitamin A group recovering successfully compared to 69% of patients in the placebo group (p=0.007). These findings correspond to the present research, which also revealed an improved clinical outcome in the Vitamin A group, which proves the efficacy of the supplement as an effective adjuvant treatment of respiratory infections.[9]

Rodrigues et al. from Ecuador found no significant benefit of moderate-dose Vitamin A supplementation in reducing the duration of uncomplicated pneumonia in underweight or normal-weight children under five years of age. However, a favorable effect was noted among those with higher baseline serum retinol levels, indicating that the benefit may depend on pre-existing nutritional status.[15] Likewise, in a meta-analysis, Zhang et al. in China determined that Vitamin A supplementation did not provide any extra value in the prevention or speed of recovery of acute respiratory infections. They also proposed that over-supplementation had the potential of raising the chances of respiratory infections amongst well-nourished children.[10]

Conversely, Hu et al., also from China, reported more encouraging results, showing that Vitamin A supplementation helped alleviate clinical symptoms, shortened hospital stays, and did not increase adverse reactions in children with pneumonia.[16] Saied et al. from Egypt found that Vitamin A used as an adjunct therapy in community-acquired pneumonia significantly reduced the duration of hospital stay and pneumonic effusion in children under five years.[17] Kanakala et al. from India also noted that Vitamin A supplementation markedly decreased the frequency of ALRTI episodes (p<0.001) and emphasized its role in reducing under-five mortality through national supplementation programs.[18]

Gebremedhin observed that Vitamin A supplementation was associated with a minor, clinically insignificant rise in common childhood illnesses.[19] Additionally, Yilmaz et al. in Turkey found that Vitamin A supplementation reduced the rate of lower urinary tract infections, with infection frequency dropping from 3.58 to 0.75 episodes in six months.[20] This indicates that the adjuvant action of Vitamin A is not limited to respiratory infections, but it can improve immunity and lower the rates of infections in other systems. In general, the current results support the immune-modulatory and supportive action of Vitamin A in childhood infectious diseases.

CONCLUSION

Vitamin A supplementation as an adjuvant therapy demonstrated significantly higher efficacy in young children with acute lower respiratory tract infections compared to placebo. This enhanced efficacy was consistent across various age, gender, and BMI groups, particularly among those with pneumonia and bronchiolitis, supporting its beneficial role in improving recovery outcomes.

LIMITATIONS & RECOMMENDATIONS

The primary strength of the given study is the randomized controlled design, the sufficient size of

the sample, and the inclusion and exclusion criteria that guaranteed the reliability of the study and reduced the bias. Internal validity was enhanced by regular monitoring by the same staff. Nevertheless, its generalizability can be limited because it is a single-center study with a short period of time. No measurement of their nutritional status or serum retinol levels was determined and this may affect the results. It is suggested to confirm and broaden these findings by conducting multicenter studies with biochemical monitoring in the future.

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