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Safety of Bronchodilators and Corticosteroids in Hyper Reactive Air Way Disease in Children Aged 1–12 Years: A Prospective Observational Study

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Abstract: ***Background: Bronchial asthma is a common, chronic inflammatory lung disease which attacks all age groups but often starts in childhood. Patients with moderate to severe asthma have to take long-term anti-inflammatory medications like inhaled corticosteroids daily to control the underlying inflammation and to prevent symptoms and attacks. If symptoms occur, short-term medications like short-acting beta2 agonists are used to relieve them. Materials & Methods: A non-experimental prospective observational study for a period of 6 months was conducted in a tertiary care teaching hospital with 147 patients from pediatrics ward. The parents of the patient were interviewed for the ADRs (Adverse Drug Reaction) and efficacy of treatment was measured using PEFR with help of breathometer. Results: Efficacy of both monotherapy (42.1%) and combination therapy (57.82%) was measured using PEFR (Peak Expiratory Flow Rate) and the success rate of monotherapy and combination therapy with PEFR was 66% and 83% respectively. Safety profile of both bronchodilators (salbutamol) and inhaled corticosteroids (budesonide) were observed and some ADRs with monotherapy and combination therapy were observed and reported. Conclusion: From this study it was found that both efficacy and safety profile is more with combination therapy (bronchodilators+corticosteroids) than with monotherapy.***

Keywords: Bronchial asthma, Bronchodilators, Corticosteroids, PEFR, Breathometer.

1. Introduction

Asthma , a chronic inflammatory airways disease is a complex condition where interaction of genetics and environment play a role and is characterized by variable and recurrent attacks of breathlessness, wheezing, chest tightness, and cough, particularly at night and/or in the early morning due to airflow obstruction, bronchial hyper-reactivity to aerobiologicals and irritants. In an attack, the lining of the passages swell causing the airways to narrow and reducing the flow of air in and out of the lungs [1]. Asthma is classified based on symptoms severity and lung function tests like PEF (Peak Expiratory Flow) and FEV1 (Forced Expiratory Volume in 1st second) as intermittent, mild, moderate and severe asthma [3]. The fundamental causes of asthma are not completely understood. The strongest risk factors for developing asthma are a combination of genetic predisposition with environmental exposure to inhaled substances and particles that may provoke allergic reactions or irritate the airways [3]. The pathophysiology of asthma is complex with participation of several interacting inflammatory cells, which result in acute and chronic inflammatory effects on the airway [7]. In the treatment of asthma we use stepwise approach according to the severity of asthma and ability to control symptoms [4]. Patients with moderate to severe asthma have to take long-term anti-inflammatory medications daily i.e. inhaled corticosteroids to control the underlying inflammation and airway remodeling in uncontrolled asthma and to prevent symptoms and attacks. If symptoms occur, short-term medications like inhaled short-acting beta2-agonists are used to relieve them. In this study we are emphasizing the safety and efficacy of bronchodilators and corticosteroids in the pediatric patients having asthma. The monotherapy with LABA (Long Acting Beta2 Agonist) may be associated with severe adverse events and asthma-related deaths, while monotherapy with ICS (Inhaled Corticosteroids) may be associated with a higher risk of growth suppression. On the other hand, the concurrent use of a LABA with an ICS has been associated with positive outcomes including symptom reduction and reduced rate and severity of exacerbations [13].

2. Literature Survey

- Ying Xia, Christina ML Kelton, Patricia R. Wigle et al; 2013 conducted a study on Safety of LABA and ICS in Children and Adolescents with Asthma and concluded that the concurrent use of a LABA with an ICS has been associated with positive outcomes including symptom reduction and reduced rate and severity of exacerbations while LABA monotherapy may be associated with SAEs and asthma-related death, while ICS monotherapy may be associated with a higher risk of growth suppression [12].
- Wim M. C. van Aalderen and Aline B. Sprikkelman, 2011; conducted a prospective observational study and They concluded that ICS are generally well tolerated in both school-aged and preschool children, and adverse events tend to be minimal in both age groups when the ICS is used in appropriate doses [16].

3. Materials and Methods

Type of study: A Non-experimental prospective observational study has been carried out to know the role of beta 2 agonists and corticosteroids and safety profile in asthmatic patients.

The study was conducted in a tertiary care teaching hospital, Government General Hospital, Guntur with 147 patients from pediatrics ward, from 01-04-2014 to 31-08-2014. The study method involves inpatients and outpatients who were selected based on inclusion and exclusion criteria and an informed consent was taken. The management of patient illness, his/ her improvement and present medical history were also recorded. The parents of the patient were interviewed for the ADR. Patient information was collected

through a data collection form from the case sheets and the data was tabulated, analyzed using suitable statistical tools.

Inclusion Criteria

- Children aged from 1 – 12 years are included in the study
- Patients of both sexes who were diagnosed to have bronchial asthma were included.
- Patients and their care givers, willing to participate in the study were included.

Exclusion Criteria

- Children <1 year and >12 years of age were excluded from the study.
- Patients diagnosed to have bronchial asthma with co-morbid conditions were not included in the study.
- Patients with congenital anomalies any systemic or physiological or pathological diseases/disorders other than bronchial asthma were excluded.

4. Observations and Results

Out of 147 cases 58(39.4%) were 1-4yrs and 89(60.6%) were 5-12yrs age distribution.

Table 1: Age Wise Distribution

Age	No. of Cases(N=147)	Percentage%
1-4yrs	58	39.4
5-12yrs	89	60.6

From this it is evident that prevalence of bronchial asthma was more in children aged 5-12yrs.

Table 2: Age Wise Sex Distribution

Age	Male(n=86)	Female(n=61)
1-4yrs	32	26
5-12yrs	54	35

Out of 147 patients 86(58.5%) were male and 61(41.49%) were female.

Table 3: Distribution Based on Family History

Category	Age	
	1-4yrs	5-12yrs
Positive Family History	43	71
No Family History	15	18

From the above table it is evident that prevalence of asthma is more with positive family history.

Table 4: Drug Prescribing Pattern in Asthmatic Patients

Namr of the Drug	*No.of Patients Used*
Salbutamol	117
Terbutaline	5
Adrenaline	2
Salmeterol	32
Amoxicillin	106
Paracetamol	94
Budesonide	73
Cetirizine	63
Chlorpheneramine maleate	41
Ipratropium + Salbutamol	38
Montelukast	22
Salmeterol + budesonide	14
Salmeterol + fluticasone	18

From the above table most commonly prescribed drugs were salbutamol, amoxicillin, paracetemol followed by budesonide.

Table 5: Therapeutic Outcome by PEFR in 5-12yrs

CATEGORY	PEFR	
	Monotherapy (n=36)	Combination therapy (n=53)
Treatment was effective	28	44
Treatment was not effective	8	9

Out of 36 cases of Monotherapy, 25 cases were Salbutamol and 11 cases were Budesonide

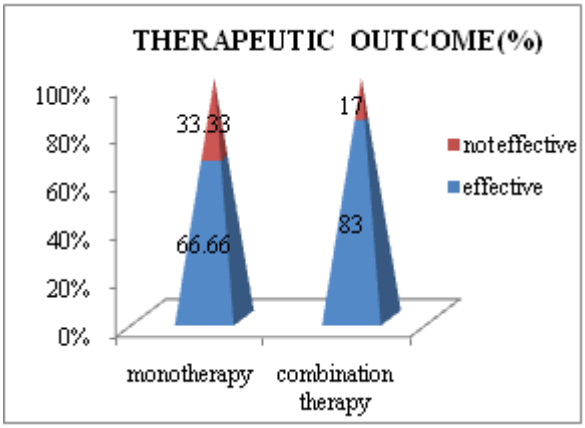

Figure 1: Measuring Treatment Outcome by PEFR

Therapeutic outcome was found to be more effective with combination therapy.

Table 6: Adverse Effects Observed With Salbutamol, Budesonide & Combination Therapy

Drug	*Adverese Drug*	*No. of Cases*
Monotherapy		
Salbutamol	Nausea	4
	Insomnia	2
	Headache	3
Budesonide	Oral candidiasis	6
	Pharyngitis	3
	Weight gain	5
Salmeterol	Sleep disturbances	4
	Tachycardia	8
	Tremor	6
Combination Therapy		
Budesonide with Salbutamol	Nausea	5
	Weight gain	3
Salmeterol with	Tachycardia	7
	Oral candidiasis	8
Salmeterol with	Pharyngitis	4
	Headache	6

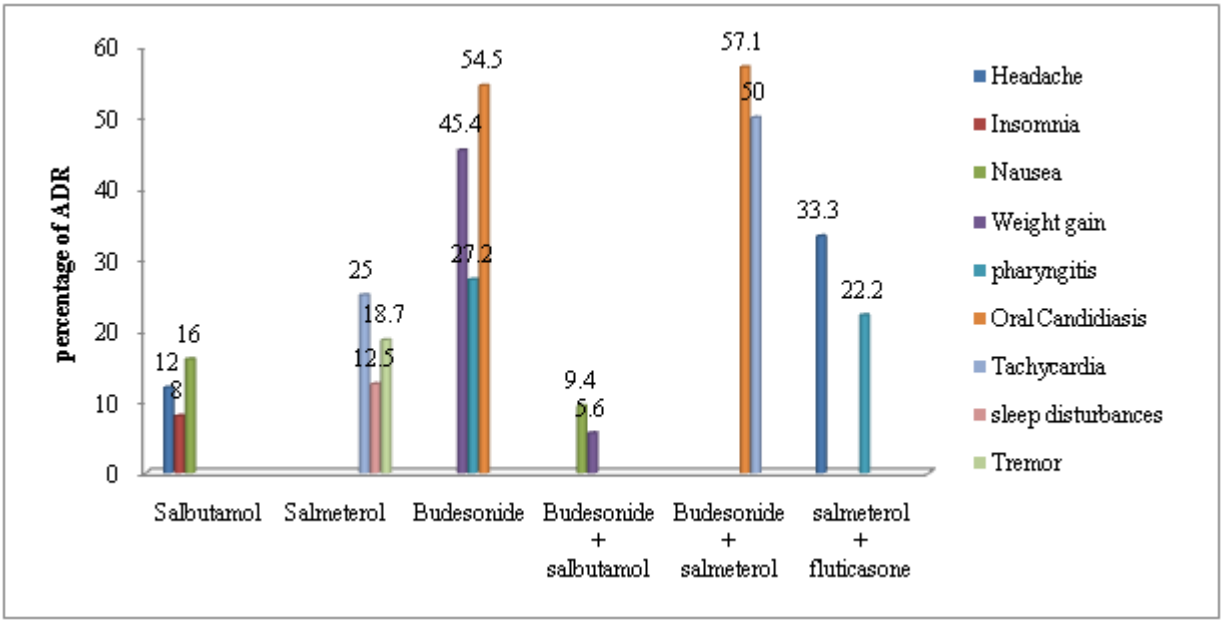

Figure 2: Incidence of ADRS

5. Discussion

A total of 147 patients were recruited in the study based on inclusion and exclusion criteria and they were classified according to their age as in table 1 as 1-4yrs (58) and 5-12yrs (89). The prevalence of asthma was much observed in the age group of 5-12yrs. In 1-4yrs of age male were 32 and females 26 and in age 5-12yrs males were 54 and females 35. Males tend to be more prone than females in childhood. Many of the patients were associated with shortness of breath and wheeze during the attack and exacerbated mostly during night. Family history of the patients supported the occurrence of bronchial asthmas in table 3. 43, 71 cases among the age group of 1-4yrs and 5-12yrs respectively were observed with a positive family history. Triggering factors has also played a vital role in occurrence of attacks i.e. winter season, food, allergens.

Ying Xia and Christina ML Kelton [12] stated that Safety of Long-Acting Beta Agonists and Inhaled Corticosteroids in Children and Adolescents with Asthma and concluded that the concurrent use of a Long acting beta 2 agonist with an Inhaled corticosteroid has been associated with positive outcomes including symptom reduction and reduced rate and severity of exacerbations while Long acting beta 2 agonist monotherapy may be associated with Serious adverse drug events and asthma-related death, while Inhaled corticosteroid monotherapy may be associated with a higher risk of growth suppression. As in our study we state that use of combination is a better choice than monotherapy.

The prescribing pattern followed in government general hospital, Guntur for asthmatic patients is salbutamol (79.5%), amoxicillin (72.1%), paracetemol (63.94%) followed by budesonide (49.65%) as stated in table 4. Comparing the monotherapy and combination therapy; combination is much advisable as the patients responded well when compared to monotherapy. It was measured using PEFR, more than 30% increase in the value of PEFR compared to initial value i.e before inhalation considered as effective outcome; value of both the therapies before and after administration as stated table 5. 42.1% were prescribed with monotherapy and 57.82% were prescribed with combination therapy. The success rate of monotherapy and combination therapy with PEFR was 66% and 83% respectively as stated in figure 1.

Safety profile of both bronchodilators (salbutamol) and inhaled corticosteroids (budesonide) were observed and documented. From table 6 following ADRs were observed Nausea (n=4), insomnia (n=2), headache (n=3) was drawn out when salbutamol was used; oral candidiasis (n=6), phyryngitis (n=3), weight gain (n=5) were observed with budesonide and with salmeterol sleep disturbances (n=4), tachycardia(n=8), tremors(n=6)were observed. combination therapy with budesonide with salbutamol resulted in nausea (n=5), weight gain (n=3), Salmeterol with Budesonide resulted in tachycardia(n=7), oral candidiasis(n=8) and salmeterol with fluticasone resulted in pharyngitis(n=4), headache(n=8) and their incidence were coded in Figure 2.

Patients were prescribed both with monotherapy and combination therapy. The results established that combination therapy was much of choice than monotherapy as its treatment outcome and safety profiles were higher than monotherapy comparatively

6. Conclusion

Patients were assessed for the outcome of therapy by PEFR (Peak Expiratory Flow Rate) the success rate for combination therapy was more than monotherapy. Safety profile of combination therapy was more when compared to monotherapy i.e combination therapy of salmeterol with budesonide, salmeterol with fluticasone and salbutamol with budesonide resulted in less and non serious side effects and more effective outcomes compared with monotherapy of salmeterol and budesonide alone. LABA monotherapy may

be associated with SAEs and asthma-related death, while ICS monotherapy may be associated with a higher risk of growth suppression and the concurrent use of a LABA with an ICS has been associated with positive outcomes including symptom reduction and reduced rate and severity of exacerbations.

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