fortune Journals

Research Article

JOURNAL OF SURGERY AND RESEARCH

ISSN: 2640-1002

Evaluation of the efficacy of a Medical device based on Magnesium alginate, Calcium carbonate, Potassium bicarbonate, Sodium hyaluronate and Chondroitin sulphate in the treatment of Laryngopharyngeal Reflux Disease

Mario Notargiacomo[1*], Enrico Maffezzoni[2], Federico Maffezzoni[3], Serena Miglio[3]

Abstract

Continuous exposure to endogenous irritants (hydrochloric acid, pepsin), that characterises the reflux of gastroduodenal contents, initiates phlogistic processes in the mucous membranes of the upper respiratory tract and causes them to become chronic. This results in the characteristic chronic reflux symptoms in the upper respiratory tract and over time, leads to an alteration of the rhino-pharyngeal-laryngeal mucous membranes, which, in combination with the chronic inflammatory factors, leads to the formation of areas of muciparous metaplasia with increasing inflammatory cell infiltrates as the alterations progress.

The treatment of laryngopharyngeal reflux disease (LPR) is based on the use of high-dose proton pump inhibitors (PPIs) for prolonged periods, but clinical experience shows that LPR patients treated with PPIs often complain of dissatisfaction with PPI monotherapy and dissatisfaction with their health-related quality of life. There is therefore a need to identify effective therapeutic approaches to be associated with the use of PPIs.

This retrospective pilot study included 93 subjects divided into two groups: 56 patients with LPR were treated by means of a medical device (Med) containing magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate of fermentative origin, while the other 37 subjects were recruited from the healthy population and were used as a control group. The 56 patients took Med after meals and before bed for 30 consecutive days. At the beginning (T0) and at the end of the 30-day treatment period (T1) and 30 days after treatment discontinuation (T2), symptoms were assessed by means of the Reflux Symptom Index (RSI) and the 22-item Sino-Nasal Outcome Test (SNOT-22), as well as by means of the Reflux Finding Score (RFS) and a cytological survey of the nasal mucosa and an assessment of health-related quality of life by means of the 12-item Short Form Survey (SF-12).

The patients treated with Med improved significantly both clinically and in rhinocytological terms. In particular, the average total scores of RSI, RFS and SNOT-22 were reduced by more than 50%, and the cytological picture improved with the reduction of lymphocyte, neutrophil and goblet cell counts. The benefits obtained by patients treated with Med resulted in a significant improvement in health-related quality of life, as evidenced by the improvement in SF-12 questionnaire scores.

Keywords: Laryngopharyngeal Reflux Disease; Magnesium Alginate; Medical Device; Nasal Cytology; Health-related Quality of Life.

Affiliation:

[1]Otorhinolaryngology unit, Melzo Hospital, Melzo (Milan), Italy

[2]Rhinocytoallergology unit, Figlie di San Camillo Institute, Cremona, Italy

[3]Clinical psychology, Oberdan Outpatient Clinic, Brescia, Italy

***Corresponding author:**

Mario Notargiacomo, Otorhinolaryngology Unit, Melzo Hospital, Melzo (Milan), Italy

E-mail: mario.notargiacomo63@gmail.com

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.

Received: March 10, 2025
Accepted: March 18, 2025
Published: April 29, 2025

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Introduction

LPR is defined as an inflammatory condition of the tissues of the upper aerodigestive tract related to the direct and indirect effects of the reflux of gastroduodenal contents, which can induce morphological changes in the upper aerodigestive tract [1]. Despite being united by the reflux of gastroduodenal contents, LPR and gastro-oesophageal reflux disease (GERD) represent two distinct nosological entities. Typical manifestations of GERD include heartburn, regurgitation, and retrosternal pain. In GERD, heartburn is the most common symptom and occurs in more than 75% of cases [2], while in LPR, fewer than 40% of patients complain of this symptom [3]. In addition, even after a modest number of reflux episodes, damage to the laryngeal cell structure can be found in patients with LPR, but no damage to the oesophageal mucosa [4].

The development of the signs and symptoms of LPR may result from direct contact between the gastroduodenal contents and the upper aerodigestive tract, but may also result from contact between the gastroduodenal contents and the mucosa of the oesophagus, as stimulation of the mucosal chemoreceptors induces vagus nerve-mediated reflexes that lead to the onset of its characteristic symptoms [5]. Preventing the reflux of gastroduodenal contents into the oesophagus and shielding it from contact with the acid reflux, are therefore therapeutic necessities for the effective treatment of LPR and justify the variety of oral medical devices authorised for the treatment of LPR.

LPR causes inflammatory reactions, alteration of the mucus layer, lesions of the respiratory mucosa, thickening of the epithelium and microtrauma [6-8]. The symptoms of LPR with the highest prevalence are the sensation of a lump in the throat, rasping, hoarseness, excess mucus in the throat and retronasal drip [1]. The most common findings of LPR are: hypertrophy of the posterior commissure, laryngeal/arytenoid inflammation and endolaryngeal mucus [1].

LPR is associated with the disorders that characterise rhinitis and non-allergic rhinosinusitis [9,10]. In clinical studies, it has been shown that LPR has a negative effect on nasal resistance and nasal congestion [11] and that the treatment of LPR can lead to a subjective and objective improvement in nasal disorders [11]. A recent systematic review shows the association between LPR and MRGE and chronic rhinosinusitis [12].

The chronic inflammatory process that characterises LPR induces an increase in the presence of inflammatory cells, such as lymphocytes and neutrophils, and leads to a progressive remodelling of the nasal mucosa, up to the manifestation of muciparous metaplasia, characterised by an increase in goblet cells [13]. Alteration of the nasal mucosa results in a progressive impairment of mucociliary clearance leading to bacterial colonisation and the onset of infection, which further intensify the inflammatory state. In this way, a vicious circle is generated with mutual reinforcement of inflammation and metaplasia [13-15].

Nasal cytology is an easily applicable and economical diagnostic method that allows, through the quantification of cell populations in the nasal mucosa, to identify the phenotypic characteristics of rhinitis and to evaluate the effect of the treatment adopted [16]. A clinical study confirmed the relationship between the cytological arrangement of the nasal mucosa, the onset of chronic rhinosinusitis and the reflux of gastroduodenal contents, comparing the results of the rhinocytogram with the outcome of pH-impedance [10].

Currently, the suppression of gastric acid production by PPIs represents the mainstay of LPR treatment. H2-receptor antagonists, prokinetic agents, and mucosal cytoprotectants may provide additional benefits [17]. Neuromodulators, such as tricyclic antidepressants, gabapentin and pregabalin, may be an option for patients with symptoms that are not relieved by acid suppression, particularly in cases where laryngeal hypersensitivity (from neuropathy) appears to contribute to LPR symptoms [17]. LPR is generally addressed with an aggressive approach, which includes high doses of PPIs for long periods [17]. Two systematic reviews with meta-analysis conclude that PPIs are more effective than placebo in the treatment of LPR, but the heterogeneity of the study design makes comparisons difficult; there is therefore uncertainty about how effective PPIs really are in the management of LPR [18,19]. From clinical experience, it is clear that LPR patients often complain about the ineffectiveness of PPI monotherapy. It can be deduced that the lack of effective LPR treatment may be the reason why patients with LPR, or with GERD and LPR, complain of a lower health-related quality of life than patients with GERD alone [20].

Based on the premises set out above, we, the authors of this study, believe that the identification of effective treatment strategies to protect the mucous membranes and reduce the symptoms and signs characteristic of LPR is desirable. In order to meet this need, for some time now, it has been our practice to treat patients with LPR who present themselves for observation with medical devices made available by pharmaceutical companies [21,22] and to systematically gather evidence of their efficacy in order to identify the formula that best suits the needs of these patients.

The purpose of this study is to evaluate the effects of treating LPR with an oral medical device that is believed to prevent reflux of gastric contents, neutralise the acid pocket that forms near the gastro-oesophageal junction during meals, and protect the oesophageal and laryngopharyngeal mucosa, as our hypothesis is that the combination of these three actions is very promising in the effective management of LPR symptoms and signs in conjunction with the use of

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

PPIs or not. Therefore, the primary objective of this study is to evaluate the efficacy of the medical device in protecting the mucosa of the upper airways from the aggression of gastric reflux and in reducing the signs and symptoms of LPR. For this purpose, both the evaluation of the change in signs and symptoms induced by the use of the medical device by LPR patients and the comparison between LPR patients and a sample of healthy, non-LPR subjects were implemented. It is considered that a truly effective treatment should bring the measured parameters as close as possible to those presented by healthy subjects and that, in any case, it should reduce the scores attributed to symptoms and signs by at least 50%.

The secondary objectives are to evaluate the change in quality of life in the group of LPR patients treated with the medical device and to assess the effectiveness and patients' satisfaction with the treatment.

Materials and Methods

Medical device tested

Medireflux® (Med, Salix S.r.l, Monte di Malo, Vicenza, Italy) is a medical device (EC Certificate No. IT299455-3, obtained on 31 July 2020) based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate (HA) with a high molecular weight, between 1800 and 2000 kDa, obtained by biotechnological processes, and sodium chondroitin sulphate (CS) of fermentative origin. Magnesium alginate was included in the formula as a gelling agent, HA and CS were included in the formula as mucoadhesive agents. The product is indicated for the treatment of gastro-oesophageal reflux to reduce associated symptoms such as heartburn, acid reflux, reflux oesophagitis, dysphagia and odynophagia.

Study design

This is a retrospective, pilot study comparing the parameters measured in LPR patients (Med Group) before starting treatment with Med, after treatment with Med and one month after stopping treatment with Med. The study also compares the parameters measured in the Med Group patients with the same parameters measured in a sample of healthy subjects.

Patients who were treated between February 2023 and January 2024, and who adhered to their treatment requirements during the treatment period, were included in the study.

The study was conducted in compliance with the Good Clinical Practice guidelines [23] and in compliance with the Declaration of Helsinki [24].

History and physical examination

The subjects underwent a physical examination and a thorough medical history with evaluation of symptoms, allergies, diet, alcohol consumption, smoking, work activity, family history of respiratory and allergic and other nasal diseases, surgery, co-morbidities and current medication.

Reflux Symptom Index

RSI is a 9-item self-administered questionnaire that accurately documents the symptoms of LPR patients. This index is considered valid and is highly reproducible. Patients are asked to rate the intensity of the symptoms listed in the RSI using the following scale: no symptom (0 points), very mild symptom (1 point), mild symptom (2 points), moderate symptom (3 points), severe symptom (4 points), very severe symptom (5 points).

An RSI greater than 13 is considered indicative of LPR. The total score range is between 0 and 45: the highest score indicates the most pronounced symptomatology [25].

Reflux Finding Score

RFS is an 8-item clinical severity rating scale based on endoscopically detectable evidence. The scale includes the most common LPR-related laryngeal findings. An individual who scores an overall RFS score greater than 7 is believed to have a greater than 95% chance of having LPR. It is believed that the RFS score can accurately document the effectiveness of the treatment to which LPR patients are subjected. The total score range is between 0 and 26: the highest score indicates the greatest clinical severity [26,27].

22-item Sino-Nasal Outcome Test

For the subjective evaluation of rhinological symptoms, the Italian version of SNOT-22 was used [28]. The test is frequently employed in clinical practice because it is simple, intuitive, and takes only a few minutes to complete. It consists of 22 items to be scored from 0 to 5 on the basis of the severity of the complaints that patients have experienced in recent weeks. The total score range is between 0 and 110; the highest scores represent worsened symptoms. The questions can be divided into 2 categories: questions concerning physical symptoms (items 1–12) covering rhinological, ear and facial symptoms and questions concerning health and quality of life (items 13–22) covering sleep function and psychological problems.

Rhinocytogram

All patients in the Med Group were sampled using the scraping technique at T0, T1 and T2, while healthy subjects were sampled only once (T0). The sample taken was laid out on a slide and stained using the May Grunwald-Giemsa method. The prepared slides were observed at 100, 400, and 1000 magnifications, counting the inflammatory cell elements (neutrophils and lymphocytes), goblet cells and any bacteria present. The outcome of the nasal cytological examination was evaluated using the classification reported in table 1 [29].

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Table 1: Quantitative classification of the results of the nasal cytological examination with regard to neutrophils, lymphocytes and goblet cells (*average of cells per 10 fields at high magnification – 1000x; from [29] modified).

Cell type	Description	Quantity	Classification
Neutrophils and lymphocytes	None	0*	0
	Sporadic	0.1 – 1.0*	½+
	A few scattered cells, small groups	1.1 – 5.0*	1+
	In discreet numbers, large groups	5.1 – 15*	2+
	Large cellular clusters that do not occupy the entire field	15.1 – 20*	3+
	Large cellular clusters occupying the entire field	> 20*	4+
Goblet cells	None	0	0
	From rare to few cells	1 - 24%	1+
	In a significant number	25 - 49%	2+
	In large numbers	50 - 74%	3+
	Lots of cells scattered all over the field	75 - 100%	4+

12-Item Short Form Health Survey

The SF-12 questionnaire is a quality-of-life assessment tool frequently employed in clinical trials as it is simple, intuitive, and takes about ten minutes to complete [30]. The evaluation of the results of SF-12 is carried out by dividing the questionnaire into two indices called Physical Component Summary (PCS) and Mental Component Summary (MCS). The PCS index concerns the patient's physical state and groups six of the twelve questions of the SF-12 questionnaire referring to various areas: two questions concern physical activity, two concern work engagement and physical health, one question concerns physical pain and one question concerns general health. The MCS index measures the patient's mental state and groups six of the twelve questions of the SF12 questionnaire referring to various areas: one question concerns vitality, one social activities, two concern emotional state and finally, two questions refer to mental health.

Opinion on the effectiveness and agreeability of the treatment

Patients in the Med Group were also asked to express an opinion on the effectiveness and agreeability of the treatment they underwent, using two scales including 5 different opinions: excellent, good, satisfactory, poor, none.

Subjects evaluated

Adult male and female LPR patients who had previously received Med treatment were included in the Med Group. Patients included had to be older than 18 years of age at the time of initiation of Med treatment, present symptoms of LPR for at least 3 months and at least 3 times a week, have an RSI score greater than 13, have morphological lesions of the larynx attributable to LPR attested by an RFS score greater than 7. This included patients who had not been on continuous treatment for the treatment of LPR prior to starting Med treatment, or patients who had already been on treatment with medical devices or dietary supplements for LPR but had discontinued them for at least 15 days at T0. To be included in the study, patients already on treatment with PPIs or H2-receptor antagonists had to have maintained a consistent dosage of the drugs in the preceding period and throughout the period of treatment with Med.

Subjects with malignant or inflammatory diseases of the upper respiratory tract and upper gastrointestinal tract, inhalant or food allergies or other disorders that, in the opinion of the study authors, could confuse the treatment results were excluded from the study. In addition, patients who had nasal cytological changes attributable to allergies or infections on the rhinocytogram were excluded. Finally, patients who had changed their diet, alcohol consumption, daily physical activities or smoking habits during treatment were excluded. In all cases, subjects who habitually smoked ≥ 10 cigarettes per day were excluded, as the signs and symptoms presented in the pharyngolaryngeal or nasal area could be attributed to smoking.

Thirty-seven healthy comparison subjects were included in the study. These were subjects who had an RSI index score of less than 13 and showed no morphological lesions of the larynx when examined by video laryngoscopy, a condition confirmed by an RFS index score of less than 7.

In line with the authors' usual practice, patients signed an informed consent form, both for the proposed treatment and for the processing of their personal data. At the start of the treatment, a medical history sheet with all the data collected was completed for each patient, and a form to be completed at the next check-up was attached.

Time schedules for checks

Patients in the Med Group were subjected to checks on three occasions: before starting Med (T0), after 30 days of

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Med intake (T1) and 30 days after stopping Med intake (T2). At T0, T1 and T2, patients completed the RSI, SNOT-22 and SF-12 questionnaires and underwent video laryngoscopy and rhinocytogram sampling. At T0, T1 and T2, the doctors completed RFS and observed the slides for the rhinocytogram. At T1, patients expressed their opinion on the effectiveness and agreeability of the treatment.

Healthy subjects were subjected to checks on a single occasion (T0).

From the time of initiation of intake (T0) and over the following 30 days (T0 to T1), patients took Med in the amount of one stick pack after each of the two main meals of the day and before going to bed to sleep at night.

Statistical analyses

Descriptive statistics were used to summarise cohort characteristics in terms of median, mean and standard deviation (SD) or frequencies when appropriate.

The effect of treatment was estimated in terms of the change in outcome in treated patients between the visit at T1 and T2 and the visit at T0, and in terms of the change in outcome between treated patients at the three visits and healthy subjects. The significance of the differences was determined by applying the non-parametric Mann-Whitney test for paired data of treated patients in the case of the comparison of T2, T1 and T0 and for unpaired data in the case of the comparison of changes between treated patients and healthy subjects. In all the analyses conducted, the results are considered statistically significant for $p < 0.05$.

GraphPad Prism software version 8.0.2 for Windows, GraphPad Software, Boston, Massachusetts USA, www.graphpad.com was used for statistical processing.

Results

93 subjects were included in the study, including 56 patients with LPR in the Med Group, and 37 healthy subjects. The demographic and medical history data of the patients enrolled in the study are shown in table 2.

The distribution of diagnoses from previous gastroenterological investigations of patients included in the Med Group is as follows: 33.9% chronic gastritis, 19.6% cardial incontinence, 14.3% hiatal hernia, 3.6% reflux oesophagitis, 3.6% ulcer.

In the Med Group patients at T0, the correlation between the results of the tests to which they were subjected is evident, confirming the correlation between the signs and symptoms presented and the diagnosis of LPR (Table III). The statistical significance of the correlation was not only achieved in the comparison between the LPR and SNOT-22 scores, between the RSI score and the neutrophil count and between the LPR score and the neutrophil count.

Table 2: The demographic and medical history data of the patients enrolled in the study and of the healthy comparison subjects. The data are expressed as mean ± SD, unless otherwise indicated.

Variable	Med Group (n=56)	Healthy subjects (n=37)
Age in years	53.2 ± 16.8	30.2 ± 8.9
Gender, % F (n)	64.3 (36)	51.3 (19)
Height (m)	1.70 ± 0.09	1.69 ± 0.07
Weight (kg)	71.0 ± 11.7	64.0 ± 9.9
BMI	24.5 ± 3.6	22.2 ± 2.3
Occasional smoking, % yes (n)	12.5 (7)	35.1 (13)
Presence of symptoms since (months)	25.4 ± 26.6	
Days with symptoms per week	5.9 ± 1.9	
PPI intake, % yes (n)	33.9 (19)	
Familiarity with respiratory tract diseases	21.4 (12)	

Table 3: Correlation between the diagnostic tools adopted in the study by calculating the Spearman correlation coefficient. In italics, the values of $P > 0.05$.

Spearman correlation	T0	
	r-value	P-value
RSI vs RFS	0.565	< 0.0001
RSI vs SNOT-22	0.366	0.0056
RFS vs SNOT-22	0.116	*0.3939*
RSI vs Neutrophils	0.227	*0.0972*
RSI vs Lymphocytes	0.601	< 0.0001
RSI vs Goblet cells	0.48	0.0002
RFS vs Neutrophils	0.244	*0.0699*
RFS vs Lymphocytes	0.601	< 0.0001
RFS vs Goblet cells	0.263	0.0498
SNOT-22 vs Neutrophils	0.35	0.0083
SNOT-22 vs Lymphocytes	0.282	0.0351
SNOT-22 vs Goblet cells	0.47	0.0003

The control at T1 was carried out on average after 30.5 ± 2.6 days from T0. The control at T2 was carried out on average after 30.0 ± 1.5 days from T1.

Reflux Symptom Index

In patients in the Med Group, the total RSI score was significantly reduced at T1 compared to T0, testifying to the improvement of LPR symptomatology. The average percentage reduction in symptoms detected by RSI was 71.0%. A total RSI score of 13 represents the threshold above which the patient is considered to suffer from LPR. After 30 days of treatment with Med (T1), 54 out of 56 patients (96.4%) had a total score of less than 12.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

The total score of the patients in the Med Group increased at T2, one month after discontinuation of Med, compared to T1, but remained significantly lower than at T0 (Table 4, Figure 1).

At T0, the total RSI score of patients in the Med Group was significantly higher than that of healthy subjects. Despite the significant improvement observed in patients in the Med Group, at T1 and T2 the difference compared to healthy subjects remained statistically significant.

Considering the individual RSI items of the Med Group separately, it can be seen that they all underwent a statistically significant reduction from T0 to T1 (Table 4). At T2, the score worsened slightly but remained significantly lower for all the individual items compared to the score at T0. At T0 and T2, the Med Group's scores remained significantly higher than those of the healthy subjects, while at T1, the scores of the items Difficulty swallowing food, liquids, or pills, Breathing difficulties or choking episodes, Sensations of something

Table 4: Median, 25th and 75th percentile and mean ± SD of the total score and the score of the individual RSI items found in healthy subjects and Med Group patients at the start of treatment (T0), after 30 days of treatment (T1) and after 30 days after discontinuation of therapy (T2) and statistical significance of the comparisons. In italics, the values of P > 0.05.

Item RSI	Parameters	Healthy subjects (n=37)	Med Group (n=56)		
			T0	T1	T2
Total	Median [25th – 75th]	2.00 [0.00 – 3.00]	21.0 [18.0 – 25.8]	6.00 [5.00 – 7.00]	8.00 [7.00 – 10.0]
	Mean ± SD	2.08 ± 1.88	21.6 ± 5.04	6.05 ± 2.58	9.16 ± 4.20
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
	Average percentage reduction from T0 to T1 Mean % (95% CI)		71.0 (66.9 – 75.0)		
1 - Hoarseness or a problem with your voice	Median [25th – 75th]	0.00 [0.00 – 1.00]	3.00 [2.00 – 3.00]	1.00 [0.00 – 1.00]	1.00 [1.00 – 2.00]
	Mean ± SD	0.32 ± 0.47	2.70 ± 0.99	0.84 ± 0.63	1.20 ± 0.92
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
2 - Clearing your throat	Median [25th – 75th]	0.00 [0.00 – 1.00]	3.00 [3.00 – 3.00]	1.00 [0.00 – 1.00]	1.50 [1.00 – 2.00]
	Mean ± SD	0.46 ± 0.61	2.95 ± 0.90	0.95 ± 0.70	1.55 ± 1.04
	P-value vs healthy subj.		< 0.0001	0.0009	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
3 - Excess throat mucus or postnasal drip	Median [25th – 75th]	0.00 [0.00 – 1.00]	4.00 [3.00 – 4.00]	1.00 [1.00 – 1.00]	1.00 [1.00 – 2.00]
	Mean ± SD	0.46 ± 0.69	3.36 ± 1.05	1.11 ± 0.71	1.43 ± 0.97
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
4 - Difficulty swallowing food, liquids, or pills	Median [25th – 75th]	0.00 [0.00 – 0.00]	1.00 [0.00 – 2.00]	0.00 [0.00 – 0.00]	0.00 [0.00 – 0.00]
	Mean ± SD	0.00 ± 0.00	1.04 ± 0.91	0.14 ± 0.59	0.23 ± 0.66
	P-value vs healthy subj.		< 0.0001	*0.1388*	0.0103
	P-value vs T0			< 0.0001	< 0.0001
5 - Coughing after you ate or after lying down	Median [25th – 75th]	0.00 [0.00 – 0.00]	3.00 [2.00 – 4.00]	1.00 [0.25 – 1.00]	1.00 [1.00 – 1.75]
	Mean ± SD	0.00 ± 0.00	2.70 ± 1.41	0.84 ± 0.56	1.16 ± 0.76
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
6 - Breathing difficulties or choking episodes	Median [25th – 75th]	0.00 [0.00 – 0.00]	1.00 [0.00 – 2.00]	0.00 [0.00 – 0.00]	0.00 [0.00 – 0.00]
	Mean ± SD	0.00 ± 0.00	1.05 ± 1.07	0.11 ± 0.41	0.27 ± 0.65
	P-value vs healthy subj.		< 0.0001	*0.1484*	0.0107
	P-value vs T0			< 0.0001	< 0.0001

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

7 - Troublesome or annoying cough	Median [25th – 75th]	0.00 [0.00 – 1.00]	3.00 [2.00 – 4.00]	1.00 [1.00 – 1.00]	1.00 [1.00 – 2.00]
	Mean ± SD	0.27 ± 0.45	3.07 ± 1.16	1.02 ± 0.62	1.27 ± 0.73
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
8 - Sensations of something sticking in your throat or a lump in your throat	Median [25th – 75th]	0.00 [0.00 – 1.00]	2.00 [1.00 – 3.00]	0.00 [0.00 – 1.00]	1.00 [1.00 – 2.00]
	Mean ± SD	0.30 ± 0.46	2.13 ± 1.28	0.57 ± 0.68	1.23 ± 0.87
	P-value vs healthy subj.		< 0.0001	*0.0641*	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
9 - Heartburn, chest pain, indigestion, or stomach acid coming up	Median [25th – 75th]	0.00 [0.00 – 1.00]	3.00 [2.00 – 4.00]	1.00 [0.00 – 1.00]	1.00 [0.25 – 1.00]
	Mean ± SD	0.27 ± 0.45	2.63 ± 1.53	0.73 ± 0.73	1.02 ± 0.77
	P-value vs healthy subj.		< 0.0001	0.002	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001

sticking in your throat or a lump in your throat of the Med Group were not significantly different from the scores of the healthy subjects.

From a statistical point of view, at T0, T1 and T2 there was no difference in RSI scores between patients in the Med Group taking PPIs and patients not taking PPIs.

Reflux Finding Score

In the Med Group, the total RFS score was significantly reduced at T1 compared to T0. The average percentage reduction in symptoms detected by RFS was 58.1%. An RFS score of 7 represents the threshold above which the patient is considered to suffer from LPR. At T1, 41 out of 56 patients (73.2%) had a score of less than 7. This confirms the significant improvement in the symptoms presented by patients. At T2, 30 days after discontinuation of Med treatment, the score worsened compared to T1, but remained significantly lower than at T0 (Table 5, Figure 1).

At T0, the total RFS score of patients in the Med Group was significantly higher than that of healthy subjects. At T1, thanks to the significant improvement observed in patients in the Med Group, the difference between the latter and healthy subjects decreased but remained statistically significant.

Considering the individual RFS items separately (Table 5), it appears that subglottic oedema, which at T0 was present in 18 patients (32.1%) of the Med group, disappeared in all patients after 30 days of Med treatment and reappeared at T2 in 2 patients (3.6%). The clear improvement achieved means that at T1 and T2, there was no statistically significant difference for this symptom between patients in the Med Group and healthy subjects. Thick endolaryngeal mucus was present at T0 in 33 patients (58.9%) of the Med Group. At T1, it was present in 2 patients (3.6%) and at T2, it was found in 3 patients (5.3%). In this case too, the improvement achieved means that at T1 and T2 there was no statistically significant difference for this symptom between patients in the Med Group and healthy subjects.

Granuloma/granulation tissue was already absent in all patients in the Med Group at T0.

At T0, the RFS score of patients in the Med Group taking PPIs was worse than that of patients not taking PPIs (P = 0.0081). At T1 (P = 0.7900) and T2 (P = 0.5429) there was no longer a statistically significant difference in RFS scores between patients taking PPIs and those not taking them.

Sino-Nasal Outcome Test

In patients in the Med Group, the total SNOT-22 score and the total score of items 1 to 12 were significantly reduced at T1 compared to T0, testifying to the improvement of LPR rhinological symptomatology. The average percentage reduction in symptoms detected by the SNOT-22 total score was 59.0%, while the average percentage reduction in rhinological symptoms detected by the total score of items 1 to 12 of SNOT-22 was 58.0%.

The two scores of the patients in the Med Group increased at T2, one month after discontinuation of Med, compared to T1, but remained significantly lower than at T0 (Table 6, Figure 1).

At T0, the total SNOT-22 score of patients in the Med Group was significantly higher than that of healthy subjects. Despite the significant improvement observed in patients treated with Med, at T1 and T2 the difference compared to healthy subjects remained statistically significant.

At T0, the total SNOT-22 score of patients in the Med Group taking PPIs was worse than that of patients not taking PPIs (P = 0.0312). At T1, the total SNOT-22 score of patients taking PPIs was not significantly different from that of patients not taking PPIs (P = 0.1324). At T2, the total SNOT-22 score of patients taking PPIs was again worse than that of patients not taking PPIs (P = 0.0120).

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Table 5: Median, 25th and 75th percentile and mean ± SD of the total score and the scores of the individual RFS items found in the Med Group at the start of treatment (T0), after 30 days of treatment (T1) and after 30 days after discontinuation of treatment (T2) and in healthy subjects and statistical significance of the comparisons. In italics, the values of P > 0.05.

Item RFS	**Parameters**	**Healthy subjects** (n=37)	**Med Group** (n=56)		
			T0	**T1**	**T2**
Total	Median [25th – 75th]	0 [0.00 – 2.50]	13 [10.00 – 14.00]	5 [4.00 – 7.00]	6 [3.25 – 8,00]
	Mean ± SD	1.00 ± 1.47	12.5 ± 2.25	5.02 ± 2.00	5.79 ± 2.72
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
	Average percentage reduction from T0 to T1 Mean % (95% CI)		58.1 (52.8 – 63.3)		
Subglottic edema	Median [25th – 75th]	0.00 [0.00 – 0.00]	0.00 [0.00 – 2.00]	0.00 [0.00 – 0.00]	0.00 [0.00 – 0.00]
	Mean ± SD	0.00 ± 0.00	0.64 ± 0.94	0.00 ± 0.00	0.07 ± 0.37
	P-value vs healthy subj.		< 0.0001	*> 0.9999*	*0.5157*
	P-value vs T0			< 0.0001	< 0.0001
Ventricular	Median [25th – 75th]	0.00 [0.00 – 0.00]	2.00 [2.00 – 2.00]	0.00 [0.00 – 2.00]	0.00 [0.00 – 2.00]
	Mean ± SD	0.22 ± 0.63	1.54 ± 0.85	0.64 ± 0.94	0.82 ± 0.99
	P-value vs healthy subj.		< 0.0001	0.0242	0.0021
	P-value vs T0			< 0.0001	< 0.0001
Erythema/ hyperemia	Median [25th – 75th]	0.00 [0.00 – 0.00]	4.00 [4.00 – 4.00]	2.00 [2.00 – 2.00]	2.00 [2.00 – 2.00]
	Mean ± SD	0.27 ± 0.69	3.54 ± 0.85	1.79 ± 0.62	1.68 ± 0.99
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
Vocal fold edema	Median [25th – 75th]	0.00 [0.00 – 0.00]	2.00 [2.00 – 2.00]	1.00 [1.00 – 1.00]	1.00 [1.00 – 1.00]
	Mean ± SD	0.19 ± 0.46	1.95 ± 0.52	0.91 ± 0.44	1.11 ± 0.53
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
Diffuse laryngeal edema	Median [25th – 75th]	0.00 [0.00 – 0.00]	2.00 [2.00 – 2.00]	1.00 [1.00 – 1.00]	1.00 [1.00 – 1.00]
	Mean ± SD	0.19 ± 0.52	2.04 ± 0.66	0.89 ± 0.41	0.98 ±0.52
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
Posterior commissure hypertrophy	Median [25th – 75th]	0.00 [0.00 – 0.00]	2.00 [1.00 – 2.00]	1.00 [0.00 – 1.00]	1.00 [0.00 – 2.00]
	Mean ± SD	0.13 ± 0.35	1.57 ± 0.63	0.71 ± 0.65	1.02 ± 0.80
	P-value vs healthy subj.		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
Granuloma/ granulation tissue	Sign absent in all patients of the Med Group				
Thick endolaryngeal mucus	Median [25th – 75th]	0.00 [0.00 – 0.00]	2.00 [0.00 – 2.00]	0.00 [0.00 – 0.00]	0.00 [0.00 – 0.00]
	Mean ± SD	0.00 ± 0.00	1.18 ± 0.99	0.07 ± 0.37	0.11 ± 0.45
	P-value vs healthy subj.		< 0.0001	*0.5157*	*0.2735*
	P-value vs T0			< 0.0001	< 0.0001

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Table 6: Median, 25th and 75th percentile and mean ± SD of the SNOT-22 total score and the total score of the physical symptoms (items 1 to 12 of SNOT-22) found in the Med Group at the start of treatment (T0), after 30 days of treatment (T1) and 30 days after the discontinuation of treatment (T2). Total SNOT-22 score found in healthy subjects and statistical significance of the comparisons.

SNOT-22	**Healthy subjects** (n=37)	**Med Group** (n=56)		
		T0	**T1**	**T2**
Median [25th–75th]	3 [0.00–4.00]	25.5 [18.00–31.80]	8 [7.00–12.00]	14 [10.30–18.00]
Mean ± SD	2.27 ± 2.12	26.0 ± 10.8	10.5 ± 6.84	15.4 ± 8.15
P-value vs healthy subjects		< 0.0001	< 0.0001	< 0.0001
P-value vs T0			< 0.0001	< 0.0001
Average percentage reduction from T0 to T1 Mean % (95% CI)		59.0 (54.1–63.9)		
SNOT-22 (items 1–12)				
Median [25th–75th]		17 [14.30–22.00]	7 [4.25–8.75]	9.5 [7.25–12.80]
Mean ± SD		18.5 ± 6.69	7.71 ± 4.77	11.0 ± 5.36
P-value vs T0			< 0.0001	< 0.0001
Average percentage reduction from T0 to T1 Mean % (95% CI)		58.0 (52.8–63.3)		

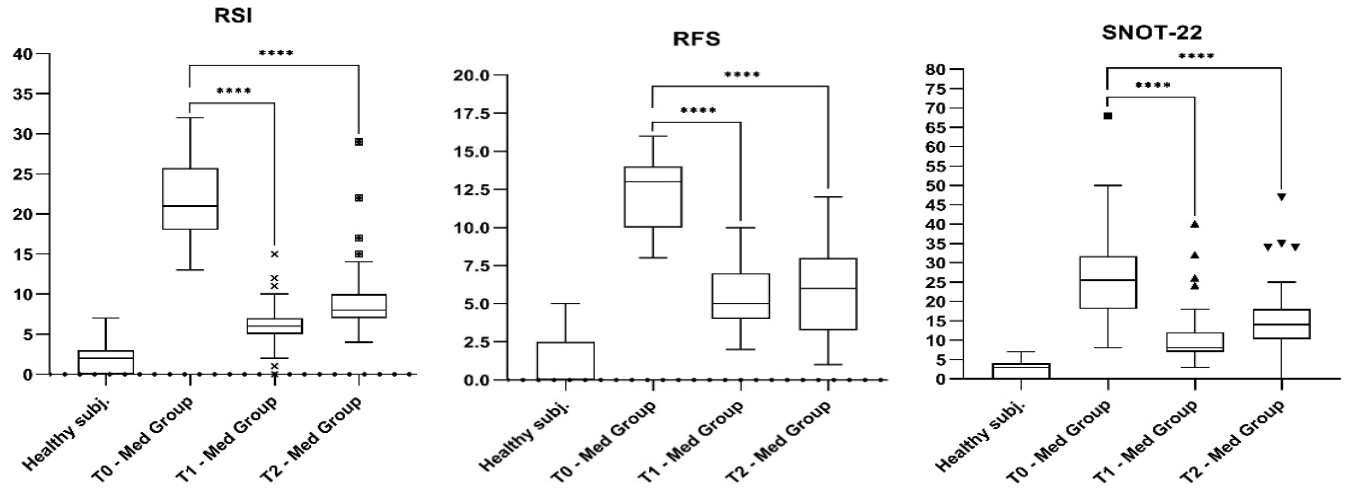

Figure 1: Treatment with Med for 30 days (T1) resulted in a significant reduction in total RSI, RFS and SNOT-22 scores. Total scores remained significantly lower than the T0 score even 30 days after discontinuation of Med (T2) treatment (****p<0.0001). The RSI, RFS and SNOT-22 score of patients with LPR always remained significantly higher than that of healthy subjects.

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Rhinocytogram

In patients in the Med Group, the presence of lymphocytes was significantly reduced at T1 compared to T0, testifying to the reduction of the inflammatory state. The presence of lymphocytes in the treated patients was further reduced at T2, one month after discontinuation of Med, compared to T1 (Table 7, Figure 2). At T0, the cell count of lymphocytes in patients with LPR was significantly higher than that of healthy subjects. Thanks to the significant improvement observed in patients in the Med group, at T1 and T2 the difference compared to healthy subjects was not statistically significant.

In patients in the Med group, the presence of neutrophils and goblet cells was significantly reduced at T1 compared to T0, testifying to the reduction of the inflammatory state. The presence of neutrophils and goblet cells increased at T2, one month after discontinuation of Med, compared to T1, but

Table 7: Median, 25th and 75th percentile and mean ± SD of lymphocyte, neutrophil and goblet cell counts found in Med Group patients at the start of Med treatment (T0), after 30 days of Med treatment (T1) and after 30 days after discontinuation of Med treatment (T2) and found in healthy subjects and statistical significance of comparisons. In italics, the values of P > 0.05.

Cell type	Parameters	Healthy subjects (n=37)	Med Group (n=56)		
			T0	T1	T2
Lymphocytes	Median [25th–75th]	0 [0.00 – 0.00]	1 [0.00 – 3.00]	0 [0.00 – 0.00]	0 [0.00 – 0.75]
	Mean ± SD	0.16 ± 0.37	1.42 ± 1.19	0.23 ± 0.43	0.25 ± 0.44
	P-value vs healthy subjects		< 0.0001	*0.446*	*0.4402*
	P-value vs T0			< 0.0001	< 0.0001
Neutrophils	Median [25th–75th]	0 [0.00 – 1.00]	3 [2.00 – 3.75]	1 [0.25 – 1.00]	1 [1.00 – 2.00]
	Mean ± SD	0.43 ± 0.59	2.98 ± 0.73	0.96 ± 0.76	1.18 ± 0.90
	P-value vs healthy subjects		< 0.0001	0.0002	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001
Goblet cells	Median [25th–75th]	1 [1.00 – 1.00]	3 [2.00 – 3.00]	1 [1.00 – 2.00]	2 [1.00 – 2.00]
	Mean ± SD	0.92 ± 0.28	2.82 ± 0.57	1.43 ± 0.57	1.59 ± 0.63
	P-value vs healthy subjects		< 0.0001	< 0.0001	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001

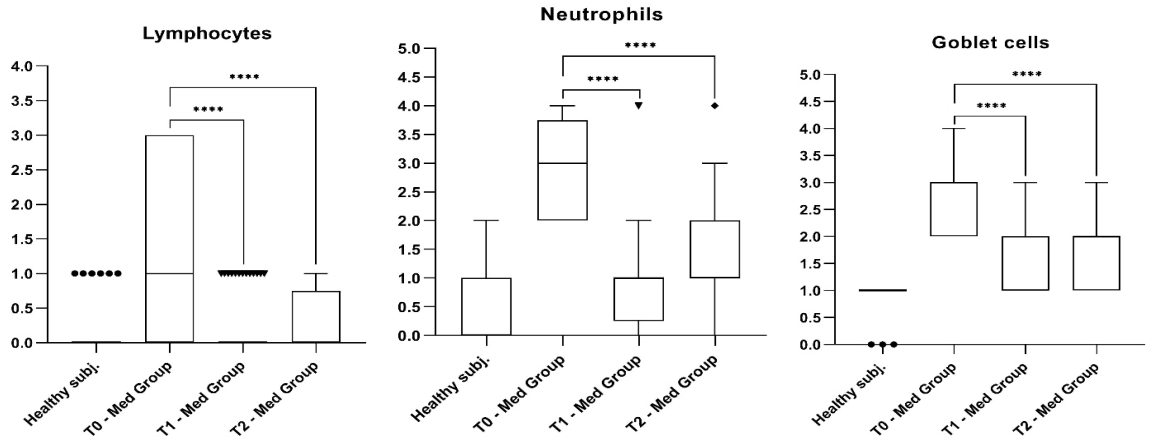

Figure 2: Treatment with Med for 30 days (T1) resulted in a significant reduction, compared to T0, in the number of lymphocytes detected. The significant difference compared to T0 was maintained even 30 days after discontinuation of Med (T2) treatment (****p<0.0001). At T1 and T2, the number of lymphocytes detected in patients with LPR was not significantly different from that detected in healthy subjects. Treatment with Med for 30 days (T1) resulted in a significant reduction in neutrophil and goblet cell counts, which rose slightly 30 days after discontinuation of treatment (T2), remaining significantly lower than T0 ****p<0.0001). The counts of neutrophils and goblet cells in patients in the Med Group always remained significantly higher than those of healthy subjects.

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Table 8: Median, 25th and 75th percentile and mean ± SD of the PCS index and MCS index found in healthy subjects and the Med Group at the start of treatment (T0), after 30 days of treatment (T1) and after 30 days after discontinuation of treatment (T2) and statistical significance of comparisons. In italics, the values of P > 0.05.

SF-12	Parameters	Healthy subjects (n=37)	Treated patients (n=56)		
			T0	T1	T2
SF-12 - PCS	Median [25th–75th]	54.9 [50.0 – 55.9]	36.1 [24.9 – 48.9]	51.2 [47.2 – 52.7]	50.7 [47.9 – 52.2]
	Mean	53.0 ± 4.36	36.0 ± 11.5	49.9 ± 4.59	49.6 ± 4.63
	P-value vs healthy subj.		< 0.0001	0.0009	0.0002
	P-value vs T0			< 0.0001	< 0.0001
SF-12 - MCS	Median [25th–75th]	53 [51.2 – 55.2]	34.7 [26.2 – 48.1]	52.1 [50.1 – 53.6]	49.6 [43.2 – 52.3]
	Mean	51.7 ± 5.75	37.2 ± 10.9	51.5 ± 3.31	47.0 ± 7.16
	P-value vs healthy subj.		< 0.0001	*0.0981*	< 0.0001
	P-value vs T0			< 0.0001	< 0.0001

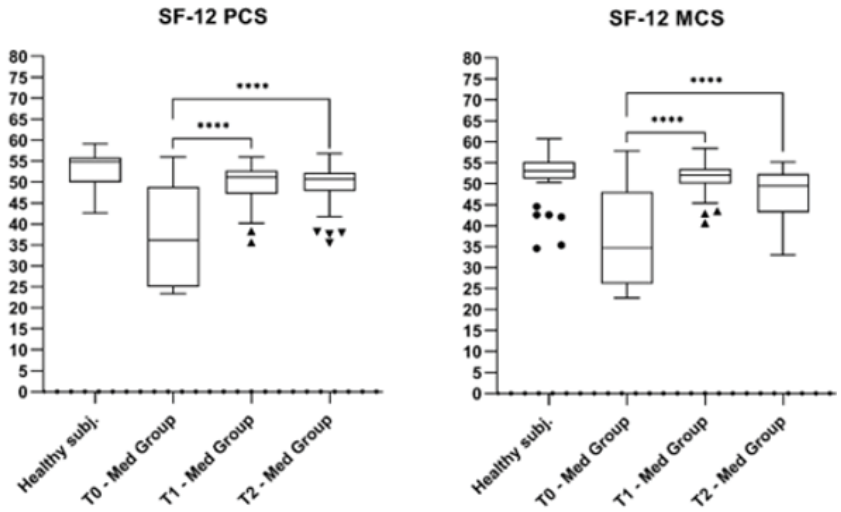

Figure 3: Treatment with Med for 30 days (T1) resulted in a significant increase in the PCS and MCS index score, which remained significantly higher than the score at T0 even 30 days after discontinuation of treatment (T2) (****p<0.0001).

remained significantly lower than at T0 (Table 7, Figure 2). At T0, the cell count of neutrophils and goblet cells in patients with LPR was significantly higher than that of healthy subjects. Despite the significant improvement observed in patients in the Med Group, at T1 and T2 the difference compared to healthy subjects remained statistically significant.

12-Item Short Form Health Survey

The results of the SF-12 questionnaire were evaluated by dividing the questionnaire into two indices called the Physical Component Summary (PCS) and the Mental Component Summary (MCS).

In the Med Group, the PCS index and MCS index scores improved significantly at T1 compared to T0, confirming the improvement of patients' physical and mental state. The scores worsened at T2, one month after discontinuation of Med, but remained significantly better than at T0 (Table 8, Figure 3). At T0, the scores of the PCS and MCS indices of patients in the Med Group were significantly lower than those of healthy subjects. At T1, the difference compared to healthy subjects remained statistically significant for the PCS index, while for the MCS index score there was no longer a statistically significant difference between patients in the Med Group and healthy subjects (P = 0.0981).

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

Opinion on the effectiveness and agreeability of the treatment

Among the 56 patients included in the Med Group, 41 patients answered the question: how many days after starting the medical device did the most troublesome symptoms disappear? The average number of days was: 12.0 ± 3.65.

After 30 days of treatment (T1), patients in the Med Group expressed an opinion on the effectiveness of the treatment. The reviews were as follows: 46.4% (26 patients) excellent, 42.9% (24 patients) good, 7.1% (4 patients) satisfactory, 3.6% (2 patients) poor.

After 30 days of treatment (T1), patients in the Med Group expressed an opinion on the agreeableness of Med. The reviews were as follows: 46.4% (26 patients) excellent, 37.5% (21 patients) good, 14.3% (8 patients) satisfactory, 1.8% (1 patient) poor.

Discussion

According to the scientific literature, a medical device that contains the appropriate amounts of magnesium alginate, calcium carbonate, and potassium bicarbonate, and in which these ingredients are present in the correct stoichiometric ratios, is expected to perform a triple action. The first action is determined by the fact that magnesium alginate, calcium carbonate and potassium bicarbonate, when in contact with the gastric contents, form what is known as a floating raft, which physically obstructs the reflux of gastric contents into the oesophagus after meals [31]. The second action is determined by the fact that calcium carbonate and potassium bicarbonate neutralise the unbuffered, extremely acidic gastric juice, which is found after meals at the gastro-oesophageal junction and is called an "acid pocket", thereby reducing its erosive power [31]. The third action is determined by the fact that the mixture of sodium hyaluronate and chondroitin sulphate is viscous and forms a transient protective film that adheres to the oesophageal mucosa [32]. As long as the film remains adherent to the epithelium of the oesophagus, it protects it against contact with material refluxed from the stomach and facilitates its reparative processes [32].

Formulations based on alginate and on carbonates and bicarbonates have demonstrated in several clinical studies their usefulness in the management of GERD and LPR [31-36]. The beneficial effects of sodium hyaluronate and chondroitin sulphate in the treatment of disorders of the upper gastrointestinal tract and in the treatment of LPR are already documented in the scientific literature [37-39].

Against this background, the intake of Med is expected to impact symptoms and thereby favourably modify the outcome of the questionnaires aimed at assessing LPR symptoms and rhinological symptoms, if any, and it is also expected to protect the pharyngolaryngeal mucosa and nasal mucosa as evidenced by direct observation of the mucosa and the favourable modification of the rhinocytogram results.

In patients with LPR, lesions such as dilation of blood vessels, increased vascular patterning within the mucosa and submucosa, ecchymosis, perivascular parenchymal oedema, inflammatory transudate and fibroblast infiltration leading to fibrosis, thickening and deformation of laryngeal structures followed by squamous metaplasia of the ciliary epithelium and secondary hypertrophy and atrophy of the muciparous glands occur. The resulting symptoms are a dry throat with a burning or velvety sensation, inducing frequent rasping, coughing and dysphonia [1]. A typical laryngeal presentation has not yet been identified on the basis of laryngoscopy: LPR may manifest with acute or chronic laryngitis, posterior laryngitis, interarytenoid oedema and hypertrophy, posterior commissure hypertrophy, Reinke's oedema, contact ulcers, stenosis of Morgagni's ventricles, vocal cord nodules, chordal hypomobility, subglottic oedema (evidenced by the appearance of pseudosulcus vocalis), up to, in very advanced cases, subglottic stenosis [1]. In severe cases, if not adequately treated, transformation of the hypopharyngolaryngeal epithelium can occur, with the appearance of precancerous lesions, such as leukoplakias and erythroplasias, which can develop into malignant hypopharyngolaryngeal neoplasms [1]. The most common lesions include hyperemia and oedema of the posterior laryngeal segment, mostly confined to the arytenoids, possibly accompanied by thickening and opacification of the interarytenoid region.

In our study, swelling and congestion of the posterior laryngeal mucosa, in particular of the posterior thirds of the vocal cords, the arytenoids, hypertrophic lesions of the posterior laryngeal commissure, and a discrete presence of mucus were more commonly presented in the Med Group patients. From a cytological point of view, in the nasal mucosa of LPR patients, the characteristic infiltration of neutrophils and lymphocytes was observed with a variable increase in the proportion of goblet cells which, normally, should not exceed 10-15%, caused by exposure to irritants, in the absence of bacteria and spores, already emphasised in previous studies [10].

After 30 days of treatment with Med, the total RSI and RFS scores improved significantly, decreasing by an average of 71.0% and 58.1% respectively, values above the 50% threshold that we considered essential to consider the treatment effective. Considering the individual RSI and RFS items separately, it can be seen that they underwent a statistically significant reduction from T0 to T1. Together, these two observations confirm that treatment with Med allows a significant improvement in the signs and symptoms of LPR.

Patients in the Med group also presented with rhinological discomfort, as evidenced by the SNOT-22 total score, the

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

sum of the scores of items 1 to 12 of SNOT-22 and the outcome of the nasal cytological investigation. After 30 days of treatment with Med, the total SNOT-22 score improved significantly, reducing by an average of 59.0%. The sum of the scores of SNOT-22 items 1 to 12, which focus on the physical aspects of the disease, was also significantly reduced. The cytological investigation shows that 30 days of treatment with Med reduced the inflammatory state of the nasal mucosa, evidenced by the significant reduction in lymphocyte and neutrophil counts and reduced the number of goblet cells, suggesting that treatment with Med facilitated the reconstitution of the physiological structure of the nasal mucosa.

Together, these observations make it possible to hypothesise that treatment with Med also contributes to the reduction of rhinological symptoms and signs that characterise LPR.

The control carried out 30 days after discontinuation of Med (T2) showed that the total score of RSI, RFS, SNOT-22 and the rhinocytogram worsened compared to T1, but remained significantly better than the condition detected at T0. These observations show that the therapeutic result obtained within 30 days of treatment with Med is partially preserved after 30 days after discontinuation of treatment and suggest that in order to resolve the signs and symptoms of LPR and stabilise the result achieved, it is desirable to extend the treatment for a period of more than 30 days.

From the comparison between patients treated with Med and healthy subjects it emerges that: at T0, the total RSI, RFS and SNOT-22 scores of patients in the Med Group were significantly higher than those of healthy subjects and at T1 the difference compared to healthy subjects decreased but remained significant in almost all cases.

As for RSI, it is considered that it is very relevant that at T1 the score of the item Sensations of something sticking in your throat or a lump in your throat in the Med Group was not significantly different from the score of the healthy subjects. Experience shows that this symptom is one of the main reasons why patients suffering from LPR undergo observation by an otolaryngologist. As confirmation of this, in the Med Group, this symptom was present at T0 with varying intensity in 48 out of 56 patients (85.7%). The situation changed radically after 30 days of treatment with Med: in fact, at T1, this symptom remained present in an attenuated form in only 26 out of 56 patients (46.4%).

At T1, the scores of the items Difficulty swallowing food, liquids, or pills and Breathing difficulties or choking episodes in the Med Group were not significantly different from the scores of the healthy subjects. However, it is not considered that this finding is particularly relevant as these two symptoms are not particularly present at T0 in patients in the Med group, and it can be assumed that this may generate an apparent amplification of the treatment's efficacy.

Also very interesting is the evidence that in RFS, the scores for the items Subglottic oedema and Thick endolaryngeal mucus undergo such a pronounced improvement after 30 days of treatment with Med that the data at T1 are not significantly different from those collected in healthy subjects.

The data collected allow us to state that patients who resort to PPI treatment are those with more intense symptoms and signs of reflux disease. Patients in the Med Group treated with PPIs, compared with patients not taking PPIs, showed more intense signs of LPR, evidenced at T0 by a significantly higher RFS score, and more intense symptoms in the upper respiratory tract, evidenced at T0 by a significantly higher SNOT-22 score, but not by the RSI score. At T1, after 30 days of treatment with Med, there were no significant differences in RFS and SNOT-22 scores between patients taking PPIs and patients not taking them. At T2, 30 days after discontinuation of Med treatment, there were no significant differences between the RFS score of patients taking PPIs and that of patients not taking PPIs, while the SNOT-22 score was significantly higher in patients taking PPIs. This makes it possible to hypothesise that in patients with more pronounced symptoms taking PPIs, the combination of these drugs with Med may significantly improve the clinical picture, and improvements may regress once the regular intake of Med is discontinued, despite continued PPI treatment.

The assessments of health-related quality of life, measured by the SF-12 questionnaire, agree with what has already been underlined: the scores of the PCS and MCS components significantly improved at T1 compared to T0 in the Med Group, confirming the improvement of the physical and mental state of patients after 30 days of treatment with Med. The scores worsened at T2, 30 days after discontinuation of Med, but remained significantly better than at T0. A comparison with healthy subjects is useful: at T0, the PCS and MCS index scores of patients in the Med Group were significantly lower than those of healthy subjects. At T1, the difference compared to healthy subjects remained statistically significant with regard to the PCS index, while with regard to the MCS index there was no longer a statistically significant difference. The marked improvement in physical and mental state is confirmed by the opinion of patients in the Med group on the effectiveness of the medical device: 89.3% of patients rated it as good to excellent.

An original aspect of this study is the comparison between patients in the Med Group and healthy subjects. It is often considered sufficient to compare the status of patients before treatment and after treatment. If the therapeutic actions taken have already proven to be effective in treating the disorder in question, a statistically significant improvement in the parameters chosen for clinical evaluation is easily achievable.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

This type of result does not allow an assessment of the extent to which the improvement achieved brings the state of patients at the end of treatment closer to the state of healthy subjects. Therefore, the comparison between treated patients and healthy subjects carried out in this study is intended to at least partially obviate this potential bias in the verification of the treatment's efficacy and is intended to help in determining how long treatment should be prolonged in order to obtain the best results.

One limitation of this study is its retrospective design. This implies the inclusion of patients who have completed the course of treatment with Med and does not allow investigation of whether there are potential reasons for discontinuing Med treatment. At the same time, what prompted us to reorganise the data collected and process it was the feeling that the patients liked the Med treatment and were therefore rather compliant with the treatment requirements. However, this is a feeling that we cannot in any way demonstrate.

The lack of a placebo-treated or PPI-treated control arm can be considered a further limitation of the present study. We would like to clarify that we do not consider a comparison with a placebo group to be necessary, primarily because alginates combined with alkalinising substances and the combination of sodium hyaluronate and chondroitin sulphate have already been tested in clinical trials versus placebo in the treatment of reflux disease. Both alginates combined with alkalinising substances [34,35] and the combination of sodium hyaluronate and chondroitin sulphate [37,38] have been shown to be more effective than a placebo, which allows us to assume that Med, which combines alginate, alkalinising substances, sodium hyaluronate and chondroitin sulphate in its formula, can easily lead to clinical effects that are superior to those of a placebo. Furthermore, our ambition is not to prescribe medical devices that exceed the effectiveness of a placebo, a very easily achievable result, but to attempt to bring our patients back to a state of health similar to that of healthy subjects. Finally, this study was conducted as part of our usual clinical activity, and we do not consider it ethically correct to treat patients who come to us with the hope of resolving their conditions with a placebo.

Conclusions

The hypothesis we formulated seems to be confirmed by the results of the study conducted: an oral medical device that physically obstructs the reflux of gastric contents, neutralises the acid pocket that forms near the gastro-oesophageal junction during meals, and protects the oesophageal and laryngopharyngeal mucosa, can effectively manage the symptoms and signs of LPR, whether with or without the use of PPI.

This study shows an improvement in all the parameters evaluated after 30 consecutive days of taking Med by patients with LPR. In fact, the symptoms and signs of LPR in the pharyngolaryngeal and nasal region were significantly improved by the treatment.

The same parameters worsen slightly in the 30 days following discontinuation of treatment, demonstrating that in the case of LPR, more prolonged treatment is preferable in order to stabilise the results obtained.

In conclusion, the results of the present clinical study demonstrate the efficacy of a medical device composed of magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in reducing the signs and symptoms commonly associated with LPR and in improving the cytological status of the mucous membranes of the upper respiratory tract in patients with LPR. The study also shows that the product under study is acceptable to patients, which makes it possible to hypothesise that adherence to treatment may be facilitated.

Aknowledgment

We thank Dr. Stefano Agostini for the precious contribution provided for the implementation of the procedures necessary for the publication of the study.

Conflict of interest

Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni and Serena Miglio declare that they do not have any business relationships (e.g., consultancy, ownership of shares, shareholding, patent/licence agreement, etc.) that could pose a conflict of interest in relation to the submitted article.

References

1. Lechien JR, Akst LM, Hamdan AL, et al. Evaluation and Management of Laryngopharyngeal Reflux Disease: State of the Art Review. Otolaryngol Head Neck Surg 160 (2019): 762-782.
2. Dent J, Brun J, Fendrick A, et al. An evidence-based appraisal of reflux disease management--the Genval Workshop Report. Gut 44 (1999): S1-16.
3. Koufman JA, Aviv JE, Casiano RR, et al. Laryngopharyngeal reflux: position statement of the committee on speech, voice, and swallowing disorders of the American Academy of Otolaryngology-Head and Neck Surgery. Otolaryngol. Head Neck Surg 127 (2002): 32-35.
4. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 101 (1991): 1-78.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

5. Amarasiri DL, Pathmeswaran A, De Silva HJ, et al. Response of the airways and autonomic nervous system to acid perfusion of the esophagus in patients with asthma: a laboratory study. BMC Pulm Med 13 (2013): 33.

6. Ali Mel-S, Bulmer DM, Dettmar PW, et al. Mucin gene expression in reflux laryngeal mucosa: histological and in situ hybridization observations. Int J Otolaryngol 2 (2014): 264075.

7. Adhami T, Goldblum JR, Richter JE, et al. The role of gastric and duodenal agents in laryngeal injury: an experimental canine model. Am J Gastroenterol 99 (2004): 2098-2106.

8. Lechien JR, Saussez S, Harmegnies B, et al. Laryngopharyngeal Reflux and Voice Disorders: a Multifactorial Model of Etiology and Pathophysiology. J Voice 31 (2017): 733-752.

9. Finocchio E, Locatelli F, Sanna F, et al. Gastritis and gastroesophageal reflux disease are strongly associated with non-allergic nasal disorders. BMC Pulm Med 21 (2021): 53.

10. Mandolesi D, Schiavon P, Ioannou A, et al. Chronic non-allergic rhinitis with neutrophils is associated with higher acid exposure time: A pH-impedance monitoring study. Dig Liver Dis 52 (2020): 414-419.

11. Dagli E, Yüksel A, Kaya M, et al. Association of oral antireflux medication with laryngopharyngeal reflux and nasal resistance. JAMA Otolaryngol Head Neck Surg 143 (2017): 478-483.

12. Aldajani A, Alhussain F, Mesallam T, et al. Association Between Chronic Rhinosinusitis and Reflux Diseases in Adults: A Systematic Review and Meta-Analysis. American Journal of Rhinology & Allergy 38 (2024): 47-59.

13. Biedlingmaier JF, Trifillis A. Comparison of CT scan and electron microscopic findings on endoscopically harvested middle turbinates. Otolaryngol Head Neck Surg 118 (1998): 165-173.

14. Berger G, Moroz A, Marom Z, et al. Inferior turbinate goblet cell secretion in patients with perennial allergic and nonallergic rhinitis. Am J Rhinol 13 (1999): 473-477.

15. Berger G, Marom Z, Ophir D. Goblet cell density of the inferior turbinates in patients with perennial allergic and nonallergic rhinitis. Am J Rhinol 11 (1997): 233-236.

16. Gelardi M, Iannuzzi L, Quaranta N, et al. Nasal cytology: practical aspects and clinical relevance. Clin Exp Allergy 46 (2016): 785-792.

17. Kuo CL. Laryngopharyngeal Reflux: An Update. Archives of Otorhinolaryngology-Head & Neck Surgery 3 (2019): 1.

18. Lechien JR, Saussez S, Schindler A, et al. Clinical outcomes of laryngopharyngeal reflux treatment: A systematic review and meta-analysis. Laryngoscope 129 (2019): 1174-1187.

19. Wei C. A meta-analysis for the role of proton pump inhibitor therapy in patients with laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 273 (2016): 3795-3801.

20. Gong EJ, Choi KD, Jung HK, et al. Quality of life, patient satisfaction, and disease burden in patients with gastroesophageal reflux disease with or without laryngopharyngeal reflux symptoms. J Gastroenterol Hepatol 32 (2017): 1336-1340.

21. Maffezzoni E, Luciano K, Maffezzoni F, et al. Efficacy of oral intake of a compound medical device in the treatment of laryngopharyngeal reflux disease: a clinical investigation and nasal cytological correlations. J Biol Regul Homeost Agents 36 (2022): 167-174.

22. Maffezzoni E, Luciano K, Maffezzoni F, et al. Treatment of Laryngopharyngeal Reflux Disease Using an Oral Medical Device: A Clinical Investigation into Signs, Symptoms and Quality of Life of Patients. Acta Scientific Medical Sciences 6 (2022): 89-102.

23. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Guidelines for Good Clinical Practice (1996).

24. World Medical Association (WMA). Declaration of Helsinki. Ethical principles for medical research involving human subjects (2013).

25. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). J Voice 16 (2002): 274-277.

26. Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope 111 (2001): 1313-1317.

27. Kim YS, Lee YS, Bang CS, et al. Su1518 Interrater Reliability of Laryngopharyngeal Reflux (LPR) Between an Otolaryngologist and Endoscopists After Laryngologic Education - a Pilot Study. Gastrointestinal endoscopy 79 (2014): AB306.

28. Mozzanica F, Preti A, Gera R, et al. Cross-cultural adaptation and validation of the SNOT-22 into Italian. Eur Arch Otorhinolaryngol 274 (2017): 887-895.

29. Gelardi M. Atlante di Citologia Nasale. Edi Ermes (2012).

30. J Ware Jr J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 34 (1996): 220-233.

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.

Notargiacomo M, et al., J Surg Res 2025
DOI:10.26502/jsr.10020444

31. Rohof WO, Bennink RJ, Smout AJ, et al. An alginate-antacid formulation localizes to the acid pocket to reduce acid reflux in patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol 11 (2013): 1585-1591.

32. Ceriotti L, Buratti P, Corazziari ES, et al. Protective Mechanisms of Liquid Formulations for Gastro-Oesophageal Reflux Disease in a Human Reconstructed Oesophageal Epithelium Model. Med Devices (Auckl) 15 (2022): 143-152.

33. De Ruigh A, Roman S, Chen J, et al. Gaviscon Double Action Liquid (antacid & alginate) is more effective than antacid in controlling post-prandial oesophageal acid exposure in GERD patients: a double-blind crossover study. Aliment Pharmacol Ther 40 (2014): 531-537.

34. Thomas E, Wade A, Crawford G, et al. Randomised clinical trial: relief of upper gastrointestinal symptoms by an acid pocket-targeting alginate-antacid (Gaviscon Double Action) - a double-blind, placebo-controlled, pilot study in gastro-oesophageal reflux disease. Aliment Pharmacol Ther 39 (2014): 595-602.

35. Wilkinson J, Wade A, Thomas SJ, et al. Randomized clinical trial: a double-blind, placebo-controlled study to assess the clinical efficacy and safety of alginate-antacid (Gaviscon Double Action) chewable tablets in patients with gastro-oesophageal reflux disease. Eur J Gastroenterol Hepatol 31 (2019): 86-93.

36. Wilkie MD, Fraser HM, Raja H. Gaviscon® Advance alone versus co-prescription of Gaviscon® Advance and proton pump inhibitors in the treatment of laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 275 (2018): 2515-2521.

37. Palmieri B, Merighi A, Corbascio D, et al. Fixed combination of hyaluronic acid and chondroitin-sulphate oral formulation in a randomized double blind, placebo controlled study for the treatment of symptoms in patients with non-erosive gastroesophageal reflux. Eur Rev Med Pharmacol Sci 17 (2013): 3272-3278.

38. Savarino V, Pace F, Scarpignato C, et al. Randomised clinical trial: mucosal protection combined with acid suppression in the treatment of non-erosive reflux disease - efficacy of Esoxx, a hyaluronic acid-chondroitin sulphate based bioadhesive formulation. Aliment Pharmacol Ther 45 (2017): 631-642.

39. Chmielecka RJ, Tomasik B, Pietruszewska W. The role of an oral formulation of hyaluonic acid and chondroitin sulphate in the treatment of patients with laryngopharyngeal reflux. Otolaryngol Pol 73 (2019): 38-49.

Citation: Mario Notargiacomo, Enrico Maffezzoni, Federico Maffezzoni, Serena Miglio. Evaluation of the efficacy of a medical device based on magnesium alginate, calcium carbonate, potassium bicarbonate, sodium hyaluronate and chondroitin sulphate in the treatment of laryngopharyngeal reflux disease. Journal of Surgery and Research. 8 (2025): 236-251.