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# The effect of Xylometazoline on the mucosa of human maxillary sinus

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SUMMARY

*A stuffy and running nose are two of the most expressed symptoms of acute rhinosinusitis and have made the use of decongestants very common. The medication, oral or nasal, gives relief from symptoms but its effect on the healing of the infection, positive or negative, is not clear.*

*The effect of Xylometazoline on the blood flow, the pulse amplitude and the gas exchange in the antral mucosa of the maxillary sinus was studied in five healthy subjects.*

*Our experiments show that the mucosal pulse amplitude and the blood flow are strongly reduced by insufflation of Xylometazoline but the gas exchange in the mucosa is only lowered to a minor extent. The reduction in gas exchange is not great enough to allow the gas mixture to be altered. The defence mechanisms in the antral mucosal lining, i.e. the mucociliary-, the immuno- and the phagocytotic mechanisms are all dependent on the blood flow and the gas exchange through narrow maxillary ostia of the pumping effect generated by the mucosal pulse wave. The reduction in blood flow and pulse amplitude in the maxillary mucosa caused by Xylometazoline leads us to consider that, although not harmful then it is at least not helpful, in healing rhinosinusitis. Since oral decongestants have almost the same effect on the mucosa as nasal decongestants, we do not think that any of the medicines faciliate the healing of infections in the upper airways even if they make the patient feel better during the infection.*

## INTRODUCTION

The paranasal sinuses, being ventilated non-collapsable gas pockets (Rahn and VanLiew, 1955) and connected to the nasal cavity or the nasopharynx by narrow ostia, have no known function. They are lined with respiratory epithelium of the same type of mucosa as in the nose and the medial part of the Eustachian tube with ventilatory (Ballenger and Ballenger, 1952; Flottes et al., 1960; Aust and

Drettner, 1974; Aust et al., 1979; Svanholm et al., 1981), secretory (Herberhold, 1982) and transporting (Hilding, 1932; Messerklinger, 1967) functions. Furthermore, the mucosal defence also includes mechanisms such as the mucociliary, the immuno and the phagocytosis systems.

All defence mechanisms must be intact to keep the paranasal antra healthy. These different systems, working together to protect the paranasal sinuses from infections, are all dependent on the mucosal blood flow, a flow of the same magnitude as that in liver, intestines and brain expressed as $cm^3$ blood/$cm^3$ tissue/min (Drettner and Aust, 1974).

In infections of the upper airways the first symptom is often a stuffy and running nose irritating the patient. This discomfort is commonly treated with nose drops or peroral alpha-adrenergic antagonists. Both kinds of medication give a reduction of the nasal blockage and to some extent of the secretion.

It is well-known that these drugs have a decongestive effect on both healthy and inflamed mucosa (Aschan, 1974; Aust et al., 1979; Melen, 1986) by reducing the nasal blood flow as shown by Bende (1983) in studies with radioactive Xenon ($^{133}Xe$). This phenomenon has been seen in both healthy and inflamed mucosa. Reduced blood flow usually disturbs normal function in organs of the body. This fact made us interested in the effect of decongestives on the mucosa of the paranasal sinus, whether the use of these drugs, especially Xylometazoline, facilitates the healing of acute infection or not.

The effect of Xylometazoline on the mucosa of the nose has been studied by earlier investigators, but not its effect on maxillary mucosa.

We therefore found it interesting to study the effect of this drug on pulse wave, blood flow and gas exchange in experimentally occluded sinuses.

The aim of this investigation is to study the effect of Xylometazoline on:

1. The pulse wave in the antral mucosa.
2. The blood flow in the antral mucosa.
3. The exchange of $O_2$, $CO_2$ and $N_2$ in the antral mucosa.

## MATERIAL AND METHODS

Five healthy persons, three women and two men, aged 24 to 47 years participated in the study.

All the studies were performed in experimentally occluded human maxillary sinuses. The variations in antral pulse were measured as pressure variations in the sinus with a manometer EMT 33 (Elema Schönander). The manometer was connected to a plastic tube with a length of 800 mm and with an inner diameter of 0.8 mm and a cannula with an inner diameter of 1.2 mm introduced into the investigated sinus through the lower nasal meatus. The signals from the manometer were amplified in a EMT 31 (Elema Schönander) amplifier and recorded with a Mingograph 32 (Elema Schönander).

The variations in blood flow were measured plethysmographically; the blood flow in the internal jugular veins was bilaterally blocked for 10 seconds by digital compression (Drettner and Aust, 1974). The blocking of the venous blood flow resulted in a pressure rise in the investigated sinus which was recorded with the manometer equipment described above. The variations in blood flow were expressed in $\mu$l/min per ml sinus volume.

The volume of the antrum was determined according to Boyle's law; 50 microliters of air were insufflated into the experimentally occluded sinus and the pressure rise together with the initial antral pressure and known volume of the insufflated gas made it possible to calculate the volume of the cavity (Figure 1).

$$P \times V = P^1 \times V^1$$

$P$ = initial pressure in the investigated sinus.
$V$ = volume of the maxillary sinus + manometrical system volume.
$P^1$ = pressure in the maxillary sinus after insufflation of 50 microliters of air.
$V^1$ = volume of the maxillary sinus + manometrical system volume − 50 microliters of air.

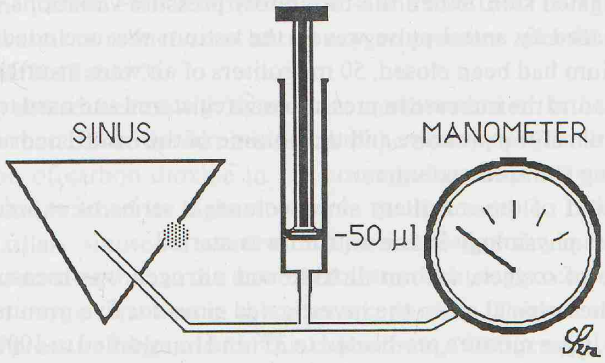


Figure 1. Equipment used for determination of the volume of the maxillary sinus.

Aust and Helmius (1974) performed experimental studies on sinus volume with X-ray contrast medium injection in maxillary sinuses of dry skulls. From these experiments they constructed formulas in which length, width and height of the sinus measured on the X-ray pictures in two projections gave both sinus volume and area of the antral mucosa.

In this study, we compared different hypothetically formed maxillary sinuses with known volume and found that variations of sinus dimensions with a given volume gave only small variations in the calculated mucosal area. We therefore approximated an ideal sinus form in which we estimated, according to Aust and Helmius, the mucosal area from the sinus volume and multiplied this area by

0.4 mm, being the thickness of the antral mucosa given by Tos (1979), thus getting a rather good estimation of the volume of the antral mucosal lining.
The variations in gas content in the investigated antrum were determined by taking samples from the sinus with a gas-tight syringe. The samples were analysed in a Varian gas chromatograph.

PROCEDURE OF THE EXPERIMENTS

The participating subjects were given a thorough history and E.N.T. investigation and if they were found healthy, with no nasal or antral infection for the last two months, they were allowed to enter the study.
The experiments started with local anaesthesia of the lower nasal meatus in the investigated persons with Xylocain® dental spray. After anaesthesia the cannula connected to the manometer was introduced into the maxillary sinus through the bony wall of the lower nasal meatus. If respiratory pressure variations synchronous to nasal breathing were registered, the ostium was regarded as patent, an indication of a normally functioning antrum.
The next step in the experiment was to close the ostium with Spongostan® mixed with Xylocain® gel by placing the Spongostan mixture in the middle nasal meatus on the investigated side. When the respiratory pressure variations disappeared and were replaced by antral pulse waves, the ostium was occluded.
When the ostium had been closed, 50 microliters of air were insufflated into the occluded sinus and the increase in pressure was registered and used together with the known initial antral pressure and the volume of the insufflated air in Boyle's law, thus giving the sinus volume.
After calculation of the maxillary sinus volume a series of experiments concerning normal physiology in the antrum was started.
The exchange of oxygen, carbon dioxide and nitrogen was measured by first washing out the original air in the investigated sinus for five minutes with, and replacing it by, a gas mixture pre-heated to 37° and humidified to 100% ($O_2$ 18.4%, $CO_2$ 2.09%, Ar 1.04% and $N_2$ 78.47%), a mixture made up of samples taken from 10 healthy maxillary sinuses with patent ostia.
After closing the system, small samples (5 microliters) were taken out from the sinus with the air-tight syringe at the beginning of the experiments and then every tenth minute for 40 minutes.
The investigation of gas exchange, pulse wave and blood flow in normal sinus was followed by a second series of experiments, similar to the one described above with the exception that in this series 1 ml, containing 1 mg of Xylometazoline (Otrivin® nasal spray 0.1%), was sprayed into the investigated sinus and before each gas sample was taken out from the sinus the antral pulse wave was recorded and a plethysmographic measurement of the blood flow in the sinus was performed.

RESULTS

The pulse waves in the antral mucosa were recorded for 30 seconds at each registration and 12 waves were measured. The largest and the smallest registrations were excluded and the amplitude of the remaining 10 were used in the calculations (Table 1).

In this study we found that the pulse amplitude in the sinus mucosa treated with Xylometazoline was reduced over time and reached a value of about 75% of its initial value after 40 minutes (Figure 2). The reactions in the antral mucosal pulse wave to nose drops within the group of investigated persons were similar and had small variations except for one subject, where only a small reaction to nose drops was seen in the antral pulse amplitude, probably due to technical reasons.

The blood flow in the sinus mucosa measured plethysmographically was also reduced after administration of Xylometazoline into the antrum (Table 2 and Figure 3).

The reduction was fastest during the first 20 minutes of our experiments. During the following 20 minutes the reduction slowed down to reach its minimum after about 40 minutes, at a reduction of nearly 40%.

The oxygen exchange in the normal, experimentally occluded maxillary sinus followed the pattern earlier showed by Aust and Drettner (1974) and Falck et al. (1989) with a mean reduction of antral oxygen pressure after 40 minutes of just above 3 vol. % (Table 3).

In maxillary sinuses treated with Xylometazoline the reduction in the oxygen fraction was smaller than before the administration of the nose drops (Table 4 and Figure 4).

The tension of carbon dioxide in the normal, experimentally occluded, sinus increased and reached its highest value in the last sample (Table 5).

In the maxillary sinuses treated with Xylometazoline the increase of carbon dioxide was smaller than in the untreated antrum which also corresponded to the decrease in oxygen fraction in the same experiment (Table 6 and Figure 5).

Within the pressure range used in this experiment, Nitrogen and Argon are biologically inactive gases and no exchange for either of them was registered during the different experiments in our study.

Table 1. Pulse amplitude (mm $H_2O$) after administration of Xylometazoline into the sinus.

| case no. time min. | 1 | 2 | 3 | 4 | 5 | M | Δ% |
|---|---|---|---|---|---|---|---|
| 0 | 0.94 | 2.09 | 2.09 | 0.90 | 2.85 | 1.77 | 0 |
| 10 | 0.93 | 2.23 | 1.98 | 0.80 | 2.35 | 1.66 | −7 |
| 20 | 0.84 | 1.97 | 1.76 | 0.79 | 1.96 | 1.46 | −17 |
| 30 | 0.75 | 2.06 | 1.97 | 0.80 | 1.81 | 1.48 | −17 |
| 40 | 0.73 | 2.10 | 1.69 | 0.63 | 1.72 | 1.37 | −23 |

Table 2. Blood flow after administration of Xylometazoline into the maxillary sinus, $\mu$L/min per ml sinus volume.

| case no. time min. | 1 | 2 | 3 | 4 | 5 | M | Δ% |
|---|---|---|---|---|---|---|---|
| 0 | 16.6 | 26.9 | 21.1 | 11.7 | 31.4 | 21.5 | 0 |
| 10 | 12.6 | 21.3 | 16.6 | 10.6 | 30.9 | 18.4 | −15 |
| 20 | 8.9 | 19.6 | 10.9 | 7.3 | 28.2 | 15.0 | −30 |
| 30 | 8.1 | 17.9 | 12.7 | 7.4 | 25.0 | 14.2 | −34 |
| 40 | 8.4 | 17.3 | 10.4 | 7.0 | 23.4 | 13.3 | −38 |

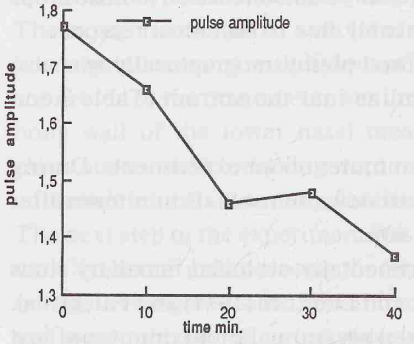


Figure 2. Pulse amplitude (mm $H_2O$) after administration of Xylometazoline into the sinus.

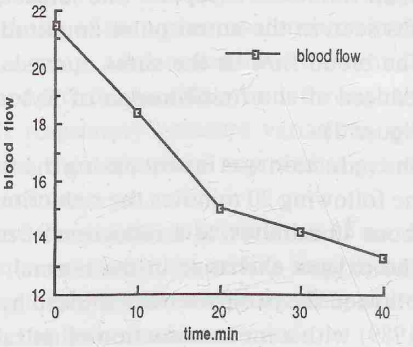


Figure 3. Blood flow after administration of Xylometazoline into the maxillary sinus, $\mu$l/min per ml sinus volume.

Table 3. Oxygen change in normal maxillary sinus with experimentally occluded ostium (vol. %).

| case no. time min. | 1 | 2 | 3 | 4 | 5 | Mean | Δ% |
|---|---|---|---|---|---|---|---|
| 0 | 17.72 | 18.23 | 17.89 | 17.86 | 17.79 | 17.90 | 0 |
| 10 | 16.87 | 17.08 | 17.35 | 17.18 | 16.70 | 17.04 | −0.86 |
| 20 | 16.28 | 16.46 | 16.60 | 16.84 | 16.02 | 16.44 | −1.46 |
| 30 | 16.03 | 15.94 | 16.33 | 16.17 | 15.42 | 15.98 | −1.92 |
| 40 | 15.52 | 15.55 | 15.78 | 15.76 | 14.94 | 15.51 | −2.39 |

Table 4. Oxygen change (vol. %) after administration of Xylometazoline.

| case no. time min. | 1 | 2 | 3 | 4 | 5 | Mean | Diff. |
|---|---|---|---|---|---|---|---|
| 0 | 16.70 | 17.64 | 17.69 | 17.86 | 17.45 | 17.47 | 0 |
| 10 | 16.28 | 16.80 | 17.19 | 16.95 | 16.84 | 16.81 | −0.66 |
| 20 | 16.20 | 16.04 | 16.55 | 16.40 | 16.09 | 16.26 | −1.21 |
| 30 | 16.07 | 15.45 | 16.33 | 16.13 | 15.28 | 15.86 | −1.61 |
| 40 | 15.88 | 15.00 | 15.81 | 15.89 | 15.07 | 15.53 | −1.94 |

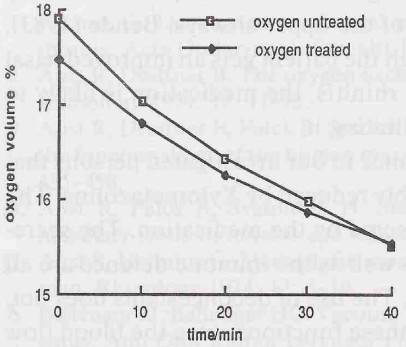


Figure 4. Oxygen change (vol. %) before and after administration of Xylometazoline.

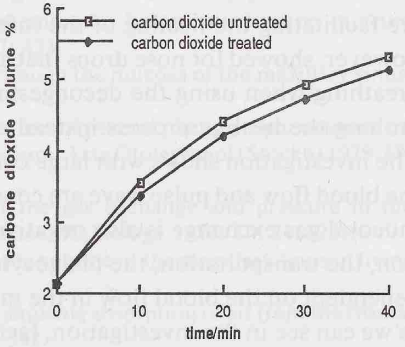


Figure 5. Carbon dioxide change before and after administration of Xylometazoline.

Table 5. Carbon dioxide change (vol. %) in the normal, experimentally occluded, maxillary sinus.

| case no. time min. | 1 | 2 | 3 | 4 | 5 | Mean | Diff. |
|---|---|---|---|---|---|---|---|
| 0 | 2.31 | 2.11 | 2.12 | 2.09 | 2.09 | 2.14 | 0 |
| 10 | 4.01 | 3.83 | 3.18 | 3.04 | 3.60 | 3.53 | 1.39 |
| 20 | 5.05 | 4.72 | 3.90 | 3.74 | 4.57 | 4.40 | 2.26 |
| 30 | 5.53 | 5.30 | 4.46 | 4.24 | 5.05 | 4.92 | 2.78 |
| 40 | 6.01 | 5.62 | 4.87 | 4.72 | 5.40 | 5.32 | 3.18 |

Table 6. Carbon dioxide change in maxillary sinuses, with occluded ostia, sprayed with 1 mg Xylometazoline.

| case no. time min. | 1 | 2 | 3 | 4 | 5 | Mean | Diff. |
|---|---|---|---|---|---|---|---|
| 0 | 2.35 | 2.07 | 2.12 | 2.09 | 2.06 | 2.14 | 0 |
| 10 | 3.70 | 3.45 | 3.24 | 3.01 | 3.47 | 3.37 | 1.23 |
| 20 | 4.88 | 4.44 | 3.81 | 3.67 | 4.15 | 4.19 | 2.05 |
| 30 | 5.20 | 5.11 | 4.30 | 4.21 | 4.73 | 4.71 | 2.57 |
| 40 | 5.69 | 5.42 | 4.62 | 4.69 | 5.27 | 5.14 | 3.00 |

## DISCUSSION

The discomfort of stuffy and running nose during rhinitis and sinusitis has made the use of decongestants very common in such conditions. We have no doubt that

the relief felt by patients when using such drugs leads them to believe that they are facilitating the healing of the infection of the upper airways. Bende (1983), however, showed for nose drops that although the patient gets an improved nasal breathing when using the decongestants in rhinitis, the medication is likely to prolong the healing process instead of facilitating it.

The investigation shows with large concordance in our investigated persons that the blood flow and pulse wave are considerably reduced by Xylometazoline. The mucosal gas exchange is also negatively affected by the medication. The secretion, the transportation, the phagocytosis as well as the immune defence are all dependent on the blood flow in the mucosa. The use of decongestants does not, as we can see in the investigation, facilitate these functions since the blood flow and pulse amplitude are reduced by the medication by about 40% and 23% respectively.

In this study, the nose drops used are such which, during normal medication, hardly get into the maxillary sinus so an objection may be raised that the investigation does not illustrate normal clinical situations. However, the maxillary sinus is an excellent "model" for physiological investigations of the mucosa of upper airways. In fact Aschan (1974) and Aust et al. (1979) have experimentally demonstrated similar effects on blood flow in the upper airways by oral and by nasal "nose drops" on maxillary and nasal mucosa and this provides us with opportunities to draw some conclusions about decongestive medication.

The ventilation through the ostium ought to be improved with nose drop medication but Ivarsson et al. (1984) have demonstrated a neglibible effect of decongestants on ostial patency. Melen (1986) showed no significant effect on the ostial size after administration of phenylpropanolamine to a patient in a sitting position, but some effect when the patient was recumbent. Furthermore, the effect of nose drops on nasal ventilation probably does not improve antral ventilation since the widening of the whole nasal cavity reduces the pressure difference between the nasal vestibulum and the nasopharynx, resulting in a less effective nasal air stream for antral ventilation.

As shown by Svanholm et al. (1981), the reduced pulse amplitude is harmful to antral ventilation through small ostia. In experimental studies in human maxillary sinuses and in models, they registered that in sinuses with very small ostia, as in many cases of sinusitis, the pumping effect of the pulse waves was important for the perostial gas exchange.

So even if the gas exchange in the maxillary mucosa is not particularly reduced, the use of decongestants on nasal and antral mucosa has a negative effect on the blood flow in the upper respiratory airways, thus reducing the effectiveness of the defence systems in the nasal and antral mucosa and their healing effect in rhinosinusitis is doubtful, if any.

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