

# Inhaled salbutamol: effects on the body



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## Introduction

Salbutamol is a first-choice bronchodilator drug used in the acute treatment of asthma. Asthma is a chronic respiratory disease which causes recurrent reversible airway obstruction. An asthma attack is often triggered by an immediate hypersensitivity reaction that occurs in response to an inhaled allergen, causing acute bronchospasm in the lungs. Salbutamol treats the symptoms of asthma by reversing this bronchoconstriction. It acts as a  $\beta$ -2-adrenoreceptor agonist, and when inhaled, it binds to beta-2-adrenoreceptors in the bronchial smooth muscle of the lungs, causing the muscle to relax. This leads to dilation of the bronchioles and improved airflow. Salbutamol has been shown to cause side effects such as tachycardia, muscle tremor, an increase in systolic blood pressure and a decrease in diastolic blood pressure. When salbutamol is absorbed into the bloodstream via the lungs, it can bind to  $\beta$ -2-adrenoreceptors present on the heart and increase the heart rate. The stimulation of beta receptors also stimulates an increase in myocardial contractility which can increase pulse pressure.

Salbutamol is usually administered by inhalation of aerosol, powder or nebulised solution, although it can also be administered intravenously. A metered-dose inhaler (MDI) is normally used for aerosol administration, which provides a standard dose of salbutamol. The spray from a MDI consists of rapidly moving propellant droplets, most of which impact in the mouth and throat where salbutamol absorption is poor, and only about 10% of the inhaled drug reaches the bronchioles.<sup>2</sup> This proportion may be further reduced by poor inhaler coordination since many patients fail,<sup>3</sup> to

synchronise the firing of the aerosol with inhalation. With good coordination about 15% of the dose would be expected to reach the lungs.'<sup>3</sup> Using a spacer device has proved to raise deposition of salbutamol in the lungs to levels similar to or greater than those obtained from a correctly used metered dose inhaler.

(Thorax 1984; 39; 935-941) The spacer is a large plastic container with a mouthpiece on one end and opening at other end where MDI is attached, and is most often used by young children and the elderly.

The aim of this study was to determine the acute effects of inhaled salbutamol on heart rate, pulse pressure, and peak expiratory flow rate and to compare the efficacy of salbutamol delivered by metered-dose inhaler (MDI) with that of salbutamol delivered by metered-dose inhaler attached to a spacer (MDI-spacer). The efficacy of the two methods of salbutamol delivery were analysed by comparing the bronchodilator and cardiovascular effects of salbutamol in subjects taking the MDI and MDI-spacer.

## **Materials and Methods**

18 healthy subjects were studied with an age range of 18-35 (14 females and 4 males). Salbutamol (Ventolin®) was supplied in pressurised, metered dose inhalers (MDI).

The 18 subjects were divided randomly into three groups: placebo, MDI and MDI-spacer. Subjects in the placebo group used the placebo MDI inhaler which acted as the control. Subjects in the MDI group used the salbutamol MDI. To administer a standard dose of salbutamol, they exhaled fully, and then inhaled slowly through the opening just as the drug was released from <https://assignbuster.com/inhaled-salbutamol-effects-on-the-body/>

the MDI, and then held their breath for 10 seconds. [manual]. Subjects in the MDI-spacer group used a salbutamol MDI with an attached spacer device. To inhale a single dose of salbutamol, the subjects attached the MDI to the end of the spacer, breathed in deeply through the mouthpiece and then held their breath for 10 seconds [Introduction to Exp Bio] . The standard dose released with each depression of the salbutamol MDI was 0. 1mg.

For each subject, control readings of heart rate, pulse pressure and peak expiratory flow rate (PEFR) were taken at 3 minute intervals for 12 minutes. At 12 minutes, two successive doses of the assigned inhaler were taken (2 x 0. 1mg doses= 0. 2mg), immediately after which the three variables were measured. This was repeated every 3 minutes until a total dose of 0. 6mg salbutamol or placebo had been administered. Heart rate was measured manually using a stethoscope and stopwatch. Diastolic blood pressure (DBP) and systolic blood pressure (SBP) were measured by using a sphyngomanometer and a stethoscope. [manual]. The pulse pressure was then calculated by subtracting the SBP from the DSB. The PEFR was measured using a Wright peak flow meter.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 16. 0. The data were assumed not to have a normal distribution, and the results obtained from the different groups were independent of each other. The non-paired, non-parametric Mann-Whitney-U test was therefore used to determine whether there were significant differences in any of the measured variables as a result of the salbutamol MDI, when compared to the placebo control. The test was also used to determine if there was a significant difference between the results of the MDI

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and MDI-spacer groups which would have been caused by the use of the spacer. For each subject, the overall change in a variable from the mean control value after a 0.6mg dose, was used to compare the results of subjects from different groups. Mann-Whitney-u test to compare results recorded for each group to see if the differences observed are significant at the 95% confidence level. A value of  $P < 0.05$  was therefore considered statistically significant.

## Results

Data are presented as mean  $\pm$  standard error

The results show that inhalation of salbutamol by MDI and MDI-spacer significantly increased PEFR and heart rate ( $n = 6$ ,  $p < 0.05$ ) compared to the placebo control, but did not cause any significant changes in pulse pressure. There were also no significant differences observed in the efficacy of salbutamol delivered by MDI compared to that delivered by MDI-spacer.

Heart rate

Graph 1 shows that inhalation of 0.6mg of inhaled salbutamol, caused the mean heart rate of Group B to increase by 10 beats per minute, and the mean heart rate of Group C to increase by 15 beats per minute.

Hand tremor and flushing of the face were most common observed effects.

## Discussion

What changes occurred in the parameters measured in the three subjects?

The study shows that inhalation of salbutamol significantly increased heart rate and PEFr in subjects who took the salbutamol, which confirms published results [1]. However, no significant changes in pulse pressure were observed, which does not agree with previous studies. As expected, no significant change in variables was observed in subjects who took the placebo, which confirmed that any changes observed in the other two groups were caused by the action of the salbutamol drug. When salbutamol is inhaled into the lungs by the MDI, it binds to  $\beta$ -2 adrenergic receptors present in the bronchiole smooth muscle. This causes the smooth muscle to relax, and increases the diameter of the bronchioles, which decreases airway resistance. This leads to an increased peak expiratory flow rate. Salbutamol entering the lungs also diffuses into the blood stream. As a result, it is able to bind to  $\beta$ -2 adrenergic receptors in the heart muscle, stimulating an increase in heart rate due to increased SA node activity. The pulse pressure would have been expected to increase, since salbutamol MDI and MDI-spacer were not significantly different, which does not confirm. Subjects were non-asthmatics, and studies carried out have been on asthmatics, Responses in non-asthmatics were slight differences, salbutamol takes up to 30 minutes to produce maximal effect. Parameters were only measured up to 18 minutes, so may have increased even further and any differences would have been amplified over a longer period. Initially there was the change in variables in MDI-spacer slightly greater, so maybe would have.

It becomes clear that the atrial and ventricular myocardium consist of both  $\beta$ -1- and  $\beta$ -2-adrenergic receptors.

5-8 It has been demonstrated that  $\beta$ -2-adrenergic

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receptors constitute 20 to 40% of the total number of [Brodde OE. Beta-1- and beta2-adrenoceptors in the human heart:

properties, function, and alterations in chronic heart failure.

Pharmacol Rev 1991; 43: 203-242]

-receptors in the human heart

Were these changes significant? What evidence do you have for this?

Relating your findings to the mechanism of action of salbutamol, how can you explain the results obtained? (N. B. Are the results what you expected? If not, suggest reasons why not and state what you would have expected to observe)

Were the results for each subject consistent across the class data? (e. g. did all Subject Bs respond in the same way?) If not, can you suggest reasons for this variation?

In one of the subjects in Group B, PEFr decreased after administration of MDI. Could be due to lack of experience with using inhaler. Were not asthmatics, so would have little experience, so inhaler may not work properly. Or tiredness. The trend of results obtained for PEFr in MDI group were not consistent in all 6 subjects. 3 subjects showed an initial increase in PEFr after 2 doses, followed by a slight drop in PEFr after the 3rd dose. However, the other subjects showed increase in PEFr after all 3 doses As the study subjects were not necessarily well trained and experienced in using

the MDI, they may not have administered the MDI correctly to obtain the dose. Also may have been error with PEFR, since

in the myocardium of the heart, causing a positive chronotropic effect, increasing AV node conduction and What deficiencies do you perceive in the experimental design? How could it be improved?

Limitation was that both subjects people taking measurements were aware of which inhaler they were taking which could have caused an increase in measured parameters due to the placebo effect. An improvement would be to make the experiment double-blind and randomised so that neither the subjects nor the data recorders know which type of drug the subject has taken, making the results more reliable, and eliminating the placebo effect.

Should measure controls over long-term to obtain accurate baseline values for different parameters in subjects, which can be used to compare any changes caused by the salbutamol.

Larger sample of people make more representative and reduce the standard error, and increase gender balance. There were more females than males, so not necessarily representative of population. Males have naturally higher mean PEFRs than females, so this could have increased the variation in the results for mean change in PEFR.

Use on asthma patients to make more clinically relevant. MDIs are used in asthma patients and rarely in non-asthmatic subjects, so it would be more conclusive to see if differences in efficacy are observed in asthma patients, and could be more reliably compared with results from previous studies



carried out in asthma patients. Also, could use varying doses of salbutamol, to see if there are significant changes in parameters with increasing doses of salbutamol.

Could do repeated measurements on subjects on different days over a longer period of time after the salbutamol has been administered to determine the maximum changes and observe the

Ensure the subjects have not taken any caffeine, have not physically exercised prior

Ensure non or smokers

Mouth rinsed immediately after inhalation to minimise the proportion of swallowed drug

Salbutamol is a short-acting agent and the maximum effect occurs within 30 minutes and the duration of action is 3-5 hours.

## **Sources Used**

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