A Prospective Study to Assess the Efficacy and Risk Associated With the Use of Bronchodilators in Pediatric Patients with Bronchiolitis – A Pilot Study

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ABSTRACT

Bronchiolitis is a common lung infection in young children and infants. It causes inflammation and congestion in the small airways (bronchioles) of the lung. Bronchiolitis is almost caused by a virus. Bronchodilators are medication which makes breathing easier by relaxing the muscles in the lungs and widening airways. To assess the efficacy and risk associated with the use of bronchodilators in pediatric patients with bronchiolitis. To assess the Efficacy of Bronchodilators, to evaluate the risk associated with bronchodilators in bronchiolitis patients and to evaluate the patient compliance in patients using bronchodilator for bronchiolitis. This study was conducted in 10 bronchiolitic pediatric patients. This study was conducted by categorizing the patients according to their Respiratory Rate, SpO2 and Heart Rate values. Patient compliance is analyzed using CRS scale and risk is assessed with Wang Scale.

Keywords: Bronchiolitis, Bronchodilators, Levosalbutamol

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INTRODUCTION

Respiratory Tract Infections
According to National Health Service (NHS) 2018 Respiratory tract infections are referred as respiratory illnesses that refer to a variety of infections of the sinuses, throat, airway or lungs. Respiratory infections are extremely prevalent, that contributes to 20.5% of mortality in children under the age of 5 in developing countries according to WHO (in 2015).[14]

Types
Respiratory Tract Infections are categorized into 2, depending on the area of respiratory tract that they affected
1. Upper Respiratory Tract Infections(URTI)
2. Lower Respiratory Tract Infections(LRTI)
According to NHS LRTI are comparatively long lasting and more serious
Respiratory Tract Infections are associated with numerous pathogens that includes viruses, bacteria and fungi.[15]

Bronchiolitis
Bronchiolitis is an inflammation of the bronchioles caused most commonly by the viruses, the most common among this is Respiratory Syncytial Virus. Human Para influenza virus type 3, some adenovirus, and others also can be responsible. Bronchiolitis is a disease that is restricted to children less than 12 years of age because this is the age at which most of the airway’s resistance is in the bronchiole. Clinically it manifests by onset of an upper respiratory infection, i.e fever and coryza. And then progresses to cough, wheezing, and signs of respiratory distress i.e, the increased respiratory rate, chest wall in drawing, thoracic- abdominal asynchrony. The child may require hospitalization because of risk for respiratory failure or need for hydration. Bronchodilator (which relaxes bronchial muscles) are the drugs causes widening of bronchi for example any of those taken by inhalation for the alleviation of Bronchiolitis.[11]

Salient Features
- Cold for 2-4 days associated with cough, wheezing and rapid breathing. There may be lower chest retraction, feeding difficulties, excessive crying due to hypoxemia, cyanosis, and respiratory failure with increasingly severe disease.
- Diagnosis is made by clinical analysis based on typical medical history and test results.
- Mild disease is characterized by breathing, no chest contraction, no feeding problems, no clinical evidence of hypoxemia, lethargy, seizures, oxygen saturation<92%.
- The finding shows that there may be a normal or minimal increase in the total number of
white blood cells with related lymphocytosis.

- Chest X-ray shows hyperinflation and small atelectasis.[1]

**Types**
- Viral bronchiolitis: Seen in infants mostly up to age 1 year. Mainly due to RSV.
- Bronchiolitis obliterans: is rare and dangerous seen in adults. This disease is scarring of bronchioles. It block air passage by airway obstruction.[6]

**CAUSES**

**Viral bronchiolitis:**
It causes by the virus get enter to respiratory tract, which causes viral bronchiolitis. Viruses mostly causing bronchiolitis are RSV, Adeno virus, Influenza virus.

Bronchiolitic obliterans: It is a rare condition. Fumes from ammonia, bleach, and chlorine, respiratory infection, adverse reaction to medications are the main causes of this condition.[2]

**Symptoms**
- Shortness of breath
- Wheezing
- Coughing
- Chest discomfort
- Nasal congestion
- Runny nose
- Insomnia
- Tachypnea

**Diagnosis**
- X-ray
- Spirometry
- Arterial blood gas test
- Check SpO2, Respiratory Rate, Heart Rate
- From Sample of mucus or nasal discharge

**Risk Factors**
High risk to patients with chronic lung disease, prematurity, Congenital heart disease, especially in patients with pulmonary hypertension or congestive heart failure, low weight, and neuromuscular disorders.[7]

Gender also plays a crucial role. Boys appears to have a higher risk of serious illness than girls.

Environmental risk factors include crowds, cigarette smoking, tobacco exposure; multiple contact
has been shown to affect the incidence and severity of bronchiolitis. Children exposed to tobacco smoke can even take them to intensive care.[3]

MANAGEMENT

Non pharmacological

- Drops of normal saline for associated nasal blockage in both nostrils when needed, especially before meals and the use of home remedies (ginger, honey, tulsi) to control cough and oral fluid intake.
- For hospitalized patients, 30-40 degree elevation and slightly extended neck.
- Be breast feded in a comfortable environment.[8]

Pharmacological

- No Antibiotics for the treatment of minor illnesses (Home outpatient treatment)
- Bronchodilators, corticosteroids, Antibiotics is mostly used in therapy.
- Cannot feed severe respiratory distress ± apnea episodes ± hypoxemic oxygen saturation
- Return the treatment to intensive care
- Oxygen to keep the SpO2 above92%
- Intravenous fluids
- Assess the need for respiratory support in the ICU.[4]

BRONCHODILATORS

Bronchodilators are medication which makes breathing easier by relaxing the muscles in the lungs and widening airways. Bronchodilators are divided into short- and long-acting groups. Short-acting bronchodilators used to relief of broncho constriction, and long-acting bronchodilators used for prevention. Short-acting bronchodilators include: Salbutamol /albuterol, Levosalbutamol / levalbuterol, pirbuterol, Epinephrine, Racemic Epinephrin, Ephedrine, Terbutaline. Long-acting bronchodilators includes: Salmeterol,Clenbuterol, Formoterol , Bambuterol.[5]

MECHANISM OF ACTION

Long-acting Bronchodilators:

Relax the muscles around your airways to help keep your airways open. Its effects last at least twelve hours.[9]

Short acting Bronchodilators:

It produces the quick relaxation on the muscle that tightens around the airways and makes the airways wider and breathing easier. It help to clear mucus from the lungs. As the airways open, the mucus can move more freely and can be coughed out more easily. It last 3 to 6 hours.

Beta-adrenergic bronchodilators:
This dilates the bronchial airways by relaxing the muscles in the airways. It is also known as beta-2 agonists. It stimulates the beta-2 receptors on the smooth muscle cells which line the airways, causing these muscle cells to relax, thus, opening airways.\textsuperscript{[10]}

**Anticholinergic bronchodilators:**

It blocks the effect of acetylcholine on airways and nasal passages. Acetylcholine is a chemical that nerves use to communicate with muscle cells. The "anticholinergic" effect of the anticholinergic bronchodilators blocks effects of cholinergic nerves, causing the muscles to relax and airways to dilate.\textsuperscript{[11]}

**Xanthine derivatives:**

It opens the airways by relaxing the smooth muscles in the walls of the airways and conjointly suppresses the response of the airways to stimuli. Xanthine dilates bronchi by interfere the action of phosphor di-esterase.\textsuperscript{[12]}

**Adverse Effects**

- Tremor
- Pupillary dilatation
- Blurred vision
- Acute glaucoma
- Gastro intestinal symptoms
- Palpitations
- Arrhythmias
- Myocardial infarction.
- Seizure

**Side Effects**

- Headaches
- Palpitations
- Muscle cramps
- Trembling in hands
- Dry mouth
- Constipation
- Cough
Contraindication
If a patient has a known hypersensitivity to the drug, then physicians should not prescribe bronchodilator. Caution is needed in case of patients on treatment with ischemic heart disease, arrhythmias, or hypokalemia, as bronchodilators may worsen the effects of these conditions.[13]

Toxicity
- Difficulty breathing
- fever/chills
- Decrease urine output
- Nausea
- Vomiting
- Tremors

MATERIALS AND METHOD

Study design:
Prospective Observational study

Data source: All the relevant information and data regarding the study was collected from case records and direct interview from patient’s parents and care givers. Data collected by using suitably designed proforma. This study was approved by the Research and Ethical Committee of Cosmopolitan Hospital, Trivandrum

Study population: Patients were selected from Pediatric Department of Cosmopolitan hospital, informed consents were obtained. This study was conducted for a period of 2 months.

Assessment of Efficacy: Details were collected from the records of bronchiolitis patients and recorded the values of SpO2, Heart Rate and Respiratory Rate by using pulse oximetry.

Assessment of Risk: Details were collected from the records of bronchiolitis patients and assessed with Wang scale.

Assessment of Patient Compliance: Patient compliance was assessed using a validated questionnaire by direct interview with the patient’s care givers.

Statistical analysis:
Statistical analysis done by and entered using SPSS software according to the nature of the data.

OBSERVATION AND RESULT
The proposed study entitled, “TO ASSESS THE EFFICACY ASSOCIATED WITH THE USE OF BRONCHODILATORS IN PEDIATRIC PATIENTS WITH BRONCHIOLITIS”

Was a prospective observational study carried out in a multispecialty tertiary care hospital. In our study we analyzed the data collected from 10 patients diagnosed with bronchiolitis.
Among the 10 patients selected, all of them are taking bronchodilator. This study aimed to assess the efficacy of the bronchodilators by comparing the before and after treatment in accordance with the Respiratory Rate, Heart Rate And SpO2. Risk assessed by Wang Score Method. Patient compliance analyzed by CRS scale and with the questionnaire.

RESULTS AND DISCUSSION

DEMOGRAPHIC DETAILS OF PATIENT

In this section, the data related to demographic details of patients were collected and recorded.

Percentage Distribution of Patients Based On Gender

The percentage distribution of patients based on gender is shown in the table.

| Gender | Frequency | Percentage |
|--------|-----------|------------|
| Male   | 5         | 50         |
| Female | 5         | 50         |
| Total  | 10        | 100        |

Figure 1: Diagrammatic representation of patients based on gender

From the Table 1, It was observed that out of the total patients with bronchiolitis, 50% were males and 50% were females. Thus from the above table we concluded that both the male and female have higher chance of occurrence of bronchiolitis.

Percentage Distribution of Patients Based On Age

The percentage distribution of patients based on age is shown in the following table:

| Age | Frequency | Percent |
|-----|-----------|---------|
| <2  | 5         | 50      |
| 2-3 | 2         | 20      |
| >3  | 3         | 30      |
| Total | 10    | 100     |
Figure 2: Diagrammatic representation of patients based on age

From the Table 2, It was observed that out of the total patients with bronchiolitis, 50% of patients causing disease of age group less than two. 30% of patients with age group greater than 3. 20% of people with age group 2 to 3.

Percentage Distribution of Patients Based On Diet

Table 3: Percentage Distribution of Patients Based On Diet

| Diet          | Frequency | Percent |
|---------------|-----------|---------|
| Non vegetarian| 7         | 70      |
| Vegetarian    | 3         | 30      |
| Total         | 10        | 100     |

Figure 3: Diagrammatic representation of patients based on diet

From the Table 3, observed that out of the total patients, 30% of patients is vegetarian and 70% is non-vegetarian. From this analyzed that non-vegetarian population has high risk of disease.

Percentage Distribution of Patients Based On Symptoms

Table 4: Percentage Distribution of Patients Based On Symptoms

| Symptoms | Frequency | Percent (%) |
|----------|-----------|-------------|
| Wheezing | 8         | 80          |
Coughing   10   100  
Runny nose  4     40    
Tachypnoea  1     10    
Shortness of breath  4     40  
Nasal congestion  3     30    
Chest discomfort  5     50    

**Figure 4: Diagrammatic representation of patients based On symptoms**

From the Table 4, observed that out of the total patients, 80% of patients has wheezing as the symptom. All the patients i.e, 100% people have cough as the major symptom. 40% people has runny nose as symptom, tachypnea is of about 10%. Again 40% of patients feel shortness of breath. 35% with nasal congestion. 50% patient feel chest discomfort. By analyzing all the data we understood that coughing is the most common symptom seen in bronchiolitis patients. Wheezing is also seen common. Chest discomfort, runny nose, shortness of breath and nasal congestion is also seen in patients. Tachypnea is the symptom less commonly seen in patients with bronchiolitis.

**Percentage Distribution of Patients Based On Past Illness**

**Table 5: Diagrammatic representation of patients based on past illness**

| Past illness                  | Frequency Percent |
|-------------------------------|-------------------|
| Tachypnoea                    | 2                 |
| Coughing                      | 8                 |
| Wheezing                      | 5                 |
| Ear infection                 | 2                 |
| other respiratory infection   | 1                 |
| Others                        | 3                 |

| Past illness                  | Frequency Percent |
|-------------------------------|-------------------|
| Tachypnoea                    | 2                 |
| Coughing                      | 8                 |
| Wheezing                      | 5                 |
| Ear infection                 | 2                 |
| other respiratory infection   | 1                 |
| Others                        | 3                 |
Table 5 shows the past illness of the bronchiolitis patient. 80% having cough as the major symptom. 50% has wheezing as severe symptom. Tachypnea, ear infections and other respiratory infections are also seen as past illness in patient. About 30% of people has other symptoms like fever, throat infection, stomach upset, nausea, vomiting. So from this we get a clear idea that coughing is the major presenting symptom and past illness in bronchiolitis.

**PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON SOCIAL HISTORY**

| Social history | Frequency | Percent |
|----------------|-----------|---------|
| Tobacco        | 1         | 10      |
| Smoking        | 0         | 0       |
| Alcohol        | 0         | 0       |

Figure 6: Diagrammatic representation of patients based on social history
From table 6, tobacco exposure, smoking, alcohol exposure are the mostly occurring social history of patient. Here we have a group of pediatric patient so chance of smoking and alcohol intake is low. And even by mistake it causes. Tobacco exposure is about 10%. special care is always given to pediatric population so mostly chance exposure to tobacco is less. And even it causes it may little bit affect baby’s condition.

**Percentage Distribution of Patients Based On Allergic History**

Table 7: Percentage Distribution of Patients Based on Allergic History Table 7, it shows dust allergy may causes bronchiolitis up to 10%.

| Allergic History | Frequency | Percent |
|------------------|-----------|---------|
| Drug allergy     | 0         | 0       |
| Dust allergy     | 1         | 10      |

**Percentage Distribution of Patients Based On Family history**

Table 8: Percentage of Distribution Based On Family History

| Family History | Frequency | Percent |
|---------------|-----------|---------|
| Father        | 1         | 10      |
| Mother        | 1         | 10      |
| Siblings      | 1         | 10      |

Figure 8: Diagrammatic representation of patients based On family history

Table 8: 10% chance for bronchiolitis if have any of the family history.

| Contact with multiple children | Frequency | Percent |
|-------------------------------|-----------|---------|
| Yes                           | 9         | 90      |
| No                            | 1         | 10      |
| Total                         | 10        | 100     |
Figure 8: Diagrammatic representation of patients has contact with multiple children

From table, it shows that 90% children has contact with multiple children their by chance of getting infection in high.

Assess Efficacy of Bronchodilator by Monitoring SpO₂

Table 9: SpO₂ before and after treatment

|       | N   | SpO₂ | Mean | Sd  | T     | P     |
|-------|-----|------|------|-----|-------|-------|
| BT    | 10  | 93.1 | 2.183| 4.839| 0.001 |
| AT    | 10  | 97.5 | 0.972| 0.011|       |

Table 9: From this table we can assess the patient spo2 level as before and after treatment. Abnormal spo2 level can be seen before treatment. But after taking bronchodilator therapy patient feels better and spo2 level is also become normal.so we get a conclusion that the bronchodilators is efficous in treatment of bronchiolitis.

Figure 9: Diagrammatic Representation of Patients SpO₂ Levels Before and After Treatment.
Assess Efficacy of Bronchodilator by Monitoring Heart rate

Figure 10: Diagrammatic representation of patient’s heart rate level in before and after treatment.

Table 10: Heart rate before and after treatment

|       | HR | Unpaired t test |
|-------|----|-----------------|
| Mean  | Sd  | T               | P    |
| BT    | 10116.4 | 30.9632.361     | 2.361| 0.043 |
| AT    | 1098.2  | 20.687          |      |      |

Table 11: From table 11 we are assessing the heart rate level of children as before and after treatment. The normal heart rate is 100-160 in pediatrics. In survey, before the treatment heart rate was about 116.4% .and after treatment it is reduced up to 98.2%.So from this we analyzed that heart rate can be maintained by the effective therapy of bronchodilator.so efficacy of bronchodilator can be clearly seen from the table

Assess Efficacy of Bronchodilator by Monitoring Respiratory Rate

Table 11: Respiratory rate before and after treatment

|       | RR | Unpaired t test |
|-------|----|-----------------|
| Mean  | Sd  | t               | P    |
| BT    | 1038.2 | 17.3131.136     | 0.285|      |
| AT    | 1032.8  | 4.442           |      |      |

Figure 11: Diagrammatic representation of patients respiratory rate level in before and after treatment.
Table 11: From table 11 we assess the respiratory rate. Before the treatment it was abnormal and after treatment with bronchodilator it becomes normal. So from this table we can understand that bronchodilators are efficacious in its treatment.

Assessing Patient Compliance

Table 12: Patient Compliance Based On CRS

| CRS   | Frequency | Percent |
|-------|-----------|---------|
| Poor  | 1         | 10      |
| Average | 1       | 10      |
| Good  | 8         | 80      |
| Total | 10        | 100     |

Figure 12: Diagrammatic representation of patient compliance based on CRS scale

Table 13.A: Patient compliance by questionnaire method

| Compliance | Frequency | Percent |
|------------|-----------|---------|
| Good       | 7         | 70      |
| Moderate   | 3         | 30      |
| Total      | 10        | 100     |

Figure 12 A: Representation of Patient Compliance Assessed By Questionnaire Method

Table 12: It is to assess the patient compliance in accordance with CRS scale. 80% people response towards the therapy is good, they were taking care of their child. Some people response was little bit low towards the therapy.

Table 12.A: patient compliance is assessed by questionnaire. 60% of the people response towards
therapy was really good and 40% have moderate. Over all the from analyzing table 10&table 10.A We reached to an assessment that bronchodilators have good effect in the treatment of the bronchiolitis and patients has high compliance towards the therapy.so it is better for further treatments.

Figure 13 Representation of effectiveness of Bronchodilators
Figure 13 represents the effect of different bronchodilators on bronchiolitis in the pediatric population. Among them Salbutamol is the most effective when compared with the other medications prescribed.
Figure 14: Risks associated in Bronchiolitis

Figure 14 represents the risk involved in bronchiolitis. When analyzed the patients who are exposed to crowded places has an increased risk of infection (90%), followed by contact with multiple children (70%), comorbid conditions (50%), premature birth (30%), and others (20%).

DISCUSSION

This study mainly aims at analyzing the efficacy and risk factors associated with the use of bronchodilators in bronchiolitis pediatric patients and to analyses the patient compliance associated with it.

Bronchodilators are the drug of choice for bronchiolitis pediatric patients with worsening conditions. Bronchodilators acts by targeting the beta 2 receptors, which is a G protein coupled receptor, in the lung airways. When the beta 2 receptor is activated the smooth muscles of the airway relaxes and patient feels better.

Levosalbutamol is the drug which has shown highest efficacy in the treatment of bronchiolitis, which acts by relaxing the smooth muscles of all airways, from trachea to the terminal bronchioles.

In this study 10 patients with bronchiolitis are selected from the pediatric population. Statistical analysis done and entered using SPSS software.

By analyzing the SpO2, Heart Rate and Respiratory Rates of the pediatric patients there is a significant improvement in the efficacy of the use of bronchodilators when compared to one without treatment.
Risk factors associated with the use of bronchodilators have been assessed by the use of Wang scale and there is a significant improvement in the risk factors on comparison with and without treatment

Patient compliance and adherence to treatment have been improved after effective interview with the care givers.

We also assessed that there is an equal distribution in gender of the children who are affected with bronchiolitis. The age group that is most commonly affected with the disease includes those under the age of 2 years followed by those in the range of 3-4 years of age.

Study also analyses that the most common symptoms shown by patients with bronchiolitis includes Coughing followed by Wheezing, Chest discomfort, Runny nose, Nasal congestion, and Tachypnea to a lesser extent.

The presence of past illness has also affected the patients with coughing, wheezing ear infections etc. are also responsible for the infection.

Exposure to tobacco can also lead to bronchiolitis.

Contact with multiple children and drug allergy are one among the main causes of the infection.

Our study has also shown a remarkable increase in the patients compliance which was performed by a validated patient compliance questionnaire and Clinician Rating Scale (CRS).

In a study by James d Keller, sowed that bronchodilators has shown modest short term improvement in clinical features of mild or moderate bronchiolitis. The effect of average score was -0.32 favoring the treatment. Secondary trials were done in 4 outpatient department trials and the results were similar and the data varied more.

In a similar study done by Ajda Praznik the respiratory syncal viruses are the frequently detected virus. Most patients who are admitted in the NICU were detected only with one type of virus. Younger age and the use of antibiotics were associated with bronchodilators severity.

Bronchodilators have shown a significant improvement in the conditions of bronchiolitis patients by improving Heart Rate, Respiratory Rates and SpO2.

CONCLUSION

From this study we concluded that Bronchodilators are efficacious in treating bronchiolitis. Among the bronchodilator levosalbutamol is the most efficient. Patient compliance improved after treatment.

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