IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
July 2023 Vol.:27, Issue:4

Demographic, Clinical Profiles and Therapeutic Outcomes of Aerosol Therapy in Children

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Keerthika. M[1], Parimalakrishnan. S[1*], Rama Praveen Kumar. R[1], Ramanathan. R[2]

1 – Department of Pharmacy, Annamalai University, Annamalai Nagar, Tamil Nadu, India

2 – Department of Paediatrics, Government Medical College and Hospital Cuddalore (RMMCH), Annamalai Nagar, Tamil Nadu, India

Submitted: 23 June 2023
Accepted: 12 July 2023
Published: 30 July 2023

HUMAN JOURNALS
ijppr.humanjournals.com

Keywords: Clinical profile, Demography, Aerosol, Respiratory Tract Infection, Paediatric

ABSTRACT

Background: Respiratory illness remains one of the leading causes of hospitalization in children. Administration of drugs in the form of aerosol plays an important role in the treatment of respiratory illnesses. Hence, it is essential to understand the use of these aerosols in clinical settings to improve efficacy with optimal utilization of drugs. **Methodology:** This study is a cross-sectional study. The study period was between January 2019 and December 2021. The patient inclusion criteria were the subjects treated with aerosol, both gender and the age group of 1 day to 12 years. Data were collected from 264 subjects. The data collection includes variables like demography, clinical presentation, therapeutic management and condition at discharge. The collected data were analyzed with descriptive and one-way ANOVA tests to find the statistical significance. **Result:** In this study, children aged between 1 day and 1 year (59.46%) were predominantly under aerosol therapy for respiratory illnesses. Crepitation was observed in 56.8% of the pediatric population and 40.1% of the population was diagnosed with bronchiolitis. Hypertonic saline was administered to 67.42% of the population in the form of an aerosol. The condition of every patient significantly improved at the time of discharge after aerosol administration. **Conclusion:** Aerosol therapy has been used in management of the paediatric respiratory illnesses widely, which has improved the therapeutic outcomes. The challenging part is the administration, use and cost of the therapy. It has the benefit of achieving the goals of therapy with improved quality of life.

INTRODUCTION

Respiratory illness is manifested as one of the leading causes of hospitalization in children. It encompasses various communicable and non-communicable diseases of the upper and lower respiratory tract contributing to mortality and morbidity among the pediatric population. According to World Health Organization (WHO), acute respiratory tract infections are responsible for 10.6 million deaths among children under 5 years with pneumonia alone being responsible for 19% of the deaths. [1] ARIs contribute to about 20-40% of hospitalization in children and mortality due to ARIs from India, Bangladesh, Indonesia, and Nepal adds up to 40% of total global deaths. [2] One of the most common pediatric non-communicable diseases, asthma, has been ranked 16th, as the leading cause of years lived with a disability, it is estimated that 300 million people have asthma and it is expected to increase by 100 million in 2025. [3] The International Society of Asthma and Allergy in Children (ISSAC) reports a prevalence of wheezing of about 7% in Indian children aged between 6 – 7 years and about 37.9 million of the Indian population suffers from asthma. [4]

The use of aerosol and inhalers as one of the therapeutic approaches plays a vital role in the management of respiratory illnesses among the pediatric population. Recent advancement in aerosol delivery devices has led to improved drug-delivery efficiency and extended ways to treat diseases with optimal use of drugs. [5,6] Aerosol therapy is the administration of solid or liquid aerosol particles to the respiratory tract for the management of a particular disease. [8] Aerosolization of medications are used to achieve high drug concentrations in the respiratory system, thereby, it is used in various pediatric respiratory illness for the management of bronchospasms, airway inflammations, mucus clearance and infections. [6,7]

Aerosol drug delivery system achieves therapeutic effect with minimal systemic adverse effects and it is considered to be a convenient and painless method of administration. [9] Small-volume nebulizers (SVN), Dry powder inhalers (DPI) and Pressurised metered-dose inhalers (MDI) are the most widely used aerosol delivery devices. [8] With the aerosol delivery system, 80% of the inhaled dose gets deposited in the oropharyngeal region and only up to 20% of the dose reaches the lungs, where it is either removed by a mucociliary escalator or gets systemically absorbed. [11] Bronchodilators, corticosteroids and mucolytic agents are some of the common drugs used as aerosols in respiratory illnesses. [8] Certain clinical considerations such as higher respiratory rates, shorter inspiratory times, lower inspiratory flows, vital capacity, functional residual capacity, and lower tidal volumes compared to

adults result in low residence time for small particles, leading to a decrease in pulmonary deposition of aerosols in children should be carefully addressed before administration of aerosols. [10] Children are known to have poor adherence to aerosol delivery devices as they lack proper knowledge of using devices effectively. Hence it becomes inevitable to explain to the patient and parent the techniques involved in the administration of aerosols with aerosol delivery devices to achieve maximum efficacy of the aerosol therapy. [8]

Hospital pharmacists can participate in various programs to understand the inhalation drug therapy policies, aerosol drug formulations and individual patient dispensing inhalation therapy by which they can provide a necessary service for better patient care. [12] Among various healthcare workers, pharmacists are easily accessible to patients and healthcare providers. Pharmacists play a key role in providing medication education, training and ongoing evaluation of optimal inhalation techniques. Thus, results in improved medication adherence, disease management and quality of life. [13] The present study aims to analyze the demographic, clinical profile and outcomes of aerosol therapy in children visiting the tertiary care teaching hospital located at Chidambaram.

METHODOLOGY

This study is a retrospective cross-sectional observational study. 264 eligible subjects were enrolled in this study from January 2019 to December 2021. The study period was 6 months. Based on the following inclusion criteria the study subjects were selected: (i) both genders of children between 1 day and 12 years; (ii) patients diagnosed with a respiratory illness; (iii) patients who received aerosol therapy; (iv) patients who were fully immunized; and (v) inpatients. The following were exclusion criteria (i) patients aged 13 and above; (ii) patients who received aerosol therapy for other illnesses; and (iii) case sheets with insufficient data. The present study protocol was approved by the Institutional Human Ethical Committee (IHEC), Government Cuddalore Medical College and Hospital (RMMCH), Annamalai Nagar. A data collection form was prepared to collect the required data from the patient. The data were collected from the MRD of the teaching hospital.

Data Collection Procedure

The following variables were collected from the individual medical records of the inpatient. The data includes demographic details, medical history, laboratory investigations and therapeutic management. Laboratory investigations include biochemical parameters such as

blood pressure (BP), oxygen saturation (SPO_2), complete blood count (CBC), liver function test (LFT), renal function test (RFT) and Imaging tests such as chest X-ray, ECG, ultrasonography and relevant data to the study were collected. The above data were collected for three years.

Statistical analysis

The collected data were represented as descriptive and analyzed using the student's t-test. The demographic data were analyzed using the chi-square test. Parameters of the clinical profile were analyzed with Fisher's test, Kruskal-Wallis test and one-way ANOVA. The p-value <0.05 was considered statistically significant.

RESULTS

Distribution of demographic and clinical profiles in various age groups of children

The demographic distribution shows that male children (54.17%) were predominant when compared with female children (45.48%). There is a significant statistical difference observed among the genders (P=0.0025), calculated by using chi-square. The majority of the children were between 0 and 1 year of age (59.46%) followed by 1-3 years (28.03%), 3-6 years (7.95%) and 6-12 years (4.54%). There is a significant statistical difference observed among the age group (P=0.0015), calculated by using Fisher's test. Presence of crepitation (56.8%) during the respiratory examination was predominant followed by the presence of wheezing (32.2%), tachypnea (29.9%), chest retractions (26.1%), conducted sounds (23.9%), low oxygen saturation (16.3%) and tachycardia (8.7%) before administration of aerosol therapy. Children were predominantly diagnosed with lower respiratory tract infections (84%) such as bronchiolitis (40%) and pneumonia (30%), followed by wheeze-associated diseases (12.8%) such as WALRI (9%), asthma (3%) and HRAD (1%). URTI was diagnosed in only 3% of the population. There is a significant statistical difference observed among the diagnosis (P=0.00128), calculated by using Fisher's test. The data are represented in Table 1.

Table 1: Demographic and clinical profile of study patients

Parameters	No. of Patients (%)	P –Value
Gender*		
Female	121 (45.83)	0.0025
Male	143 (54.17)	
Age**		
0-1 year	157 (59.46)	0.0015
2-3 years	74 (28.03)	
4-6 years	21 (10.98)	
7-12 years	12 (7.95)	
Clinical findings**		
Crepitation	150 (56.8)	0.0567
Conducted sounds	63 (23.9)	
Wheeze	85 (32.2)	
Tachypnea	79 (29.9)	
Tachycardia	23 (8.7)	
Low Oxygen saturation	43 (16.3)	
Chest retractions	69 (26.1)	
Diagnosis**		
Bronchiolitis	106 (40.1)	0.0128
Pneumonia	78 (29.5)	
LRTI	37 (14)	
WALRI	24 (9)	
URTI	10 (3.7)	
Asthma	7 (2.6)	
Hyperreactive airway disease	2 (1)	

* - P value calculated by using the Chi-square test

** - P value calculated by using Fisher's test

Male children were predominant between age 0 and 1 year whereas female children were predominant between age 1 to 3 years. In children of age 0-1year crepitation (57%),

conducted sounds (25%), wheeze (28%), tachypnea (29%), tachycardia (7.6%), low oxygen saturation (16%), chest retractions (30%) was observed. In children of age >1-3years crepitation (58%), conducted sounds (30%), wheeze (38%), tachypnea (31%), tachycardia (11%), low oxygen saturation (19%), chest retractions (24%) was observed. In children of age 4-6years crepitation (57%), conducted sounds (9%), wheeze (38%), tachypnea (24%), tachycardia (4%), low oxygen saturation (9%), chest retractions (14%) was observed. In children of age 7-12years crepitation (41%), wheezing (58%), tachypnea (42%), tachycardia (17%), low oxygen saturation (17%) and chest retractions (8%) were observed.

Bronchiolitis was observed in children aged between 0-1 year (62%), >1-3 years (9%), 4-6years (4%). Pneumonia was predominant in children aged between 0 – 1 year (29%), >1 – 3 years (32%), 4 – 6 years (25%) and 7 – 12 years (4%). LRTI was predominant in children aged between v (4.4%), >1 – 3 years (33%), 4 – 6 years and 7 – 12 years (17%). WALRI was predominant in children aged between 0-1 year (1%), >1-3 years (22%) and 4-6 years (24%). URTI was predominant in children aged between 0 – 1 year (1%), >1 – 3 years (1%), 4 – 6 years (14%) and 7 – 12 years (17%). Asthma was predominant in children aged between >1 – 3 years (1%), 4 – 6 years (14%) and 7 – 12 years (33%). Hyperreactive airway disease was predominant in children aged between 4 and 6 years (5%) and 7 – 12 years (8%).

Table 2: Distribution of study patients according to age and clinical presentation

Parameters	Age of Children (years)				Total	P -Value
	0-1	2-3	4-6	7-12		
Gender						
Male	91	32	12	8	143 (54.17%)	0.0193
Female	66	42	9	4	121 (43.83%)	
Clinical findings						
Crepitation	90	43	12	5	150 (56.81%)	0.0278
Conducted sounds	39	22	2	-	63 (23.86%)	
Wheeze	42	28	8	7	85 (32.19%)	
Tachypnea	46	23	5	5	79 (29.9%)	
Tachycardia	12	8	1	2	23 (8.71%)	
Low Oxygen saturation	25	14	2	2	43 (16.2%)	
Chest retractions	47	18	3	1	69 (26.13%)	
Diagnosis						
Bronchiolitis	98	7	1	-	106 (40.1%)	0.0091
Pneumonia	46	24	5	3	78 (29.5%)	
LRTI	7	25	3	2	37 (14%)	
WALRI	3	16	5	-	24 (9%)	
URTI	3	1	3	2	10 (3.7%)	
Asthma	-	1	3	4	7 (2.6%)	
Hyperreactive airway disease	-	-	1	1	2 (1%)	

* - P value calculated by using Kruskal – Wallis Test

Aerosolized medications in pediatric respiratory illness

3% NaCl (67.42%) is the most aerosolized drug followed by budesonide with levosalbutamol (40.53%), adrenaline (33.71%), levosalbutamol with ipratropium bromide (26.9%), budesonide (21.21%), levosalbutamol (16.3%), salbutamol (10.6%) and ipratropium bromide

(3.4%) for the treatment of respiratory illness. There is a significant statistical difference among the administration of aerosolized medications in pediatric respiratory illness (P value=0.0409). The P value was calculated using one-way ANOVA.

Table 3: Distribution of aerosolized medications among pediatric respiratory illnesses

Aerosolized drug	Frequency (%)	P – value
Budesonide	56 (21.21)	0.0409
3% NaCl	178 (67.42)	
Levosalbutamol with Ipratropium bromide	71 (26.9)	
Levosalbutamol	43 (16.3)	
Adrenaline	89 (33.71)	
Salbutamol	28 (10.6)	
Ipratropium bromide	9 (3.4)	
Budesonide with Levosalbutamol	107 (40.53)	

* - P value calculated by using one-way ANOVA

Table 4: Distribution of aerosolized medications based on their use for respiratory diseases in study patients

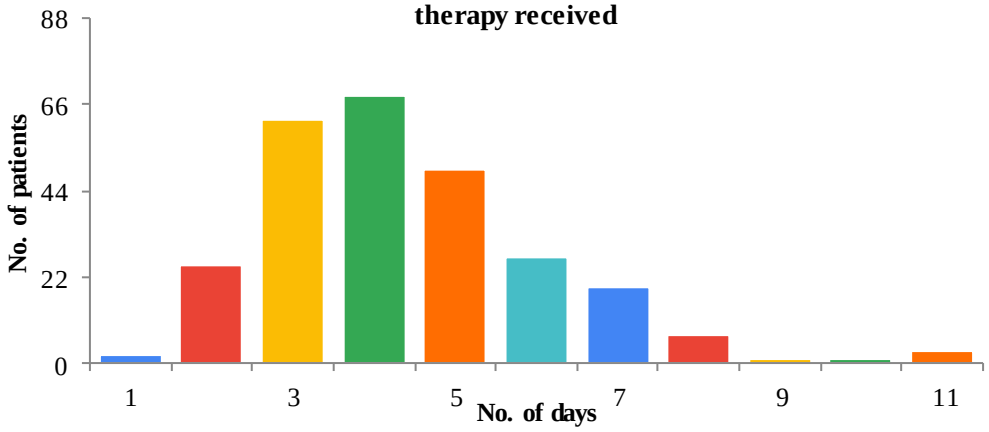
Disease	Percentage							
	3% NaCl	Adrenaline	Budesonide	Budesonide with levosalbutamol	Levosalbutamol	Salbutamol	Ipratropium bromide	Ipratropium bromide with levosalbutamol
Bronchiolitis	83	54	16	44	16	10	0	9
WALRI	50	16	37	29	25	8	8	54
LRTI	51	11	11	43	22	5	5	35
Pneumonia	67	23	17	9	9	9	0	32
Asthma	12	12	50	50	36	25	50	87
URTI	44	0	0	0	0	11	0	0
Hyperreactive airway disease	0	0	0	0	50	0	50	100

3% NaCl has been administered largely in bronchiolitis (83%), pneumonia (67%), LRTI (51%), WALRI (50%), URTI (44%) and asthma (12%). Adrenaline has been administrated predominantly in bronchiolitis (54%) followed by pneumonia (23%), WALRI (16%), asthma (12%) and LRTI (11%). Budesonide has been used predominantly in asthma (50%), further in WALRI (37%), pneumonia (17%), bronchiolitis (16%) and LRTI (11%). A fixed-dose combination of budesonide with levosalbutamol has been administrated largely in asthma (50%), bronchiolitis (44%), LRTI (43%), WALRI (29%) and pneumonia (3%). Levosalbutamol has been administrated predominantly in HRAD (50%) further in asthma (36%), WARLI (25%), LRTI (22%), bronchiolitis (16%) and pneumonia (9%). Salbutamol has been used predominantly in asthma (25%), further in URTI (11%), bronchiolitis (10%), pneumonia (9%), WALRI (8%) and LRTI (5%). Ipratropium bromide has been administrated predominantly in HRAD (50%), and asthma (50%), followed by WALRI (8%) and LRTI (5%). FDC of ipratropium bromide with levosalbutamol has been administrated predominantly in HRAD (100%), followed by asthma (87%), WALRI (54%), LRTI (35%), pneumonia (32%) and bronchiolitis (9%). Overall, in paediatric respiratory illness, 3% NaCl (67.42%) has been administered extensively followed by budesonide with levosalbutamol (33%), adrenaline (29.1%), levosalbutamol with ipratropium bromide (23.86%). Budesonide (18.2%), levosalbutamol (12.12%), salbutamol (8.7%) and ipratropium bromide (2.7%). The data are provided in Table 3.

Number of days aerosol therapy received by patients

From the below graph, most of the patients received aerosol therapy from 3 to 5 days (67.8%), specifically most patients received aerosol therapy for 4 days (25.76%) followed by 3 days (23.48%), 5 days (18.56%), 6 days (10.23%), 2 days (9.48%), 7 days (7.1%), 8 days (2.65%), 11 days (1.13%), 1 day (0.75%), 9 days (0.38%) and 10 days (0.38%).

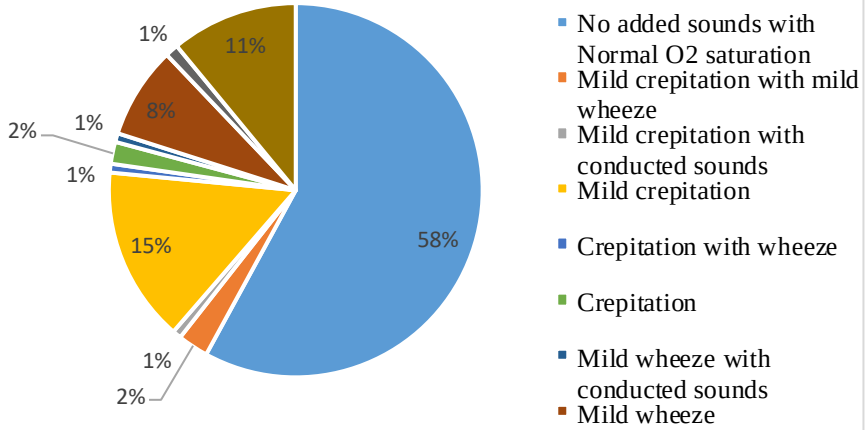
Fig. No. 1: Distribution of patients based on number of days aerosol therapy received



Examination of the respiratory system at the time of discharge after receiving aerosol therapy

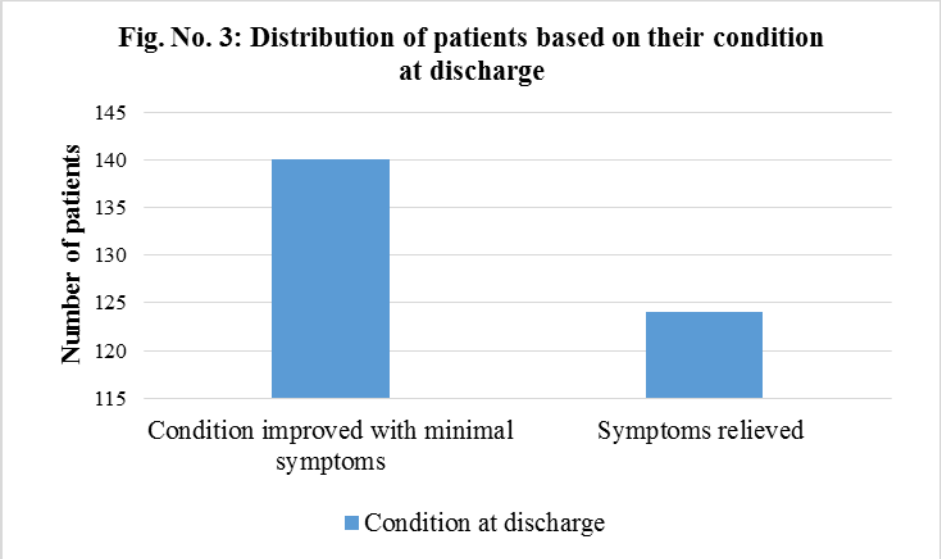
From the below graph, 58% of patients after treatment with aerosols and other therapeutic management have shown normal respiratory rate and normal O_2 saturation with no added sounds in respiratory system examination, followed by mild crepitation (15%), conducted sounds (11%), mild wheeze (8%), mild crepitation with mild wheeze (3%), crepitation (2%), mild crepitation with conducted sounds (1%), crepitation with wheeze (1%), wheeze (1%) and mild wheeze with conducted sounds (1%).

Fig. No. 2: Distribution of patients based on the examination of respiratory system during discharge



Condition at discharge after receiving aerosol therapy

From the below graph, about 53% of patients' conditions improved with minimal symptoms and about 47% of patients' symptoms were relieved and became clinically normal after treatment with aerosol therapy and other appropriate therapeutic agents. Almost all patients' general condition got improved at the time of discharge.



DISCUSSION

Respiratory diseases, both communicable and non-communicable, are one of the most common diseases around the world and it continues to be a major threat to the pediatric population. With the ongoing increase in air pollution and other environmental crisis, children are further prone to increased risk of respiratory diseases. Hence, understanding the antibiotics and supportive care in pediatric respiratory illness is much needed. In developing countries like India, a wide variety of cooking fuels such as biomass fuel, and coal, causes increased inhalation of particles which leads to exacerbation of respiratory systems and increased mortality rates. In India, around 23% of death in preschool children is caused due to respiratory diseases. [14]

Children have been known to have various barriers to the administration of aerosols as they differ anatomically in various factors from adults. Behavioral factors such as crying decrease the lung deposition of aerosols by four to tenfold leading to increased deposition in the upper airway tract which may lead to systemic absorption of the drug causing various adverse effects such as tachycardia. [6]

The use of inhalation of aerosols in children is based on clinical presentation rather than diagnostic disease and they play an important in the improvement of symptoms reducing the number of days of hospitalization. The efficiency of aerosol therapy could be achieved by understanding the differences between delivery devices and interfaces and knowledge of selecting appropriate interfaces and delivery devices that could comply with the patient's age

and condition. This study is to present a clearer picture of the use of aerosols in various respiratory conditions among the hospitalized pediatric population.

About 87% of the subjects enrolled in the study were diagnosed with acute respiratory tract infections including upper and lower tract, in which, lower respiratory tract infection alone contributes 84%. Though there is no high-end quality evidence to support the use of aerosols in respiratory tract infections, good quality data and clinical experience support the use of bronchodilators such as salbutamol, anti-infectives such as tobramycin, aztreonam and colistin, and anti-inflammatory agents such as budesonide, which is a mainstay therapy in respiratory diseases like asthma. [7] The study included 264 patients with respiratory illness with a mean age of 1.63years, crepitation was observed in 56.81% of the population followed by patients presented with wheeze (32.19%), tachypnea (29.9%), chest retractions (26.13%), conducted sounds (23.86%), low oxygen saturation (16.2%) and tachycardia (8.71%).

In this study, hypertonic saline has been used to a great degree in almost all respiratory illnesses (67.42%) and predominantly in bronchiolitis (83%). A meta-analysis study with 4186 children from 32 publications concluded that the use of 3% saline decreases the length of hospital stay compared to 0.9% saline in acute bronchiolitis. [15] Another study which is a systemic review concluded that treatment of hypertonic saline in moderate to severe bronchiolitis has small or no effect. [16] Adrenaline has been used for up to 29.1% of respiratory illnesses, predominantly in Bronchiolitis. Evidence-based research with a total of 238 patients in seven clinical trials concluded that the use of adrenaline (1:1000) in bronchiolitis (acute inflammatory airway obstruction) is a safe treatment. [17]

The combination of budesonide with levosalbutamol has been widely used in various diseases such as asthma (50%), Bronchiolitis (44%), WALRI (29%), LRTI (43%) and pneumonia (9%). Overall it has been used in 33% of the cases. 23.86% of the cases were prescribed with the fixed-dose combination of ipratropium bromide and levosalbutamol. Budesonide (50%) and a combination of ipratropium bromide with levosalbutamol (87%) have been chiefly used in the management of asthma. Salbutamol (8.7%) is the least used among the nebulized drugs.

A double-blind, randomized, placebo-controlled study with 434 children aged between 2 to 18 years concluded that has concluded that combination of ipratropium bromide with a corticosteroid has significantly reduced the number of days of hospitalization. [18] 58% of

the population were discharged with no lung signs such as added sounds, respiration rate and normal oxygen saturation after therapeutic management. 53% of the population got their condition improved along with some minimal symptoms and 47% of the population became clinically normal.

A double-blind, randomized, placebo-controlled clinical trial with 85 patients in the nebulizer group and 83 in the MDI spacer group concluded that MDI with spacers may be as efficacious as nebulized in children aged between 2 to 24 months with wheezing episodes as bronchodilator therapy. [19] One of the common problems addressed in aerosol therapy is the education on the proper use of aerosol delivery devices by patients. Hence patient counseling regarding the appropriate procedures and assembly of the device for the administration of the aerosol plays a vital role. The patient should be educated about the delivery devices and interfaces to reach their maximum efficacy.

Limitations:

Limitations of the study include (i) the severity of the disease was not addressed for the use of aerosols (ii) the study was conducted in a small population confined within pediatric inpatients of Government Medical College Cuddalore and Hospital (RMMCH) (iii) Types of delivery devices used for the administration of the aerosols were not addressed.

CONCLUSION

With the rapid onset of action and lower systemic adverse effects, aerosolized medication has been shown to improve the clinical presentation of respiratory illnesses and also the goals of therapy can be achieved effectively along with other therapeutic management such as antibiotics, corticosteroids, supplements etc. Due to its efficacy, aerosolized medication has been administered in most pediatric respiratory infections and disorders even from the initial phase and also eventually throughout treatment. The use of proper aerosol delivery devices/ attachments has resulted in achieving the treatment goals better in various respiratory illnesses. Numerous studies have demonstrated the advantages of the administration of aerosols. Appropriate drugs which are used to treat respiratory illness may be developed as aerosol formulations and their therapeutic outcomes can be compared with other traditional dosage forms to achieve the goals of treatment in respiratory illness.

Declarations:

Conflict of interest:

The authors have no conflicts of interest regarding this investigation.

REFERENCES

1. Oguonu T, Adaeze Ayuk C, Edelu BO, Ndu IK. Pattern of respiratory diseases in children presenting to the pediatric emergency unit of the University of Nigeria Teaching Hospital, Enugu: a case series report. BMC Pulmonary Medicine. 2014 Dec;14:1-8.
2. Vashishtha VM. Current status of tuberculosis and acute respiratory infections in India: much more needs to be done!. Indian Pediatrics. 2010 Jan;47(1):88-9.
3. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. Frontiers in pediatrics. 2019 Jun 18;7:246.
4. Krishna MT, Mahesh PA, Vedanthan PK, Mehta V, Moitra S, Christopher DJ. The burden of allergic diseases in the Indian subcontinent: barriers and challenges. The Lancet Global Health. 2020 Apr 1;8(4):e478-9.
5. Rau JL. The inhalation of drugs: advantages and problems. Respiratory care. 2005 Mar 1;50(3):367-82.
6. DiBlasi RM. Clinical controversies in aerosol therapy for infants and children. Respiratory Care. 2015 Jun 1;60(6):894-916.
7. Dhanani J, Fraser JF, Chan HK, Rello J, Cohen J, Roberts JA. Fundamentals of aerosol therapy in critical care. Critical Care. 2016 Dec;20(1):1-6.
8. Gardenhire DS, Burnett D, Strickland S, Myers TR. Aerosol delivery devices for respiratory therapists. American Association for Respiratory Care: Irving, TX, USA. 2017;61.
9. Hess DR. Aerosol delivery devices in the treatment of asthma. Respiratory care. 2008 Jun 1;53(6):699-725.
10. Goralski JL, Davis SD. Breathing easier: Addressing the challenges of aerosolizing medications to infants and preschoolers. Respiratory Medicine. 2014 Aug 1;108(8):1069-74.
11. Alharbi AS, Yousef AA, Alharbi SA, Al-Shamrani A, Alqwaiee MM, Almeziny M, Said YS, Alshehri SA, Alotaibi FN, Mosalli R, Alawam KA. Application of aerosol therapy in respiratory diseases in children: A Saudi expert consensus. Annals of Thoracic Medicine. 2021 Apr;16(2):188.
12. Puckett Jr WH. The pharmacist and inhalation therapy. American Journal of Health-System Pharmacy. 1972 Jul 1;29(7):556-63.
13. Petite SE, Hess MW, Wachtel H. The role of the pharmacist in inhaler selection and education in chronic obstructive pulmonary disease. Journal of Pharmacy Technology. 2021 Apr;37(2):95-106.
14. Awasthi S, Glick HA, Fletcher RH. Effect of cooking fuels on respiratory diseases in preschool children in Lucknow, India. The American journal of tropical medicine and hygiene. 1996 Jul;55(1):48-51.
15. Hsieh CW, Chen C, Su HC, Chen KH. Exploring the efficacy of using hypertonic saline for nebulizing treatment in children with bronchiolitis: a meta-analysis of randomized controlled trials. BMC Pediatrics. 2020 Dec;20(1):1-5.
16. Axelsson I, Sollander S. Is inhalation of hypertonic saline for bronchiolitis effective in infants and toddlers?. Lakartidningen. 2019 Oct 22;116:FPFF-.
17. Zhang L, Sanguebsche LS. The safety of nebulization with 3 to 5 ml of adrenaline (1: 1000) in children: an evidence-based review. Jornal de pediatria. 2005;81:193-7.
18. Qureshi F, Pestian J, Davis P, Zaritsky A. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. New England Journal of Medicine. 1998 Oct 8;339(15):1030-5.
19. Delgado A, Chou KJ, Silver EJ, Crain EF. Nebulizers vs metered-dose inhalers with spacers for bronchodilator therapy to treat wheezing in children aged 2 to 24 months in a pediatric emergency department. Archives of pediatrics & adolescent medicine. 2003 Jan 1;157(1):76-80.