**Data tables**

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| **Author;**  **Year Published**  **(References)** | **Study Type** | **Setting** | **Population** | **Intervention** | **Comparison** | **Outcomes** | **Results/Key findings Related to Harm** |
| DaCruz D, Holburn C. Serum potassium responses to nebulized salbutamol administered during an acute asthmatic attack. Arch Emerg Med. 1989 Mar;6(1):22-6. doi: 10.1136/emj.6.1.22. PMID: 2712984; PMCID: PMC1285553. | Case series | Emergency department (ED) in Leicester England | 20 patients with a mean age of 39 years (range not given) who were treated in the ED with nebulized salbutamol for “reversible airways disease.” | 5 mg of nebulized salbutamol | NA | Primary:  Hypokalemia | 8 patients had a decrease in serum potassium concentration by >0.3 mmol/L.  The greatest drop was 1 mmol/L with a mean on 0.54 mmol/L.  Two patients had an increase in serum potassium concentration of 0.3 mmol/L and 1.3 mmol/L, respectively. |
| Duarte M, Camargos P. Efficacy and safety of a home-made non-valved spacer for bronchodilator therapy in acute asthma. Acta Paediatr. 2002;91(9):909-13. doi: 10.1080/080352502760272579. PMID: 12412864. | Randomized Controlled Trial | Emergency department in Juiz de Fora a, Brazil | 196 participants age 4-15 years with a history of asthma who presented to the ED with an acute mild to moderate asthma exacerbation. | Up to 3 treatments of salbutamol MDI (5 puffs of 100 mcg per puff) through a homemade  non-valved spacer at 15-minute intervals. | Salbutamol nebulization (0.15 mg/kg per dose (minimum  1.25 mg dose, maximum 5 mg dose) for 15 min. | Primary:  Clinical parameters (asthma clinical score, heart rate, respiratory rate, electrocardiogram, peak expiratory flow rate, venous blood gas analysis, potassium level, cAMP, levels). | Side effects were reported in 17.2% of the nebulizer group and in  4.1% of the MDI group (p = 0.003).  Side effects included generalized muscle tremors, pallor, hand  tremors, headache, palpitation, vomiting, dizziness and extrasystoles on cardiac auscultation.  There was an increase in HR in both groups but the number of beats per min was similar in both groups  (p = 0.32). |
| Hung CH, Chu DM, Wang CL, Yang KD. Hypokalemia and salbutamol therapy in asthma. Pediatr Pulmonol. 1999 Jan;27(1):27-31. Doi: 10.1002/(sici)1099-0496(199901)27:1<27::aid-ppul6>3.0.co;2-p. PMID: 10023788. | Case Series | Emergency department | 17 children age 3-14 years who presented to the ED with respiratory due to presumed asthma. | 0.125 mg/kg nebulized salbutamol. | NA | Primary:  Efficacy (peak expiratory flow rate)  Secondary:  Safety | Blood potassium concentrations before nebulization and 30 minutes after nebulization decreased from a mean of 3.80 ± 0.44 to 3.28 ± 0.44 (MD −0.52 mmol/L; p < 0.001). |
| Jerrard DA, Olshaker J, Welebob E, Caraballo V, Hooper F. Efficacy and safety of a rapid-sequence metaproterenol protocol in the treatment of acute adult asthma. Am J Emerg Med. 1995 Jul;13(4):392-5. doi: 10.1016/0735-6757(95)90121-3. PMID: 7605520. | Case Series | Academic emergency department with a described inner-city population in Baltimore, Maryland, US | 50 patients age 19-86 years (mean 38.3) with a history of asthma who presenting to the ED with an acute asthma exacerbation and had wheezing on auscultation | Three rapid sequence nebulization of 15 mg metaproterenol within a 45-minute period from the first dose. | NA | Primary:  Side effects | Baseline HR increased from 96.4 ± 2.6 beats/min to 109.62 ± 2.9 beats/min at the conclusion of three nebulizations (95% CI, 8.1, 18.3).  Systolic blood pressure increased from 136.6 ± 2.0 mm Hg to  143.5 ± 2.8 mm Hg at the end of therapy (95% CI, 2.5, 11.3).  Diastolic blood pressure decreased from 78.2 ± 1.8 mm Hg to 74.9 ± 2.1 mm Hg (95% CI, -7.2, .8). Three (6%) patients discontinued therapy because of severe tremulousness.  One (2%) patient experienced a two-minute run of supraventricular tachycardia at a rate of 200 beats/rain, which spontaneously converted to a sinus tachycardia of 115 beats/min. |
| Kenyon CC, Fieldston ES, Luan X, Keren R, Zorc JJ. Safety and effectiveness of continuous aerosolized albuterol in the non-intensive care setting. Pediatrics. 2014 Oct;134(4):e976-82. doi: 10.1542/peds.2014-0907. PMID: 25266428. | Retrospective Cohort | Pediatric inpatient unit at the Children’s Hospital of Philadelphia, Pennsylvania, US | 3003 children age 2-18 with a diagnosis of asthma who were admitted to pediatric inpatient floor and were entered in the hospitals asthma treatment pathway and treated at least every two hours with albuterol nebulizers or MDI. | Continuous albuterol nebulizers | Intermittent albuterol nebulizers or MDI | Primary:  Clinical deterioration, prolonged therapy, adverse medication effects  Secondary:  Duration of therapy, overall length of stay | Serum potassium levels <3 mEq/L or patients experiencing dysrhythmias were not statistically different between continuous and intermittent albuterol patients (12.2% vs 11.0%; p=0.74 and 0.5% vs 0.8%; p=0.30, respectively) |
| Kokulu K, Öner H, Özen C, Eroğlu SE, Altunok İ, Akça HŞ. Pharmacologic anisocoria due to nebulized ipratropium bromide: A diagnostic challenge. Am J Emerg Med. 2019 Jun;37(6):1217.e3-1217.e4. doi: 10.1016/j.ajem.2019.03.047. Epub 2019 Mar 28. PMID: 30948255. | Case Report | Emergency Department, Turkey | 35-year-old female with dyspnea attributed to asthma. | Nebulized ipratropium and albuterol | NA | NA | Unilateral mydriasis developed after exposure to ipratropium that resulted in CT/CTA to evaluate for an intracranial process. |
| McGonigle R, Woods RA. Take my breath away: a case of lactic acidosis in an asthma exacerbation. CJEM. 2011 Jul;13(4):284-8. doi: 10.2310/8000.2011.110236. PMID: 21722560. | Case Report | Own residence, emergency department | 36 year old male with a history of asthma who presented to the ED with a 4 day history of difficulty breathing | Salmeterol use by metered dose inhaler 3-4 puffs 4 times a day for “several days.” Salmeterol 2.5 mg and ipratropium bromide 250 mcg were nebulized by ED staff prior to assessment and Salmeterol 5 mg and ipratropium bromide 500 mcg were nebulized every 20 minutes for 3 additional doses. | NA | NA | Laboratory investigations revealed a bicarbonate of 20 mmol/L potassium 2.8 mmol/L and lactate of 5.3 mmol/L. |
| Muchão FP, Souza JM, Torres HC, De Lalibera IB, de Souza AV, Rodrigues JC, Schvartsman C, da Silva Filho LV. Albuterol via metered-dose inhaler in children: Lower doses are effective, and higher doses are safe. Pediatr Pulmonol. 2016 Nov;51(11):1122-1130. Doi: 10.1002/ppul.23469. Epub 2016 May 12. PMID: 27171324. | Randomized Controlled Trial | Emergency department | Participants 2-17 years old who had two or more prior episodes of wheezing who presented with moderate to severe acute asthma exacerbations. | High dose albuterol (900-1800 mcg depending on weight) via MDI and chamber and mask or mouthpiece | Low dose albuterol (600-1200 mcg depending on weight) via MDI and chamber and mask or mouthpiece | Primary:  length of stay in emergency room, admission rate  Secondary:  side effects, drug levels | ED length of stay and admission rates were similar between the two groups, p = 0.55 and p = 0.48, respectively.  Potassium concentrations drop in both the high dose (4.42±0.59 initial), (4.03±0.64 final) and low dose (4.60±0.61 initial 4.01±0.50 final) groups (p <0.001).  Glucose concentrations elevated in both high dose (91.55±18.24 initial, 126.27±45.80 final) ad low dose (92.53±13.42 initial 115.43±29.24 final) groups (p<0.001).  Bicarbonate concentrations dropped in both the high dose (22.76±2.21 initial, 21.01±2.30 final) and low dose (23.02±2.35 initial, 21.57±1.97 final) groups (p<0.001). |
| Newhouse MT, Chapman KR, McCallum AL, Abboud RT, Bowie DM, Hodder RV, Paré PD, Mesic-Fuchs H, Molfino NA. Cardiovascular safety of high doses of inhaled fenoterol and albuterol in acute severe asthma. Chest. 1996 Sep;110(3):595-603. doi: 10.1378/chest.110.3.595. PMID: 8797398. | Randomized Controlled Trial | Emergency department | 257 participants 18-45 years old who had a diagnosis of asthma and presented for asthma exacerbations | Fenoterol MDI, 4 puffs (200 mcg/puff) via chamber and facemask, 2 additional puffs could be given every 10 minutes to a maximum of 16 puffs. | Albuterol MDI, 4 puffs (100 mcg/puff) via chamber and facemask, 2 additional puffs could be given every 10 minutes to a maximum of 16 puffs. | Primary:  Efficacy (forces expiratory value).  Secondary:  Safety (serum potassium level, QTc interval, incidence of serious cardiac dysrhythmia). | 32 (12%) patients (14 fenoterol, 18 albuterol) had premature ventricular contractions. 34 (13%) patients (17 fenoterol, 17 albuterol) had premature supraventricular contractions.  There was a decrease in serum potassium level that was significantly greater in the fenoterol (0.23±0.04 mmol/L) than in the salbutamol (0.06±0.03 mmol/L) group (p=0.0002).  There was also a greater increase in the Q-Tc interval in the fenoterol group, 0.011±0.003 sec compared with 0.003±0.003 sec in the albuterol group (p<0.05).  There was no increased risk of serious cardiac disturbances. |
| Olshaker J, Jerrard D, Barish RA, Brandt G, Hooper F. The efficacy and safety of a continuous albuterol protocol for the treatment of acute adult asthma attacks. Am J Emerg Med. 1993 Mar;11(2):131-3. doi: 10.1016/0735-6757(93)90105-k. PMID: 8476452. | Case Series | Emergency department, Baltimore, Maryland, US. | 67 patients 18 years of age or older with a history of asthma and presenting to the ED with an acute asthma attack | Three continuous albuterol nebulizer treatments (2.5mg each) completed within 45-minutes of first treatment. | NA | Primary: Safety, efficacy. | 2 (2.6%) patients felt flushed, 3 (4%) patients felt tremulous, and 1 (1.3%) patient had the feeling of palpitations. |
| Patel B, Assad D, Wiemann C, Zughaib M. Repeated use of albuterol inhaler as a potential cause of Takotsubo cardiomyopathy. Am J Case Rep. 2014 May 19;15:221-5. doi: 10.12659/AJCR.890388. PMID: 24855502; PMCID: PMC4029766. | Case Report | Outpatient and emergency department. | 78-year-old female with a history of chronic obstructive pulmonary disease presented to the ED with chest discomfort and shortness of breath for 2 days. | She was reported to use her albuterol inhaler “several times and at least 4 times in 12 hours.” She used albuterol up to 2 times a day at baseline. | NA | NA | Electrocardiogram demonstrated ST segment elevation in leads II, III, aVF and V1-4. Coronary angiography demonstrated apical ballooning on the left ventricle typical of Takotsubo cardiomyopathy. |
| Payares-Salamanca L, Contreras-Arrieta S, Florez-García V, Barrios-Sanjuanelo A, Stand-Niño I, Rodriguez-Martinez CE. Metered-dose inhalers versus nebulization for the delivery of albuterol for acute exacerbations of wheezing or asthma in children: A systematic review with meta-analysis. Pediatr Pulmonol. 2020 Dec;55(12):3268-3278. doi: 10.1002/ppul.25077. Epub 2020 Sep 25. PMID: 32940961. | Systematic Review with Meta-analysis | Emergency department or hospital inpatient | 15 RCTs (n=2057) enrolling participants 17 years of age or younger with a diagnosis of symptoms suggestive of asthma that presented to an emergency department or inpatient with an acute asthma exacerbation that compared albuterol delivered by nebulizer with metered dose inhaler. | In studies, albuterol administered varied from 20–30 min in seven  studies, 5–10 min in two studies, and a  single administration in four studies.  Albuterol delivered through nebulizer, 0.15 mg/kg (max  5 mg) was the most frequently used dosage,  Albuterol MDI doses from single doses of 600 mcg to cumulative doses up to 3000 mcg. | NA | Primary:  Rate of hospitalization.  Secondary:  Oxygen arterial saturation, heart rate, respiratory rate, pulmonary index score, adverse effects, need for additional treatment | Hospital admission was reported in 8 studies. No differences were found between the two delivery methods for this outcome (RR, 0.89; 95% CI, 0.55–1.46; p = .65)  Heart rate (HR) was reported in three studies and pooled analysis showed a significantly smaller increase in HR when albuterol was delivered through MDI than when it was delivered through nebulizer (MD, −6.47; 95% CI, −11.69 to −1.25; I2 = 0%; p = .02).  No significant differences were found between the two methods of delivery of albuterol for other adverse effects such as nausea (RR, 0.71; 95% CI, 0.41–1.22; I2 = 27%; p = .22),11,13,23,27 palpitations (RR, 0.60; 95% CI, 0.22–1.64; I2 = 44%; p = .32), and tremor (RR, 0.60; 95% CI, 0.22–1.64; I2 = 44%; p = .32. |
| Spooner LM, Olin JL. Paradoxical bronchoconstriction with albuterol administered by metered-dose inhaler and nebulizer solution. Ann Pharmacother. 2005 Nov;39(11):1924-7. doi: 10.1345/aph.1G248. Epub 2005 Sep 20. PMID: 16174783. | Case Report | Outpatient clinic, emergency department | 92 year old male with history of chronic obstructive pulmonary disease and asbestosis | Albuterol inhaler | NA | NA | Severe bronchospasm 30-minutes after use of the albuterol inhaler. He was taken to the emergency department and was given an albuterol nebulizer treatment about 2 hours after the initial inhaler use, bronchospasm recurred immediately |

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