Eur J Clin Pharmacol (2011) 67:19–23
DOI 10.1007/s00228-010-0941-z

SPECIAL ARTICLE

A comparative analysis of the decongestive effect of oxymetazoline and xylometazoline in healthy subjects

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Received: 17 July 2010 / Accepted: 21 October 2010 / Published online: 11 November 2010

Abstract
Background Oxymetazoline and xylometazoline are locally effective and direct acting drugs that relieve nasal congestion. The aim of this study was to objectively determine and compare the decongestive effects of oxymetazoline and xylometazoline in healthy subjects.
Methods The study population comprised thirty healthy adults. All subjects underwent active anterior rhinomanometry (AARhm) and acoustic rhinometry (AR) tests following the application of oxymetazoline, xylometazoline, or placebo (physiological saline). The change in nasal resistance, nasal airflow, and different cross-sectional areas (CSAs) of the nasal cavity in the subjects were examined for each solution separately. The measurements were obtained over a 1-h period (baseline and 1, 15, 30, and 60 min post-dosing). All results were analyzed using the Kruskal–Wallis test and the Mann–Whitney *U* test.
Results A total of 6,300 measurements of AARhm and AR were obtained. The application of placebo did not cause a statistically significant change in nasal resistance, nasal airflow, and CSAs (CSA1, 2, and 3, respectively) of the nasal cavity. In contrast, statistically significant changes in nasal resistance (inspiration p=0.000 and p= 0.004; expiration p=0.000 and p=0.000), nasal airflow (inspiration p= 0.000 and p= 0.004; expiration p=0.000 and p=0.000), and CSAs of the nasal cavity (CSA2 p=0.000 and p=0.000, CSA3 p=0.000 and p=0.00), with the exception of CSA1 (p= 0.982 and p=0.994), were obtained after the application of oxymetazoline and xylometazoline. A comparison of oxymetazoline and xylometazoline based on nasal resistance, nasal airflow, and CSAs of the nasal cavity demonstrated no statistically significant difference, except for CSA3.
Conclusion Oxymetazoline and xylometazoline are fast-acting and potent topical decongestants that have similar decongestive effects.

Keywords Nose · Rhinomanometry · Rhinometry · Nasal decongestants · Oxymetazoline · Xylometazoline

Introduction

Nasal congestion is one of the most frequent and prominent findings in sinonasal diseases. It occurs due to congestion of the venous sinusoids lining the nasal mucosa, which is mainly triggered by infectious rhinosinusitis, allergic or non-allergic rhinitis, and/or the improper use of some medications.

Topical nasal decongestants are fast-acting, potent drugs which are especially effective for the reduction of nasal congestion. They can be classified into two major groups: (1) sympathomimetic amines (cocaine, amphethamine, adrenaline, ephedrine) and (2) imidazolines (oxymetazoline and xylometazoline). Of the imidazolines, oxymetazoline, a selective α-1 and partial α-2 agonist, and xylometazoline, an α-2 agonist, are the most popular and clinically used derivatives. Both achieve their decongestive effect via activation of α-adrenergic receptors, resulting in vasoconstriction of the blood vessels and, consequently, resumption of nasal airflow.

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Nasal airflow can be objectively assessed by rhinomanometry and/or acoustic rhinometry (AR) [1, 2]. Rhinomanometry provides an objective assessment of nasal resistance and measures the rate of airflow in the nasal cavity during respiration. It can be performed using active or passive methods and by anterior or posterior techniques. In practice, active anterior rhinomanometry (AARhm) is the most commonly used method for the clinical measurement of nasal patency [1, 3]. AR is a quick, noninvasive, and reliable method which evaluates the configuration of the nasal cavity through the use of reflected sound waves. It provides an objective assessment of nasal airway patency by obtaining information on nasal cross-sectional areas (nCSAs) and nasal volumes within a given distance. Consequently, it is especially useful for the anatomic evaluation of the nasal cavity. The combination of both of these objective methods provides insight into nasal airflow physiology and nasal airway anatomy.

The aim of this study was to investigate and objectively analyze the decongestive effects of oxymetazoline and xylometazoline using AARhm and AR procedures and to compare the changes in nasal resistance, nasal airflow, and nCSAs over time and location.

Material and methods

Subjects and study design

Thirty healthy volunteers (17 men, 13 women) with a mean age of 26 years (range of 21–33 years) were enrolled in the study. Our inclusion criteria were (1) no nasal symptoms (nasal obstruction, rhinorrhea, etc.), septal deviation, nasal polyps, allergic rhinitis, nasal trauma or surgery, or recurrent upper respiratory tract infections and (2) no use of topical and/or systemic drugs. All subjects underwent a standard clinical and endoscopic examination of the nasal cavity. Upon arrival at the laboratory, subjects acclimatized for 30 min in a comfortable upright seated position; the study was briefly explained to the subjects during this period.

All of the solutions (oxymetazoline 0.05% solution; xylometazoline 0.1%; physiological saline, 0.9% NaCl) were put in standard spray bottles. The solutions were administered randomly and applied to both nostrils of the subjects. Two puffs (50 microlt/puff) from each solution were administered to each nostril of every subject without disclosing any information on the type of solution. Both AARhm and AR tests were performed by a well-trained examiner (Z.H.), who was also blinded for the content of the spray bottle. All measurements were obtained over a 1-h period (baseline and at 1, 15, 30, and 60 min post-dosing).

Active anterior rhinomanometry

Active anterior rhinomanometry was performed using the Rhinostream built-in system in the SRE 2100 acoustic rhinometer (Rhinometrics, Lynge, Denmark). A nasal nozzle was applied to one nostril, and the other nostril was closed off with tape to obtain an airflow seal. Subjects were instructed to breathe through the nozzle. The measurements of nasal resistance [Avg: Pa/(cm^3/sn)] and nasal airflow (cm^3/sn) were made according to the standards set by the Standardization Committee on Objective Assessment of Nasal Airway [4].

Acoustic rhinometry

Acoustic rhinometry was performed according to the guidelines of the Standardization Committee on Acoustic Rhinometry. The acoustic rhinometer (SRE2100PC; Rhinometrics) was calibrated before each set of measurements. Each subject was allowed to breathe through his/her mouth before the test. The anatomical nosepiece with lubricating gel, which is a hypertonic solution that consists of ocean salt, macrogol, propyl parahydroxybenzoate, and methyl parahydroxybenzoate, was positioned on the nostril so as to obtain an acoustic seal without distorting the nose. The subjects were then requested to stop breathing for about 5 s. At least three consecutive measurements with a standard deviation (SD) of less than 5% were obtained. Measurements of nCSAs (cm^2) were obtained at the anterior end of the inferior turbinate and nasal valve (nCSA1), at the anterior half of the inferior turbinate and the anterior end of the middle turbinate (nCSA2), and at the posterior end of inferior turbinate (nCSA3) for each nostril separately.

Data analysis

The statistical analysis was performed by the third author (B.Ö). The results were evaluated using SPSS ver. 10.0 for Windows (SPSS, Chicago, IL). All measurements were entered into an SPSS file for further analysis, allowing evaluation of the mean values of nasal resistance, nasal airflow and nCSAs for all solutions. The decongestive effects of oxymetazoline, xylometazoline, and physiological saline were analyzed by the Kruskal–Wallis test. The time–nasal resistance, time–nasal airflow, and time–nasal area differences of all solutions were compared by the Mann–Whitney U test. The significance level was set at $p<0.05$.

Ethics

Approval for this study was obtained from the Institutional Review Board of Celal Bayar University.

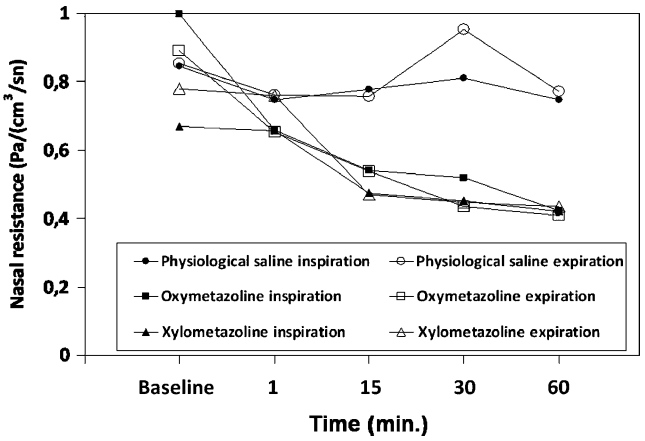

Fig. 1 Changes in nasal resistance from baseline to 1 h after the application of all solutions

Results

All subjects completed the study successfully. Both nasal cavities of all subjects were examined separately, resulting in a total of 6,300 measurements of AARhm and AR.

The effects of all solutions on nasal resistance were examined during respiration (Fig. 1). The application of physiological saline did not cause a statistically significant change in nasal resistance during inspiration and expiration (Table 1). However, statistically significant decreases in nasal resistance during respiration were detected after the application of oxymetazoline (inspiration p=0.000, expiration p=0.000) and xylometazoline (inspiration p=0.004, expiration p=0.000). Although the decrease in nasal resistance during inspiration and expiration following treatment with oxymetazoline or xylometazoline were observable at 1 min post-dosing, statistically significant differences were first determined at 15 min post-dosing and continued until 60 min post-dosing (Fig. 1, Table 2). When the decongestive effects of oxymetazoline and xylometazoline were compared for their effects on nasal resistance, no statistically significant difference was detected during inspiration or expiration (Table 2).

The effects of all solutions on nasal airflow were examined during respiration (Fig. 2). Based on the measurements, application of physiological saline did not cause a statistically significant difference during inspiration (p=0.797) or expiration (p=0.791). In contrast, treatment with oxymetazoline and xylometazoline resulted in a measurable increase in the volume of nasal airflow at 1 min post-dosing, although statistically significant differences in nasal airflow volumes were first detected at 15 min post-dosing, continuing to the end of the experiment (60 min post-dosing) (Table 2). There was no statistically significant difference between the effects of oxymetazoline and those of xylometazoline in terms of changes in nasal airflow (Table 2).

The changes in the different CSAs of the nasal cavity after the application of all solutions were examined (Fig. 3). None of the solutions (oxymetazoline, xylometazoline, physiological saline) caused a statistically significant difference at nCSA1, which marked the internal nasal valve (p=0.982, p=0.994, p=0.966, respectively). In contrast, statistically significant increases at nCSA2 and nCSA3 were determined after the application of both oxymetazoline and xylometazoline (Table 1), although at different time points: at 1 min post-dosing with oxymetazoline and at 15 min post-dosing with xylometazoline (Table 2). When oxymetazoline and xylometazoline were compared according to area differences of nCSAs, xylometazoline caused statistically significant increases only at nCSA3, which marked the posterior end of the inferior turbinate; this was particularly evident at 15 and 30 min post-dosing (p=0.038 and p= 0.035, respectively).

Discussion

Oxymetazoline and xylometazoline are powerful and locally effective decongestants that decrease the workload of breathing through a congested nose and improve drainage of the nasal cavities. Despite their widespread

Table 1 Kruskal–Wallis test for analysis of the decongestive effects of all solutions according to nasal resistance, nasal airflow, and nCSA

Measurement conditions	Physiological saline (p values)	Oxymetazoline (p values)	Xylometazoline (p values)
Nasal resistance (inspiration)	0.730	0.000	0.004
Nasal resistance (expiration)	0.803	0.000	0.000
Nasal airflow (inspiration)	0.797	0.000	0.004
Nasal airflow (expiration)	0.791	0.000	0.000
nCSA1	0.966	0.982	0.994
nCSA2	0.093	0.000	0.000
nCSA3	0.059	0.001	0.000

nCSA, Nasal cross-sectional area: nCSA1. at the anterior end of the inferior turbinate and nasal valve; nCSA2, at the anterior half of the inferior turbinate and the anterior end of the middle turbinate; nCSA3, at the posterior end of inferior turbinate

Table 2 *p* values (according to Mann–Whitney *U* test) of the changes in nasal resistance, nasal airflow, and nCSAs of, oxymetazoline, and xylometazoline over time

Measurement conditions	Experimental solution	Time post-dosing				
		Baseline	1 min	15 min	30 min	60 min
Nasal resistance (inspiration)	PS-OM	0.337	0.208	0.048	0.002	0.003
	PS-XM	0.379	0.304	0.002	0.001	0.003
	OM-XM	0.096	0.607	0.074	0.957	0.588
Nasal resistance (expiration)	PS-OM	0.808	0.137	0.038	0.002	0.002
	PS-XM	0.534	0.776	0.002	0.004	0.004
	OM-XM	0.570	0.756	0.056	0.645	0.797
Nasal airflow (inspiration)	PS-OM	0.317	0.317	0.050	0.005	0.003
	PS-XM	0.379	0.310	0.002	0.001	0.005
	OM-XM	0.093	0.516	0.064	0.978	0.579
Nasal airflow (expiration)	PS-OM	0.417	0.172	0.035	0.005	0.002
	PS-XM	0.552	0.776	0.003	0.003	0.003
	OM-XM	0.285	0.925	0.055	0.903	0.787
nCSA1	PS-OM	0.118	0.968	1.000	0.102	0.978
	PS-XM	0.818	0.935	0.871	0.386	0.626
	OM-XM	0.126	0.818	0.839	0.344	0.655
nCSA2	PS-OM	0.457	0.076	0.015	0.003	0.010
	PS-XM	0.892	0.039	0.001	0.000	0.003
	OM-XM	0.351	0.839	0.110	0.298	0.425
nCSA3	PS-OM	0.829	0.053	0.083	0.001	0.035
	PS-XM	0.946	0.030	0.001	0.000	0.006
	OM-XM	0.735	0.323	0.038	0.035	0.490

PS, Physiological saline; OM, oxymetazoline; XM, xylometazoline

use, limited objective and comparative data related to their decongestive effects are available in the English literature. Bickford et al. studied the effect of oxymetazoline in healthy subjects and concluded that normal subjects are good candidates for the examination of the effects of topical decongestants due to easy subject recruitment and low variability [5]. Therefore, we also used healthy volunteers in our study. Bickford et al. also reported that oxymetazoline caused a significant vasoconstrictor effect in normal healthy subjects [5].

We first evaluated the decongestive effects of oxymetazoline and xylometazoline according to the changes

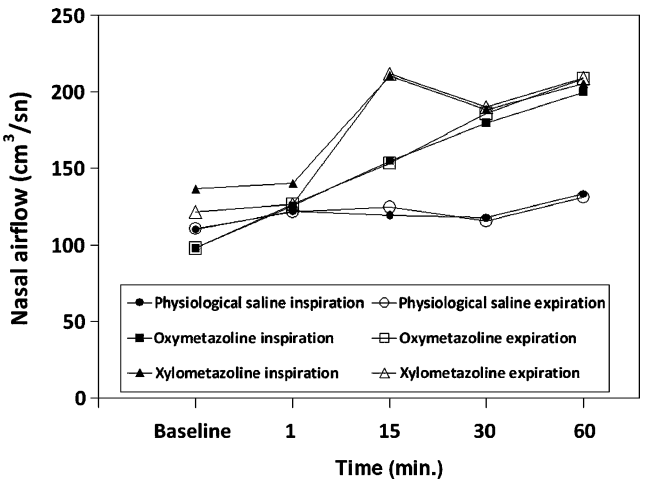

Fig. 2 Changes in nasal airflow from baseline to 1 h after the application of all solutions

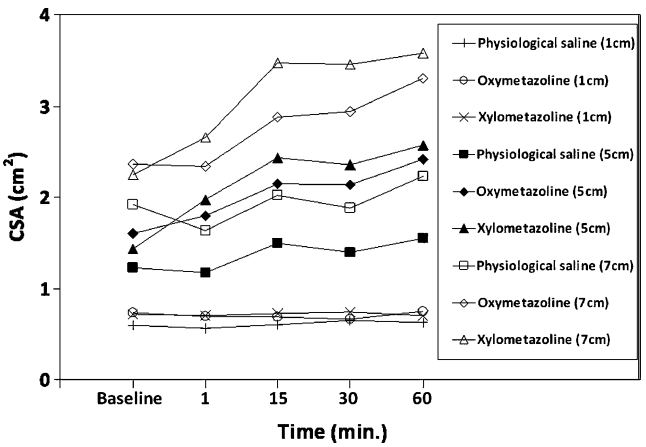

Fig. 3 Changes in nasal cross-sectional areas (CSAs) from baseline to 1 h after the application of all solutions

in nasal resistance, nasal airflow, and nCSAs and observed that the application of both topical decongestants resulted in a progressive decrease in nasal resistance during inspiration and expiration (Fig. 1). The values of nasal resistance obtained following the application of oxymetazoline and xylometazoline were significantly different from that of the control group (Table 2). Both topical decongestants also caused statistically significant increases in the volume of nasal airflow (Fig. 2, Table 1) as well as statistically significant progressive changes in the nCSAs at CSA2 and CSA3 (Fig. 3). However, none of the topical decongestants caused a statistically significant change at the internal nasal valve, which constitutes rigid structures, such as quadrangular and upper lateral cartilages (CSA1) (Table 1). These data indicate that both oxymetazoline and xylometazoline are potent decongestants which achieve their decongestive effect by acting on nasal mucosa throughout the nasal cavity, with the exception of the internal nasal valve. Although this study was performed on healthy subjects, similar decongestive effects are to be expected in patients with congested nose. In a double-blind study, Eccles et al. objectively evaluated the decongestive effect of xylometazoline in patients with common cold and found a statistically significant difference between xylometazoline and placebo. In addition, they emphasized that xylometazoline significantly relieved nasal congestion [6].

Secondly, we evaluated the changes in the decongestive effects of oxymetazoline and xylometazoline over time (1 h). Although the application of both oxymetazoline and xylometazoline caused a decrease in nasal resistance and an increase in nasal airflows as early as 1 min post-dosing, statistically significant differences were first observed at 15-min post-dosing (Figs. 1, 2, Table 2). In addition, xylometazoline caused statistically significant increases in nCSA2 and nCSA3 at 1 min post-dosing, while oxymetazoline caused statistically significant increases in nCSA2 and nCSA3 at 15 min post-dosing (Table 2). These data demonstrate that xylometazoline seems to have a faster onset of action, even though decongestive effects were observed within minutes with both of the topical decongestants, with a similar duration of effect. In a similar study, Connell and Linzmayer compared the decongestive effects of topical oxymetazoline and systemic pseudoephedrine according to the change in nasal airflow; they reported that oxymetazoline had a more rapid onset and duration of action, greater improvement in airway patency, and longer action than pseudoephedrine [7].

In the last part of our study, we compared the decongestive effects of oxymetazoline and xylometazoline. During the evaluation of nasal resistance and airflow, we did not observe any statistically significant difference between oxymetazoline and xylometazoline (Table 2). The evaluation of nCSAs revealed that xylometazoline seemed to produce better results than oxymetazoline (Figs. 1, 2, 3); however, none of the results was statistically significant with the exception of the difference at nCSA3 at 15 and 30 min post-dosing. Although our objective results indicate that xylometazoline had a more potent decongestive effect at the posterior end of the turbinate, this can be a misinterpretation which may be related to the inaccuracies in the measurements made beyond 6 cm from the entrance of the nostril [8]. Therefore, we relied on the results of nCSA1 and nCSA2, for which the differences between oxymetazoline and xylometazoline were statistically insignificant. Likewise, Hochban et al. reported that they did not find a statistically significant difference between different concentrations of various imidazoline derivatives in terms of efficacy [9]. Based on these results, we conclude that both oxymetazoline and xylometazoline have similar decongestive effects over the relatively short term; however, studies that focus on the decongestive effects of these drugs over the long term (3–6 h) are also required.

Conclusion

Oxymetazoline and xylometazoline are potent, fast-acting drugs that exert their decongestive effects through the nasal cavity. However, neither drug was observed to alter nasal resistance or nasal airflow at the internal nasal valve. Our comparison revealed that oxymetazoline and xylometazoline had similar decongestive effects in our study subjects and that these occurred within minutes of application and had a similar duration of action.

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