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**Search details**

Use of nebulised salbutamol for the alleviation of bronchospasm.improvement in breathing of adult (16-60 years) asthmatic patients.

**Resources searched**

NHS Evidence; TRIP Database; Cochrane Library; BNI; CINAHL; MEDLINE; Google Scholar

**Database search terms:** asthma*; exp ASTHMA; salbutamol adj2 (nebuli* OR atomi*); albuterol adj2 (nebuli* OR atomi*); salbutamol; ALBUTEROL; albuterol; nebulis*; nebuliz*; atomis*; atomiz*; vaporiz*; vaporis*; evaporate*; NEBULIZERS AND VAPORIZERS; bronchospasm*; “bronchial spasm*”; bronchospasm; Ventolin; Apo-Salvent; Accuneb; ProAir and HFA; Proventil; breath*; respiration; exp RESPIRATION

**Evidence search string(s):** asthma* (salbutamol OR albuterol) (nebuli* OR atomi* OR vapori*) ("bronchial spasm*" OR bronchospasm* OR breath* OR respirat*)

**Google search string(s):** ~asthma (~salbutamol OR ~albuterol) (~nebulizer OR ~atomizer OR ~vaporizer) (~"bronchial spasm" OR ~bronchospasm OR ~breathing OR ~respiration)

**Summary**

There is quite a lot of research on the use of salbutamol for the alleviation of bronchospasm in adult asthmatic patients. As children are usually defined by the databases as 0-18, for 16-18 year olds, some of the research will include children younger than 16 years old.
Guidelines

British National Formulary

3.1.2 Antimuscarinic bronchodilators 2013

Acute angle-closure glaucoma has been reported with nebulised ipratropium, particularly when given with nebulised salbutamol (and possibly other beta₂ agonists); care needed to protect patient’s eyes from nebulised drug or from drug powder.

Salbutamol 2013

British National Formulary for Children

Management of acute asthma 2013

1. Treatment of life-threatening asthma should be initiated with nebulised salbutamol 2.5 mg or terbutaline 5 mg (via an oxygen-driven nebuliser if available); nebulised doses may be doubled for children over 5 years. Repeat the dose every 20–30 minutes or as necessary, then reduce the frequency on improvement.

2. If the condition does not respond or is life-threatening, transfer the child to an intensive care unit and treat with a parenteral short-acting beta₂ agonist (e.g. salbutamol, section 3.1.1.1) or parenteral aminophylline (section 3.1.3).

Salbutamol 2013

Canadian Paediatric Society

Managing the paediatric patient with an acute asthma exacerbation 2012

Short-acting beta₂-agonists: Salbutamol (albuterol) is the bronchodilator of choice [3][8][12]. A metered-dose inhaler (MDI) with a spacer is the preferred device for salbutamol administration because it is more efficient than a nebulizer for bronchodilator delivery (22). An MDI can be used in almost all situations except for very severe episodes with impending respiratory failure. Even in the presence of hypoxemia, oxygen can be given by nasal canulae at the same time that salbutamol is given by MDI and spacer. In children without initial oxygen requirements, beta₂-agonists administered by MDI and spacer are less likely to provoke hypoxemia and tachycardia than a nebulizer [22].

The recommended doses for MDI and nebulizer beta₂-agonists delivery are listed in Table 2. The dose and frequency of intermittent salbutamol therapy depend on the severity of an acute attack and the patient’s response to treatment. The first dose of salbutamol should be given as soon as possible after rapid triage and evaluation in the ED. In patients having a severe asthma attack, the continuous administration of nebulized beta₂-agonists may have a better and more prolonged bronchodilator effect compared with intermittent therapy [23]. Side effects of salbutamol include tachycardia, hyperglycemia and hypokalemia, which are generally well tolerated. There is no evidence in the paediatric age group of reversible arrhythmias following treatment with beta₂-agonists, but this side effect has been reported in adults. Paediatric patients treated with continuous nebulized beta₂-agonists should be monitored for cardiac arrhythmias.

College of Emergency Medicine

Guideline for the management of acute allergic reaction 2009

Some trials of nebulised adrenaline have been performed in acute severe asthmatic patients with symptoms of wheeze and breathing difficulty, who are similar in many ways to patients with acute allergy. These are briefly discussed below.

Zeggwagh et al (1998)31 concluded from a prospective randomised controlled trial in 44 patients that nebulised adrenaline is as effective as nebulised salbutamol. They also concluded that nebulisation could reduce the systemic side effects of adrenaline.

Turpeinen et al (1984)32 compared injected adrenaline with nebulised salbutamol in 46 children with asthma. They concluded that nebulised salbutamol was a more effective
bronchodilator than injected adrenaline in children.

eMedicines Compendium
Combivent metered aerosol and UDVs (salbutamol, ipratropium) - Revised SPC 2009
Ventolin 2.5 and 5mg Nebules, Respirator solution, 500mcg injection, solution for IV infusion (salbutamol) - Revised SPC 2009

Finnish Medical Society Duodecim
Long-term management of asthma 2011
Treatment of acute exacerbation of asthma 2011

Joint Royal Colleges Ambulance Liaison Committee
UK Ambulance Service Clinical Practice Guidelines 2006
Alternatively see separately published sections: Asthma in Children and Asthma in Adults.
1. In acute severe or life threatening asthma ipratropium should be given concurrently with the first dose of salbutamol. In acute asthma or COPD unresponsive to salbutamol alone a single dose of ipratropium may be given concurrently with the second or later dose of salbutamol. Salbutamol often provides initial relief. In more severe attacks however, the use of steroids by injection or orally and further nebuliser therapy will be required. Do not be lulled into a false sense of security by an initial improvement after salbutamol nebulisation.

2. Salbutamol is less effective in children <12 months and a single dose of 2.5 milligrams should be administered. If this is ineffective, further doses should not be given.

3. administer salbutamol 6-9 via O2 driven nebuliser, running at 6-8 litres per minutes (refer to salbutamol drug protocol for dosages and information). In acute severe or life-threatening cases ipratropium bromide (refer to ipratropium bromide drug protocol for dosages and information) should be added to the salbutamol. Continue high concentration O2 after nebulisation if no clinical improvement after 5-10 minutes, administer further salbutamol via nebuliser and consider continuous nebulised salbutamol. Ipratropium bromide should be administered if not given earlier.

Repeat or continuous nebulised salbutamol may be given until arrival at hospital or side effects become clinically significant (extreme tachycardia >140 beat per minute in adults, tremors etc.)

Medicines and Healthcare products Regulatory Agency
Salbutamol 1mg ml and 2 mg ml Nebuliser Solution, PL 36390 0035-6 2011
UKPAR Salbutamol Sulphate 100 micrograms Inhaler PL 36390 0034 2011

New South Wales Health
Infants and Children - Acute Management of Asthma 2012

SIGN
British Guideline on the Management of Asthma - Quick reference guide 2011
1. Salbutamol HFA can be substituted for salbutamol CFC at 1:1 dosing.

2. Paramedics attending to children with acute asthma should administer nebulised salbutamol driven by oxygen if symptoms are severe whilst transferring the child to the
Welsh Medicines Information Centre
Which commonly used nebuliser solutions are compatible? 2012

Evidence-based reviews

BestBETs
Oral versus inhaled salbutamol for acute paediatric asthma 2011
Oral salbutamol is ineffective in the treatment of paediatric asthma and is associated with an increased incidence of adverse events compared with inhaled formulations. Paediatric masks and spacers can facilitate administration of inhaled salbutamol to all patients; therefore, there is no role for oral salbutamol. Oral salbutamol should be excluded from use in the treatment of childhood asthma.

Nebulised salbutamol or nebulised adrenaline for wheeze in anaphylaxis 2009
Patients with severe (life-threatening) acute allergic reactions should be treated with intramuscular adrenaline according to the Resuscitation Council Guidelines (2008).

Clinical Immediate Reference
Acute Severe Asthma and Status Asthmaticus 2012
1. There is no evidence for any difference in efficacy between salbutamol and terbutaline.
2. For adults with severe asthma that is poorly responsive to an initial bolus dose of beta₂, consider continuous nebulisation of salbutamol at 5-10 mg/hour with an appropriate nebuliser. Continuous nebulised beta₂ agonists are of no greater benefit than the use of frequent intermittent doses in the treatment of children with acute asthma.
   Add nebulised ipratropium bromide (0.5 mg 4-6-hourly) to beta₂ agonist treatment for adults with acute severe or life-threatening asthma, or those with a poor initial response to beta₂ agonist therapy.
3. Children: frequent doses of ipratropium bromide up to every 20-30 minutes (250 micrograms/dose mixed with 5 mg of salbutamol solution in the same nebuliser) should be used for the first few hours of admission. The salbutamol dose should then be weaned to 1-2-hourly according to clinical response and the ipratropium dose should be weaned to 4-6-hourly or discontinued.

Cochrane Database of Systematic Reviews
Addition of intravenous beta2-agonists to inhaled beta2-agonists for acute asthma 2012
There is very limited evidence from one study (Browne 1997) to support the use of IV beta₂-agonists in children with severe acute asthma with respect to shorter recovery time, and similarly there is limited evidence (again from one study Browne 1997) suggesting benefit with regard to pulmonary index scores; however this advantage needs to be considered carefully in relation to the increased side effects associated with IV beta₂-agonists. We identified no significant benefits for adults with severe acute asthma. Until more, adequately powered, high quality clinical trials in this area are conducted it is not possible to form a robust evaluation of the addition of IV beta₂-agonists in children or adults with severe acute asthma.

Hospital Pharmacy
Stability of Levalbuterol in a Mixture of Levalbuterol and Ipratropium Nebulizer Solution 2008
Over the time period of 28 days at room temperature, no significant decrease in
concentrations could be detected for levalbuterol or ipratropium.

### Published research

#### 1. beta2-agonist therapy in lung disease

**Author(s)** Cazzola M., Page C.P., Rogliani P., Matera M.G.

**Citation:** American Journal of Respiratory and Critical Care Medicine, April 2013, vol./is. 187/7(690-696), 1073-449X;1535-4970 (01 Apr 2013)

**Publication Date:** April 2013

**Abstract:** beta$_2$-Agonists are effective bronchodilators due primarily to their ability to relax airway smooth muscle (ASM). They exert their effects via their binding to the active site of beta$_2$-adrenoceptors on ASM, which triggers a signaling cascade that results in a number of events, all of which contribute to relaxation of ASM. There are some differences between beta$_2$-agonists. Traditional inhaled short-acting beta$_2$-agonists albuterol, fenoterol, and terbutaline provide rapid as-needed symptom relief and short-term prophylactic protection against bronchoconstriction induced by exercise or other stimuli. The twice-daily beta$_2$-agonists formoterol and salmeterol represent important advances. Their effective bronchodilating properties and long-term improvement in lung function offer considerable clinical benefits to patients. More recently, a newer beta$_2$-agonist (indacaterol) with a longer pharmacodynamic half-life has been discovered, with the hopes of achieving once-daily dosing. In general, beta$_2$-agonists have an acceptable safety profile, although there is still controversy as to whether long-acting beta$_2$-agonists may increase the risk of asthma mortality. In any case, they can induce adverse effects, such as increased heart rate, palpitations, transient decrease inPa$_O_2$, and tremor. Desensitization of beta$_2$-adrenoceptors that occurs during the first few days of regular use of beta$_2$-agonist treatment may account for the commonly observed resolution of the majority of these adverse effects after the first few doses. Nevertheless, it can also induce tolerance to bronchoprotective effects of beta$_2$-agonists and has the potential to reduce bronchodilator sensitivity to them. Some novel once-daily beta$_2$-agonists (olodaterol, vilanterol, abediterol) are under development, mainly in combination with an inhaled corticosteroid or a long-acting antimuscarinic agent. Copyright 2013 by the American Thoracic Society.

**Source:** EMBASE

#### 2. Noninvasive ventilation coupled with nebulization during asthma crises: A randomized controlled trial

**Author(s)** Galindo-Filho V.C., Brandao D.C., Ferreira R.C.S., Menezes M.J.C., Almeida-Filho P., Parreira V.F., Silva T.N., Rodrigues-Machado M.G., Dean E., Andrade A.D.

**Citation:** Respiratory Care, January 2013, vol./is. 58/2(241-249), 0020-1324;1943-3654 (01 Jan 2013)

**Publication Date:** January 2013

**Abstract:** BACKGROUND: Despite the clinical improvements attributed to noninvasive ventilation (NIV) during asthma crises, and the well-established effects of nebulization, there are few studies on the effects of these interventions together. We hypothesized that nebulization coupled to NIV should raise radio-aerosol pulmonary deposition in asthmatics. The aims of this study were to assess the effects of coupling beta-agonist nebulization and NIV during asthma exacerbations on radio-aerosol pulmonary deposition, using scintigraphy and cardiopulmonary parameters, to correlate pulmonary function with radio-aerosol deposition index, radio-aerosol penetration index, and pulmonary clearance.

**METHODS:** In this controlled trial, 21 adults with moderate to severe asthma attack were randomized to a control group (n = 11) or experimental group (NIV + nebulizer group, n = 10). All subjects inhaled bronchodilators for 9 minutes, and after particles were counted with a gamma camera to analyze regions of interest and pulmonary clearance at 0, 15, 30, 45, and 60 min. RESULTS: Breathing frequency (P < .001) and minute ventilation (P = .01) were reduced, and tidal volume was increased (P = .01) in the NIV + nebulizer group,
compared with the control group. The NIV + nebulizer group had improvement from baseline values, compared to the control group in the following parameters: FEV1 46.7 +/- 0.5% of predicted vs 29.8 +/- 8.9% of predicted, P = .02), FVC (41.2 +/- 1.5% of predicted vs 23.2 +/- 7.1% of predicted, P = .02), peak expiratory flow (67.3 +/- 38.3% of predicted vs 26.9 +/- 12.1% of predicted, P = .01), and inspiratory capacity (54.9 +/- 28.8% of predicted vs 31.2 +/- 9.1% of predicted, P = .01). No differences were observed between groups regarding radio-aerosol deposition index or pulmonary clearance. Negative correlations were found between FEV1, forced expiratory flow during the middle half of the FVC maneuver (FEF25-75%), inspiratory capacity, and radio-aerosol penetration index.

CONCLUSIONS: Coupling nebulization and NIV during asthma exacerbation did not improve radio-aerosol pulmonary deposition, but we observed clinical improvement of pulmonary function in these subjects. (ClinicalTrials.gov registration NCT01012050). 2013 Daedalus Enterprises.

Source: EMBASE

Available in fulltext from Respiratory Care at Highwire Press

3. Efficacy of nebulized ipratropium bromide in the treatment of acute asthma in children: Randomised, double blind, placebo-controlled trial [English;Turkish]

Cocukluk cagı akut astım atagi tedavisinde nebulize ipratropium bromurun etkinliği:
Cift kor randomize kontrollu calisma

Author(s) Sengul Gokalp A., Bicer S., Siraneci R.

Citation: Nobel Medicus, January 2013, vol./is. 9/1(67-75), 1305-2381 (January-April 2013)

Publication Date: January 2013

Abstract: Objective: To determine the effect of adding nebulized ipratropium bromide to standard therapy compared with standard therapy alone in children presenting with acute severe and moderate asthma to the pediatric emergency department. Material and Method: One hundred children aged between 3-17 years who presented with moderate or severe asthmatic attack (status asthmaticus) were randomly assigned to two groups in a prospective, double blind, placebo-controlled study performed in the pediatric emergency department of teaching children's hospital. All patients received nebulized salbutamol every 20 minutes and intramuscular metilprednisolon after the first dose of salbutamol. Children in group 1 received three doses of nebulized ipratropium bromide after the third dose of salbutamol; those in group 2 received normal saline placebo every 20 minutes. Percentage of the predicted peak expiratory flow rate (PEFR), clinical asthma scores, pulse oximetry and physiologic measurements were assessed at the start of the ED visit, after salbutamol treatment and combined treatment and at 72. hour. Results: Baseline demographics and clinical characteristics of all two groups were similar. An intention to treat analysis showed that there was no statistically significant difference in the clinical asthma score at 1 and 72 hours between two groups (p>0.05). PEFR changed from 54.28 +/- 17.22 (%) to 90.60 +/- 7.45 (p<0.05) in the first group and from 50.11 +/- 12.23 to 82.02 +/- 12.21 in the second group. There were significant differences between groups on PEFR measured at 72 hours (p<0.05). No side effects were documented in any of the patients. Conclusion: In conclusion, this study demonstrates that addition of ipratropium bromide to salbutamol and corticosteroid therapy have a significant improvement in PEFR values and oxygen saturation even after 72<sup>th</sup> hour of treatment.

Source: EMBASE

4. Effectiveness of a breath-actuated nebulizer device on asthma care in the pediatric emergency department.

Author(s) Titus MO, Eady M, King L, Bowman CM

Citation: Clinical Pediatrics, December 2012, vol./is. 51/12(1150-4), 0009-9228;1938-2707 (2012 Dec)

Publication Date: December 2012

Abstract: The breath-actuated nebulizer (BAN) is a new respiratory device to deliver short-
acting -agonists to patients with asthma exacerbations. This pediatric convenience sample experimental study compares the BAN with conventional nebulizers and demonstrates that the BAN allows for shorter treatment times to achieve improved clinical asthma scores with less albuterol, shorter emergency department length of stay, and fewer hospitalizations.

Source: Medline
Available in fulltext from Clinical Pediatrics at EBSCOhost

5. Effectiveness of a breath-Actuated nebulizer device on asthma care in the pediatric emergency department

Author(s) Titus M.O., Eady M., King L., Bowman C.M.

Citation: Clinical Pediatrics, December 2012, vol./is. 51/12(1150-1154), 0009-9228;1938-2707 (December 2012)

Publication Date: December 2012

Abstract: The breath-Actuated nebulizer (BAN) is a new respiratory device to deliver short-Acting A-Agonists to patients with asthma exacerbations. This pediatric convenience sample experimental study compares the BAN with conventional nebulizers and demonstrates that the BAN allows for shorter treatment times to achieve improved clinical asthma scores with less albuterol, shorter emergency department length of stay, and fewer hospitalizations. The Author(s) 2012.

Source: EMBASE
Available in fulltext from Clinical Pediatrics at EBSCOhost

6. Emergency department treatment of adults with acute asthma exacerbations: Effect on exhaled nitric oxide levels

Author(s) Silverberg J.I., Rodenas M., Sinert R., Joks R.

Citation: Allergy and Asthma Proceedings, November 2012, vol./is. 33/6(514-518), 1088-5412;1539-6304 (November-December 2012)

Publication Date: November 2012

Abstract: Measurement of exhaled nitric oxide levels (eNO) from asthmatic patients is a noninvasive marker of airway inflammation in both adults and children and has been used as an outpatient measure of asthma control. We examined eNO in acute asthma exacerbations and how it is affected by treatment in the emergency department (ED) setting. Both eNO and peak expiratory flow (PEF) rate were measured at arrival and before discharge for adult asthmatic subjects (n = 28) treated for acute exacerbations in the ED at Kings County Hospital Center during spring and fall pollen seasons. Total serum Immunoglobulin E (IgE), peripheral blood leukocyte numbers, and tobacco smoking history were determined. Routine ED treatment included oral prednisone at 60 mg and inhalation of nebulized albuterol and ipratropium. Both PEF (p = 0.0005) and eNO (p < 0.0001) increased after treatment of subjects. Initial eNO was associated with age (p = 0.0004), absolute eosinophil count (p = 0.003), Asthma Control Test (p = 0.004), and Asthma Quality of Life Questionnaire (p = 0.04). Change in pre- versus posttreatment eNO (eNO) was associated with change in PEF (PEI p < 0.0001). Initial PEF was associated with oxygen saturation (p < 0.0001). PEF was associated with serum IgE levels. ED visit duration was associated with initial PEF (p = 0.0004), eNO (p = 0.004), and number of albuterol treatments (p = 0.001). These associations remained significant in multivariate models that controlled for demographic factors, asthma control, smoking, and measures of inflammation and ventilation. eNO levels increase after ED treatment of acute asthma exacerbations in adults. Improved ventilation may allow for more accurate measurement of NO produced in inflamed airways. Copyright 2012, OceanSide Publications, Inc.

Source: EMBASE
Available in fulltext from Allergy and Asthma Proceedings at EBSCOhost
7. The patient with asthma in the emergency department

Author(s) Adams J.Y., Sutter M.E., Albertson T.E.

Citation: Clinical Reviews in Allergy and Immunology, August 2012, vol./is. 43/1-2(14-29), 1080-0549;1559-0267 (August 2012)

Publication Date: August 2012

Abstract: Asthma is a highly prevalent disease that presents commonly to the emergency department (ED) in acute exacerbation. Recent asthma treatment guidelines have added content dedicated to the management of acute exacerbations. Effective management of an exacerbation requires rapid assessment of severity through physical examination, measurement of peak expiratory flow rate, and response to initial treatment. Most therapies are directed at alleviating bronchospasm and decreasing airway inflammation. While inhaled short-acting beta-agonists, systemic corticosteroids, and supplemental oxygen are the initial and often only therapies required for patients with mild moderate exacerbations, high-dose beta agonists and inhaled anti-cholinergics should also be given to patients with severe exacerbations. Adjunctive therapy with intravenous magnesium and Heliox-driven nebulization of bronchodilators should be considered for patients presenting with severe and very severe exacerbations. Early recognition and appropriate management of respiratory failure are required to mitigate the risk of complications including death. Disposition should be determined based on serial assessments of the response to therapy over the first 4 h in the ED. Patients stable for home discharge should receive medications, asthma education including a written asthma action plan, and should have follow-up scheduled for them by ED staff. Rapid implementation of evidence-based, multi-disciplinary care is required to ensure the best possible outcomes for this potentially treatable disease. Springer Science+Business Media, LLC 2011.

Source: EMBASE

8. [Salbutamol in asthma treatment: with nebulizer or inhaler?] [Turkish] Astım tedavisinde salbutamol; nebulizerle mı inhalerle mı?

Author(s) Cakkaytar O., Sekerel B.E.

Citation: Tuberkuloz ve toraks, June 2012, vol./is. 60/2(193-198), 0494-1373 (Jun 2012)

Publication Date: June 2012

Abstract: Breath relieving and protective drugs in asthma treatment are applied through pressurized metered dose inhaler (pMDI), nebulizer or dry powder inhaler. The short acting beta-2 agonist salbutamol used in acute asthma exacerbation is found in the forms of nebule or pMDI in Turkey. Nebule form is used more frequently in emergency services. The aim of this review is to compare these two routes of administration through clinical efficacy, the amount of drug reaching to the lungs and adverse events comprehensively by way of looking through the studies. Additionally effect of different inhalation techniques through chambers, different methods used in cleaning of them and different types of nebulizers, to the efficacy are investigated. As a result, asthma exacerbation can be treated with pMDIs used through holding chambers in emergency room successfully when applied with dosing scheme appropriate for the patient's age, weight and severity of exacerbation (usually 1/4th of nebule dosing) on the contrary to ordinary method of nebulizers.

Source: EMBASE

Available in fulltext from Tuberculosis and Thorax / Tuberkoloz ve Toraks at EBSCOhost

9. A comparison on the effectiveness of Symbicort vs Pulmicort with as-needed salbutamol in reducing eosinophilic bronchial inflammation as measured using fractional exhaled nitric oxide

Author(s) Chew K.S., Kamarudin H.

Citation: Academic Emergency Medicine, June 2012, vol./is. 19/6(766), 1069-6563 (June 2012)

Publication Date: June 2012
Abstract: Objectives: The purpose of this paper is to study the effectiveness of budesonide/formoterol (Symbicort AstraZeneca) as an alternative in reducing eosinophilic bronchial inflammation and improving clinical control over a four-week duration. Fraction of exhaled nitric oxide (FENO) is a surrogate marker of the severity of the underlying inflammation. Asthma Control Test (ACT) is a validated, patient-centered questionnaire to assess control for the past four weeks. Methods: We performed a randomized, open label study (March until August 2011) comparing the bronchodilatory effects of Symbicort (160/4.5 mcg per inhalation) vs that of nebulized salbutamol as the initial reliever in acute exacerbation of mild to moderate bronchial asthma. The first FENO reading was measured from all patients using the portable, hand-held electrochemical device, NIOX MINO Airway Inflammation Monitor (Aerocrine AB, Solna, Sweden). Patients who were fit for discharge were given an appointment 4 weeks later for follow-up assessment. Patients in the Symbicort group were instructed to take two inhalations of Symbicort twice daily at home. Patients in the nebulized salbutamol arm were given inhaled budesonide (Pulmicort 100 mcg per inhalation, AstraZeneca), two inhalations twice daily besides the as-needed salbutamol. During follow-up, a second FENO level (FENO2) was obtained together with an ACT score evaluation. We dichotomized the ACT score into "well-controlled" (>=20) and "uncontrolled" (<=19). Results: Only 14 out of 32 patients enrolled (43.8%) came back for follow-up. The mean reduction of FENO level for Symbicort was 6.25 (SD 36.0) pbb; whereas for the comparison arm, the mean reduction in FENO level was 31.0 (SD 28.8) pbb. In the Symbicort arm 4/8 (50%) patients were categorized as "well controlled". All six patients (100%) in the comparison arm were categorized as "well controlled" on ACT re-evaluation. No correlation between ACT scoring and FENO level was noted. Conclusion: This study suggest that Symbicort is an effective alternative in improving patient's clinical asthma control as well as reducing underlying eosinophilic bronchial inflammation although the improvement in the comparison arm seems to be greater.

Source: EMBASE
P = 0.417). Beta-adrenoceptor blocker induced bronchoconstriction was demonstrated by spirometry and impulse oscillometry. For the placebo visit, FEV<sub>1</sub> fell 4.7% 2 hours post propranolol (95% CI 1.8, 7.5, P = 0.008) whilst total airway resistance (R5%) increased 31.3% (95% CI 15.6, 47.0, P = 0.04). On both visits FEV<sub>1</sub>% and R5% returned to baseline after salbutamol post histamine. Conclusion: Nebulized salbutamol and ipratropium produced a full recovery after propranolol and histamine induced bronchoconstriction, independent of hydrocortisone use. Since the greatest risk of beta-adrenoceptor blockade is after first dose, our findings offer reassurance to those undertaking further evaluation of chronic beta-adrenoceptor blockade as a potential treatment for mild-to-moderate asthma. 2011 The Authors. British Journal of Clinical Pharmacology 2011 The British Pharmacological Society.

Source: EMBASE

Available in fulltext from British Journal of Clinical Pharmacology at National Library of Medicine

Available in fulltext from British Journal of Clinical Pharmacology at EBSCOhost

12. Increased serum albuterol concentrations may be associated with elevations of serum lactate in subjects with acute asthma exacerbations

Author(s) Aubuchon K., Matsuda K., House S.L., Ferguson I., Schneider J., Lewis L.

Citation: Academic Emergency Medicine, April 2012, vol./is. 19/(S312-S313), 1069-6563 (April 2012)

Publication Date: April 2012

Abstract: Background: We have previously described increased serum lactate concentrations in subjects with acute asthma exacerbation. It is not clear if this is due to increased work of breathing or possibly a side effect of treatment. Objectives: 1) Determine if there is a significant correlation between increased treatment lactate or lactate and serum albuterol concentrations during treatment of an acute asthma exacerbation after adjusting for dyspnea score (DS). 2) Determine if elevated treatment lactate concentrations or lactate concentrations are associated with increased hospital admissions. Methods: This is an interim, subgroup analysis of a prospective, interventional, double-blind study performed in an academic urban ED. Subjects who were consented for this trial presented with acute asthma exacerbations with FEV1 <= 50% predicted within 30 minutes following initiation of “standard care” (includes a minimum of 2.5 mg nebulized albuterol, 0.5 mg nebulized ipratropium, and 50 mg of a corticosteroid). ED physicians who were unaware of the study objectives administered all treatments. Subjects were randomized in a 1:1 ratio to either placebo or investigational intravenous beta agonist arms. Blood was obtained at 1 and 1.25 hours after the start of the hour long infusion. Blood was centrifuged and serum stored at -80 degree C, and then shipped on dry ice for albuterol and lactate measurements at a central lab. The treatment lactate and lactate were correlated with 1 hr serum albuterol concentrations and hospital admission using partial Pearson correlations to adjust for DS. Results: 38 subjects were enrolled to date, 20 with complete data. The mean baseline serum lactate level was 18.1 mg/dL (SD +/- 8.6). This increased to 32.7 mg/dL (SD +/- 15.0) at 1.25 hrs. The mean 1 hr DS was 3.85 (SD +/- 2.0). The correlations between treatment lactate, lactate, 1 hr serum albuterol concentrations (R, S and total) and admission to hospital are shown (see table). Both treatment and lactate were highly correlated with total serum albuterol, R albuterol, and S albuterol. There was no correlation between treatment lactate or lactate and hospital admission. Conclusion: Lactate and lactate concentrations correlate with albuterol concentrations in patients presenting with acute asthma exacerbations after adjusting for dyspnea score, but do not correlate with hospital admission. (Table presented).

Source: EMBASE

Available in fulltext from Academic Emergency Medicine at EBSCOhost

13. Management of acute bronchospasm respiratory distress with CPAP ventilation associated with nebulization in the prehospital emergency setting
**Author(s)** Cuny J., Berteloot C., Goldstein P., Wiel E.

**Citation:** Critical Care, March 2012, vol./is. 16/(S48), 1364-8535 (20 Mar 2012)

**Publication Date:** March 2012

**Abstract:** Introduction In emergency medicine, noninvasive ventilation (NIV) has grown up for COPD and acute pulmonary edema through the use of continuous positive airway pressure (CPAP). Recently, several studies have reported the use of NIV coupled with nebulized bronchodilators to optimize the management of acute asthma patients in emergency departments and ICUs. This has indicated an improvement in gas exchanges, decreased lung resistances and decreased work of breathing. The purpose of this study is to assess prehospital practices in CPAP for these patients, to target patients for its use, and to compare clinical data before and after achievement of CPAP with nebulization.

**Methods** We have conducted a retrospective, descriptive and observational study, by collecting all files (EMA, Dispatching Center) for each patient receiving CPAP associated with nebulization, for pulmonary bronchospasm (excluding acute pulmonary edema), and supported by the emergency medical service. Several data were analyzed: age, sex, history, severity signs, cardiac and respiratory rate, blood pressure, pulse oxymetry, need for intubation, nebulization of beta2-agonists, anticholinergics, intravenous corticosteroids, and arterial blood gases. Results Over an 18-month period, 21 patients were enrolled: 38% for severe asthma, and 62% for COPD exacerbation. Regarding the history: 67% were under long-term corticosteroid, 48% smokers, 29% received antibiotics, and all of them presented a clinical bronchospasm, and severity criteria for respiratory distress. Sixty percent of patients were hypoxic (SpO2 <92%). All patients received salbutamol inhalation, associated with inhaled anticholinergic agent in 71.4%. Intravenous glucocorticoid drug was dispensed in 71.4% and intravenous salbutamol in 23.8%. None of the asthma patients was intubated, five COPD patients (24.8%) were intubated. Twelve patients were admitted to the ICU (one with asthma and 11 with COPD). Comparison of clinical parameters between prehospital care and the emergency room shows a significant difference (P <0.05) for respiratory rate (35.9 +/- 7.48 vs. 24.95 +/- 8.25) and pulse oxymetry (81.8 +/- 15.8 vs. 96.4 +/- 3.54). Conclusion NIV through CPAP associated with nebulizations appears to provide benefit by reducing respiratory work (decreased respiratory rate) and improving alveolar ventilation (increased SpO2) in patients with asthma. However, in COPD patients, no improvement of symptoms has been observed.

**Source:** EMBASE

Available in fulltext from Critical Care at National Library of Medicine

14. The effectiveness of two different methods of salbutamol nebulization in children with asthma

**Author(s)** Emeryk A., Kowalska M., Czerwinska- Pawluk I., Bartkowiak-Emeryk M.

**Citation:** World Allergy Organization Journal, February 2012, vol./is. 5/(S82), 1939-4551 (February 2012)

**Publication Date:** February 2012

**Abstract:** Background: Short acting beta-2 agonists (SABA) inhalation is commonly used in bronchodilatatory test, which is still an important research tool in the diagnosis of respiratory diseases with bronchial obstruction. Bronchodilatatory effect of SABA depends primarily on the degree of patency of the airway, the type and dose of SABA, as well as the type of inhaler and inhalation technique. The aim of the study was to evaluate the spirometric effectiveness of 2 different methods of salbutamol nebulization in asthmatic children. Methods: The study group included 132 children aged 6 to 18 years (mean: 11.7), 91 (69%) boys and 41 (31%) girls with partly controlled asthma treated in the Allergy or Pulmonology Outpatient Clinics in Children's University Hospital in Lublin. The study was randomized and single blind design. Patients were randomly assigned to one of 2 groups. The first group used 2.2 mg of salbutamol (mean calculated dose) in the breath-actuated nebulizer (BAN) (Marine, Medbryt, Poland), while the second one-5 mg salbutamol (constans dose) in the constant-output nebulizer (CON) (Porta-Neb, MEDICAID, UK). Flow-volume curve (dynamic spirometry) was measured before and 20 minutes. after drug nebulization (bronchodilatatory test). FEV1 (expiratory volume in first second) and FEF25-75 (forced expiratory flow at 25 to 75% of forced vital capacity) values were analyzed. The
change in FEV1 and FEF25-75 after treatment with respect to baseline was calculated. Results: The mean baseline value of FEV1 was 67.4% in BAN and 70.5% in CON group and there was no statistical difference between these groups. The significant improvement of measured ventilatory parameters was observed. There was the significant difference in the bronchodilator response to salbutamol between 2 methods of nebulization. The value of FEV1 increased at 16.2% in BAN group and at 12.6% in CON group (P = 0.026). The value of FEF25-75 increased in both groups at 37.7% and 32.7% respectively and there was no statistical difference between these groups. Conclusions: We observed greater bronchodilatatory effect of salbutamol inhaled via breath-actuated nebulizer while delivering a double lower dose. 2. Bronchodilatory test using nebulized salbutamol in breath-actuated nebulizer should be recommended for children.

Source: EMBASE

15. Salbutamol in asthma treatment: With nebulizer or inhaler? [English;Turkish] Asti(dotless)m tedavisinde salbutamol; nebulizerle mi inhalerle mi?

Author(s) Cavkaytar O., Sekerel B.E.

Citation: Tuberkuloz ve Toraks, 2012, vol./is. 60/2(193-198), 0494-1373 (2012)

Publication Date: 2012

Abstract: Breath relieving and protective drugs in asthma treatment are applied through pressurized metered dose inhaler (pMDI), nebulizer or dry powder inhaler. The short acting beta-2 agonist salbutamol used in acute asthma exacerbation is found in the forms of nebule or pMDI in Turkey. Nebule form is used more frequently in emergency services. The aim of this review is to compare these two routes of administration through clinical efficacy, the amount of drug reaching to the lungs and adverse events comprehensively by way of looking through the studies. Additionally effect of different inhalation techniques through chambers, different methods used in cleaning of them and different types of nebulizers, to the efficacy are investigated. As a result, asthma exacerbation can be treated with pMDIs used through holding chambers in emergency room successfully when applied with dosing scheme appropriate for the patient's age, weight and severity of exacerbation (usually 1/4<sup>th</sup> of nebule dosing) on the contrary to ordinary method of nebulizers.

Source: EMBASE

Available in fulltext from Tuberculosis and Thorax / Tuberkoloz ve Toraks at EBSCOhost

16. Severe intraoperative bronchospasm treated with a vibrating-mesh nebulizer.

Author(s) Golden LR, DeSimone HA, Yeroshalmi F, Pranevicius M, Saraghi M

Citation: Anesthesia Progress, 2012, vol./is. 59/3(123-6), 0003-3006;0003-3006 (2012)

Publication Date: 2012

Abstract: Bronchospasm and status asthmaticus are two of the most dreaded complications that a pediatric anesthesiologist may face. With the occurrence of severe bronchospasm and the inability to ventilate, children are particularly vulnerable to apnea and ensuing hypoxia because of their smaller airway size, smaller lung functional residual capacity, and higher oxygen consumption rates than adults. Nebulized medication delivery in intubated children is also more difficult because of smaller endotracheal tube internal diameters. This case demonstrates the potentially lifesaving use of a vibrating-mesh membrane nebulizer connected to the anesthesia circuit for treating bronchospasm.

Source: Medline

Available in fulltext from Anesthesia Progress at EBSCOhost
Available in fulltext from Anesthesia Progress at National Library of Medicine

17. Fighting for air.

Author(s) Goss, James F, Philipson, Tyrone, Yergenson, Randy, Brocato, Chad

Citation: JEMS: Journal of Emergency Medical Services, 01 December 2011, vol./is.
18. Albuterol, An uncommonly recognized culprit in lactic acidosis

Author(s) Dodda V., Spiro P.

Citation: Chest, October 2011, vol./is. 140/4 MEETING ABSTRACT, 0012-3692 (October 2011)

Publication Date: October 2011

Abstract: INTRODUCTION: Albuterol, an uncommonly recognized cause for lactic acidosis, should be considered by physicians dealing with acute asthmatic patients. CASE PRESENTATION: A twenty year old African American female, with history of asthma and HIV, presented to the emergency room with a chief complaint of shortness of breath. It progressively got worse over the past couple of days inspite of increased use of albuterol. Patient had asthma since childhood, with one episode of intubation. Overall, her asthma was well controlled and the last attack was three years ago. Her asthma triggers include pollen and dust. She never smoked and denied having any pets. She was taking albuterol, fluticasone/ salmeterol 250/50 and montelukast and is not on any anti-retroviral medications. Patient received prednisone and a total of five albuterol nebulizations (2.5 mg) in the ER. Physical exam showed a normotensive, tachycardic and tachypneic patient in mild distress. She was able to talk in full sentences and was saturating 100% on 2 liters. Her best peak flow was reportedly 300, and she only did 150. Other pertinent positives include bilaterally decreased air entry and significant expiratory wheezing. ABG on arrival showed a lactate level of 3 with a peak flow of 120. Surprisingly by the time of ICU evaluation, in spite of improvement in her peak flow to 150, she looked more tachypneic and lactate level increased to 6.8. Rest of the labs were normal including a negative drug screen and normal liver function tests. Chest x-ray was normal. In the absence of hypoxemia, evidence of tissue hypoperfusion, liver abnormality or any other drugs that can cause lactic acidosis, albuterol was assumed to be the prime suspect for her hyperlactemia. She was managed with systemic steroids, ipratropium and lactic acidosis eventually resolved. DISCUSSION: Albuterol is an uncommonly recognized culprit in lactic acidosis. It seems to be caused by a combination of factors but the exact etiology and why only a proportion of patients develop it remains to be elucidated. Reports of lactic acidosis induced by high dose beta agonists used for tocolysis and bronchodilation have been described in obstetric and asthmatic patients. Type A lactic acidosis is usually secondary to hypoxia and tissue hypoperfusion. In contrast, albuterol is postulated to cause type B lactic acidosis due to increase in both endogenous and exogenous catecholamines. Enhanced ?2 receptor activation leads to increased glycogenolysis, gluconeogenesis, lipolysis and ultimately to increased conversion of pyruvate to lactic acid. Concurrent corticosteroid use may enhance the beta receptor sensitivity further potentiating the lactic acidosis. Alternate explanations like increased respiratory muscle work has also been postulated but lactic acidosis was shown to occur in mechanically ventilated and in some cases even in paralyzed patients where respiratory muscle fatigue is not a concern. Albuterol induced lactic acidosis creates a paradoxical situation where there is enhanced bronchodilation but worsening tachypnea as a compensation for metabolic acidosis. This might mislead the physicians to give more albuterol leading to further lactic acidosis creating a vicious cycle. Serial peak flow measurements and examination is the ideal way to identify this situation. CONCLUSIONS: So while treating asthmatic patients for severe bronchospasm any discrepancy between exacerbation of dyspnea and resolution of bronchospasm, with no other explanation for lactic acidosis, should lead the physician to suspect albuterol induced hyperlactemia. A need for further studies is essential to establish the exact etiology and management of this unique paradoxical situation.
study

Author(s) Mangunnegoro H., Novariska F., Wiyono W.H., Setiawati A., Louisa M.

Citation: International Journal of Clinical Pharmacology and Therapeutics, October 2011, vol./is. 49/10(614-621), 0946-1965 (October 2011)

Publication Date: October 2011

Abstract: Objective: beta<sub>2</sub> agonists have been used widely as relievers in asthma management. Procaterol is a selective beta<sub>2</sub> agonist, claimed to be more selective than salbutamol. The present study aimed to compare the efficacy of nebulized procaterol with nebulized salbutamol in the treatment of moderate acute asthma.

Methods: This was a randomized, double-blind, parallel group study in 140 patients with moderate acute asthma according to modified GINA 1998 who visited emergency department of Persahabatan Hospital, Jakarta. Patients were randomly assigned to receive three doses of either nebulized procaterol or salbutamol. The primary efficacy variable was the improvement in predicted peak expiratory flow rate (PEFR), while the secondary efficacy variable was the improvement in asthma score and the incidence and severity of adverse events. This study is registered at Current Controlled Trials, number ISCTRN25669625.

Results: Baseline characteristics were similar in both groups. After treatment, there were significant improvement of % PEFR (p < 0.001) and asthma score (p < 0.001) in procaterol (n = 68) and salbutamol (n = 69) groups. It was shown that procaterol and salbutamol produced similar efficacy in improving % predicted PEFR and decreasing asthma score. Both treatments were well tolerated. Palpitation and sinus tachycardia were found as adverse events with low incidence. Conclusion: In moderate acute asthma, nebulized procaterol and nebulized salbutamol were both effective in improving PEFR and decreasing asthma score. Both treatments were well tolerated, adverse reactions were rare. 2011 Dustri-Verlag Dr. K. Feistle.

Source: EMBASE

Available in fulltext from International Journal of Clinical Pharmacology and Therapeutics at EBSCOhost

20. Assessment of the use of non invasive continuous positive airway pressure associated with nebulization in pre-hospital management

Author(s) Berteloot C., Cuny J., Wiel E., Goldstein P.

Citation: Intensive Care Medicine, September 2011, vol./is. 37/(S192), 0342-4642 (September 2011)

Publication Date: September 2011

Abstract: INTRODUCTION. These lasts few years, Non Invasive Ventilation (NIV) has grown up for Chronic Obstruction Pulmonary Disease (COPD), and Acute Pulmonary Edema (APE) through the use of Continuous Positive Airway Pressure (CPAP). Recently, several studies have reported the use of NIV coupled with nebulized bronchodilators to optimize the management of acute asthma patients in emergency departments and intensive care units. This has indicated an improvement in gas exchanges, decreased lung resistances and decreased work of breathing. OBJECTIVES. The purpose of this study is to assess the workable in pre-hospital management, to target patients for its use, to compare clinical data before and after achievement of CPAP with nebulization. METHODS. We have conducted a retrospective, descriptive and observational study. We have collected all files (EMA, Dispatching center) for each patient who had received CPAP NIV associated to nebulisation, for pulmonary bronchospasm (excluded Acute Pulmonary Edema), and supported by emergency medical service. Several data were analyzed: age, sex, history, severity signs, cardiac and respiratory rate, blood pressure, pulse oxymetry, intubation, nebulization of beta-2 agonists, anticholinergics, intravenous corticosteroids, arterial blood gases. RESULTS. Over an 18 months period, 21 patients were enrolled: 8 patients were ventilated with CPAP nebulisation for a Severe Acute Asthma (38%), and 13 patients for a COPD exacerbation (62%). The mean age for asthma patients was 48 years, and 68 for COPD. Regarding to the history: 67% were under long-term corticosteroid, 48% were smokers, 29% received antibiotics, all patients presented a clinical bronchospasm, and severity criteria for respiratory distress. 67% of patients were hypoxic (SpO<sub>2</sub>&lt;92%). All patients have received salbutamol inhalation, associated in
71.4% of cases with inhaled anticholinergic agent. Intravenous glucocorticoid drug was dispensed in 71.4% of cases and intravenous salbutamol in 23.8% of cases. None of asthma patients were intubated, 5 COPD patients (24.8%) patients were intubated. 12 patients were admitted in intensive care units (1 with asthma and 11 with COPD).

Comparison of clinical parameters between pre-hospital care and emergency room shows a significant difference (p<0.05) for respiratory rate (35.9 +/- 7.48 vs. 24.95 +/- 8.25) and pulse oxymetry (81.8 +/- 15.8 vs. 96.4 +/- 3.54). CONCLUSIONS. First, it is interesting to note that the recommendations of management of acute severe asthma are not always followed. NIV through CPAP associated with nebulizations appears to provide benefit by reducing respiratory work (decreased respiratory rate) and improving alveolar ventilation (increased SpO2) in patients with asthma. However in COPD patients, no improvement of symptoms has been observed. Nevertheless, we cannot know which of CPAP or drug inhalation have improved asthma patients.

Source: EMBASE
Available in fulltext from Intensive Care Medicine at EBSCOhost

21. Management of acute asthma exacerbations

Author(s) Pollart S.M., Compton R.M., Elward K.S.
Citation: American Family Physician, July 2011, vol./is. 84/1(40-47), 0002-838X;1532-0650 (July 1, 2011)
Publication Date: July 2011
Abstract: Asthma exacerbations can be classified as mild, moderate, severe, or life threatening. Criteria for exacerbation severity are based on symptoms and physical examination parameters, as well as lung function and oxygen saturation. In patients with a peak expiratory flow of 50 to 79 percent of their personal best, up to two treatments of two to six inhalations of short-acting beta<sub>2</sub> agonists 20 minutes apart followed by a reassessment of peak expiratory flow and symptoms may be safely employed at home. Administration using a hand-held metered-dose inhaler with a spacer device is at least equivalent to nebulized beta<sub>2</sub> agonist therapy in children and adults. In the ambulatory and emergency department settings, the goals of treatment are correction of severe hypoxemia, rapid reversal of airflow obstruction, and reduction of the risk of relapse. Multiple doses of inhaled anticholinergic medication combined with beta<sub>2</sub> agonists improve lung function and decrease hospitalization in school-age children with severe asthma exacerbations. Intravenous magnesium sulfate has been shown to significantly increase lung function and decrease the necessity of hospitalization in children. The administration of systemic corticosteroids within one hour of emergency department presentation decreases the need for hospitalization, with the most pronounced effect in patients with severe exacerbations. Airway inflammation can persist for days to weeks after an acute attack; therefore, more intensive treatment should be continued after discharge until symptoms and peak expiratory flow return to baseline. 2011 American Academy of Family Physicians.
Source: EMBASE
Available in fulltext from American Family Physician at EBSCOhost

22. Randomized Controlled Trial of a Breath-Actuated Nebulizer in Pediatric Asthma Patients in the Emergency Department.

Author(s) Sabato, Katie, Ward, Priscilla, Hawk, William, Gildengorin, Virginia, Asselin, Jeanette M.
Citation: Respiratory Care, 01 June 2011, vol./is. 56/6(761-770), 00201324
Publication Date: 01 June 2011
Abstract: BACKGROUND: Bronchodilator treatment for asthma can be provided with various aerosol-generating devices and methods. There have been no randomized trials of a breath-actuated nebulizer versus continuous 1-hour nebulization and/or small-volume constant-output nebulizer in pediatric asthma patients. METHODS: We conducted a randomized study of one-time albuterol treatment with the AeroEclipse breath-actuated
nebulizer versus standard therapy (single treatment via small-volume nebulizer or 1-hour of continuous nebulized albuterol) in pediatric asthma patients in the emergency department. Eligible patients were those admitted to the emergency department, 0 months to 18 years of age, who presented with asthma or wheezing. We assessed all the patients with our clinical asthma scoring system and peak-flow measurement if possible. We stratified the patients by clinical asthma score and weight, and then randomized them to receive their initial albuterol treatment in the emergency department via either AeroEclipse or standard therapy. We recorded time in the emergency department, change in clinical asthma score, need for additional bronchodilator treatments, need for admission, patient response, ability to actuate the AeroEclipse, and adverse effects.

RESULTS: We enrolled 149 patients between October 14, 2004 and November 11, 2005, and we randomized 84 patients to AeroEclipse and 65 to standard therapy. The cohort's average age was 5.5 years. There were no significant differences in demographics. The initial mean clinical asthma scores were 5.1 ± 2.4 in the AeroEclipse group, and 5.1 ± 2.1 in the standard-therapy group. Time in the emergency department was not different (AeroEclipse 102 min, standard therapy 125 min, P = .10), but the AeroEclipse group had a significantly greater improvement in clinical asthma score (1.9 ± 1.2 vs 1.2 ± 1.4, P = .001) and respiratory rate (P = .002), and significantly lower admission rate (38% vs 57%, P = .03). There was no difference in adverse effects.

CONCLUSIONS: Although AeroEclipse did not reduce the time in the ED, it significantly improved clinical asthma score, decreased admissions, and decreased respiratory rate.

Source: CINAHL
Available in fulltext from Respiratory Care at Highwire Press

23. Reversal of acute sequential beta-blocker and histamine induced bronchoconstriction

Author(s) Short P.M., Williamson P.A., McKinlay L., Lipworth B.J.

Citation: American Journal of Respiratory and Critical Care Medicine, May 2011, vol./is. 183/1 MeetingAbstracts, 1073-449X (01 May 2011)

Publication Date: May 2011

Abstract: Rationale Beta-blockers are contraindicated for patients with asthma because they can cause bronchoconstriction after acute dosing. Prior to embarking on a double blinded randomised controlled trial to evaluate the therapeutic potential of chronic dosing with propranolol and its effects on AHR, we wished to investigate the safety of first dose exposure to propranolol in asthmatics who were subsequently challenged with histamine to mimic recovery from an acute exacerbation. Methods Mild-moderate-persistent stable asthmatics taking <=1000mug day budesonide or equivalent performed a randomised double blinded controlled trial. After receiving 10mg or 20mg of oral propranolol, patients were administered either 400mg of hydrocortisone i.v or placebo (as 10ml of saline i.v) on separate days, and then underwent histamine bronchial challenge testing (PC10) immediately followed by recovery to nebulised salbutamol 5mg and ipratropium 0.5mg. Spirometry, impulse oscillometry (airway resistance @5Hz : R5), and heart rate were recorded (see fig1). (Figure presented) Results 13 patients completed per protocol. 11 patients had < 10% fall in FEV1 after 10mg of propranolol and subsequently were given 20mg. There were no significant differences at any time points when comparing the respective visits for iv hydrocortisone vs iv saline - ie. steroid did not potentiate the effect of salbutamol FEV1 recovery. For the hydrocortisone visit there was a non significant fall in FEV1% predicted post propranolol, whilst at the placebo visit a significant fall of 4.7% was observed at 2 hours post propranolol. There was however a significant increase in R5% predicted at 2 and 4 hours post propranolol on both visits, with a mean increase of 31.3% on the placebo visit at 2 hours (p=0.008). On both visits FEV1% predicted at 2 and 4 hours post propranolol on both visits, with a mean increase of 31.3% on the placebo visit at 2 hours (p=0.04). On both visits FEV1% returned to baseline values after nebulised salbutamol and ipratropium bromide post histamine challenge (see table 1). Heart rate was significantly lower 2 hours post propranolol at the hydrocortisone (mean change 20bpm, p<0.001) and saline visits (mean change 16bpm, p<0.001). (Figure presented) Conclusions We have demonstrated that a single dose of oral propranolol caused a small but significant deterioration in airway calibre, which was more evident with impulse oscillometry rather than spirometry. Moreover nebulised salbutamol and ipratropium produced a full recovery of FEV1 and airway resistance after subsequent acute histamine induced bronchoconstriction.
bronchoconstriction. Since the greatest risk of beta-blockade is after 1st dose exposure we are now proceeding to evaluate effects of chronic dosing with propranolol with concurrent tiotropium, given that beta-2 receptor up regulation will also have occurred.

Source: EMBASE

24. A comparative study of efficacy and safety of arformoterol and salbutamol nebulization as rescue therapy in acute non-severe asthma

Author(s) Das S.K., Biswas I., Bandyopadhyay A.K., Bairagya T.D., Bhattacharya S.

Citation: Indian Journal of Pharmacology, May 2011, vol./is. 43/4(463-465), 0253-7613;1998-3751 (May 2011)

Publication Date: May 2011

Abstract: Arformoterol, a long-acting beta-2 agonist, has a rapid onset and long duration of action. Its role as rescue medication in acute asthma attack is undetermined. To compare the efficacy and tolerability of arformoterol with salbutamol nebulization, a study was conducted among 50 patients with acute non-severe asthma. Patients were randomly assigned to group 1 (n = 25) and group 2 (n = 25) who received three doses of salbutamol and arformoterol nebulization, respectively, at 20-min intervals. The peak expiratory flow rate (PEFR) was measured at the baseline and 5 min after each dose. The demographics and baseline characteristics were comparable between the two groups. The mean PEFR significantly increased in both these groups when compared with the baseline. The increases in the PEFR in two groups were similar after the third dose. The adverse effects in both these groups were minor. Arformoterol was as effective and safe as salbutamol in acute non-severe asthma.

Source: EMBASE

Available in fulltext from Indian Journal of Pharmacology at National Library of Medicine

25. Comparison of salbutamol efficacy in children- via themetered-dose inhaler (MDI) with Volumatic spacer and via the dry powder inhaler, Easyhaler, with the nebulizer - in mild to moderate asthma exacerbation: A multicenter, randomized study

Author(s) Direkwatanachai C., Teeratakulpisarn J., Suntornlohanakul S., Trakultivakorn M., Ngamphaiboon J., Wongpitoon N., Vangveeravong M.

Citation: Asian Pacific Journal of Allergy and Immunology, March 2011, vol./is. 29/1(25-33), 0125-877X;2228-8694 (March 2011)

Publication Date: March 2011

Abstract: Background: beta<sub>2</sub> agonist administered via nebulizer is the standard treatment for acute asthma exacerbation. There are some limitations for the use of nebulization. We conducted a study to determine the efficacy of salbutamol administered via the pMDI with Volumatic<sup></sup> spacer and the Easyhaler<sup></sup>(DPI) compared to nebulization in mild to moderate asthma exacerbations in children. Methods: A multicenter, randomized, controlled study was conducted in children between 5 and 18 years of age who presented at an emergency or outpatient department. They were randomized to receive either 6 puffs of salbutamol via the pMDI with Volumatic<sup></sup> spacer, or via the Easyhaler<sup></sup>, or 0.15 mg/kg of salbutamol nebulized via oxygen (or compressed air). The primary outcome was the clinical response which was assessed using the modified Wood's asthma score. The secondary outcomes were: hospitalization, asthma revisit within 3 days, systemic corticosteroid use and adverse events. The clinical score, oxygen saturation, PR, RR, BP and adverse events were recorded at time 0 (before treatment) and 20, 40 and 60 minutes after drug administration. Results: There were no statistically significant differences in the clinical response between the three groups at the 1<sup>st</sup>, 2<sup>nd</sup> or 3<sup>rd</sup> dose or for the SpO<sub>2</sub> or the respiratory rate while the children in the Easyhaler<sup></sup> group had significantly less tachycardia after the 2<sup>nd</sup> dose. No significant adverse events were noted among the three groups. Conclusions: Salbutamol administered via pMDI with Volumatic<sup></sup> spacer or DPI (Easyhaler<sup></sup>) areas effective as salbutamol given via a
nebulizerin providing effective relief of mild to moderate severity acute asthma exacerbation in children between 5 and 18 years of age.

Source: EMBASE

26. Testing of nebulizers for delivering magnesium sulfate to pediatric asthma patients in the emergency department

Author(s) Coates A.L., Leung K., Vecellio L., Schuh S.

Citation: Respiratory Care, March 2011, vol./is. 56/3(314-318), 0020-1324;1943-3654 (March 2011)

Publication Date: March 2011

Abstract: BACKGROUND: As the use of intravenous magnesium sulfate (MgSO$_4$) for the treatment of refractory asthma is becoming more common, the incidence of MgSO$_4$-related systemic hypotension is also rising. One option is to deliver MgSO$_4$ via aerosol, but compared to most inhaled medications, which are active in the microgram dose range, the MgSO$_4$ dose requirement is in the milligram range. This, along with inefficient aerosol delivery systems, may be the reason that some studies have found lack of efficacy with aerosol MgSO$_4$. In preparation for a multicenter study of inhaled MgSO$_4$ in asthmatic children 2-17 years old, we conducted an in vitro study to choose the best MgSO$_4$ nebulizer system that would be effective over the entire age range.

METHODS: We tested the Pari LC Star jet nebulizer, Omron MicroAir vibrating-mesh nebulizer, and the Aeroneb Go vibrating-mesh nebulizer with the Idehaler valve-less holding chamber. Aerosol delivery was via face mask. RESULTS: The Pari LC Star had an appropriate particle size distribution but a very slow aerosol output rate. The Omron MicroAir had an even slower output rate and a larger particle size distribution, which would be inappropriate for smaller children. In vitro lung deposition with the Aeroneb Go with Idehaler was 16.0 +/- 0.4 mg/min in older children and approximately a fifth of that in toddlers. CONCLUSIONS: The Aeroneb Go with Idehaler was chosen for the multicenter clinical study. 2011 Daedalus Enterprises.

Source: EMBASE

Available in fulltext from Respiratory Care at Highwire Press

27. Efficacy of racemic albuterol versus levalbuterol used as a continuous nebulization for the treatment of acute asthma exacerbations: A randomized, double-blind, clinical trial

Author(s) Wilkinson M., Bulloch B., Garcia-Filion P.A.M., Keahey L.

Citation: Journal of Asthma, March 2011, vol./is. 48/2(188-193), 0277-0903;1532-4303 (March 2011)

Publication Date: March 2011

Abstract: Objective. To compare racemic albuterol (RAC) with levalbuterol (LEV) in continuous form for the treatment of acute pediatric asthma exacerbations in the emergency department. Study design. Children between the ages of 6 and 17 inclusive were enrolled if they had a history of asthma, presented to the emergency department with an acute asthma exacerbation, and had an initial forced expiratory volume in 1 second (FEV1) <70% predicted. Patients were then randomized to receive either 7.5 mg of RAC or 3.75 mg of LEV over 1 hour, in addition to standard asthma therapies. Spirometry and asthma scoring were performed at the end of the first hour, and a second hour-long nebulization with the same drug was administered if deemed necessary. Spirometry and asthma scoring were again performed and the final disposition was recorded. As a second, optional part of the study, baseline serum albuterol levels were collected on some patients before treatment. Results. A total of 99 patients completed the study (44 RAC and 55 LEV). Baseline characteristics were similar except that the RAC group had a higher baseline asthma score. Children in the RAC group had a greater improvement in their FEV1 (p = .043) as well as in their asthma scores (p = .01) after 1 hour of continuous treatment compared to the LEV group. The greater improvement in asthma scores was maintained
after the second hour of continuous therapy in the RAC group (p = .008) but not for FEV1 measurements (p = .57). There were no differences between groups for changes in heart rate, respiratory rate, oxygen saturation, or rates of admission. Conclusions. At the doses used, RAC appears to be superior to LEV with respect to changes in FEV1 and asthma score. There was no significant difference between the drugs with respect to admission rates or side-effect profile. Copyright 2011 Informa Healthcare USA, Inc.

Source: EMBASE
Available in fulltext from Journal of Asthma at EBSCOhost

28. Efficacy and cost comparisons of bronchodilator administration between metered dose inhalers with disposable spacers and nebulizers for acute asthma treatment

Author(s) Dhuper S., Chandra A., Ahmed A., Bista S., Moghekar A., Verma R., Chong C., Shim C., Cohen H., Choksi S.
Citation: Journal of Emergency Medicine, March 2011, vol./is. 40/3(247-255), 0736-4679 (March 2011)
Publication Date: March 2011
Abstract: Background: Despite demonstration of equivalent efficacy of beta agonist delivery using a metered dose inhaler (MDI) with spacer vs. nebulizer in asthma patients, use of a nebulizer remains standard practice. Objectives: We hypothesize that beta agonist delivery with a MDI/disposable spacer combination is an effective and low-cost alternative to nebulizer delivery for acute asthma in an inner-city population. Methods: This study was a prospective, randomized, double-blinded, placebo-controlled trial with 60 acute asthma adult patients in two inner-city emergency departments. Subjects (n = 60) received albuterol with either a MDI/spacer combination or nebulizer. The spacer group (n = 29) received albuterol by MDI/spacer followed by placebo nebulization. The nebulizer group (n = 29) received placebo by MDI/spacer followed by albuterol nebulization. Peak flows, symptom scores, and need for rescue bronchodilator were monitored. Median values were compared with the Kolmogorov-Smirnov test. Results: Patients in the two randomized groups had similar baseline characteristics. The severity of asthma exacerbation, median peak flows, and symptom scores were not significantly different between the two groups. The median (interquartile range) improvement in peak flow was 120 (75-180) L/min vs. 120 (80-155) L/min in the spacer and nebulizer groups, respectively (p = 0.56). The median improvement in the symptom score was 7 (5-9) vs. 7 (4-9) in the spacer and nebulizer groups, respectively (p = 0.78). The median cost of treatment per patient was $10.11 ($10.03-$10.28) vs. $18.26 ($9.88-$22.45) in the spacer and nebulizer groups, respectively (p < 0.001). Conclusion: There is no evidence of superiority of nebulizer to MDI/spacer beta agonist delivery for emergency management of acute asthma in the inner-city adult population. MDI/spacer may be a more economical alternative to nebulizer delivery.
Source: EMBASE

29. Evaluation of non-invasive ventilation in management of acute severe asthma

Author(s) Chaudhry D., Indora M., Sangwan V., Sehgal I.P.S., Chaudhry A.
Citation: Thorax, December 2010, vol./is. 65/(A32-A33), 0040-6376 (December 2010)
Publication Date: December 2010
Abstract: Objectives To study the role of non-invasive positive pressure ventilation (NIPPV) in management of acute severe asthma. Study design Open randomised controlled trial. Methods 50 patients of acute severe asthma having asthma for at least 1 year duration with exacerbation of less than 7 days duration, FEV<sub>1</sub> <50% of predicted, respiratory rate of >25 breaths/min and pulse rate >110/min after half hour of 5 mg nebulised salbutamol were included in the study over 1 year. Patients with known COPD, history of smoking >10 years, HR >140/min, systolic BP <90 mm Hg, facial deformity, pulmonary oedema, pneumonia and pregnancy were excluded. Patients were divided into two groups A and B. All patients received nebulisation with salbutamol 5 mg and ipratropium bromide 0.5 mg and hydrocortisone 100 mg IV at zero hour and later 5 mg
salbutamol with small volume oxygen driven nebuliser @ 6 l/min at 1, 2, 3, 5 h of the study. Group B patients were given NIV support in addition to medical therapy for 6 h. All patients received O2 at 6e6 l/min for 6 h. NIV and medical treatment were stopped after 6 h. Spirometry, ABG, respiratory rate (RR), accessory muscles of respiration (AMR) and Borg dyspnoea score were assessed at 0, 1, 3, 6 and 7th hour of study. Results: Out of 308 patients 246 were excluded because of nonfulfillment of inclusion criteria. Eight patients refused consent, three had pneumonia and claustrophobia to mask respectively. One patient deteriorated in Group A and was withdrawn. The use of accessory muscles of respiration (AMR) reduced significantly in group B at 3, 6 and 7 h (p<0.01), BORG dyspnoea score improved significantly (p<0.01) in group B after 1 h. There was no difference between two groups in terms of improvement in RR, HR, FEV/sub>1</sub> and ABG. In group B, the mean IPAP and EPAP used was 14.3260.945 and 7.1660.472 cm of water, respectively. Conclusion: The use of NIPPV in patients with acute severe asthma though found to be useful in terms of faster resolution of dyspnoea and decrease in use of AMR but did not improve pulmonary functions significantly.

Source: EMBASE
Available in fulltext from Thorax at Highwire Press

30. The efficacy of nebulized salbutamol, hypertonic saline and salbutamol/hypertonic saline combination in first bronchiolitis attack

Author(s) Sezer G.R., Bozaykut A., Ipek I.O., Uyur E., Seren P.L., Paketci C.

Citation: Acta Paediatrica, International Journal of Paediatrics, December 2010, vol./is. 99/(114), 0803-5253 (December 2010)

Publication Date: December 2010

Abstract: Introduction: The mainstay of treatment in bronchiolitis includes supportive care, maintenance of hydration, oxygenation and follow-up for possible complications. Since the symptoms resemble asthmatic attacks, the first choice becomes nebulized bronchodilators in clinical practice although the place of nebulized bronchodilators in treatment is controversial. Purpose: We aimed to compare the efficacy of nebulized salbutamol, nebulized hypertonic (3%) saline and salbutamol/ hypertonic saline combination in the treatment of bronchiolitis in the emergency department. Material and methods: One hundred and twenty infants admitted to emergency department for their first bronchiolitis attack were included in this randomised, doubleblind, prospective study. Infants were grouped according to the nebulized treatment they received: group I - salbutamol + saline, group II - salbutamol + hypertonic saline, group III- hypertonic saline, group IV - saline. Results: The mean values of posttreatment breath count per minute, oxygen saturation, corticosteroid usage and hospitalization ratio were not statistically different among the groups. Breath counts per minute were significantly decreased after the treatment in all groups (P = 0.005, P = 0.0001, P = 0.0001, P = 0.004, respectively). The mean clinical scores after the treatment were lower in all groups (P = 0.0001). In group I, improvement percentage in breath count values and clinical scores were significantly low among infants without the family history of atopy (P = 0.019, P = 0.021, respectively). Differently, in groups III and IV, improvement percentage in breath count values and clinical scores were significantly high among infants with the family history of atopy (P = 0.023, P = 0.0001, respectively). Conclusions: In conclusion, in infants with the history of atopy, improvement percentage of breath counts and clinical scores are higher with nebulized salbutamol + saline treatment than saline and HS treatments. Moreover, nebulized saline and HS improved the breath count and clinical score values in infants without history of atopy. So, salbutamol could be accepted as 'effective' in the first bronchiolitis attack of infants with the history of atopy.

Source: EMBASE
Available in fulltext from Acta Paediatrica at EBSCOhost

31. Management of exercise-induced bronchospasm in adolescents with asthma.

Author(s) Morris KJ
Citation: Nurse Practitioner, 01 December 2010, vol./is. 35/12(18-27), 03611817

Abstract: Physical activity in persons with asthma is important at any age but even more so in adolescents. Collaboration between the nurse practitioner and adolescent is essential to develop an asthma management plan that will provide for optimal physical activity and prevent asthma exacerbations while exercising.

Source: CINAHL

32. Apical ballooning syndrome in a male with status asthmaticus; role of exogenous beta 2 agonists in reversible cardiomyopathy

Author(s) Salahuddin F.F., Agarunov L., Sloane P.

Citation: American Journal of Respiratory and Critical Care Medicine, May 2010, vol./is. 181/1 MeetingAbstracts, 1073-449X (01 May 2010)

Abstract: Apical ballooning syndrome (ABS), also known as takotsubo cardiomyopathy is a reversible left ventricular dysfunction thought to be precipitated by exaggerated sympathetic stimulation. It was first reported by Dote and colleagues in the Japanese literature in 1991 in a review of five cases which highlighted severe psychological stressors as the major precipitating factor in this syndrome. Status epilepticus and subarachnoid hemorrhage are also now established independent etiologies for this phenomenon in patients without coronary artery disease. We report a case of reversible ABS in a 50-year-old male presenting with status asthmaticus who quickly underwent intubation. Before running out of inhalers just prior to the emergency admission, he was using albuterol sulfate metered dose inhaler 2 puffs (90 mcg each) and 3 ml (2.5 mg) of inhalation solution in a nebulizer at least every two hours, perhaps as frequently as every 15 minutes. It was confirmed that he had consumed 1 month's prescriptions of inhaler as well as nebulizer forms of albuterol sulfate in less than 1 week. Following intubation and admission, he had ST elevation in precordial leads with mild cardiac enzyme leak. Subsequent cardiac catheterization revealed akinetic anteroseptal and apical wall segments with a hypokinetic left ventricle. No obstructive coronary artery disease was seen. Three days later there was marked clinical improvement, patient was extubated, and repeat echocardiography revealed a return to normal ventricular size and systolic function with complete resolution of apical ballooning. Our case demonstrates that excess use of beta-agonists may be associated with and raises the possibility of beta-receptor mediated cardiotoxicity in the absence of severe psychological stress. The case also highlights that apical ballooning syndrome may develop in male asthmatics, even though it has been predominantly reported in women.

Source: EMBASE

33. Comparative study on the efficacy of procaterol and salbutamol nebulizing solutions in mild and moderate asthma exacerbations in children

Author(s) Arellano M.A., Jiao A.

Citation: American Journal of Respiratory and Critical Care Medicine, May 2010, vol./is. 181/1 MeetingAbstracts, 1073-449X (01 May 2010)

Abstract: Objectives: This study was undertaken to compare the efficacy of inhaled procaterol and inhaled salbutamol in the management of mild and moderate asthma exacerbations in children aged 6 to 18 years. Design: Randomized, double-blind clinical trial Setting: Emergency room and out-patient department of the Philippine Children's Medical Center. Participants: Asthmatic children aged 6 to 18 years with mild and moderate asthma attacks. Methodology: Treatment was allocated randomly to 44 patients. Group1 received salbutamol nebulizing solution (2mg/inhalation) while group2 received procaterol nebulizing solution (20muq/inhalation) every 20 minutes for 3 doses. Peak expiratory flow rate (PEFR), Modified Wood-Downes (MWD) clinical asthma score, heart rates, and respiratory rates were re-assessed after the 3rd nebulization and at hourly intervals until
the 8th hour. The need for additional treatment and adverse effects were determined. Results: Mean percent predicted PEFR normalized and mean percent change in PEFR increased and were comparable in both groups until the 2nd hour. The procaterol group exhibited higher PEFR levels after the 3rd hour up to the 7th hour and these were significant after the 3rd hour (p<0.05). The duration of action of procaterol was at least 6 to 8 hours and 4 to 6 hours for salbutamol. Significant reduction in the MWD clinical asthma scores was noted in the procaterol group after the 4th hour. There was also a significant reduction in respiratory rates and lesser increase in heart rates in the procaterol group. All patients in the salbutamol group needed additional treatment compared to 8 patients (36.4%) in procaterol group. Less adverse effects were observed in patients given procaterol (86.4%). All patients were discharged. Conclusion/Recommendation: Inhaled salbutamol and inhaled procaterol were both efficacious in mild to moderate asthma exacerbation in children. Procaterol is safe and showed better and prolonged bronchodilator response. Thus, procaterol nebulizing solution can be used in the management of mild and moderate asthma exacerbations. Subsequent frequency of drug administration and longer observation time as well as its use in severe exacerbation are recommended for further study.

Source: EMBASE

34. Comparative effects of caffeine and albuterol on the bronchoconstrictor response to exercise in asthmatic athletes.

Author(s) VanHaitsma TA, Mickleborough T, Stager JM, Koceja DM, Lindley MR, Chapman R

Citation: International Journal of Sports Medicine, 01 April 2010, vol./is. 31/4(231-236), 01724622

Publication Date: 01 April 2010

Abstract: The main aim of this study was to evaluate the comparative and additive effects of caffeine and albuterol (short-acting beta (2)-agonist) on the severity of EIB. Ten asthmatic subjects with EIB (exercise-induced bronchoconstriction) participated in a randomized, double-blind, double-dummy crossover study. One hour before an exercise challenge, each subject was given 0, 3, 6, or 9 mg/kg of caffeine or placebo mixed in a flavored sugar drink. Fifteen minutes before the exercise bout, an inhaler containing either albuterol (180 microg) or placebo was administered to each subject. Pulmonary function tests were conducted pre- and post-exercise. Caffeine at a dose of 6 and 9 mg/kg significantly reduced (p<0.05) the mean maximum % fall in post-exercise FEV (1) to -9.0+/−9.2% and -6.8+/−6.5% respectively compared to the double-placebo (-14.3+/−11.1%) and baseline (-18.4+/−7.2%). There was no significant difference (p>0.05) in the post-exercise % fall in FEV (1) between albuterol (PLUS CAFFEINE PLACEBO) (-4.0+/−5.2%) and the 9 mg/kg dose of caffeine (-6.8+/−6.5%). Interestingly, there was no significant difference (p>0.05) in the post-exercise % fall in FEV (1) between albuterol (PLUS CAFFEINE PLACEBO) (-4.0+/−5.2%) and albuterol with 3, 6 or 9 mg/kg of caffeine (-4.4+/−3.8, -6.8+/−5.6, -4.4+/−6.0% respectively). Similar changes were observed for the post-exercise % fall in FVC, FEF (25−75%) and PEF. These data indicate that moderate (6 mg/kg) to high doses (9 mg/kg) of caffeine provide a significant protective effect against EIB. It is feasible that the negative effects of daily use of short-acting beta (2)-agonists by asthmatic athletes could be reduced simply by increasing caffeine consumption prior to exercise.

Source: CINAHL

35. Repeat dosing of albuterol via metered-dose inhaler in infants with acute obstructive airway disease: a randomized controlled safety trial.

Author(s) Kaashmiri M, Shepard J, Goodman B, Lincourt WR, Trivedi R, Ellsworth A, Davis AM

Citation: Pediatric Emergency Care, 01 March 2010, vol./is. 26/3(197-202), 07495161

Publication Date: 01 March 2010

Abstract: BACKGROUND: Airway obstruction and bronchial hyperactivity often times lead to emergency department visits in infants. Inhaled short-acting beta2-agonist
bronchodilators have traditionally been dispensed to young children via nebulizers in the emergency department. Delivery of bronchodilators via metered-dose inhalers (MDIs) in conjunction with holding chambers (spacers) has been shown to be effective. STUDY OBJECTIVE:: Safety and efficacy evaluations of albuterol sulfate hydrofluoroalkane (HFA) inhalation aerosol in children younger than 2 years with acute wheezing caused by obstructive airway disease. METHODS: A randomized, double-blind, parallel group, multicenter study of albuterol HFA 180 microg (n = 43) or 360 microg (n = 44) via an MDI with a valved holding chamber and face mask in an urgent-care setting. Assessments included adverse events, signs of adrenergic stimulation, electrocardiograms, and blood glucose and potassium levels. Efficacy parameters included additional albuterol use and Modified Tal Asthma Symptoms Score ([MTASS] reduction in MTASS representing improvement). RESULTS: Overall, adverse events occurred in 4 (9%) and 3 (7%) subjects in the 180-microg and 360-microg groups, respectively. Drug-related tachycardia (360 microg) and ventricular extrasystoles (180 microg) were reported in 1 patient each. Three additional instances of single ventricular ectopy were identified from Holter monitoring. No hypokalemia or drug-related QT or QTc prolongation was seen; glucose values and adrenergic stimulation did not significantly differ between treatment groups. In the 180-microg and 360-microg groups, mean change from baseline in MTASS during the treatment period was -2.8 (-49.8%) and -2.9 (-48.4%), and rescue albuterol use occurred in 4 (9%) and 3 (7%) subjects, respectively. CONCLUSIONS: Cumulative dosing with albuterol HFA 180 microg or 360 microg via MDI-spacer and face mask in children younger than 2 years did not result in any significant safety issues and improved MTASS by at least 48%.

Source: CINAHL

36. Adding osteopathic intervention may improve outcome in acute asthma exacerbation

Author(s) Karagic M., Gomez S., Wilson A., Lee-Wong M.

Citation: Journal of Allergy and Clinical Immunology, February 2010, vol./is. 125/2 SUPPL. 1(AB199), 0091-6749 (February 2010)

Publication Date: February 2010

Abstract: RATIONALE: Will adding non-traditional asthma therapies to traditional interventions improve outcome? METHODS: Patients often ask that non-pharmacologic remedies either replace or supplement their medical therapy. Previously diagnosed chronic asthmatic patients presenting to our outpatient clinic for acute asthma exacerbation were given standard traditional care including albuterol nebulizer treatments. Then, patients were offered supplemental Osteopathic Maneuver Technique (OMT) known as "rib raising." This technique has been utilized to treat children and adults with asthma to stimulate thoracic sympathetic chain ganglia to enhance respiration. Forty five adult patients consented to receive OMT. In addition to standard medical asthma therapy, they received OMT "rib raising" for five minutes. Peak flows (PF), and asthma symptom scores were obtained pre/post albuterol nebulizer and post OMT. T-test statistical analysis compared peak flows post OMT and post albuterol and OMT were compared. RESULTS: Analysis of the data using t-test at 95% CI showed a mean improvement after nebulizer treatment to be 13.64 L/min, after OMT to be 7.95 L/min, with the overall difference after both albuterol nebulizer treatment and OMT to be 14.38 L/min (p<0.05). No adverse effects were reported. All 45 patients stated feeling more "relaxed" after therapy with albuterol and OMT compared to no OMT and treatment with albuterol alone. CONCLUSIONS: Patients given both albuterol and OMT did better objectively (peak flows) and subjectively (symptom scores) than with albu- terol alone. Perhaps osteopathic treatments may be offered to supplement standard traditional asthma management in acute settings.

Source: EMBASE

37. Treatment of asthma in children

Author(s)

Citation: Journal of Investigational Allergology and Clinical Immunology, 2010, vol./is.
38. A study of serum electrolyte levels during nebulised salbutamol therapy

Author(s) Vittal B.G., Rudresha B.M., Aliya N., Priyadarshini K.S.

Citation: Journal of Clinical and Diagnostic Research, 2010, vol./is. 4/6(3460-3464), 0973-709X (2010)

Publication Date: 2010

Abstract: Background and objectives: asthma is a very common disease with immense social impact. nebulised salbutamol is the mainstay of therapy in acute severe asthma. this prospective study was done to determine the magnitude of changes in serum magnesium, Potassium, Phosphate and calcium during the treatment of acute severe asthma with nebulised salbutamol alone in a larger sample size. As previous studies were carried on a smaller sample size and yielded ambiguous results. subjects and methods: sixty patients who met the inclusion criteria were included and their baseline electrolyte levels were measured. nebulised salbutamol was administered every thirty minutes till the symptoms subsided and repeat serum levels of electrolytes were determined after 90 minutes. results: serum magnesium levels decreased significantly (p < 0.001) from 2.058 +/-0.0263 mg/dl to 2.048 +/-0.0268 mg/dl. serum potassium levels decreased from 4.053 +/-0.0485 meq/l to 3.983 +/-0.0482 meq/l (p < 0.001). serum phosphate levels decreased significantly (p < 0.001) from 3.899 +/-0.0299 mg/dl to 3.872 +/-0.0296 mg/dl. But no statistical difference was seen in the serum calcium levels. interpretation and conclusion: nebulised salbutamol therapy is associated with statistically significant decreases in serum magnesium, Potassium and phosphate levels.

Source: EMBASE


Author(s) Williams DM

Citation: Journal of Pediatric Healthcare, 01 November 2009, vol./is. 23/6(357-370), 08915245

Publication Date: 01 November 2009

Source: CINAHL

40. Levosalbutamol vs racemic salbutamol in the treatment of acute exacerbation of asthma

Author(s) Punj A., Prakash A., Bhasin A.

Citation: Indian Journal of Pediatrics, November 2009, vol./is. 76/11(1131-1135), 0019-5456 (November 2009)

Publication Date: November 2009

Abstract: Objective: To compare efficacy and tolerability of levosalbutamol (Group 1) and racemic salbutamol (Group 2) for the treatment of acute exacerbation of asthma in children age 5 to 18 yr. Methods: A randomized double blind clinical study involving 60 children was undertaken between October’ 06 to December’ 07. Results: The following baseline clinical characteristic were recorded initially and after giving 3 nebulizations at 20 min intervals in the 1st hour of presentation viz respiratory rate (RR), heart rate (HR), oxygen saturation in room air SPO2, PEFR (peak expiratory flow rate), serum K+ level and asthma score. In Group 1 patients (levosalbutamol), there was significant increment in SPO2 and PEFR (P<0.05) values with decrease in tachypnea and asthma score while no significant difference was found in pre and post treatment HR & Serum K+ levels. In Group 2 patients although there was clinical improvement in terms of SPO2 and PEFR, RR and asthma score, it resulted in significant tachycardia and
decrease in K<sup>+</sup> levels. Conclusion: Levosalbutamol appears to be more efficacious than racemic salbutamol in terms of improvement in PEFR, SPO2 and asthma score while deleterious effects of tachycardia and fall in serum K<sup>+</sup> were seen with racemic salbutamol. 2009 Dr. K C Chaudhuri Foundation.

**Source:** EMBASE

41. Beneficial Effects of Warmed Humidified Oxygen Combined with Nebulized Albuterol and Ipratropium in Pediatric Patients with Acute Exacerbation of Asthma in Winter Months

**Author(s)** Nibhanipudi K., Hassen G.W., Smith A.

**Citation:** Journal of Emergency Medicine, November 2009, vol./is. 37/4(446-450), 0736-4679 (November 2009)

**Publication Date:** November 2009

**Abstract:** Background: The objective of this study was to determine whether a combination of nebulized albuterol and ipratropium with warmed humidified oxygen would be more beneficial when compared to the same combination with humidified oxygen at room temperature. Albuterol alone was tested in the same settings. Methods: All patients between 6 and 17 years of age who presented to a pediatric emergency department in the winter months with acute exacerbation of bronchial asthma were given a combination of nebulized albuterol and ipratropium with warmed or room temperature humidified oxygen. Peak flow was measured before and after the treatment. Results: Sixty patients were enrolled in the study, with 15 subjects in each group. The mean increase in peak flow in the albuterol-ipratropium with warm humidified oxygen group was 52.6, and in the albuterol-ipratropium with humidified oxygen at room temperature group, it was 26.2. The results of the albuterol with warmed humidified oxygen and with humidified oxygen at room temperature groups were 20.6 and 34.3, respectively. The differences between the groups were statistically significant. Conclusion: Our study shows that warmed humidified oxygen given along with the combination of nebulized albuterol and ipratropium is more beneficial for pediatric patients having an acute exacerbation of bronchial asthma in the winter months when compared to nebulized albuterol alone with warmed humidified oxygen, nebulized albuterol alone with room temperature humidified oxygen, or a combination of nebulized albuterol and ipratropium with room temperature humidified oxygen. 2009 Elsevier Inc. All rights reserved.

**Source:** EMBASE

42. Clinical evaluation and treatment of acute asthma exacerbations in children


**Citation:** International Journal of Immunopathology and Pharmacology, October 2009, vol./is. 22/4(867-878), 0394-6320 (October-December 2009)

**Publication Date:** October 2009

**Abstract:** This update on treatment of asthma exacerbations in children is the result of an Italian Pediatric Society Task-force, made up of a panel of experts working in 2007-2008. The aim is to give clear indications on the use of the drugs most employed in children, grading the quality of evidence and the strength of recommendations. Suggestions on their limits due to unlicensed and off-label use are reported. The level of evidence and the strength of recommendations for different therapeutic approaches demonstrate that frequently the use of drugs in children is extrapolated from the experience in adults and that more studies are required to endorse the correct use of different drugs in asthmatic children. Copyright by Biolife, s.a.s.

**Source:** EMBASE
43. High-dose continuous nebulized levalbuterol for pediatric status asthmaticus: a randomized trial.

Author(s) Andrews T, McGintee E, Mittal MK, Tyler L, Chew A, Zhang X, Pawlowski N, Zorc JJ

Citation: Journal of Pediatrics, 01 August 2009, vol./is. 155/2(205-), 00223476

Publication Date: 01 August 2009

Source: CINAHL

Available in print at Lincoln County Hospital Professional Library

44. Love it or lev it: levalbuterol for severe acute asthma--for now, leave it.

Author(s) Kercsmar CM, McDowell KM

Citation: Journal of Pediatrics, 01 August 2009, vol./is. 155/2(162-164), 00223476

Publication Date: 01 August 2009

Source: CINAHL

Available in print at Lincoln County Hospital Professional Library

45. Acute severe asthma: New approaches to assessment and treatment

Author(s) Papiris S.A., Manali E.D., Kolilekas L., Triantafillidou C., Tsangaris I.

Citation: Drugs, 2009, vol./is. 69/17(2363-2391), 0012-6667;1179-1950 (2009)

Publication Date: 2009

Abstract: The precise definition of a severe asthmatic exacerbation is an issue that presents difficulties. The term 'status asthmaticus' relates severity to outcome and has been used to define a severe asthmatic exacerbation that does not respond to andor perilously delays the repetitive or continuous administration of short-acting inhaled beta2-adrenergic receptor agonists (SABA) in the emergency setting. However, a number of limitations exist concerning the quantification of unresponsiveness. Therefore, the term 'acute severe asthma' is widely used, relating severity mostly to a combination of the presenting signs and symptoms and the severity of the cardiorespiratory abnormalities observed, although it is well known that presentation does not foretell outcome. In an acute severe asthma episode, close observation plus aggressive administration of bronchodilators (SABAs plus ipratropium bromide via a nebulizer driven by oxygen) and oral or intravenous corticosteroids are necessary to arrest the progression to severe hypercapnic respiratory failure leading to a decrease in consciousness that requires intensive care unit (ICU) admission and, eventually, ventilatory support. Adjunctive therapies (intravenous magnesium sulfate andor others) should be considered in order to avoid intubation. Management after admission to the hospital ward because of an incomplete response is similar. The decision to intubate is essentially based on clinical judgement. Although cardiac or respiratory arrest represents an absolute indication for intubation, the usual picture is that of a conscious patient struggling to breathe. Factors associated with the increased likelihood of intubation include exhaustion and fatigue despite maximal therapy, deteriorating mental status, refractory hypoxaemia, increasing hypercapnia, haemodynamic instability and impending coma or apnoea. To intubate, sedation is indicated in order to improve comfort, safety and patient-ventilator synchrony, while at the same time decrease oxygen consumption and carbon dioxide production. Benzodiazepines can be safely used for sedation of the asthmatic patient, but time to awakening after discontinuation is prolonged and difficult to predict. The most common alternative is propofol, which is attractive in patients with sudden-onset (near-fatal) asthma who may be eligible for extubation within a few hours, because it can be titrated rapidly to a deep sedation level and has rapid reversal after discontinuation; in addition, it possesses bronchodilatory properties. The addition of an opioid (fentanyl or remifentanil) administered by continuous infusion to benzodiazepines or propofol is often desirable in order to provide amnesia, sedation, analgesia and respiratory drive suppression. Acute severe asthma is characterized by severe pulmonary hyperinflation due to marked limitation of the expiratory flow. Therefore, the main objective of the initial ventilator management is 2-fold: to ensure
adequate gas exchange and to prevent further hyperinflation and ventilator-associated lung injury. This may require hypoventilation of the patient and higher arterial carbon dioxide (PaCO$_2$) levels and a more acidic pH. This does not apply to asthmatic patients intubated for cardiac or respiratory arrest. In this setting the post-anoxic brain oedema might demand more careful management of PaCO$_2$ levels to prevent further elevation of intracranial pressure and subsequent complications. Monitoring lung mechanics is of paramount importance for the safe ventilation of patients with status asthmaticus. The first line of specific pharmacological therapy in ventilated asthmatic patients remains bronchodilation with a SABA, typically salbutamol (albuterol). Administration techniques include nebulizers or metered-dose inhalers with spacers. Systemic corticosteroids are critical components of therapy and should be administered to all ventilated patients, although the dose of systemic corticosteroids in mechanically ventilated asthmatic patients remains controversial. Anticholinergics, inhaled corticosteroids, leukotriene receptor antagonists and methylxanthines offer little benefit, and clinical data favouring their use are lacking. In conclusion, expertise, perseverance, judicious decisions and practice of evidence-based medicine are of paramount importance for successful outcomes for patients with acute severe asthma.

Source: EMBASE
Available in fulltext from Drugs at EBSCOhost

46. Population pharmacodynamic model of bronchodilator response to inhaled albuterol in children and adults with asthma.

Author(s) Blake K, Madabushi R, Derendorf H, Lima J
Citation: CHEST, 01 November 2008, vol./is. 134/5(981-989), 00123692
Publication Date: 01 November 2008

Abstract: BACKGROUND: Because interpatient variability in bronchodilation from inhaled albuterol is large and clinically important, we characterized the albuterol dose/response relationship by pharmacodynamic modeling and quantified variability. METHODS: Eighty-one patients with asthma (24% African American [AA]; 8 to 65 years old; baseline FEV$_1$, 40 to 80% of predicted) received 180 mug of albuterol from a metered-dose inhaler (MDI), and then 90 mug every 15 min until maximum improvement or 540 mug was administered; all then received 2.5 mg of nebulized albuterol. FEV$_1$ was measured 15 min after each dose. The population cumulative dose/response data were fitted with a sigmoid maximum effect of albuterol (Emax) [maximum percentage of predicted FEV$_1$ effect] model by nonlinear mixed-effects modeling. The influence of covariates on maximum percentage of predicted FEV$_1$ reached after albuterol administration (Rmax) and cumulative dose of albuterol required to bring about 50% of maximum effect of albuterol (ED$_{50}$) and differences between AA and white patients were explored. RESULTS: ED$_{50}$ was 141 mug, and Emax was 24.0%. Coefficients of variation for ED$_{50}$ and Emax were 40% and 56%, respectively. Ethnicity was a statistically significant covariate (p < 0.05). AA and white patients reached 82.4% and 91.9% of predicted FEV$_1$, respectively (p = 0.0004); and absolute improvement in percentage of predicted FEV$_1$ was 16.6% in AA patients vs 26.7% in white patients (p < 0.0003). There were no baseline characteristic differences between AA and white patients. Nebulized albuterol increased FEV$_1$ $\geq$ 200 mL in 21% of participants. Heart rate and BP were unchanged from baseline after maximal albuterol doses. CONCLUSIONS: Our model predicts that 180 mug of albuterol by MDI produces a 14.4% increase in percentage of predicted FEV$_1$ over baseline (11.7% in AA patients, and 17.5% in white patients). Emax varies widely between asthmatic patients. AA patients are less responsive to maximal doses of inhaled albuterol than white patients.

Source: CINAHL
Available in print at Grantham Hospital Staff Library
Available in fulltext at Chest; Notes: Username: ULHTKIS/Password: Library
47. Nebulization therapy for asthma: A practical guide for the busy pediatrician

Author(s) Welch M.J.

Citation: Clinical Pediatrics, October 2008, vol./is. 47/8(744-756), 0009-9228 (October 2008)

Publication Date: October 2008

Source: EMBASE

Available in fulltext from Clinical Pediatrics at EBSCOhost

48. When breathing goes bad.

Author(s) Waddell B

Citation: EMS Magazine, 02 September 2008, vol./is. /(2-3), 19464967

Publication Date: 02 September 2008

Source: CINAHL

49. Effects of acute salbutamol inhalation on quadriceps force and fatigability.

Author(s) Decorte N, Verges S, Flore P, Guinot M, Wuyam B

Citation: Medicine & Science in Sports & Exercise, 01 July 2008, vol./is. 40/7(1220-1227), 01959131

Publication Date: 01 July 2008

Abstract: INTRODUCTION: Oral beta2-agonist administration improves muscle function in persons without asthma. We performed a double-blind, randomized, controlled crossover study to assess whether acute inhaled salbutamol administration improves muscle strength and fatigability in healthy moderately trained subjects. METHODS: Quadriceps muscle strength was measured during maximal voluntary contraction (MVC) and femoral nerve magnetic stimulation (potentiated single twitch, TwQpeak) before and after (i) a maximal incremental cycling test (n = 10) and (ii) 50 maximal isometric one-leg extensions (n = 9). Each exercise test was performed on three occasions, after salbutamol (200 and 800 microg) or placebo inhalation. RESULTS: Before exercise, treatments had no significant effect on MVC [(placebo) 597 +/- 146 N vs (200 microg) 629 +/- 151 N vs (800 microg) 610 +/- 148 N] and TwQpeak [(placebo) 215 +/- 83 N vs (200 microg) 227 +/- 69 N vs (800 microg) 250 +/- 84 N]. Maximal power during cycling and maximal force during leg extensions did not differ between treatments. Treatments had no effect on MVC and TwQpeak reductions at 30 min [MVC: (placebo) -8 +/- 9% vs (200 microg) -9 +/- 7% vs (800 microg) -8 +/- 5%; TwQpeak: (placebo) -29 +/- 13% vs (200 microg) -23 +/- 15% vs (800 microg) -20 +/- 8%] and 60 min [MVC: (placebo) -12 +/- 17% vs (200 microg) -6 +/- 9% vs (800 microg) -8 +/- 8%; TwQpeak: (placebo) -20 +/- 21% vs (200 microg) -19 +/- 23% vs (800 microg) -8 +/- 7%] after cycling. Similarly, reductions in MVC and TwQpeak were not significantly different between treatments at 30 [MVC: (placebo) -11 +/- 9% vs (200 microg) -12 +/- 7% vs (800 microg) -8 +/- 16%; TwQpeak: (placebo) -37 +/- 12% vs (200 microg) -33 +/- 20% vs (800 microg) -32 +/- 16%] and 60 min [MVC: (placebo) -10 +/- 11% vs (200microg) -11 +/- 6% vs (800 microg) -8 +/- 20%; TwQpeak: (placebo) -30 +/- 11% vs (200 microg) -28 +/- 24% vs (800 microg) -27 +/- 15%] after leg extensions. Treatments did not modify maximal voluntary activation at any time of the protocol. CONCLUSION: Acute therapeutic or supratherapeutic doses of inhaled salbutamol have no effect on quadriceps strength, fatigue, and recovery in men without asthma.

Source: CINAHL

50. Formoterol fumarate inhalation powder vs albuterol nebulizer for the treatment of asthma in the acute care setting

Author(s) Lee-Wong M., Chou V., Ogawa Y.

Citation: Annals of Allergy, Asthma and Immunology, February 2008, vol./is. 100/2(146-
Abstract: Background: Although albuterol remains the standard treatment for asthma in the emergency department, formoterol fumarate may be more advantageous, with its rapid and long-lasting bronchodilation. Objective: To compare formoterol fumarate with albuterol in controlling acute asthma exacerbation. Methods: Patients aged 18 to 65 years who presented to the emergency department with mild to moderate asthma exacerbation (peak expiratory flow rate [PEFR], 40%-60% of predicted) were randomized to receive either formoterol fumarate aerolizer (12 mg) or albuterol nebulizer (2.5 mg) every 30 minutes up to 2 treatments. Symptom scores and PEFRs were measured at each treatment. Results: Thirty-four patients (19 in the albuterol arm and 15 in the formoterol fumarate arm) were enrolled. At 30 and 60 minutes, the mean PEFR of the albuterol group increased from 43.7% of predicted to 51.9% of predicted and 54.6% of predicted, respectively, and the formoterol fumarate group had changes in the mean PEFR from 49.3% of predicted to 55.5% of predicted and 57.3% of predicted, respectively, and the mean change in the 2 groups was not significantly different at 30 and 60 minutes (P = .64 and .57, respectively, by t test). The albuterol group improved in symptom scores by 3.7 and 5.5 from 0 minutes to 30 and 60 minutes, respectively, and in the formoterol fumarate group these values were 3.1 and 4.9 at 30 and 60 minutes, respectively, and the mean change in the 2 groups was not significantly different at 30 and 60 minutes (P = .61 and .76, respectively, by t test). Conclusion: Formoterol fumarate is as effective as albuterol inhalation for the treatment of adults with mild to moderate asthma exacerbations in the acute care setting.

Source: EMBASE

51. Comparison of levalbuterol and racemic albuterol in hospitalized patients with acute asthma or COPD: A 2-week, multicenter, randomized, open-label study


Citation: Clinical Therapeutics, 2008, vol./is. 30/PART 1(989-1002), 0149-2918;1879-114X (2008)

Publication Date: 2008

Abstract: Background: The National Heart, Lung, and Blood Institute guideline recommends that dosing racemic albuterol be administered every 1 to 4 hours for treating patients with asthma or chronic obstructive pulmonary disease (COPD) in the hospital. Previously published preliminary and retrospective studies suggested that levalbuterol can be administered every 8 hours for the treatment of bronchoconstriction in hospitalized patients. However, it is unclear how the different dosing regimens affect the total number of nebulizations (scheduled plus as-needed treatments) and the costs of treatment of bronchoconstriction in a hospital setting. Moreover, it is not clear how the different dosing regimens affect symptom outcomes and health status in hospitalized patients with asthma or COPD. Objective: The aim of this study was to evaluate these issues in hospitalized patients with acute asthma or COPD. Methods: In this prospective, multicenter, randomized, open-label study, hospitalized patients aged >=18 years were randomly assigned to receive 14-day treatment with levalbuterol 1.25 mg q6-8h or racemic albuterol 2.5 mg q1-4h, administered per routine hospital practice at each institution. The primary efficacy end point was total number of nebulizations during hospitalization. Pulmonary function, symptom evaluation [subject general well-being score [SGWB], disease symptom assessment [DSA], and beta-mediated adverse effect scores], hospital costs (excluding medication costs) and hospital length of stay (LOS) were also evaluated. Results: In the intent-to-treat population (n = 479; levalbuterol, 241;racemic albuterol, 238), the mean (SE) age was 55.3 (16.9) years, the majority of patients were white (57.8%), and the mean (SE) weight was 80.9 (24.5) kg. Demographic characteristics were similar between the 2 treatment groups, except that there were more females with COPD in the levalbuterol treatment group (63.8%) compared with the racemic albuterol treatment group (57.8%) (P = 0.005). Patients treated with levalbuterol required significantly fewer median total nebulizations (10 vs 12; P = 0.031) and scheduled nebulizations (9 vs 11; P = 0.009) compared with those in the racemic albuterol group. The 2 treatment groups required 0 rescue nebulizations. Mean (SD) forced expiratory volume in 1 second improved from baseline with both levalbuterol and racemic albuterol (0.06 [0.43] and 0.10 [0.37] L, respectively); these improvements were maintained throughout the hospital stay (0.11
and 0.16 L). DSA and SGWB scores improved significantly from baseline in both treatment groups, and beta-mediated adverse effects mean scores were significantly greater with levalbuterol versus racemic albuterol (P < 0.001). In the levalbuterol and racemic albuterol treatment groups, hospital LOS (70.6 and 65.7 hours, respectively), time to discharge (66.0 and 62.8 hours), and total hospital costs (least squares mean [SE], US $4869.30 [$343.58] and $4899.41 [$343.20]) were similar. Conclusions: In these hospitalized patients with acute asthma or COPD treated with levalbuterol every 6 to 8 hours or racemic albuterol every 1 to 4 hours, significantly fewer total nebulizations were required with levalbuterol, without an increased need for rescue nebulizations during 14 days of hospitalization. Both treatments were associated with improvements from baseline in symptoms and health status. The costs of treating bronchoconstriction in hospitalized patients were similar between the levalbuterol and racemic albuterol groups. 2008 Excerpta Medica Inc. All rights reserved.

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