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Effect of pseudoephedrine on nasal airflow in patients with nasal congestion associated with common cold

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SUMMARY

The aim of this study was to investigate the efficacy of pseudoephedrine as a nasal decongestant. Patients with nasal congestion associated with common cold received two doses of medication separated by 4 hours, either 60 mg pseudoephedrine ($n = 20$), or placebo ($n = 20$). Unilateral nasal airflow was measured over a 7-hour period to record the spontaneous changes in nasal airflow associated with the nasal cycle. Minimum (F MIN) and maximum (F MAX) unilateral nasal airflows were defined as the minimum and maximum nasal airflow values for each nasal passage recorded during the 7-hour period of the study. There was no significant difference in F MAX between the two treatment groups yet there was a significant difference in F MIN ($p < 0.05$). No difference in total nasal airflow (TNAF) between treatment groups was found, either before or after treatment ($p > 0.05$). The results demonstrate that (TNAF) is not as sensitive a measure of decongestion as F MIN. The findings of this study show that pseudoephedrine had no effect on the decongestion phase of the nasal cycle, but did significantly limit the congestion phase. The decongestant action may be explained by the sympathomimetic supplementing the natural sympathetic nervous activity to the nasal blood vessels.

Key words: nose, nasal cycle, nasal airflow, pseudoephedrine

INTRODUCTION

Pseudoephedrine is widely used for the treatment of nasal congestion associated with common cold, and although there is some support for a decongestant action from a study using subjective scores of nasal patency (Berkowitz et al., 1989), there are no published clinical data using objective measures of patency to support the efficacy of pseudoephedrine as a nasal decongestant in common cold. The majority of studies on the decongestant action of pseudoephedrine are on patients with allergic rhinitis, but these studies have used only subjective measures of nasal congestion to determine the efficacy of pseudoephedrine (Howarth et al., 1993; Williams et al., 1996).

The aim of the present study was to investigate the efficacy of pseudoephedrine as a nasal decongestant in patients with nasal congestion associated with common cold, using an objective measure of nasal patency. In a previous study, measurements of nasal airway resistance in patients with common cold symptoms, demonstrated that the most sensitive measure of nasal congestion was maximum unilateral nasal airway resistance (Eccles et al., 1996). Total nasal airway resistance was shown to increase by around 30% with common cold, whereas an 80% increase in unilateral nasal airway resistance was recorded. Therefore, in the present study unilateral measures of nasal airflow were used to assess the degree of decongestion related to treatment.

MATERIALS AND METHODS

The study was a single center, open, randomized, stratified, parallel group design conducted at the Common Cold Center. Patients with nasal congestion associated with a history of common cold of less than 96 hours, were recruited by local advertisement. Patients were excluded from the study if they had: anatomical nasal obstruction or gross anatomical deformity, including moderate or severely deviated nasal septum or the presence of nasal polyps; taken menthol lozenges or a menthol containing product in the past hour; taken any nasal decongestant in the past 12 hours; taken any antihistamine in the last 72 hours or astemizole in the last 30 days; taken any analgesic in

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the last 24 hours; taken any prescribed medication within the last 30 days (with the exception of the contraceptive pill); a history of hyperthyroidism, diabetes mellitus, heart disease prostatic hypertrophy or hypertension. The study was conducted over two consecutive days. The study was approved by the Local Research Ethics Committee.

Day 1

Patients presenting at the Centre were asked to score their common cold symptoms of cough, runny nose, blocked nose and sore throat on a five point box scale with symptoms labeled 0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe. To enter the trial, patients had to score 2 (moderate) for blocked nose, and at least 1 (mild) for any other cold symptom. Patients were screened by the physician and a medical history was taken; blood pressure and pulse were measured and then patients were trained in the technique of posterior rhinomanometry. Total nasal resistance was measured so that patient treatments could be randomised and stratified on day 2 as high and low total airflow groups.

Day 2

Patients returned to the Centre at approximately 09:00 hr and received the first dose of medication at approximately 09:15 hr and the second dose at approximately 13:15 hr. Measurements of unilateral nasal airflow were made at 1 hour after the first dose of medication and then every hour over a 7-hour period. On completion of the study patients had their blood pressure measured.

Medication

Treatments consisted of either placebo (Sanatogen Multivitamin tablet) or pseudoephedrine 60 mg tablet. Total nasal airflow was measured on Day 1 and treatments for Day 2 were allocated according to a randomisation list. Those patients with a total nasal airflow of 175 cm^3/sec or less were randomised to a low treatment group and those with a total nasal airflow of 176 cm^3/sec or greater were randomized to a high treatment group.

Measurement of nasal airflow

Unilateral nasal airflow was measured using posterior rhinomanometry (NR6 rhinomanometer, GM Instruments) at an inspiratory reference pressure of 75 Pa with an oral cannula to sense posterior nasal pressure. Measurements were made with the patients seated upright. Unilateral measurements were obtained by alternately occluding each nostril with surgical tape. The instrument was programmed to give a mean nasal resistance measurement for four consecutive breaths. For each patient two measurements were used to calculate an overall mean nasal resistance with the patient repositioning the mask between each measurement. If the coefficient of variation of the eight breaths was greater than 15% the measurements were repeated until the coefficient of variation for two consecutive measurements was less than 15% and then the overall mean was recorded. In this study nasal patency has been expressed in terms of nasal airflow at a reference pressure of 75 Pa, rather than as nasal resistance. This is because nasal resistance tends towards infinity with nasal obstruction whereas nasal airflow tends towards zero which is more easily handled in statistical analysis. In those patients with complete unilateral nasal obstruction, nasal airflow was deemed to be zero.

Minimum and maximum unilateral nasal airflow

Minimum and maximum unilateral nasal airflows were defined as the minimum (F MIN) and maximum (F MAX) nasal airflow values for each nasal passage recorded during the 7-hour period of the study.

Statistical analysis

F MIN and F MAX were shown to have a skewed distribution and therefore results are given as medians (with interquartile range) and the Mann Whitney U test for unpaired data was used for statistical comparisons between the treatment groups. Total nasal airflow TNAF was shown to have a normal distribution and results are given as means (with standard deviation) and the unpaired Students T test was used for statistical comparisons between treatment groups.

RESULTS

Forty patients, 22 females and 18 males (mean age 23; range 18–49 years) took part in the study; 20 patients were treated with pseudoephedrine (16 randomised to high flow group, and 4 to low flow group) and 20 patients with placebo (16 randomised to high flow group, and 4 to low flow group). An example of the spontaneous changes in unilateral nasal airflow recorded in one patient is shown in Figure 1. There was considerable variation in the patterns of unilateral nasal airflow associated with the nasal cycle. In both of the treatment groups some patients exhibited spontaneous reciprocal changes in nasal airflow similar to those shown in Figure 1, whereas other patients exhibit-

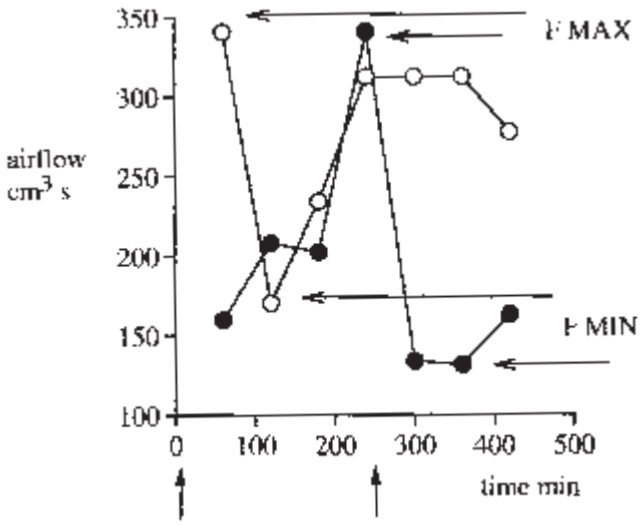

Figure 1. Spontaneous changes in left (open symbols) and right (filled symbols) unilateral nasal airflow recorded in one patient treated with pseudoephedrine. The points of maximum and minimum unilateral airflow (F MAX and F MIN) are illustrated on the graph. The arrows below the graph indicate the time points at which a dose of pseudoephedrine 60 mg was administered.

ed one nasal passage with the dominant nasal airflow throughout the study, and in others the spontaneous changes in nasal airflow on each side of the nose sometimes were in phase .

There was no significant difference in the median F MAX for the two treatment groups with F MAX being 234 cm^3 sec (161) for the placebo group, and 234 cm^3 sec (92) for the pseudoephedrine group ($p = 0.4$). However, there was a significant difference in median F MIN between the treatment groups, with F MIN being 45 cm^3 sec (86) for the placebo group, and 79 cm^3 sec (83) for the pseudoephedrine group ($p = 0.036$).

There was no significant difference between the two treatment groups for TNAF on day 1 (TNAF placebo, 293 cm^3 sec +/–133; TNAF pseudoephedrine 270 cm^3 sec +/–138; $p = 0.595$) or TNAF at the end of treatment (420 min) on day 2 (TNAF placebo, 316 cm^3 sec +/–118; TNAF pseudoephedrine 343 cm^3 sec +/–107; $p = 0.466$). However, comparisons within treatment groups showed a significant increase in TNAF for the pseudoephedrine treated group between day 1 and day 2 ($p=0.029$), but no difference in the placebo treated group ($p=0.542$). There were no significant differences in blood pressure between the treatment groups either before or after treatment ($p > 0.05$).

DISCUSSION

Pseudoephedrine is a sympathomimetic which is believed to increase nasal airflow by causing constriction of nasal venous sinuses. In the present study we have assessed the decongestant action of pseudoephedrine by measuring changes in unilateral nasal airflow. Patients with common cold symptoms may often have one nasal passage congested whilst the other is quite patent (Bende et al., 1989; Eccles et al., 1996). It is the congested side of the nose that is of interest in assessing the action of a nasal decongestant such as pseudoephedrine as one would expect the greatest decongestant action on the congested side of the nose.

A single measurement of airflow in a nasal passage does not provide any useful information in assessing the decongestant action of pseudoephedrine as the nasal passages often exhibit spontaneous phases of congestion and decongestion over a period of 2–4 hours associated with the 'nasal cycle' (Heetderks, 1927; Stoksted, 1953; Hasegawa et al., 1977). In the present study we have measured the nasal airflow in each nasal passage over a period of 7 hours in order to determine the range of congestion and decongestion exhibited in each nasal passage. The extremes of congestion and decongestion in each nasal passage can be quantified by the minimum and maximum airflows (F MIN and F MAX) (Flanagan et al., 1996; Flanagan et al., 1998). Previous studies have shown that topical nasal decongestants have little decongestant action on the patent side of the nose (Principato et al., 1970; Williams et al., 1992; Flanagan et al., 1998). These findings indicate that the venous sinuses on the patent side of the nose are already in a state of maximal vasoconstriction due to the presence of a high sympathetic nervous tone and that application of a topical sympathomimetic medication does not cause any further vasoconstriction. In contrast, the venous sinuses on the congested side of the nose readily respond to a topical sympathomimetic and this results in a large change in nasal airflow.

The findings of the present study on the effects of an oral decongestant on nasal airflow agree with the previously published work on the actions of topical nasal decongestants, in that pseudoephedrine did not cause any change in nasal airflow on the naturally decongested side of the nose, i.e. there was no change in F MAX. However, pseudoephedrine did cause a significant increase in airflow on the naturally congested side of the nose, i.e. there was an increase in F MIN. This action of pseudoephedrine may be explained in the same way as the action of topical nasal decongestants, with the sympathomimetic having its greatest effect on the side of the nose with the least sympathetic nervous activity (Flanagan et al., 1998).

The results also demonstrate that total nasal airflow (TNAF) is not as sensitive a measure of decongestion as F MIN. Statistical comparisons between treatment groups after treatment with both doses of pseudoephedrine at the end of day 2 showed that there was no difference in TNAF between treatment groups. No adverse events were associated with treatment and there were no significant changes in blood pressure.

The results of this study provide support for the efficacy of pseudoephedrine as a nasal decongestant in the treatment of nasal congestion associated with common cold. This study has shown that two doses of pseudoephedrine (60 mg) reduce the degree of unilateral congestion associated with common cold. The pronounced unilateral nasal congestion, which often results in periods of complete unilateral nasal obstruction, is one of the most bothersome symptoms of common cold, and may predispose to obstruction of the ostia of the paranasal sinuses and obstruction of the Eustachian tube. The decongestant action of pseudoephedrine may not only help to limit the severity of unilateral congestion associated with common cold but may also help to maintain the ventilation and drainage of the paranasal sinuses and middle ear and therefore help prevent secondary bacterial infection of the upper airway.

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ANNOUNCEMENT

BOOKS

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