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[Intervention Review]

Inhaled anticholinergics and short-acting beta$_2$-agonists versus short-acting beta2-agonists alone for children with acute asthma in hospital

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ABSTRACT

Background

Inhaled anticholinergics given in addition to β_2-agonists are effective in reducing hospital admissions in children presenting to the emergency department with a moderate to severe asthma exacerbation. It seems logical to assume a similar beneficial effect in children hospitalised for an acute asthma exacerbation.

Objectives

To assess the efficacy and safety of anticholinergics added to β_2-agonists as inhaled or nebulised therapy in children hospitalised for an acute asthma exacerbation. To investigate the characteristics of patients or therapy, if any, that would influence the magnitude of response attributable to the addition of anticholinergics.

Search methods

We identified trials from the Cochrane Airways Group Specialised Register of trials (CAGR), which is derived through systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED and PsycINFO and through handsearching of respiratory journals and meeting abstracts. The search is current to November 2013.

Selection criteria

Randomised trials comparing the combination of inhaled or nebulised anticholinergics and short-acting β_2-agonists versus short-acting β_2-agonists alone in children one to 18 years of age hospitalised for an acute asthma exacerbation were eligible.

Data collection and analysis

Two review authors independently assessed the methodological quality of trials and extracted data; disagreement was resolved by consensus or with the input of a third review author, when needed. Primary outcomes were duration of hospital stay and serious adverse

events. Secondary outcomes included admission and duration of stay in the intensive care unit (ICU), ventilation assistance, time to short-acting β_2-agonists spaced at four hours or longer, supplemental asthma therapy, duration of supplemental oxygen, change from baseline in asthma severity, relapse after discharge, adverse health effects and withdrawals.

Main results

Seven randomised trials were included, four of which reported usable data on 472 children with asthma one to 18 years of age who were admitted to paediatric wards. No trials included patients admitted to the ICU. The anticholinergic used, ipratropium bromide 250 μg, was given every one to eight hours over a period from four hours to the entire length of the hospital stay. Two of four trials (50%) contributing data were deemed of high methodological quality. The addition of anticholinergics to β_2-agonists showed no evidence of effect on the duration of hospital admission (mean difference (MD) -0.28 hours, 95% confidence interval (CI) -5.07 to 4.52, 3 studies, 327 participants, moderate quality evidence) and no serious or non-serious adverse events were reported in any included trials. As a result of the similarity of trials, we could not explore the influence of age, admission site, intensity of anticholinergic treatment and co-interventions on primary outcomes. No statistically significant group difference was noted in other secondary outcomes, including the need for supplemental asthma therapy, time to short-acting β_2-agonists spaced at four hours or longer, asthma clinical scores, lung function and overall withdrawals for any reason.

Authors' conclusions

In children hospitalised for an acute asthma exacerbation, no evidence of benefit for length of hospital stay and other markers of response to therapy was noted when nebulised anticholinergics were added to short-acting β_2-agonists. No adverse health effects were reported, yet the small number of trials combined with inadequate reporting prevent firm reassurance regarding the safety of anticholinergics. In the absence of trials conducted in ICUs, no conclusion can be drawn regarding children with impending respiratory failure. These findings support current national and international recommendations indicating that healthcare practitioners should refrain from using anticholinergics in children hospitalised for acute asthma.

PLAIN LANGUAGE SUMMARY

Are inhaled anticholinergics added to β_2-agonists beneficial in children hospitalised with acute asthma?

Background: Anticholinergics (e.g. ipratropium bromide, atropine sulfate) are inhaled drugs. They relax the airway muscles and decrease secretions. Anticholinergics are sometimes used in addition to beta$_2$-agonists (such as salbutamol and terbutaline), which are potent drugs given to relax smooth muscles in the airways in children with acute asthma. We do not know whether the addition of inhaled anticholinergics to beta$_2$-agonists is beneficial for children hospitalised with acute asthma.

Review question: We wished to examine the efficacy and safety of inhaled or nebulised (mist inhaled into the lungs) anticholinergics added to beta$_2$-agonists compared with beta$_2$-agonists alone in children one to 18 years of age hospitalised for an acute asthma exacerbation.

Study characteristics: In reviewing evidence available until November 2013, we found seven eligible studies of children hospitalised with acute asthma; four of these studies (472 children one to 18 years of age) contributed data to the review. Four studies compared the combination of anticholinergics (ipratropium bromide) and beta$_2$-agonists versus the same dose of beta$_2$-agonists alone. Included studies enrolled both girls and boys, with a gender ratio ranging from 59% to 73% males.

Results: No additional benefit was noted by adding anticholinergics to β_2-agonists in terms of duration of hospital stay in patients compared to those who received beta$_2$-agonists alone. Two of four trials (50%) contributing data were deemed of high methodological quality. No trial reported information on serious adverse events. No statistically significant group difference was noted in other markers of response to therapy, that is, the need for supplemental asthma therapy, time to short-acting beta$_2$-agonists spaced at four hours or longer, asthma clinical scores, lung function and overall withdrawals for any reason.

Conclusion: No apparent benefit is derived from adding anticholinergics to beta$_2$-agonists in children hospitalised for an acute asthma exacerbation, that is, beyond initial treatment in the emergency department. No adverse health effects were reported, yet the small number of trials combined with inadequate reporting prevents firm reassurance regarding the safety of anticholinergics. In the absence of trials conducted in the intensive care unit (ICU), no conclusion can be drawn regarding children with very severe exacerbations who are admitted to the ICU. Our findings support the ongoing recommendations provided by national and international guidelines.

Quality of the results: This review is based on a small number of identified trials conducted in children with acute asthma. All trials contributing to the primary outcome are of high methodological quality, but they are few. As the addition of new trials may change the conclusion, the quality of evidence was downgraded from high to moderate. Additional and larger trials are needed.