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Comparison of decongestive capacity of xylometazoline and pseudoephedrine with rhinomanometry and MRI*

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SUMMARY

Topical and systemic sympathicomimetics have been used for many years as a treatment of nasal congestion in diseases such as coryza and sinusitis. The aim of this study was to perform an objective measurement of the decongestive capacity of topical xylometazoline and oral pseudoephedrine in normal subjects and patients with chronic sinusitis.

Ten healthy subjects and 10 patients with chronic sinusitis were included in this study. Xylometazoline (0.1%) and pseudoephedrine (120 mg) were each administered to 5 healthy subjects and to 5 patients with chronic sinusitis. Decongestion was measured with active anterior rhinomanometry before, 15 minutes, 30 minutes and 1, 2, 4, 6 and 8 hours after administration. Before and about 90 minutes after drug administration a MRI was performed to visualize the decongestive effect on the turbinates and the mucosa of the sinuses. Xylometazoline reduces the nasal airway resistance for an average 37.3% in all patients and healthy subjects during 8 hours. Pseudoephedrine does not show a clear and long lasting decongestive effect on the turbinates. Important interindividual differences are also noted. MRI clearly shows a clear cut superiority of xylometazoline over pseudoephedrine concerning decongestion of the nasal mucosa. However, there was no decongestive effect whatsoever on the mucosa of the sinuses with either sympathicomimetic.

Key words: decongestion, MRI, rhinomanometry, xylometazoline, pseudoephedrine

INTRODUCTION

Topical and systemic sympathicomimetics have been used for many years to treat nasal congestion in diseases such as coryza and sinusitis. There are two groups of sympathicomimetics: the imidazoline derivatives (e.g xylometazoline, oxymetazoline) and the sympathicomimetic amines (e.g. pseudoephedrine, phenylephrine). Both are α-adrenoreceptor agonists. The imidazoline derivatives have a specific action on the α_2-adrenoreceptors while the sympathicomimetic amines act on the α_1-adrenoreceptors. Through this mechanism they produce a vasoconstriction of the submucosal vessels in the nose that results in decongestion. However, the imidazoline derivatives can also cause a reduction in the mucosal blood flow as has been shown by Bende [1] in 1983, due to their

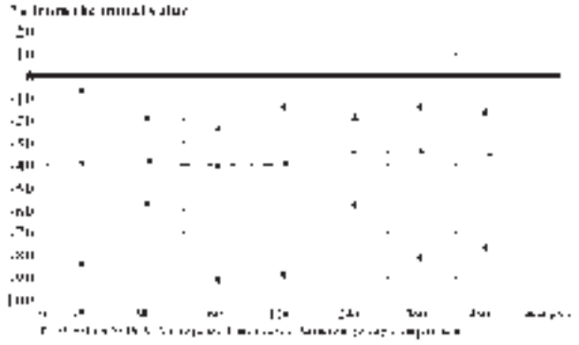

Figure 1. Decongestion after xylometazoline administration.

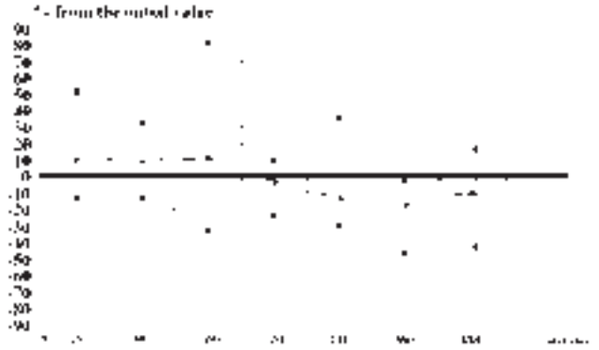

Figure 2. Decongestion after pseudoehphedrine administration.

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A

B

Figure 3. MRI in healthy subjects before (3a) and after (3b) xylometazoline administration: note the marked decongestive effect after ninety minutes on the inferior turbinates and no effect on the mucosa of the sinuses.

A

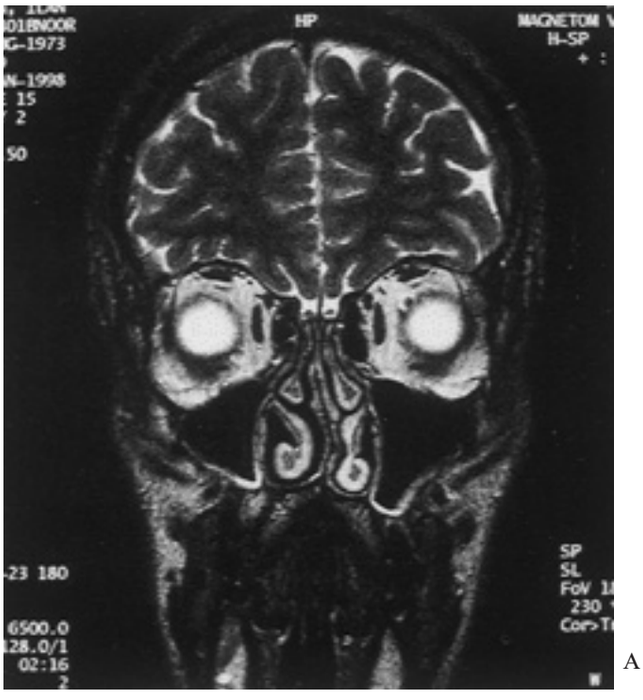
B

Figure 4. MRI in chronic sinusitis patients before (4.) and after (4b) xylometazoline administration: note the marked decongestive effect after ninety minutes on the inferior turbinates and no effect on the mucosa of the sinuses.

specific activity on the resistance vessels.

Sympathicomimetic amines are used both topically and systemically as a decongestant; sometimes in combination with other drugs e.g. antihistamines, but also as a treatment of obesity.

Imidazoline derivatives are used topically. The aim of this study was to perform an objective measurement of the decongestive capacity of topical xylometazoline and oral pseudoephedrine in normal subjects and patients with chronic sinusitis.



A

B

Figure 5. MRI in healthy subjects before (5a) and after (5b) pseudoephedrine administration: note the absence of any effect after ninety minutes on the inferior turbinates and on the mucosa of the sinuses.

A

B

Figure 6. MRI in chronic sinusitis patients before (6a) and after (6b) pseudoephedrine administration: note the absence of any effect after ninety minutes on the inferior turbinates and on the mucosa of the sinuses.

MATERIAL AND METHODS

Ten healthy subjects and 10 chronic sinusitis patients were selected for the study. Healthy subjects (6 male, 4 female) had no nasal complaints and had no obvious rhinoscopic abnormalities.

Chronic sinusitis patients (7 male, 3 female) 1 day prior to FESS-surgery were included in the study. Tobacco, alcohol, coffee, drugs, physical activities, changes of temperature and hot meals or beverages had to be avoided during the study. For the objective assessment of the nasal airway resistance

active anterior rhinomanometry (Atmos 300) was used. Nasal airway resistance was measured left and right and the total nasal airway resistance, in Pa/cm3.s-1, was calculated at 75 Pascal: R tot = RL X RR / RL + RR. Rhinomanometry was performed before and 30', 1, 2, 4, 6 and 8 hours after drug administration.

MRI (Siemens Vision 1.5T) was used to determine the effect of the decongestant on nasal and sinus mucosa and was chosen for absence of radiation and better soft tissue differentiation.

T2- weighted coronal images were obtained before and approximately 90 minutes after drug administration. The decongestive effect on inferior turbinates and mucosa of the sinuses was evaluated.

The images were scored blind by a senior radiologist in the university hospital.

Hundred and twenty mg pseudoephedrine was orally administered as a slow release drug. Xylometazoline was topically administered as a 0.1% spray (140μg per spray). One spray in each nostril was given and repeated after 10 minutes.

Statistics

The ANOVA test for repeated measures was used for statistical analysis of the total nasal airway resistance values, compared with baseline values. A p-value less than 0.05 was considered as statistically significant.

RESULTS

Rhinomanometry

In all patients with chronic sinusitis and all healthy subjects there was a clear and rapid decongestion after xylometazoline administration. An average decrease of the total nasal airway resistance of 37.3% was noted. Decongestion was obvious during 8 hours in all patients and healthy subjects after xylometazoline administration (Figure 1). All healthy subjects showed an increase of the total nasal airway resistance at one or more rhinomanometric measurements after pseudoephedrine administration. In three out of five patients with chronic sinusitis an increase of the total nasal airway resistance was seen at several measurements after pseudoephedrine administration. An average decongestion of 15.9% and 24.1% was noted in two patients, although the total nasal airway resistance remained unchanged during one rhinomanometric measurement. The duration of action of pseudoephedrine can not be determined, taking the irregular results into account (Figure 2).

MRI

MRI findings coincide with rhinomanometric results. Ninety minutes after xylometazoline administration, there is an obvious reduction of the volume of the inferior turbinates in all healthy subjects and in all patients with chronic sinusitis (Figures 3, 4). In the pseudoephedrine group no effect on the nasal mucosa was seen (Figures 5, 6). There was no decongestive effect whatsoever on mucosa of the sinuses with either sympathicomimetic.

Statistics

ANOVA for repeated measures showed significant changes in total nasal airway resistance in both xylometazoline and pseudoephedrine groups. Pair-wise mean comparison testing with Bonferroni correction showed however that there was no difference between the values obtained in the pseudoephedrine group compared with the T0 value in this group. Using the same comparison testing, all values in the xylometazoline group where significantly decreased compared with the baseline values. A p-value less than 0.05 is considered as statistically significant.

DISCUSSION

The effect of topical and oral decongestants has already been studied in the past by several authors using different methods. However, the aim of this study was to compare the decongestive capacity of a topically applied imidazoline derivative and orally administered sympathicomimetic amine during 8 hours using an objective method of evaluation. Bende and Loth [2] used anterior rhinomanometry to assess the duration of action of topical oxymetazoline and the effect of the drug on the nasal mucosal blood flow. They found a rapid decongestive effect which lasted for 6 hours. The reduction of the nasal mucosal blood flow coincided with the reduction of the nasal airway resistance. The authors suggested that the long duration of action of the imidazoline derivatives could be due to the reduced blood flow [2]. In 1994, Hamels et al. [3] studied the effect of topical phenylephrine and xylometazoline using MRI and rhinomanometry. They too found a clear cut superiority of xylometazoline.

Maranta et al. [4] also used rhinomanometry to compare topical xylometazoline and phenylephrine in 60 patients. Although both drugs had a rapid onset of action, the effect of xylometazoline lasted for more than 6 hours and less than 2 hours after phenylephrine administration. Graf et al. [5] used acoustic rhinometry and rhinostereometry to assess the decongestive capacity of orally administered phenylpropanolamine and topically applied oxymetazoline. The recommended dose of phenylpropanolamine showed no significant decongestive effect although the efficacy of twice the recommended dose was comparable with that of oxymetazoline. There was, however, a dose related increase in blood pressure.

In the present study, the important decongestive effect of xylometazoline was confirmed. There was a rapid onset and duration of action of at least 8 hours. There was, however, no significant decongestive effect of orally administered pseudoephedrine.

Falck et al. [6] studied the effect of xylometazoline on the pulse wave and the blood flow in the antral mucosa as well as the gas exchange in the sinus. Blood flow, pulse and

gas exchange are all negatively affected by xylometazoline administration and could therefore impair healing since secretion, transportation, phagocytosis and immune defence are dependent on mucosal blood flow. Paulsson et al. [7] recently studied the ventilation of the paranasal sinuses before and after oxymetazoline administration in healthy subjects and found no significant effect in either group. Further studies on the diseased sinus are however required.

Ackerhans et al. [8] studied the effects of a new nasal drug administration form ('nasal bellows container') in healthy subjects and patients with acute rhinitis. There seems to be an increase in the maxillary ostial diameter after oxymetazoline administration with the nasal bellows container, compared to placebo spray and oxymetzoline spray. Clearly, the study and the new administration form can be of use for further research in rhinitis and sinusitis treatment.

In the present study, MRI showed no effect on the sinus mucosa after xylometazoline or pseudoephedrine administration. As a result, the efficacy of pseudoephedrine or xylometazoline in the treatment of sinusitis is questionable and, as mentioned below, needs further study.

In the past the superiority of imidazoline derivatives over sympathicomimetic amines has been shown by several authors [3, 4, 9]. This was confirmed in the present study.

Although there was an obvious and long lasting decongestive effect of topically administered xylometazoline on the nasal mucosa, no effect whatsoever on the mucosa or inflammatory lesions of the sinuses was noted. The authors conclude that xylometazoline is an effective symptomatic treatment for nasal congestion when compared to orally administered pseudoephedrine.

There is, however no influence on the ventilation or drainage of the sinuses in patients with objective signs of soft tissue involvement. Taking the short term measurements and drug administration in this study into account, repeated MRI studies and long term administration of drugs, for example 10 days, are necessary in the future to evaluate the long term effects of drugs on the sinus mucosa. Kanfer et al. [10] studied the effects of oral decongestants in 1993. They found a half-life of pseudoephedrine of 6 hours. Peak-plasma concentrations vary from 0.5 to 2 hours. Since a slow-release formulation was used in the present study, repeated MRI and rhinomanometry measurements could be useful in the future.

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REFERENCES

1. Bende M. (1983) The effect of topical decongestant on blood flow in normal and infected nasal mucosa. Acta ORL 96: 523-527.
2. Bende M, Loth S (1986) Vascular effects of topical oxymetazoline on human nasal mucosa. J Laryngol Otol 100: 285-288.
3. Hamels K, Clement P(1994) Decongestiecapaciteit van twee frequent gebruikte topische nasale decongestiva bij gezonde proefpersonen. Acta Oto-Rhino-Laryngologica Belgica 48: 265-269.
4. Maranta CA, Simmen D (1996) Decongestant nasal spray. Results of a rhinomanometric double-blind study. Schweiz Med Wochenschr 126: 1875-1880.
5. Graf P, Toll K, Palm J, Hallen H (1999) Effects of sustained-release oral phenylpropanolamine on the nasal mucosa of healthy subjects. Acta Otolaryngologica 119: 837-842.
6. Falck B, Svanholm H, Aust R (1990) The effect of xylometazoline on the mucosa of human maxillary sinus. Rhinology 28: 239-247.
7. Paulsson B, Lindberg S, Ohlin P (2002) Effects of oxymetazoline on the ventilation of paranasal sinuses in healthy subjects. Am J Rhinology 16: 125-129.
8. Ackerhans M, Jannert M, Tonnesson M (1994) Effects of a new administration form of oxymetazoline on maxillary ostial patency in healthy individuals and patients with acute rhinitis. Acta Otolaryngologica Suppl 515: 49-52.
9. Andersson K, Bende M (1984) Adrenoceptors in the control of human nasal mucosal blood flow. Annal Otol Rhinol Laryngol 93: 179-182.
10. Kanfer I, Dowse R, Vuma V (1993) Pharmacokinetics of oral decongestants. Pharmacother 13: 116S-128S.

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