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Treatment with xylometazoline (Otrivin®) nosedrops over a six-week period

Björn Petruson, Göteborg, Sweden

SUMMARY

Twenty healthy subjects were treated with xylometazoline 1 mg/ml for six weeks in order to study the occurrence of tachyphylaxis and rhinitis medicamentosa. Each subject instilled 0.15 ml of xylometazoline nose-drops into each nostril three times a day. Posterior rhinomanometry was performed before the trial started, after 1, 2, 4 and 6 weeks treatment and 20, 27, 40 and 48 hours after the subject had taken the nose-drops for the last time.

With rhinomanometry it was possible in this study to show that the same dose was adequate during the whole six-week period, i.e. no tachyphylaxis was observed. No reactive congestion was observed after the trial was finished.

When nose-drops containing ephedrine and naphazoline are used over a period of time tachyphylaxis and rhinitis medicamentosa frequently are observed (Kluger, 1959; Sählbrandt, 1960; Freiman and Puchta, 1963).

Only a few cases of rhinitis medicamentosa have been reported, however, after the use of xylometazoline (Feinberg and Feinberg, 1971). In this investigation 20 healthy subjects were tested with xylometazoline for 6 weeks in order to study the occurrence of tachyphylaxis and rhinitis medicamentosa.

SUBJECTS

The study group consisted of 16 women and 4 men, aged 22–55 years (mean age 32 years), working at the hospital. One of the subjects had not had a common cold for several years, eleven had a cold once a year and eight had 2–4 colds a year. Ten of the subjects never had crusting in the nose, nine had it sometimes and one had it often. Eight of the subjects smoked.

When rhinoscopy was performed none of the subjects showed changes that diverged from the normal. None had had a common cold during the month preceding the trial.

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METHODS

Nose-drops

Each subject took the nose-drops three times daily at fixed times for 6 weeks. The contents of one plastic pipette containing 0.15 ml of xylometazoline solution 1 mg/ml were instilled into each nostril.

Olfaction test

Olfaction was tested before and two days after the trial in the following way. Four 100 ml bottles were filled with 20 ml of eau de cologne, oil of lemon, turpentine or tar. Two plastic tubes were connected to each bottle. A nasal tip was connected to the outgoing tube and a 20 ml syringe to the other one. By means of the syringe, different amounts of air could be passed through the bottle to the test subject's nostril. It was noted whether 5, 10, 15 or 20 ml of air was needed for olfaction.

Rhinomanometry

Posterior rhinomanometry was performed with a Rinoma 12S (Dr. Ing. Heinz Gohlke, 8251 Kirchdorf ü/Dorfen, West-Germany). The pressure and flow of air were measured at the same time. The air flow at a pressure of 1.5 mbar was shown on the scale during inspiration. During the trial the rhinomanometer was tested against known airflow and pressure.

At each test 15–25 inspirations were recorded and the mean value was then calculated. On average the variation between the readings in one test was less than two per cent.

Rhinomanometry was performed before the trial started, after the use of nose-drops for 1, 2, 4 and 6 weeks and 20, 27, 40 and 48 hours after the subjects had taken nose-drops for the last time (approximately at 11 a.m., 6 p.m., 7 a.m. and 3 p.m.). During the trial the recordings were made 1–4 hours after administration of the drops. The tests were always performed in the seated position while the subjects quietly breathed atmospheric air.

Side-effects

On each day during the trial the subjects recorded the answers to the following questions on a form: Have you got a cold? Do you have a stuffy nose, a runny nose, irritation or dryness of the nose? Any other side-effects? One week after the trial was finished each subject was asked to answer the following questions: Have you at any time during the last week had a stuffy nose, a runny nose, irritation or dryness of the nose? Have you observed any other side-effects?

Statistics

The statistical calculations were performed with the sign-test.

RESULTS

Olfaction test

Before the trial two subjects needed 20 ml of air to catch the odour, three needed 10 ml and the rest could do so after 5 ml of air. Two days after the end of the trial all subjects could catch the odour after 5 ml of air. Diminished olfaction was thus not observed after the use of the nose-drops for 6 weeks. Nor had any of the subjects observed that their ability to smell was reduced.

Rhinomanometry

The nasal air-flow increased significantly during the trial. The mean values were at the same level which means that no tachyphylaxis was observed (Figure 1, Table 1 and 2). After the trial the nasal air-flow in the study group was the same as before the trial, no rebound-effect was seen.

Side-effects

Five of the subjects had an upper respiratory throat infection during the trial. Two had a sore throat for a couple of days, one had a runny nose for 6 days with no other symptoms and one bled a few drops from the nose. No subject reported irritation or dryness of the nose.

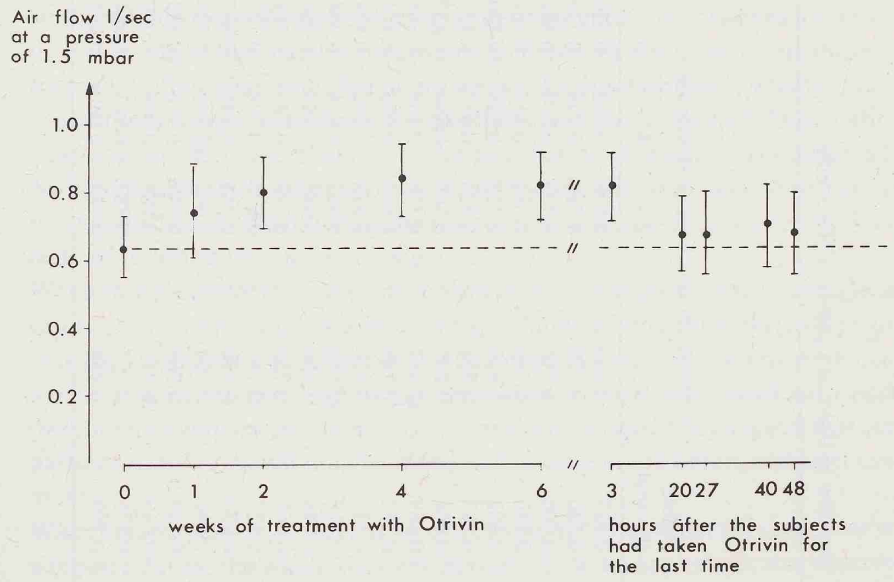

Figure 1. The mean values and standard deviations of air-flow in 20 subjects treated with nose-drops over a six-week period.

Table 1. Air-flow in l/sec. at a pressure of 1.5 mbar.

Subject No.	Before the trial	Weeks of treatment with Otrivin				Hours after the subject had taken Otrivin for the last time				Subjects who	
		1	2	4	6	20	27	40	48	contracted a common cold during the trial	had a stuffy nose at times after the trail
1	0.527	0.636	0.629	0.772	0.770	0.764	0.747	0.722	0.663		
2	0.580	0.759	0.780	0.736	0.779	0.703	0.704	0.676	0.575		2 days
3	0.700	0.710	0.729	0.779	0.694	0.639	0.570	0.657	0.596		
4	0.740	0.746	0.680	0.857	0.761	0.715	0.645	0.701	0.624		
5	0.602	0.639	0.768	0.920	x0.800	0.673	0.751	0.694	–	x	
6	0.793	0.838	0.926	0.857	0.823	0.695	0.652	0.682	0.646		
7	0.604	0.803	0.765	0.794	0.837	0.727	0.731	0.627	0.746		1 day
8	0.469	x0.457	0.718	0.636	0.666	0.492	0.424	0.458	0.439	x	
9	0.562	0.768	0.843	0.905	0.814	0.668	0.658	0.674	0.748		
10	0.511	0.570	0.812	0.782	0.818	0.480	0.551	0.533	0.548		
11	0.710	x0.551	0.862	0.936	0.964	0.743	0.735	0.725	0.743	x	
12	0.746	1.000	0.948	0.987	0.984	0.634	0.846	0.791	0.786		2 mornings
13	0.661	0.738	0.723	0.737	0.711	0.616	0.689	0.654	0.696		2 days
14	0.537	0.745	0.670	0.708	0.727	0.514	0.538	0.541	0.473		2 days
15	0.620	0.629	0.745	0.745	0.807	0.556	0.539	0.619	–		
16	0.666	0.794	0.667	x0.745	0.799	0.619	0.578	0.810	0.652	x	
17	0.709	0.863	0.949	0.978	x0.823	0.831	0.575	0.838	0.818	x	2 mornings
18	0.719	0.915	0.989	0.926	1.000	0.826	0.928	0.997	0.926		
19	0.575	0.757	0.787	0.961	0.864	0.634	0.688	0.625	0.634		
20	0.759	0.953	0.984	0.960	0.961	0.879	0.765	0.868	0.719		

Table 2. Air-flow in l/sec. at a pressure of 1.5 mbar.

	Before the trial	Weeks of treatment with Otrivin				Hours after the subject had taken Otrivin for the last time			
		1	2	4	6	20	27	40	48
Mean value	0.639	0.743	0.797	0.836	0.820	0.670	0.665	0.695	0.668
S.D.	0.093	0.137	0.109	0.105	0.095	0.110	0.118	0.124	0.121
Statistical comparison with the pre-trial value, sign test		$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p>0.3$	$p>0.2$	$p>0.11$	$p>0.3$

During the week after the trial two subjects felt a slightly stuffy on the first two mornings and four subjects had a stuffy nose at times during the first two days. The nasal air-flow was tested on four occasions in each of these six subjects (see methods). In four tests in four different subjects it was possible to show that the air-flow had decreased by about ten per cent. In the other tests the air-flow was the same or better than in the test before the trial. One subject experienced slight dryness of the nose during the first three days. No other side-effects were reported.

DISCUSSION

Nose-drops have been used for many years for treatment of a common cold with a stuffy or runny nose. When nose-drops containing ephedrine or naphazoline were used side-effects like reactive congestion, tachyphylaxis and rhinitis medicamentosa were often observed after some weeks. Xylometazoline is widely used in nose-drops but only a few cases of side-effects have been reported. This might be due to failure to report them or to the fact that no side-effects are observed.

No rhinomanometric study on long-term therapy with xylometazoline has ever been published. In order to evaluate the occurence of side-effects, 20 healthy subjects were tested over a six-week period.

When rhinomanometry is used in clinical trial it is not possible to use single test values as the coefficient of variation is high. Kumlien and Schiratzki (1979) found that the coefficient was 20 per cent when duplicate determinations were made within a short interval and 50 per cent when a small was tested with posterior rhinomanometry once a day on 3–5 consecutive days. They suggest that comparisons in trials should only be made in the same group before and after treatment.

With rhinomanometry it was possible in this study to show that the same dose was adequate during the whole six-week period, i.e. no tachyphylaxis was observed. No reactive congestion was observed after the trial was finished. The nasal air-flow was approximately the same as before the trial. Thirteen subjects showed a

decreased air-flow in at least one test after the trial. The decrease was always less than 20 per cent, however, and thus less than the day-to-day variation.
The side-effects during the trial were few – one subject had a runny nose for a few days and one bled a few drops from the nose. None of the subjects suffered from impaired olfaction.
During the week after the trial six subjects had a stuffy nose at times. Only in four out of twenty-four rhinomanometric tests was it possible to show a decreased air-flow, the reduction being about ten per cent. A possible explanation is that during the trial the subjects became used to breathing more easily through the nose. When the congestion returned to normal after the trial some subjects probably experienced a false sensation of stuffiness.

ZUSAMMENFASSUNG

20 gesunde Personen wurden 6 Wochen lang mit 1 mg/ml Xylometazoline behandelt, um das Auftreten der Tachyphylaxie und medikamentösen Rhinitis zu studieren. Jeder nahm dreimal täglich 0,15 ml Xylometazoline als Tropfen in jede Nasenhälfte. Posteriore Rhinomanometrie wurde vor dem Versuch 1, 2, 4 und 6 Wochen nach der Behandlung sowie 20, 27, 40 und 48 Stunden nach der letzten Einnahme der Nasentropfen durchgeführt. Mit der Rhinomanometrie konnte gezeigt werden, dass die gleiche Dosis im Zeitraum von 6 Wochen gleich wirksam war, dass also eine Tachyphylaxie nicht beobachtet wurde. Auch eine reaktive Schwelling konnte nach Beendigung des Versuches nicht festgestellt werden.

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Björn Petruson
Assoc. professor
University ENT-Clinic
Sahlgren's Hospital
S-41345 Göteborg
Sweden