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Effect of mucolytic and bronchodilator aerosol therapy on airway resistance in mechanically ventilated patients

D. F. Zandstra, C. P. Stoutenbeek and D. R. Miranda

Institute of Anaesthesiology and Intensive Care, University Hospital Groningen, The Netherlands

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Abstract. Nebulisation of a 10% solution of Mesna (Mistabron) in 10 postoperatively ventilated patients without preexisting pulmonary disease caused a significant increase in inspiratory resistance. This increase is effectively blocked by addition of a bronchodilator (i.e. Salbutamol) to the aerosol. No significant changes in airway resistance were observed in the 10 patients receiving salbutamol alone or isotonic saline. The expiratory resistance did not change suggesting that only the larger airways are involved in the constrictive effect of the drug. Although no patient showed clinical signs of bronchospasm, it is worth considering that even in patients without history of obstructive pulmonary disease nebulisation of Mesna should be performed in combination with a bronchodilator.

Key words: Airway resistance – Respiratory therapy – Bronchodilator agents – Mucolytic agents

Aerosol therapy with mucolytic agents and bronchodilators can be considered to be a routine treatment in artificially ventilated patients. The rationale behind it is prevention and treatment of airway problems resulting from an increase in viscosity of bronchial secretion, impaired clearance, stasis, atelectasis, and infection [9]. Side effects have been observed after mucolytic therapy, in particular increase in airway resistance due to bronchoconstriction. The purpose of the present study was to evaluate the effects of aerosol therapy on airway resistance (Raw) using a mucolytic agent (Mesna), a bronchodilator (salbutamol) and isotonic saline, alone or in various combinations.

Material and methods

Four comparable groups of 10 patients each who were postoperatively ventilated after coronary artery bypass grafting received either a 10% solution of Mesna (Mistabron), or a 0.5% solution of salbutamol (Ventolin) or a combination of these two agents or isotonic 0.9% saline. Nebulisation was done by means of a Bird nebuliser during 5 min on manual ventilation. Thereafter mechanical ventilation was again continued with a Servo ventilator (Siemens Elema Solna, Sweden). Inspiratory and expiratory resistance were measured by means of a Servo 940 lung mechanics calculator, before starting spray therapy and 5, 15 and 30 min after spraying. Airway resistances by means of the Servo 940 are calculated according the formulae:

$$\text{inspiratory resistance} = = \frac{\text{peak airway pressure} - \text{pause pressure}}{\text{end inspiratory flow}}$$

$$\text{expiratory resistance} = = \frac{\text{pause pressure} - \text{early expiratory pressure}}{\text{early expiratory flow}}$$

No patient suffered from chronic obstructive pulmonary disease (COPD). Peroperative anaesthetic technique was identical for all patients (oxygen/air/etomidate, fentanyl, pancuronium bromide).

Postoperative sedatives used were morphine and diazepam. Preoperatively the inspired air was humidified by means of a Bennet cascade system, postoperatively with a condensor humidifier (Siemens 150). Data were statistically analyzed using the Students t-test for paired samples.

Table 1.

Spray regimen	Before spray		5′ after spray		15′ after spray		30′ after spray	
	Insp. resist.	Exp. resist.	Insp. resist.	Exp. resist.	Insp. resist.	Exp. resist.	Insp. resist.	Exp. resist.
Salbutamol 0.5%	9.1±0.7	12.4±3.9	8.8±1.8	11.8±4.0	8.6±2.6	11.7±4.0	9.1±2.3	12.6±3.6
Saline 0.9%	8.4±1.4	10.6±1.3	8.0±1.9	10.4±1.8	7.9±1.4	10.5±1.4	7.9±1.4	10.6±1.6
Salb. 0.5% + mesna 10%	9.7±2.3	12.9±5.0	8.8±1.4	12.2±4.8	8.6±1.0	12.4±4.5	8.9±1.1	12.4±4.0

Data are given as mean ±SD

Results

Resting values of both inspiratory and expiratory resistance were higher than normal in all the different groups (see Fig. 1 and Table 1). In the group receiving the mucolytic drug we observed a significant increase in Raw inspiratory (Fig. 1). This effect was observed only 5 min after cessation of the nebulization. After 15 min the inspiratory resistance had returned to starting values. In this group no significant changes were observed in the expiratory resistance. In the groups treated with either salbutamol or saline or the combination of mesna and salbutamol no significant changes were found in either inspiratory or expiratory resistance (Table 1).

Discussion

Various compounds used in this study are known to change inspiratory resistance in both artificially ventilated and spontaneously breathing patients. Nebulization of isotonic saline may result in bronchoconstriction in subjects with and without chronic obstructive pulmonary disease [3, 4, 10]. Increase in airway resistance after nebulization of saline can be blocked with atropine suggesting a vagal reflex. The lack of response on airway resistance in the saline treated group could be explained by the fact that the patients were still anaesthetized thereby blocking reflex bronchoconstriction. Mucolytic drugs have also been reported to provoke bronchoconstriction in both COPD and non-COPD patients [5, 14, 18]. These unwanted side effects may be reduced either by adding bronchodilators to the aerosol [8, 13] or by reducing the concentration of the nebulized drug [6] or by reflex blocking with atropine [10]. However, an increase in pulse rate, especially after coronary bypass grafting has to be prevented and therefore is the addition of isoprenaline to the aerosol, or the administration of atropine relatively contraindicated. Salbutamol is a sympatho-

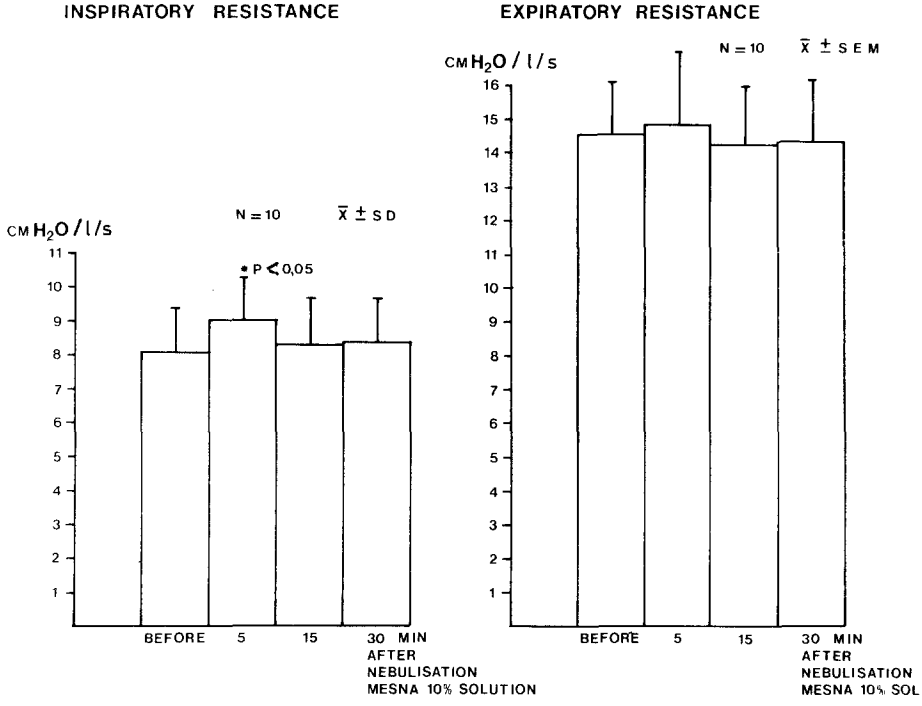

Fig. 1.

mimetic bronchodilator with similar effects on the bronchi as isoprenaline, but without many of the adverse haemodynamic effects [7, 16, 17]. Adverse effects on arterial oxygen tension observed after bronchodilator therapy with isoprenaline are absent or less pronounced in patients treated with salbutamol [1, 2, 11, 12]. However, these effects on arterial oxygen tension can be prevented in artificially ventilated patients by adding PEEP, because this adverse effect is the result of a decrease in FRC due to reduction in hyperinflation rather than the effect on pulmonary vasodilatation [11, 12]. Although a slow onset of action (more than 1 min) of salbutamol can be expected it is probably sufficiently rapid to prevent the significant increase in inspiratory resistance induced by Mesna.

The significant increase in inspiratory resistance after mesna without significant changes in expiratory resistance could possibly be explained by the fact that all patients received 2–4 cm H_2O of PEEP, thereby mechanically preventing constriction of the smaller airways. This could also explain the higher than normal expiratory resistance in the studied patients. Another explanation for the isolated increase in inspiratory resistance could be the size of the particles leading to a deposition in the major airways [16]. The condenser humidifier may be responsible for 2–4 cm H_2O increase in Raw explaining the high resting values of airway resistance.

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Dr. D. F. Zandstra
Institute of Anaesthesiology
and Intensive Care
University Hospital Groningen
Oostersingel 59
NL-9713 EZ Groningen
The Netherlands