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Comparative Randomised Clinical Study of Tolerability and Efficacy of Rhinomer® Force 3 versus a Reference Product in Post-Operative Care of the Nasal Fossae after Endonasal Surgery

Key Words

Endonasal surgery
Sea water
Washing of the nasal cavities

Abstract

Twenty-eight patients undergoing rhinologic surgery were enrolled in a clinical study to compare two post-operative cleansing preparations. Patients were asked to wash their nasal fossae for 1 month, either with Rhinomer®, a cleansing preparation of isotonic, sterile, undiluted sea water, presented in a slightly pressurised bottle with neither CFC nor preservative, or with Prorhinel®, a marketed solution containing an antiseptic agent. Patients were randomly allocated to treatment beginning 2 days after surgery. Nasal status was assessed by symptoms (blocking nose, rhinorrhoea, sneezing, itching and impaired smell) and rhinologic endoscopy (colour of the nasal mucosa, swelling of the mucosa, secretions, presence of crusts or pus). Patients attended control visits on days 9, 15 and 30 following surgery. They were asked to record symptom intensity and use of a rescue medication (Vibrocil®, dimetindene 0.25 mg and phenylephrine 2.5 mg/ml) on a diary card. Twenty-six of 28 patients were eligible for efficacy analysis, 14 in the Rhinomer group and 12 in the Prorhinel group. In both groups, intensity of complaints decreased markedly over the study period. No severe adverse drug reactions were reported in either treatment. Evoked complaint frequency was comparable between groups, but patient's and physician's opinion on tolerability was significantly different between treatments, in favour of Rhinomer. In addition, the test preparation was found to be easier to use than Prorhinel. The weekly average frequency of use of the rescue medication was not significantly different between treatments. When both patients and physicians were asked about treatment efficacy, they expressed an opinion significantly more favourable to Rhinomer than to the reference drug. In this study, Rhinomer has shown efficacious results that justify its use in washing of the nasal cavities following endonasal surgery.

Introduction

The affections of the upper and lower respiratory tract are constantly increasing in developed countries, probably due to pollution. The nose has a key role in the respira-

tory function by filtrating and conditioning the inspired air to the lungs. In this respect, the nose and paranasal sinuses are prone to inflammatory diseases. When medical treatment has failed to improve a patient, a surgical approach is necessary. Nasal lavage is a common feature

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of treatment after nasal surgery. Until now, this procedure has always been achieved by passive local instillation of saline. Recently, a new compound has become available on the market, Rhinomer®. Rhinomer is a cleansing preparation of undiluted sea water brought to isotonicity by electro dialysis. It appeared very promising for two reasons. First, the way of use, i.e. a pressurised bottle delivering a constant flow of liquid. Secondly, the preparation itself, undiluted sea water brought to isotonicity by electro dialysis. In this regard, although the reason being unelucidated, the spectacular improvement of patients during a stay at the seaside is well known.

Toxicological experiments have shown very good skin and ocular tolerability in rabbits [1, 2] and good tolerability was also demonstrated after repeated applications on the hamster cheek mucosa [3]. Moreover, Rhinomer did not induce any inhibition of ciliary beat [4].

Clinical studies in patients suffering from various rhinological conditions have been performed, either with Physiomer® (trade mark in France) or with Rhinomer. An open, non-comparative trial in 25 infants and young children showed that coughing and noisy breathing disappeared after washing the nasal cavities with Rhinomer [5]. An open study in adults showed that 4 daily irrigations in both nostrils for 6-10 days improved the nasal condition in various types of rhinitis and in pre- and post-operative care [6]. In an open multicentre trial, Rhinomer was tested in rhinitis of various types and in post-operative care nasal surgery in 209 patients. The beneficial effect on nasal signs and symptoms, from entry to the final visit, was found to be highly significant [7].

Lavages of the nasal fossae, as painless as possible, following endonasal surgery, are a very important element of post-operative care. This procedure is necessary to achieve complete recovery. It depends on the good tolerability and the efficacy of the preparation, requiring high compliance [8]. The objective of this study was to compare the tolerability and efficacy of Rhinomer versus Prorhinel in post-operative care of the nasal fossae following endonasal surgery.

Material and Method

The study design was randomised, comparative, and parallel. Patients of both sexes, aged between 18 and 60, had nose surgery, i.e. rhinoplasty, septoplasty, ethmoidectomy. After surgery, patients had an intranasal haemostatic dressing applied for 2 days. When this dressing was removed, patients were allocated randomly to two treatment groups, either Rhinomer or Prorhinel, which is a nose rinsing preparation containing 5 mg/100 ml of benzododecinium bromide,

an antiseptic agent. Patients were instructed in the use of both preparations. They were asked to wash their nasal cavities for 4 weeks, 4 times a day with Rhinomer (weeks 1 and 2: double washing in each nostril, i.e. nose blowing in between, then single washing until treatment completion), twice a day with Prorhinel, according to the manufacturer's product information. Nose drops (Vibrocil®, dimetindene 0.25 mg and phenylephrine 2.5 mg/ml) were prescribed as rescue medication. Visits were scheduled on the 2nd, 9th, 15th and the 30th post-operative day.

At each visit, based on information from the patient's diary card, a physician appraised the severity of the nasal symptoms, according to a four-level scale (from 0 = absent to 3 = severe). Symptoms were: blocked nose, rhinorrhoea, sneezing/itching, impaired smell. A rhinoscopic examination was completed to assess the colour of the nasal mucosa, its swelling, nasal secretions (rated normal or abnormal), and the presence or absence of crusts and pus. Use of rescue medication was to be reported in the diary card.

Global opinions on treatment efficacy and on treatment tolerability were given by both patients and physicians. Efficacy was rated from 'not satisfactory' to 'very satisfactory' (4 levels) and tolerability from 'very bad' to 'very good' (4 levels). Patients' and physicians' global evaluation of efficacy and frequency of use of rescue medication were the two primary efficacy criteria, the secondary criteria being physician's appraisal of the drug efficacy, nasal symptom intensity, the presence of rhinoscopic signs, and time of symptom disappearance. In addition, patients were asked to report on unpleasantness of use such as smarting, burning, impaired breathing, or bad taste. Patients had to give their opinion about the ease of use of the two products. In the case of an adverse drug reaction a specific form was to be filled in and submitted. Premature treatment cessation was to be mentioned. Statistical analysis was performed with the Mann-Whitney U test to compare opinions on efficacy at each visit. Mean frequencies of use of rescue medication were compared by Student's t test. The intensity of nasal symptoms, separately and together, was analysed by analysis of variance for repeated measures. Times of symptom recovery were compared by survival analysis.

Results

Patients

Twenty-eight patients undergoing rhinologic surgery between February and August 1993 entered the trial (table 1). Two failed visit controls, thus 26 were kept for statistical analysis. Patients underwent various surgical procedures, i.e. rhinoplasty, septoplasty, ethmoidectomy (table 2).

Tolerability

Globally both patients' and physicians' opinions were statistically favourable to Rhinomer (fig. 1). Spontaneous complaints were reported by 8 patients in each group. None of these reactions necessitated countermeasures. These reactions were mostly of mild intensity and related to pain after surgery as well as to nasal lavages. All

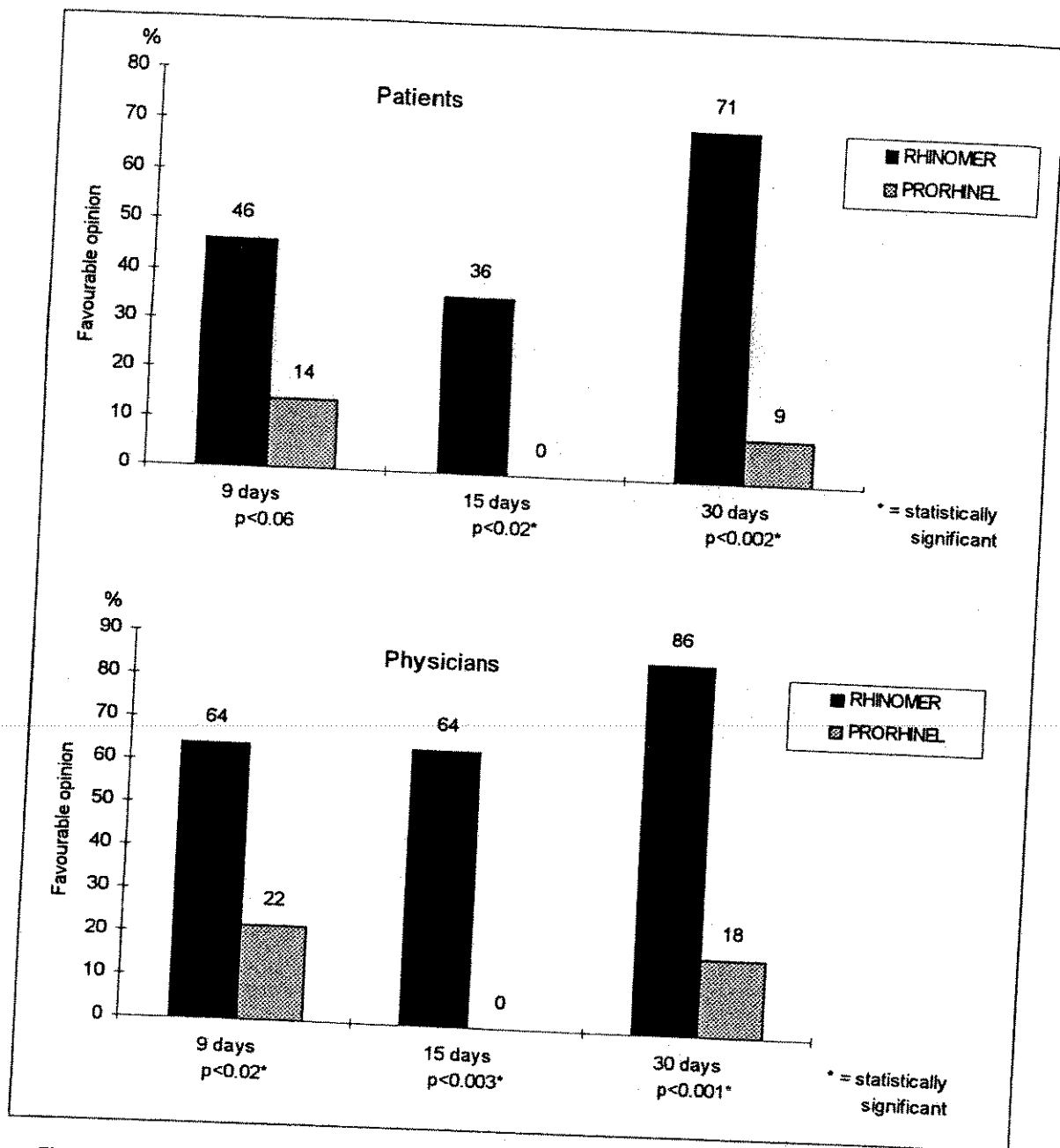


Fig. 1. Patients' and physicians' opinions on treatment tolerability.

Table 1. Demographic data

| | n | Age | | Men | Women |
|-----------|----|------|----|-----|-------|
| | | mean | SD | | |
| Rhinomer | 14 | 29 | 7 | 10 | 4 |
| Prorhinel | 12 | 36 | 11 | 11 | 1 |
| Total | 26 | 32 | 9 | 21 | 5 |

Table 2. Surgical procedure

| | Rhinomer | Prorhinel | Total |
|---------------|----------|-----------|-------|
| Rhinoplasty | 5 | 6 | 11 |
| Septoplasty | 7 | 6 | 13 |
| Ethmoidectomy | 2 | 2 | 4 |
| Total | 14 | 14 | 28 |

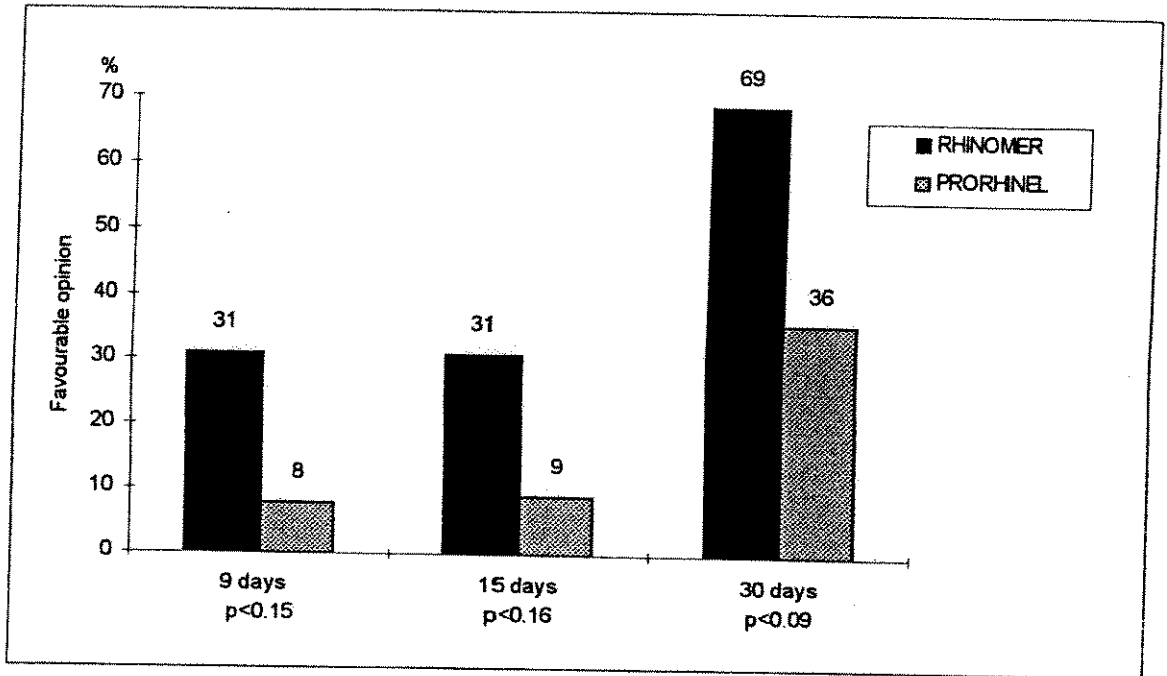


Fig. 2. Evaluation of efficacy by patients.

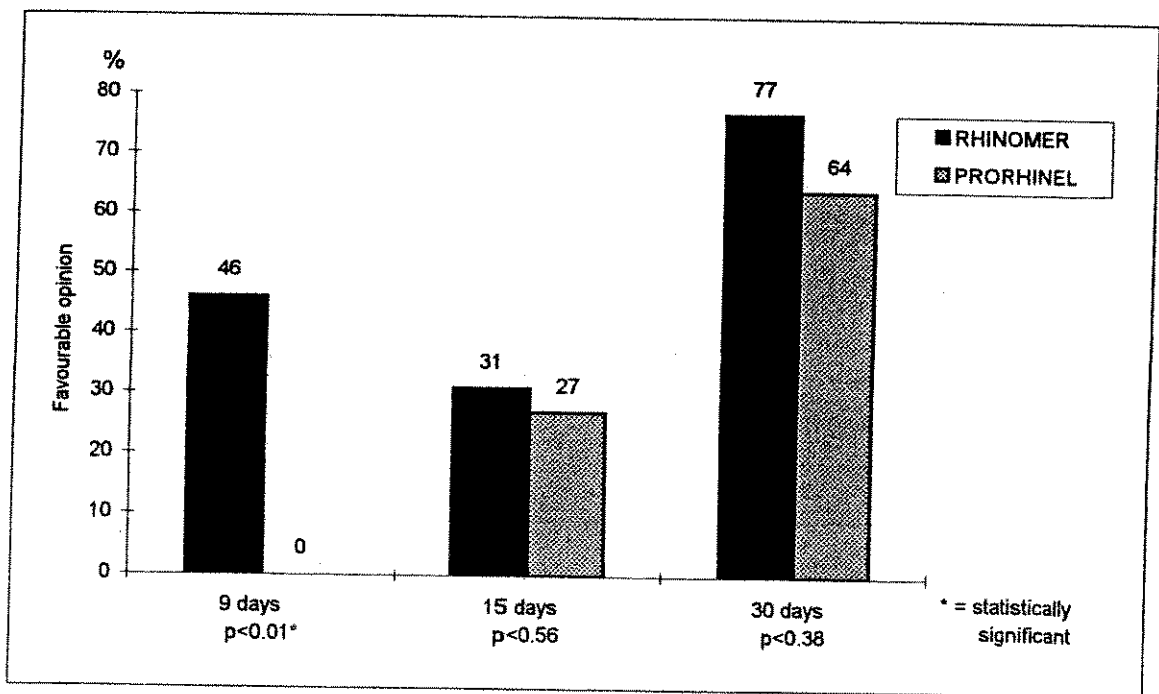


Fig. 3. Evaluation of efficacy by physicians.

Table 3. Product handiness

| | Compli- cated | Difficult | Easy | Very easy | p (Mann- Whitney) |
|---------------|------------------|-----------|------|--------------|----------------------|
| <i>Day 9</i> | | | | | |
| Rhinomer | 0 | 0 | 8 | 6 | 0.005 |
| Prorhinel | 1 | 5 | 7 | 1 | |
| <i>Day 15</i> | | | | | |
| Rhinomer | 0 | 0 | 7 | 7 | 0.141 |
| Prorhinel | 1 | 1 | 6 | 3 | |
| <i>Day 30</i> | | | | | |
| Rhinomer | 0 | 0 | 5 | 9 | 0.020 |
| Prorhinel | 1 | 0 | 8 | 2 | |

Table 4. Total score of nasal symptoms (mean \pm SD)

| | Rhinomer | Prorhinel |
|--------|---------------|---------------|
| Week 1 | 5.3 \pm 2.2 | 5.1 \pm 2.2 |
| Week 2 | 2.9 \pm 1.4 | 3.9 \pm 1.6 |
| Week 3 | 1.6 \pm 1.1 | 2.6 \pm 1.6 |
| Week 4 | 1.2 \pm 1.3 | 1.8 \pm 1.7 |

patients in the Rhinomer group agreed both on the easiness and quickness of the lavage. Patients on Prorhinel needed more time (2 weeks) to get familiar with the lavages (table 3).

Efficacy

Following nasal surgery, the majority of signs and symptoms disappeared at the end of 4 weeks' treatment in both groups. When the whole period of treatment is taken into account by Mantel-Haenszel extended test for 3 tables 2×4 [9], patients' opinions were globally favourable to Rhinomer at $p < 0.025$ ($x = 5.72$, 1 d.f., fig. 2). The assessment of the physicians was in favour of Rhinomer throughout the treatment. On the 9th day following surgery, the efficacy was statistically significant for Rhinomer (fig. 3).

When analysed by Mantel-Haenszel extended test, examination by the physicians was favourable to Rhinomer at $p < 0.02$ ($x = 6.27$, 1 d.f.). Use of Vibrocil as rescue medication was recorded daily in the patient diary. Vibrocil was on average used less frequently in the Rhinomer group (64% of the patients) than in the Prorhinel group

(83% of the patients). These differences did not reach statistical significance.

Scores of nasal symptoms (obstruction, rhinorrhoea, sneezing/itching, impaired smell) were recorded daily in the patient diary using a 4-level scale. The average for each week and for each symptom separately was calculated as the variable to be analysed. The data were analysed by repeated measures analysis of variance. There was no statistically significant difference for each symptom between treatments. A total score was evaluated as the sum of the individual daily scores and for each symptom and averaged over weeks (table 4).

Discussion

Patients and physicians expressed a statistically significant preference for the investigated preparation (Rhinomer) when they were asked about the tolerability. Moreover, Rhinomer was found to be easier to use. These two features led to better compliance. Indeed, nasal lavages are often uncomfortably felt, especially following surgery, thus encountering 'resistance' from patients. In this respect, Rhinomer appears to be a very promising compound.

Similarly, the assessment of efficacy from a clinical standpoint both by physicians and patients was favourable to Rhinomer throughout the trial. This difference was statistically significant on day 9 as evaluated by physicians familiar with nasal surgery follow-up. In terms of nasal surgery, prompt recovery is of crucial importance to ensure quick restoration of nasal functions. This reduces the need for repeated visits and alleviates discomfort to the patients.

The difference between the two compounds was less marked during the last visits: as expected, most of the signs and symptoms related to the post-operative condition disappeared due to normal healing after 4 weeks.

The quick recovery 1 week following surgery in the Rhinomer group is most likely due to the original concept of the product. Undiluted sea water brought to isotonicity probably favours respiratory epithelium regeneration. This was shown in vitro on tracheal epithelium [10]. Furthermore, by delivering nasal lavages under pressure, as opposed to passive instillation, Rhinomer achieves a new concept, i.e. active and dynamic cleansing of the nose.

In this clinical trial, the investigational cleansing preparation Rhinomer has shown good results that justify its choice in the washing of the nasal cavities following endonasal surgery.

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