

Inhaled Salbutamol plus Ipratropium in Moderate and Severe Asthma Crises in Children

BACKGROUND

- Inhaled salbutamol, a β_2 agonist, is the standard treatment for children with mild to moderate asthma crises. The addition of ipratropium, an anticholinergic, is recommended for severe or life-threatening asthma emergencies.
- Not many studies exist to validate the efficacy of these guidelines. Of the studies available, few have classified patients based on age or clinical severity.

OBJECTIVE

- To analyze whether the combination of salbutamol plus ipratropium bromide administered by nebulizer in the emergency department improved oxygenation and lung function and reduced the frequency of hospital admission among children with asthma crises, compared with salbutamol alone, with a differential analysis according to age and severity of the asthma crisis.

METHODS

- **Design:** Single site, double-blinded, randomized parallel trial; Duration: 6 nebulizer treatments
- **Inclusion criteria:** Not clearly stated
- **Exclusion criteria:** Mild asthma crisis, administration of corticosteroids in previous 48 hours, presence of severe respiratory failure requiring immediate admission to intensive care or mechanical ventilation, history of respiratory failure requiring admission to intensive care, cardiac or pulmonary malformations, chronic lung disease (pulmonary bronchodysplasia, cystic fibrosis), stridor, foreign body aspiration, neurological alterations, or contraindications for the use of beta2 agonists or anticholinergic medication.
- **Primary outcome measure:** Change from baseline to end point in pulmonary asthma score, oxygen saturation, forced expiratory volume in first second (FEV₁), and peak expiratory flow (PEF).
- **Secondary outcome measures:** Number of hospital admissions.
- 100 patients (51 salbutamol plus ipratropium and 49 salbutamol plus placebo) received either
 - 5mg of salbutamol and 500 μ g of ipratropium in 5mL of normal saline (1/2 dose for children less than 20kg)
 - OR
 - 5mg of salbutamol in 5mL of normal saline (1/2 dose for children less than 20kg)
- Patients were given six nebulizer treatments, one every 20 minutes. Each treatment lasted for 7 minutes.
- Power of 80% with an alpha level of 0.05 to detect a 30% difference in the frequency of hospital admission between the two groups. This was calculated to be sufficient for 45 people per group, or 90 total patients.
- Data handling method was per protocol.

RESULTS

- 3 patients were lost-to-follow up and their data was not included.
- **Primary outcome measure:** There was a statistically significant difference in change from baseline between groups in asthma score (p=0.0001), oxygen saturation (p=0.0001), % of predicted FEV₁ (p=0.0001), and % of predicted PEF (p=0.0001).
- **Secondary outcome measures:** There was a statistically significant difference between the groups in the number of hospital admissions (p=.007; RR = 0.29, 95% CI, 0.1-0.8). The NNT was 3.9 (95%CI, 2-13). In the severe asthma crisis subgroup, the number of hospital

admissions was statistically significant ($p=0.004$; $RR=0.2$, 95% CI, 0.1-0.7). The NNT was 2.9 (95% CI, 2-8). In the moderate asthma crisis subgroup, the difference between the group who received salbutamol plus ipratropium and the group who received salbutamol plus placebo in the need for hospitalization was not statistically significant.

- **Author's conclusion:** Salbutamol plus ipratropium significantly improves the pulmonary asthma score, oxygen saturation, and lung function in children with moderate to severe asthma crises, while reducing the need for hospitalization.

STRENGTHS

- Double-blind, placebo-controlled, randomized design
- Few drop-outs
- Sub-group analyses based on age and severity

LIMITATIONS

- Method of recruitment
- Excluding children who had received a corticosteroid in the past 48 hours
- Small sample size in moderate crisis subgroup
- Did not account for the use of chronic medications or previous hospitalizations

CONCLUSION

- The combination of salbutamol and ipratropium significantly improves the lung function of patients with moderate to severe asthma crises.
 - Ipratropium, in combination with salbutamol, should be administered early on in patients with severe asthma crises.
 - In children of all ages, salbutamol plus ipratropium reduces the risk of hospitalization.
- Future research:
 - Future studies need to focus on a larger sample size of patients with moderate asthma crisis to see if there is actually a statistically significant reduction in hospital admission and pulmonary asthma score.

Reference: Iramain R, Lopez-Herce J, Coronel J, Spitters C, Guggiari J, Bogado N. Inhaled salbutamol plus ipratropium in moderate and severe asthma crises in children. *Journal of Asthma*. 2011;48:298-303.

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