Original Research Paper

Volume-9 | Issue-8 | August - 2019 | PRINT ISSN No. 2249 - 555X

Paediatrics

STUDY ON COMPARISON OF NEBULIZATION WITH SALBUTAMOL ALONE WITH COMBINATION OF SALBUTAMOL AND IPRATROPIUM BROMIDE IN THE TREATMENT OF ACUTE EXACERBATION OF BRONCHIAL ASTHMA

Dr. Boddupalli Ramakrishna — Professor, Department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh 534005, India

Dr. Thirupathi Koppala* — Assistant Professor, Department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh 534005, India *Corresponding Author

Dr.G. Snigdha — Postgraduate, Department of Pediatrics, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh 534005, India

ABSTRACT

Introduction: Asthma is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction. This chronic inflammation heightens the airway hyper responsiveness (AHR). Asthma is defined by the history of respiratory symptoms like wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity together with variable expiratory airflow limitation.1

Aims & Objectives: To compare the effectiveness of a combination of inhaled anticholinergics (ipratropium bromide) and beta 2 agonists (salbutamol) compared with beta 2 agonists (salbutamol) alone for the treatment of children with acute exacerbation of asthma.

Methods: This is a randomized comparative study conducted in the Department of pediatrics ASRAM Medical College during the period May 2018 to June2019. Total 66 children between the age group of 1-15 years with eligible diagnostic criteria were included in the study.

Results: The percentage increase in predicted PEFR is better in Group II with a mean of 24.74 compared to Group I with a mean of 13.35. The p value is highly significant 0.001. The mean PAS at the start of the study is 10.5 in Group I and 10.7 in Group II. The mean PAS at the end of the study is 7.19 in Group I and 5.77 in Group II. The p value is 0.001 and is highly significant. The outcome is better in Group II when compared to Group I with a better decrease in PAS and better increase in percentage predicted PEFR.

Conclusion: In the present study it has been proven the repeated doses of Ipratropium bromide combined to Salbutamol is beneficial and it reduces the broncomotor cholinergic tone.

KEYWORDS : Bronchial asthma, Ipratropium bromide, PAS Score, PEFR, Salbutamol.

INTRODUCTION:

Asthma is a chronic inflammatory condition of the lung airways resulting in episodic airflow obstruction. This chronic inflammation heightens the airway hyper responsiveness (AHR). Asthma is defined by the history of respiratory symptoms like wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity together with variable expiratory airflow limitation.[1]

These variations are triggered by factors such as exercise, allergen or irritant exposure change in weather or viral respiratory infections.

The prevalence of asthma is increasing worldwide with an estimate of 1 - 18%. Nearly 14% of the world children experience asthma symptoms. The International study of Asthma and Allergies in Childhood (ISAAC) estimated asthma prevalence in India to be 6.2–6.8% in 6–7 year old and 6.4–6.7% in 13 – 14 year olds with more males affected than females.[2] According to the Centre for Disease Control, Government of Indiathe asthma prevalenceis 3.8 % in children aged 0 – 4 years, 10.1 % in children aged 5 -14 years and 10% in children aged 15 – 19 with more male preponderance.[3]

AIMS AND OBJECTIVES

The aim of this study is to compare the effectiveness of a combination of inhaled anticholinergics (ipratropium bromide) and beta 2 agonists (salbutamol) compared with beta 2 agonists (salbutamol) alone for the treatment of childrenwith acute exacerbation of asthma.

Methods:

This is a randomized control comparative study conducted in the Department of pediatrics ASRAM Medical College during the period May2018 to June2019. Total 66 children between the age group of 1-15 years with eligible diagnostic criteria were included in the study.

Inclusion Criteria

All children with acute exacerbation who were diagnosed as bronchial asthma according to the GINA guidelines 2017 [1]

All children of the age group 1 - 5 years with the following

1. recurrent non productive cough
2. recurrent wheezing
3. shortness of breath occurring with exercise, laughing or crying reduced activity
4. family history of asthma in 1st degree relatives
5. clinical improvement during 3 months of controller treatment and worsening when treatment isstopped

Children 6 – 15 years with the following
History of variable respiratory symptoms
Wheeze shortness of breath, chest tightness and cough

- more than one type of respiratory symptom
- symptoms vary with time and intensity
- symptoms often worse at night or on waking
- Symptoms triggered by exercise, allergens
- symptoms often appear or worsen with viral infections

Exclusion Criteria:

1) Life threateningasthma
2) Persistent localizedwheezing
3) Asthma with complications like pneumothorax,collapse
4) Administration of corticosteroids in the previous 24hours,
5) Presence of severe respiratory failure or pulmonary malfunction, chronic lung disease (bronchopulmonary dysplasia, cysticfibrosis)
6) Contraindications for the use of SABAs or anticholinergic medications.

An informed consent was taken from the parents
All the children who were included into the study were divided into two groups based on simple randomization.

2) confirmed variable expiratory airflow limitation

Group I:

Each child was treated with nebulized salbutamol 0.15 mg/kg/dose (150 ug/kg/dose) of asthalin respirator solution to which contains 2.5mg in 2.5 ml. It was diluted in 0.9% Isotonic saline to a volume of 3ml and nebulized over a period of 10 minutes. The same dose was repeated thrice at an interval of 20 minutes

Group II:

Each child was nebulized with a combination ipatropium bromide and salbutamol sulphate 250 mcg/dose of duolinrespule 0.02 % (contains levosalbutamol 1.25mg and ipratropium bromide 500mcg per 2.5ml) thrice at 20 minutes interval

All the children were assessed as follows

The initial PAS score including Oxygen saturation, respiratory rate, auscultation, retractions and dyspnea were taken for eachchild.

Initial PEFR was measured in each child 5 years and older using Mini Wright Peak flow meter before the start of the study.

Later at the end of 20,40,60,80 and 120 minutes the PAS score and the PEFR was assessed for each child 5 years and older in both the groups.

Children with signs of respiratory failure, PAS score persistently >12 at the end of three nebulization were excluded from the study.

The category of asthma was graded into mild, moderate and severe based on Paediatric Asthma Score[4]
Mild asthma – score of5-7
Moderate asthma – score of 8 –11
Severe asthma – score of > 12

The PEFR response was measured in percentage increase in predicted PEFR.
Predicted PEFR = Observed PEFR/ Actual PEFR ×100

The observed PEFR is the one which is measured and the actual PEFR is calculated based on height.[5]

Statistical analysis:
SPSS version statistical software and Chi Square test and P value of 0.05 is considered as significant.

RESULTS:
In the present study the Pediatric asthma score [4] was evaluated at the end of at 20, 40, 60, 80 and 120 minutes.

At the end of 20 minutes, 40 minutes and 60 minutes a better response was found in Group I compared to Group II. The p value is statistically significant at 20 minutes but not significant at 40 and 60minutes.

At the end of 80 minutes and 120 minutes more number of children shifted to the mild category in Group II compared to Group I. The p value is highly significant.

This may be because of the late onset of action of ipratropium bromide ie 60 - 120 minutes compared to salbutamol.

Table:1. Categorization of asthma based on PAS with nebulization in different times.

PAS at Time (Minutes)	Category of Asthma	Group-I (n=31)	Group-II (n=31)	Total (n=62)	P- value
Initial	Moderate	26(83.9%)	23(74.2%)	49(79.0%)	0.349(NS)
	Severe	5(16.1%)	8(25.8%)	13(21.0%)	
20	Moderate	29(93.5%)	23(74.2%)	52983.9%)	0.038(S)
	Severe	2(6.5%)	8(25.8%)	10(16.1%)	
40	Mild	3(9.7%)	0(0.00%)	3(4.8%)	0.076(NS)
	Moderate	28(90.3%)	31(100.0%)	59(95.2%)	
60	Mild	6(19.4%)	2(6.5%)	8(12.9%)	0.130(NS)
	Moderate	25(80.6%)	29(93.5%)	54(87.1%)	
80	Mild	6(19.4%)	19(61.3%)	25(80.6%)	0.001(S)
	Moderate	25(80.6%)	12(38.7%)	37(59.7%)	
120	Mild	20(64.5%)	26(83.9%)	46(74.2%)	0.082(NS)
	Moderate	11(35.5%)	5(16.1%)	16(25.8%)	

The mean initial PEFR is 102.5 in Group I and 105.8 in Group II. The mean PEFR is increasing gradually in each group with more increase in Group II. This increase in PEFR is maximum at 120 minutes with a p value of 0.01 which is highly significant.

Table:2 Peak Expiratory Flow Rate Comparison At Different Times

		GROUP	MEAN (L/min)	STD. Deviation	P value
Intial PEFR		**Group I**	102.581	35.7741	0.719 (NS)
		Group II	105.806	34.5229	
PEF20min	**AT**	**Group I**	105.48	34.913	0.766 (NS)
		Group II	108.06	33.007	
PEFR 40min	**AT**	**Group I**	111.94	33.607	0.701 (NS)
		Group II	115.48	38.630	
PEFR 60min	**AT**	**Group I**	115.81	34.907	0.113 (NS)
		Group II	131.29	40.722	
PEFR 80min	**AT**	**Group I**	122.26	35.469	0.075 (NS)
		Group II	140.97	45.193	
PEFR 120min	**AT**	**Group I**	124.19	35.569	0.01 (S)
		Group II	150.48	41.580	

The percentage increase in predicted PEFR in Group II with an initial moderate PAS is more than compared to Group I with an initial moderate PAS. The percentage increase in predicted PEFR in Group II severe is more compared than Group I severe and p value is significant(p value0.001).

The mean PAS at the start of the study is 10.5 in Group I and 10.7 in Group II. The mean PAS at the end of the study is 7.19 in Group I and 5.77 in Group II. The p value is 0.001 and is highly significant.

The percentage increase in predicted PEFR is better in Group II with a mean of 24.74 compared to Group I with a mean of 13.35. The p value is highly significant 0.001.

The outcome is better in Group II when compared to Group I with a better decrease in PAS and better increase in percentage predicted

DISCUSSION:
The primary outcome of this study was to assess the efficacy of adding ipratropium to salbutamol by observing the percentage increase in the predicted PEFR and decrease in PAS score.

Table 3: Comparison of the category of asthma based on initial PA Sscore in different studies

		Moderate Asthma In %		Severe Asthma In %	
	Year	Group I	Group Ii	Group I	Group Ii
Qureshi et al[6]	1997	38.4	36.7	61.6	63.3
Watanasomsiri et al[7]	2003	73	74	27	26
Menon et al[8]	2010	62	59	38	41
Present study	2018	83.9	74.2	16.2	25.8

In the present study 83.9% children in Group I and 74.2% children in Group II came under moderate asthma. Under severe asthma category 16.2% in Group I and 25.8% in Group II are present. The difference between the two groups is not statistically significant.

It is comparable to the study done by Qureshi et al[6] where a similar scoring system was used. In that study 38.4% in Group I and 36.7 % in Group II were present in the moderate category and 61.6% in Group I and 63.3% in Group II were present in severe category. That includes more children in severe asthma category than moderate asthma.

The present study includes more children presenting with moderate asthma at the time of admission than severe asthma. It is comparable to the study done by Watanasomsiri et al[7]based on different asthma scoring systems.

while the one done by Menon et al [8] included children of moderate and severe asthma.

The study of Kartiningsih et al[9] included children of the moderate asthma category, The mean initial pediatric asthma score is 10.5 in Group I and 10.7 in GroupII. It is comparable to the study done by Qureshi et al.[6]

The mean PEFR at the time of admission is 102.5 L/min in Group I and 105.8 in Group II with no statistical difference between the two groups. In the study done by Chakraborti et al[10] the mean initial PEFR is 158.3 L/min in Group I and 155.6 L/min in GroupII. In this study mainly included children with mild to moderate asthma, while in our study most children belonged to moderate and severe category.

Comparison of PAS score at various times of nebulization:

In the present study the Pediatric asthma score [4] was evaluated at the end of at 20, 40, 60, 80 and 120 minutes.

At the end of 20 minutes, 40 minutes and 60 minutes a better response was found in Group I compared to Group II. The p value is statistically significant at 20 minutes but not significant at 40 and 60minutes.

At the end of 80 minutes and 120 minutes more number of children shifted to the mild category in Group II compared to Group I. The p value is highly significant.

This may be because of the late onset of action of ipratropium bromide ie 60 -120 minutes compared to salbutamol.

The study conducted by Qureshi et al [6] showed a better decrease in asthma in children treated with combination of ipratropium and salbutamol compared to salbutamol alone.

Chakraborti et al[10] conducted a similar study where there was a greater improvement in clinical asthma score in experimental group than the control group, though it was not statistically significant.

In the study done by Watanasomsiri et al [7] there was no statistical significance in the asthma score between the two groups.

Kartininingsih et al [9] observed that the combination group showed a better decrease in the clinical score than the control group. However statistical significance was observed at 20 minutes and 100 minutes.

Harumdini et al [11] also showed a similar observation of a decrease in clinical asthma score at 40, 60 and 120minutes.

Menon et al [8] also observed a better improvement of score in the experimental group compared to the control group at the end of the study.

Comparison of The Improvement Of The PEFR At The End Of The Study:

In the present study the mean PEFR shows a better increase in Group II when compared to Group I. This increase in PEFR is maximal at 120 minutes and p value is highly significant.

Qureshi et al [6] reported that increase in the predicted PEFR was greater in experimental group when compared to the control group.

Reisman et al[12] showed that peak response with an increase in FEV1 was noted at 60 minutes in the ipratropium group. There was further increase in the bronchodilator response upto the end of study in the experimental group compared to control.

Chakraborti et al [10]also observed similar result with a significant improvement in FEV1 and percent predicted PEFR in combination group than with salbutamol alone.

Watanasomsiri et al [7] showed that the percent predicted PEFR was a higher in the ipratropium group.

Harumdini et al [11] observed a higher PEFR percentage increase from the baseline at 20 – 120 minutes in the experimental group than in the control group.

Comparison of the % Increase in predicted PEFR in different studies

		% Increase in predicted PEFR	
	YEAR	GROUP I	GROUP II
Qureshi et al[6]	1997	31	32
Chakraborti et al[10]	2006	12.2	17.9
Iramain et al[13]	2008	8.9	29.5
Present study	2018	13.3	24.7

In the present study the % increase in the predicted PEFR was compared between the two groups and it was found to better in Group II with p value is highly significant.

A percentage increase in the predicted PEFR > 20 % was considered as a good response. The combination group showed an increase of 24.7% while the salbutamol group showed an increase of 13.3%.

It is comparable to the study done by Chakraborti et al [10] who reported that there was a significant improvement in the experimental group compared to the control.

Qureshi et al [71] did not find any significant change in the predicted PEFR between the control and experimental groups.

This may be because the PEFR measured could be performed in only 40% and the asthma score was used primarily to assess theoutcome.

Iramain et al[13] observed a greater improvement in the % predicted PEFR in the ipratropium and salbutamol group compared to the only salbutamol group.

CONCLUSION:

- The role of anticholinergics in the management of acute exacerbation of asthma in children have shown varying results.
- In the present study it has been proven the repeated doses of ipratropium bromide combined to salbutamol is beneficial and it reduces the broncomotor cholinergictone.
- It has been proven that the addition of ipratropium to salbutamol shows a better outcome in asthmatic exacerbations when compared to salbutamol alone.

REFERENCES

1. Global Initiative for Asthma. Global Strategy for Asthma Managementand Prevention, 2017. Available from:www.ginasthma.org/ Accessed on13August2018
2. K R Bharat Kumar Reddy, Samantha Sonappa,Preschool Wheeze and Bronchial Asthma, PG textbook of Pediatrics, Vol 2, secondedition;2022
3. Centre for Disease Control and Prevention, National Current Asthma Prevalence, May 2018.Available fromwww.cdc.govt/asthma/national current asthma prevalence 2016
4. Maue DK, Krupp N, Rowan CM. Pediatric asthma severity score is associated with critical care interventions. World J Clin Pediatr 2017; 6(1): 34-39
5. Lung function by J.E.Cotes (3rd edition). For EU scale Mini Wright peak flowmeter.
6. Qureshi F, Pestian J, Davis P, Zaritsky A. Effect of nebulisedipatropium on the hospitalization rates of children with asthma.NEngl J Med 1998 ; 338; 1030-5
7. Watanasomsiri A, PhipatanakulW. Comparison of nebulized ipratropium bromide with salbutamol vs salbutamol alone in acute asthma exacerbation in children.Annals of Allergy, Asthma, & Immunology 2006;96(5):701–6.
8. Memon, Bilquis Naeem et al. "Response to nebulized salbutamol versus combination with ipratropium bromide in children with acute severe asthma." JPMA. The Journal of the Pakistan Medical Association 66 3 (2016):243-6.
9. Kartininingish L, Setiawati L, MS M. Comparison of clinical efficacy and safety between salbutamol -ipratropium bromide nebulization and salbutamol alone in children with asthmatic attack. PaediatricaIndonesiana 2006; 46: 241-5.
10. Chakraborti A, Lodha R, Pandey RM, Kabra SK. Randomized controlled trial of ipratropium bromide and salbutamol versus salbutamol alone in children with acuteexacerbation of asthma. Indian Journal of Pediatrics. 2006;73(11):979–83
11. Harumdini M, Supriyatno B, Sekartini R. Efficacy of salbutamol-ipratropium bromide nebulization compared to salbutamol alone in children with mildto moderate asthma attacks. PaediatricaIndonesiana. 2012 Aug 31;52(4):200-8
12. Reisman J, Galdes-Sebalt M, Kazim F, Canny G, Levison H. Frequent administration by inhalation of salbutamol and ipratropium bromide in the initial management of severe acute asthma in children. J Allergy Clin Immunol1988;81:16-20.
13. Ricardo Iramain, Jesús López-Herce, Julia Coronel, Cristopher Spitters, Jaime Guggiari& Norma Bogado(2011) Inhaled Salbutamol Plus Ipratropium in Moderate and Severe Asthma Crises in Children, Journal of Asthma, 48:3,298-303,