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Prehospital use of ipratropium bromide paired with salbutamol as treatment for shortness of breath.

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Paramedic Critically Appraised Topic

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Topic: Prehospital use of ipratropium bromide paired with salbutamol as treatment for shortness of breath.

Clinical Scenario: Two primary care paramedics respond code 4 for a 55 year old male patient severely short of breath. Questioning his wife reveals that the patient has chronic obstructive pulmonary disease (COPD), takes Ventolin (salbutamol) when necessary and takes Atrovent (ipratropium bromide) daily. He took his Atrovent today, but experienced sudden onset shortness of breath after walking up the flight of stairs in his home.

PICO Question: In patients with shortness of breath from respiratory diseases, does the use of prehospital ipratropium bromide paired with salbutamol provide a better outcome than salbutamol treatment alone?

Search Strategy: see Appendix 1

Relevant Papers: eight relevant articles were found, but four were reviewed because they were most directly related to the topic

Key Words: FVC: forced vital capacity, amount of air which can be forcibly exhaled from the lungs after taking a full breath in
FEV_1: forced expiratory volume, volume of air exhaled in one second of forced expiration
ED: emergency department
COPD: chronic obstructive pulmonary disease
COAD: chronic obstructive airway disease

Author, Date	**Population**	**Design**	**Outcomes**	**Results**	**Strengths/Weaknesses**
Davis, D., 2005	371 adult patients, 18 years of age or older, transported to the University of California ED and treated for suspected reactive	Prehospital retrospective study	• Change in heart rate, respiratory rate, blood pressure and/or oxygen saturation. • Clinical improvement or deterioration	*Avg. change in vital signs, Albuterol alone cohort (n=192)* • ΔHR: -3 bpm • ΔBP: -7mmHg • Δresp. rate: 0 • ΔSaO_2: +8% • Improved clinical status: 34% of pts *Avg. change in vital signs, Albuterol/Ipratropium cohort (n=179)*	***Strengths*** Used vitals as an objective way to obtain data of patient improvement. Fairly large sample size. Study could be reproduced in other regions. ***Weaknesses*** Retrospective design, so patients were not randomized to receive each treatment. Data relies on

	airway disease (RAD). Pts were treated with either nebulized albuterol and ipratropium bromide or just albuterol.		as assessed by paramedics.	• ΔHR: -6 bpm • ΔBP: -10mmHg • Δresp. rate: -4 breaths/min • ΔSaO_2: +8% • Improved clinical status: 33% of pts There was no statistically significant difference, p-value < 0.05, between groups.	past EMS and ED records. Approximately one third of patients included in study were diagnosed with a cardiac etiology for their dyspnea. Analyzing treatment effect during short prehospital transport times does not indicate the longer-term effects.

Author, Date	**Population**	**Design**	**Outcomes**	**Results**	**Strengths/Weaknesses**
Moayyedi, P., 1995	62 patients admitted to hospital for acute exacerbation of COPD. Pts treated with either 5mg nebulized salbutamol and 500µg ipratropium bromide, or just 5mg salbutamol, both four times a day.	Randomized controlled trial	• Change in spirometric values (forced vital capacity and FEV_1) on days 1, 3, 7, 14 and then weekly and on the day of discharge. • Simple subjective symptom score recorded daily. Pts asked to report whether they feel better, worse, or the same as the day before. • Duration of hospital stay.	*Mean change in FEV_1* *Salbutamol only* • Day 1 – 3: +0.17 mL • Day 1 – 7: +0.21 mL • Day 1 – 14: +0.06 mL • Discharge: +0.23 mL *Mean change in FVC* *Salbutamol only* • Day 1 – 3: +0.25 mL • Day 1 – 7: +0.39 mL • Day 1 – 14: +0.33 mL • Discharge: +0.56 mL *Mean change in FEV_1* *Salbutamol + ipratropium bromide* • Day 1 – 3: +0.05 mL • Day 1 – 7: +0.15 mL • Day 1 – 14: +0.26 mL	***Strengths*** Examines changes over time to get a better picture of the long-term effects of the two treatments. Extensive exclusion criteria to ensure minimal confounding variables. Spirometric values obtained at 1800 hrs each time. ***Weaknesses*** Small sample size, also restricted to patients with COPD. Some patients did receive other IV steroid and

	All pts were not taking nebulized bronchodilators at home, were 45 years of age or older, and had a history of smoking more than 10 pack years.		• Numbers of days on nebulizer treatment.	• Discharge: +0.15 mL *Mean change in FVC Salbutamol + ipratropium bromide* • Day 1 – 3: +0.04 mL • Day 1 – 7: +0.17 mL • Day 1 – 14: +0.62 mL • Discharge: +0.42 mL No statistically significant difference, $p < 0.05$ between groups.	antibiotic medication, but study states there was no statistically significant difference between groups.

Author, Date	**Population**	**Design**	**Outcomes**	**Results**	**Strengths/Weaknesses**
Koutsogiannis, Z., 2000	50 adult patients admitted to the emergency department with COAD. Pts received 5mg nebulized salbutamol and 500µg ipratropium bromide and 250mg IV hydrocortisone at time=0. Then randomized to receive 5mg salbutamol and 500µg ipratropium	Prospective, randomised, double blind trial	• Mean percent change in FEV_1 measured at time=0 and time=90 mins. • Absolute change on pulmonary function test	*Mean percentage change in FEV_1* • comb. treatment: 6.4% • salbutamol: 18.6% • ipratropium: 4.8% *Mean absolute change on pulmonary function test* • comb. treatment: 0.06L • salbutamol: 0.13L • ipratropium: 0.023L	***Strengths*** Different perspective considering ipratropium bromide was given to both groups as an initial treatment, then studied subsequent treatments of ipratropium. Explains the cost of ipratropium bromide and the seemingly minimal benefits when paired with salbutamol in the prehospital environment. ***Weaknesses*** Small sample size and only one diagnostic tool used for comparison of improvement. Standard deviation in absolute change in FEV_1 is large in all

	bromide, or 5mg salbutamol alone, or 500µg ipratropium bromide alone, at 15min and 30min.			No statistically significant difference between groups.	groups, suggesting there are subgroups within the sample that may benefit from the combined treatment.

Author, Date	**Population**	**Design**	**Outcomes**	**Results**	**Strengths/Weaknesses**
Lanes, S.F., 1998	1064 pts aged 18 to 55 years admitted to the emergency department with acute asthma. Pts randomized for treatment of a combination of nebulized 2.5mg salbutamol plus 0.5mg ipratropium bromide, or 2.5mg salbutamol alone.	Pooled analysis of three randomized double-blinded clinical trials conducted in the United States, Canada and New Zealand.	• FEV_1 measured at baseline, 45 mins and 90 mins. Pts followed up for 48h after hospital discharge for occurrence of asthma exacerbation and hospitalization. • Reduced risk of need for additional treatment, subsequent asthma exacerbations and hospitalizations	*Mean difference between FEV_1 change from time=0* *Ipratropium + salbutamol* *45 minutes* • CAN: 587mL • NZ: 461mL • US: 651mL *90 minutes* • CAN: 633mL • NZ: 519mL • US: 831mL *Salbutamol* *45 minutes* • CAN: 542mL • NZ: 369mL • US: 645mL *90 minutes* • CAN: 542mL • NZ: 416mL • US: 851mL	***Strengths*** Account for all differentiating factors in the populations studied. Extensively explains and accounts for all study biases, including the original claims of each of the studies, which did not coincide with the overall conclusions when looking at all three studies. ***Weaknesses*** Outcome of seemingly positive effects of the combination treatment was <10% of the overall improvement of FEV_1 from baseline, indicating only a small improvement. Also stated that the data could be

				Small improvement in lung function indicated for combination treatment.	obscured by outliers in the U.S.A. study.

Comments:

One major challenge that presents with this PICO question is the specificity of observing prehospital, emergency medicine data of the benefits of pairing ipratropium bromide and salbutamol. None of the studies analyzed in this CAT occurred within the last 10 years, and took place in either the emergency department or longer in-hospital stays. Moayyedi et al. completed their study over several days until patient discharge, evaluating FEV_1 and FVC, as well as some subjective symptom questions (1995). This prospective study produced no statistically significant difference between treatment groups, further suggesting that ipratropium bromide paired with salbutamol does not give any additional benefit to patients with SOB due to airway diseases. Contraindicative to these results, Lanes et al. examine FEV_1 at 0 mins, 45 mins, and 90 mins after arrival in the ED (1998). A small improvement was noted for patients who received the combination treatment, as well as reduced risk for subsequent symptoms of asthma. The large total sample size and cross-country meta-analysis study design enhances the efficacy of the results and the ability to detect small differences in data (Lanes et al. 1998). Only one of the studies mentioned a reason for questioning the effect of the combination treatment. The cost of using a medication that does not seem to have significant benefit in prehospital treatment, is a factor to consider because that money can be put towards something else. Emergency medicine in Canada is always in need of improvements in equipment, education, community programs, and many other things. Though the cost of PCPs using ipratropium bromide may seem small, the savings of not using it over a year could have a significant benefit to another aspect of paramedicine. There is also always a risk of patients having adverse reactions to medications. So if the latest evidence-based medicine shows little to no benefit of the pairing of ipratropium bromide and salbutamol in the prehospital environment, it should be considered to be removed from PCP scope of practice.

Consider: ***Why would you NOT change practice, based on these articles?***

Since these studies mainly look at short term treatment of ipratropium bromide and salbutamol, the long term effects of the combination is not well observed. Perhaps continuous treatment of the paired medications has a significant effect in patient presentation after several weeks. The use of the combination treatment in the prehospital environment could be beneficial for patients who are going to be prescribed these two medications and will be using them consistently from that point forward. Using it to treat these critical patients will theoretically begin their treatment at the earliest moment possible.

Clinical Conclusion:

The use of ipratropium bromide for shortness of breath due to chronic airway diseases, appears to be of little additional benefit than salbutamol treatment alone, in the prehospital environment. Paramedics should perhaps consider the costs of using the drugs paired together when deciding what to use to treat SOB. Salbutamol alone is a very effective way to dilate bronchioles, enhance ventilation and allow for reperfusion in a short period of time.

Appendix 1

	Key Word	Results (CINAHL & EBSCO)	Results (MEDLINE)
S1	Ipratropium bromide/albuterol	246	626
S2	Albuterol/ipratropium bromide	22	422
S3	Ipratropium bromide/salbutamol	173	689
S4	Salbutamol/ipratropium bromide	17	689
S5	Salbutamol	318	11492
S6	Albuterol	1363	10061
S7	Ipratropium bromide	160	2233
S8	Prehospital	11606	9338
S9	Pre hospital	1114	38437
S10	Pre-hospital	710	3279
S11	Out of hospital	5582	95408
S12	S1 OR S3	249	724
S13	S5 OR S6	1486	12220
S14	S8 OR S9 OR S10 OR S11	17160	136985
S15	S12 AND S13 AND S14 AND S7	1	9
S16	S14 AND S7	52	

Back-sourcing used
Nova Scotia EHS: Canadian Prehospital Evidence-Based Practice website used
https://emspep.cdha.nshealth.ca/LOE.aspx?VProtStr=Asthma&VProtID=200

References:

Davis, D.P., Wiesner, C., Chan, T.C., and Vilke, G.M. (2005). The efficacy of nebulized albuterol/ipratropium bromide versus albuterol alone in the prehospital treatment of suspected reactive airways disease. *Prehospital Emergency Care*, *9*(4), 386-390. DOI: 10.1080/10903120500255404

Koutsogiannis, Z., and Kelly, A.M. (2000). Does high dose ipratropium bromide added to salbutamol improve pulmonary function for patients with chronic obstructive airways disease in the emergency department? *Aust NZ J Med, 30*(1), 38-40. DOI: 10.1111/j.1445-5994.2000.tb01052.x

Lanes, S.F., Garrett, J.E., Wentworth, C.E. III., Fitzgerald, J.M., and Karpel, J.P. (1998). The effect of adding ipratropium bromide to salbutamol in the treatment of acute asthma: a pooled analysis of three trials. *Chest, 114*(2), 365-372.

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