ORIGINAL ARTICLE

INDEX COPERNICUS INTERNATIONAL

Indications and Long-term Outcomes of Open Augmentation Rhinoplasty with Autogenous L-shaped Costal Cartilage Strut Grafts – A Single Plastic Surgeon's Experience

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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ABSTRACT:

Introduction: We present a single surgeon's experience of open augmentation rhinoplasty with autogenous L-shaped costal cartilage grafts, with long-term patient-reported outcome data. We highlight the salient operative steps and outline the peri-operative care required to optimise outcomes.

Materials and Methods: A retrospective review of eleven such augmentation rhinoplasties performed between 2008 and 2016 was undertaken. Indications included saddle nose deformity [granulomatosis with polyangiitis (n=7) and relapsing polychondritis (n=1)], post-traumatic nasal collapse (n=1) and advanced cosmetic westernisation of the nose (n=2). Long-term patient-reported outcome was assessed with a patient questionnaire.

Results: All patients achieved marked improvement in nasal position, shape and function. There was no cartilage exposure, warping or resorption and no recurrent deformities. One patient's dorsal graft was fractured two years later during an ophthalmological procedure and the deformity was re-corrected successfully, again with the above technique. Average follow up was 5.2 years. Of the nine patients who responded to the follow-up questionnaire, 100% were satisfied with their nasal appearance. 100% of responders at follow-up reported that they have had no problems relating to their nose (n=9).

Discussion: L-shaped costal cartilage grafts provided a reliable, reproducible approach in augmentation rhinoplasty for disparate indications (inflammatory, traumatic and cosmetic) in the hands of a low-volume operator. With careful patient selection and planning, this technique can provide pleasing aesthetic outcomes and high patient satisfaction, with good long-term outcomes.

KEYWORDS: augmentation rhinoplasty, costal cartilage grafts, autoimmune inflammatory disease, granulomatosis with polyangiitis, relapsing polychondritis, screw fixation of grafts

INTRODUCTION

Granulomatosis with polyangiitis (GP) and relapsing polychondritis (RPC) are both immune-mediated conditions associated with saddle nose deformity with physical, functional and psychological implications. RPC is a multi-systemic inflammatory disease associated with cartilage destruction with an annual incidence of 0.7-3.5 cases per million [1, 2]. GP has an incidence of 3-14.4/million per year in Europe and is a multi-systemic necrotising granulomatous vasculitis [3]. It results in inflammation of small and medium sized blood vessels, and subsequent mucosal inflammation. The cycle of inflammation and healing leads to granulation, scar formation, and tissue contracture. This process causes the weakening of the cartilagino-

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us part of the septum, leading to septal perforation, weakening of the middle portion of the nose and a resultant saddle-nose deformity [4]. Symptomatic management of autoimmune-related saddle nose deformities includes nasal saline rinses, intranasal corticosteroids, mucolytics, and emollients for nasal crusting and mucosal-sparing techniques. However, nasal reconstruction is the only definitive treatment of the deformity. Surgical reconstruction of saddle-nose deformities using cartilage grafts has rarely been explored [5].

Nasal deformity secondary to trauma is often initially managed with closed reduction ideally within 10 days of the injury but post-reduction deformity persists in 14-50% of patients [6]. These patients may require a secondary rhinoplasty for function and/or cosmesis.

African nose westernisation entails the challenge of correcting an acute columellar-labial angle, bulbous and poorly-projecting tip, short columella and flaring alae with rounded nostrils and broad alar bases [7].

The foregoing disparate indications are amenable to correction using similar complex rhinoplasty techniques. We present a single surgeon's experience of performing open augmentation rhinoplasty using autogenous L-shaped costal cartilage dorsal and columellar strut grafts to correct marked nasal deformity secondary to autoimmune conditions, trauma-related injuries to the dorsum of the nose and Westernisation of African noses. Costal-cartilage grafting of the nose is at best a challenging operation, which is not commonly used in aesthetic rhinoplasty surgery; we reflect upon key intra-operative and peri-operative features to optimise outcomes.

MATERIALS AND METHODS

A retrospective review was undertaken of eleven augmentation rhinoplasties performed between 2008 and 2016 by a single consultant plastic surgeon. Patients were identified using theatre records, the consultant's logbook and electronic billing records. Surgery was performed at a tertiary university teaching hospital and two private hospitals. Patients were followed up in the relevant outpatient clinics. Case notes were reviewed retrospectively, focusing on demographics, cause and severity of deformity, operative indication and technique, complications and cosmetic outcomes.

Surgical technique

All patients underwent general anaesthesia with endotracheal intubation. An open rhinoplasty approach was used, with

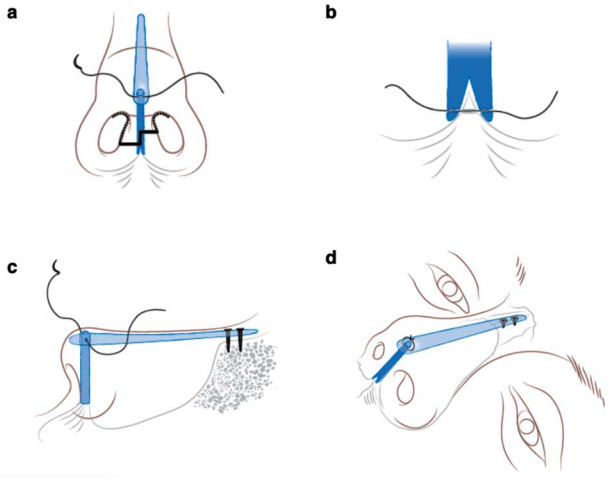

Fig. 1. Artist's illustration showing key stages of the open augmentation rhinoplasty approach using costal cartilage; a) stair-step columellar and infra-cartilaginous (rim) incisions, b) the split columellar strut sitting astride the nasal spine prior to suture fixation of the two via a drill hole through the nasal spine, c) securing the dorsal strut to the nasal bone with monocortical titanium screws. The dorsal and columellar struts are secured to each other using a single 4/0 PDS suture, d) the completed open augmentation rhinoplasty with the columellar and dorsal struts in position.

a stair-step transcolumellar incision extending into bilateral infracartilaginous (rim) incisions (Figure 1). After exposure of the lower lateral cartilages, the underlying nasal bones and cartilage remnants were exposed taking care not to breach the mucosa. An additional 1 cm skin crease incision over the radix was made to allow direct access to the nasal bone cranially. The dorsal cartilaginous and bony structures were examined for damage, followed by rasping and trimming, as necessary, to create a receptive graft bed.

Costal cartilage was harvested from the sixth or seventh rib. Following subperichondrial costochondral harvest, a water test via the valsalva manoeuvre was performed to demonstrate any pleural leaks.

A dorsal (length 3.5-5.0 cm; variable width) and columellar strut (length 2.5-3.5 cm; width 5 mm; height 2-3 mm) of cartilage were carved using the balanced forces concept of Gibson and Davis with a focus on symmetry in order to reduce the risk of post-operative warping [9]. The dorsal graft was secured to the nasal bone with two titanium self-tapping monocortical screws (6-8 mm length, Leibinger Wurzburg Miniplating System, Wurzburg, Germany) to ensure a stable and symmetrical reconstruction.

The posterior end of the columellar graft was carefully split

Tab. I. Patient Characteristics.

PATIENT	GENDER	AGE	PRIMARY OR SECONDARY RHINOPLASTY	INDICATION	CO-MORBITIES	IMMUNOSUPPRESSION AT SURGERY	FOLLOW-UP (YEARS)	COMPLICATIONS
1	F	25	Secondary	GP	None	Prednisolone 10mg daily Budesonide nebulisers 1mg BD	8.7	none
2	F	74	Primary	GP	Spinal degeneration Hypertension	Prednisolone 1.5mg/day Methotrexate 22.5mg/week	7.7	Slow healing on small area over donor site
3	F	32	Primary	RPC	None	None	6.3	none
4	M	30	Primary	GP	Crohn's disease	Presnisolone 10mg/day Azathioprine 150mg/day Mesalazine 1g/day	5.2	none
5	F	30	Primary	GP	None	Prednisolone 1mg/day Azathioprine 100mg/day	5.2	none
6	F	48	Primary	GP	None	Rituximab 4-monthly Methotrexate 15mg/week	3.7	Cartilage graft fractured post dacryocystorhinostomy
7	F	51	Secondary	GP	None	Rituximab infusions 8-monthly Methotrexate 12.5 mg/week	1.2	none
8	F	58	Primary	GP	Breast cancer, gastro-intestinal ulcers	Prednisolone 1mg/week (weaning off at time of surgery)	3.5	none
9	F	22	Primary	Westernisation of African Nose	Mental health disorder	None	4.6	Pseudomonas infection to radix access incision 3 weeks post-operatively
10	M	27	Primary	Westernisation of African Nose	Non-allergic perennial rhinitis	None	9.6	Painful screw from rhinoplasty nasal bridge graft
11	M	46	Primary	Post-traumatic dorsal collapse	Hypertension	None	6.3	none
Median		32					5.2	

by approximately 5 mm to allow it to sit astride the anterior nasal spine. This was fixed to the nasal spine with a 4/0 PDS suture through a hole drilled in the spine with a 1.5 mm dental drill (Leibinger Wurzburg Miniplating System, Wurzburg, Germany). The two grafts were then connected to each other using a 'hole and dowel' arrangement and secured with a single 4/0 PDS suture (Figure 1). The overall structure was then examined and the cartilage further trimmed as necessary to improve contour.

After securing the L-shaped graft, the rim columellar incision was closed with 4/0 Vicryl Rapide to the mucosa and 5/0 nylon to the skin. The radix incision was closed in two layers (5/0 Vicryl and 6/0 Nylon). Half-inch wound closure strips (3M Steri-Strip) and a thermoplastic external nasal splint were then applied and left in place for 7 days. [8]

RESULTS

Indications included saddle nose deformity (granulomatosis with polyangiitis (n=7), relapsing polychondritis (n=1)) post-traumatic nasal collapse (n=1) and advanced cosmetic westernisation of the nose (n=2). The majority were primary rhinoplasties (n=9), but two were revision rhinoplasties (Table 1) The median age at operation was 32, and eight of the eleven

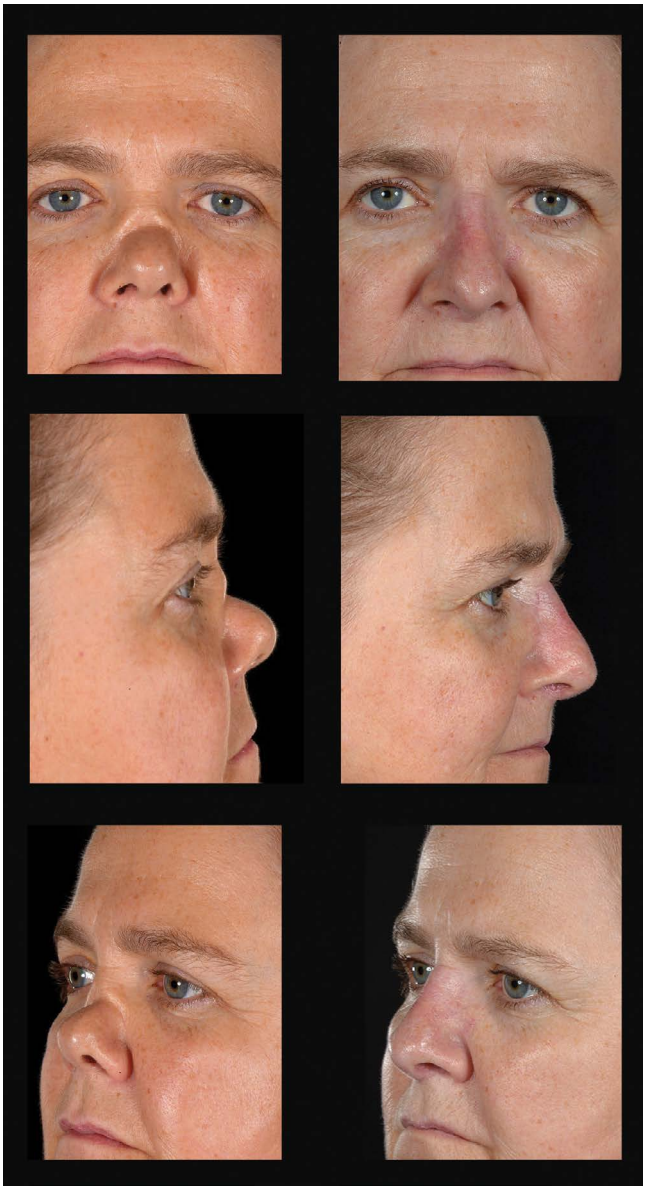

Fig. 2. Pre (left) and three-year postoperative (right) appearances of a patient with a saddle-nose deformity secondary to Granulomatosis with Polyangiitis (patient 6). Note the correction of the saddle-nose A-frame deformity between the bony and soft tissue part of the nose, elongation of the foreshortened nose and improved dorsal profile. The nose is also straighter in the front view.

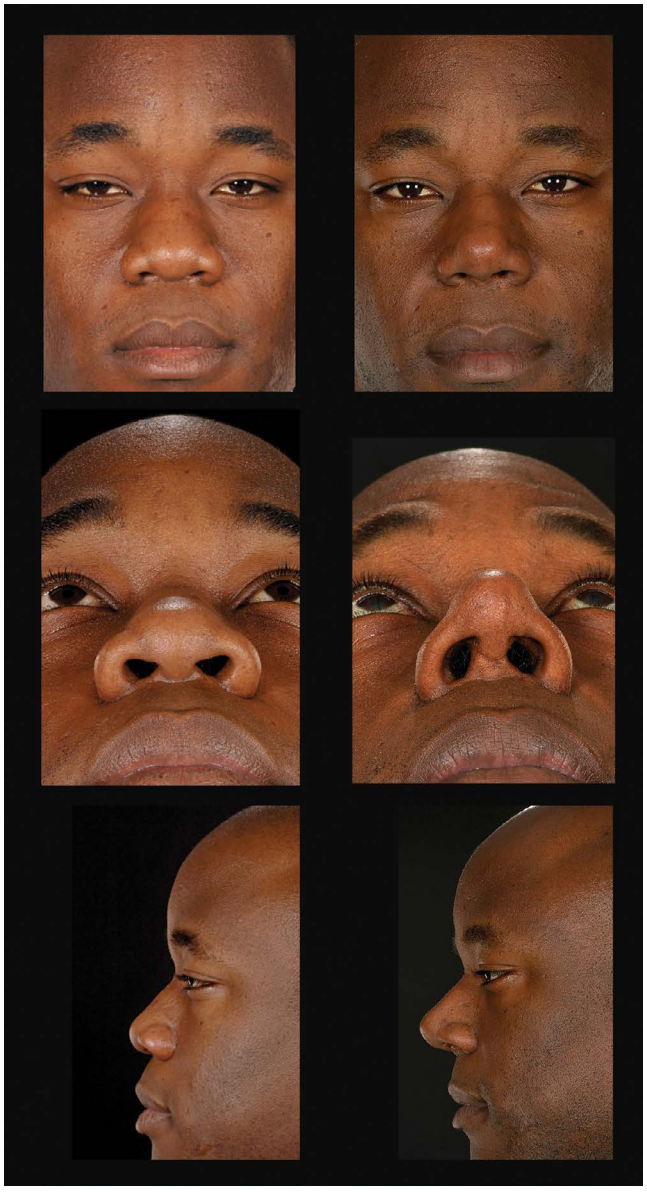

Fig. 3. Westernisation rhinoplasty in a man of mixed ethnicity (patient 9) Post-operative photographs (right side) were taken 6 years after surgery. Note the partially visible V-shaped columellar incision scar, improvement in the bulbous and poorly-projecting tip, and reduction in size of the alar bases. The cartilage grafts refined the tip, improved the projection and straightened the dorsal profile.

rhinoplasties were on caucasian patients. Length of follow-up from the operation date was a median of 5.2 years (average 5.6, range 1.2-9.6).

All patients achieved marked improvement in nasal position and shape (Figures 2-4). There was no cartilage exposure or resorption and no recurrent deformities. There were no incidences of nasal deviation due to cartilage warping. Long-term patient reported outcome was assessed with a questionnaire at a median of 5.2 years post-operatively. 90% of patients (n=9) responded, of whom 100% were satisfied with their nasal appearance. One of these patients (with GP) reported that their nose had some residual nasal dorsal deviation however they felt that it was markedly improved compared to the pre-operative appearance and they were therefore satisfied with the improvement. A second patient with GP stated that they were "hap-

py enough" with the appearance but reported they had some minor nasal deviation. At follow-up all nine reported that they have had no problems relating to their nose.

Most patients with autoimmune disease did not experience a relapse during this period, however, patient 5 experienced a mild flare in GP symptoms two months post-operatively. Despite requiring the addition of rituximab to her immunosuppression regime, there were no resultant nasal complications. There were no early complications apart from patient 8 who developed a pseudomonas infection of the radix access incision three weeks post-operatively. This was treated successfully with antibiotics and washout, with no permanent sequelae in the 4.6 years of follow-up postoperatively. Patient 9 underwent removal of a persistently painful fixation screw at one year post--operatively, without causing loosening of the dorsal graft (Figure 3). Patient 6 had cartilage graft fracture with deviation to the left two years later during an ophthalmological procedure (dacryocystorhinostomy) and the deformity re-corrected successfully with the above technique using rib cartilage from the contralateral side to that of the primary operation (Figure 4).

There were no donor site surgical complications such as bleeding, pneumothorax, infection or poorly-controlled pain. Patient 2 (on immunosuppression for GP) had a small area over the donor site which was initially slow to heal, however this subsequently healed satisfactorily.

DISCUSSION

In this study, we have demonstrated that the technique of using L-shaped cartilage grafts can be used successfully for nasal deformity due to a range of pathologies including autoimmune conditions, trauma and cosmetic westernisation of the nose.

The complex nature of these deformities requires a careful consideration of perioperative factors to ensure optimal outcome of augmentation rhinoplasty, and a multidisciplinary perioperative approach is necessary to create a safe and individualised service for patients. Those with autoimmune conditions require specialist input from a rheumatologist to monitor disease progression, and preoperative assessment by an anaesthetist and otolaryngologist to exclude airway pathologies including subglottic and tracheobronchial stenosis [9].

In our experience, with careful patient selection and adequate multidisciplinary optimisation, augmentation rhinoplasty is safe and effective in patients with saddle deformity secondary to GP and RPC. These patients all underwent pre-operative consultations with a specialist rheumatologist who maintained them on a maximum of

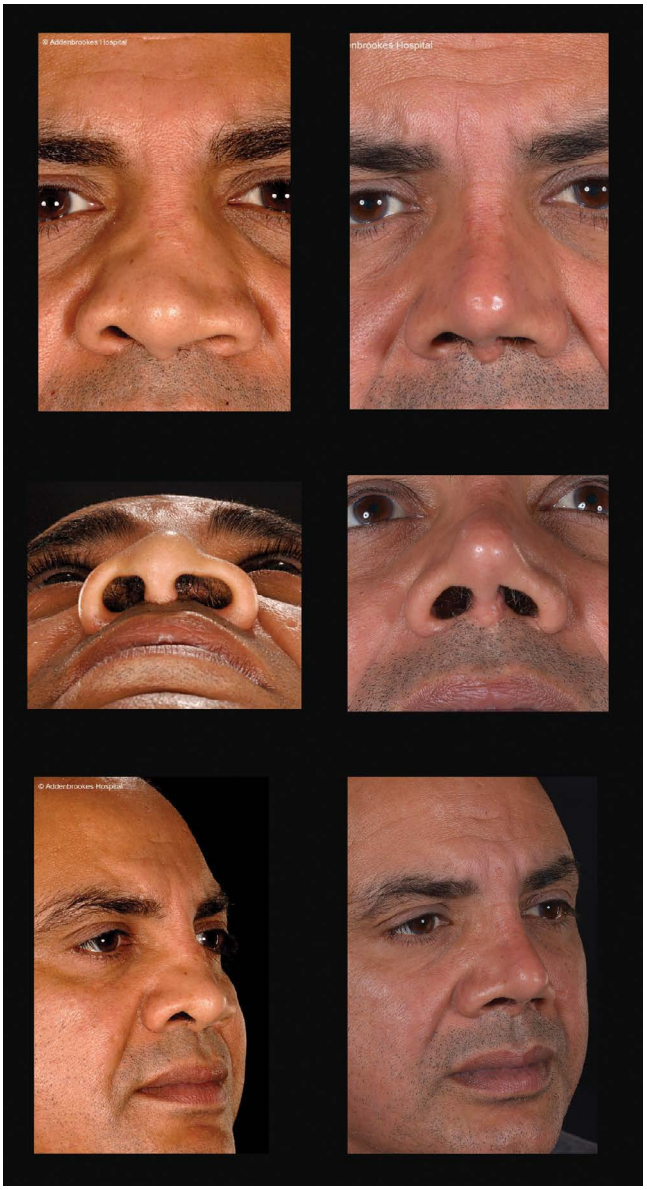

Fig. 4. Open augmentation rhinoplasty with costal cartilage for post-traumatic appearances (patient 10). Post-operative photographs (right) were taken at 5 years. Note the improved dorsal aesthetic lines (AP view), refined tip and nostrils and increased tip projection. With the internal scarring from multiple previous surgeries prior to referral and the complexity of the deformity, it is not surprising that there was still some residual alar and dorsal asymmetry.

10mg prednisolone daily as per local guidelines developed from our joint experience. Postoperatively, patients were given three doses of intravenous dexamethasone to reduce swelling. A further concern regarding operating on patients with autoimmune conditions is the potentially increased risk of infection, secondary to immunosuppressive therapies as well as a chronic microbial colonisation of the nasal epithelium. In our protocol, we address this by prescribing a

48-hour course of intravenous antibiotics postoperatively and a further seven days of topical antibiotics. Multidisciplinary team pre- and post-operative medical optimisation of disease is a key factor to successful operative outcomes.

Surgical challenges that have been addressed

In African and Asian noses there is often inadequate septal cartilage for augmentation rhinoplasty [10]. Furthermore, thickness of the soft tissue envelope means that conchal cartilage grafts are not strong enough and therefore result in insufficient definition and refinement. Our study suggests that costal cartilage grafts may therefore be superior in this patient population.

Traditionally surgeons are cautious to operate on saddle nose deformity in autoimmune conditions due to the potential risk of graft failure secondary to disease flare-up that will result in suboptimal long-term cosmetic results. However, with an average of 5.2 years follow-up of seven patients with autoimmune conditions, we have not seen post-operative recurrence of nasal deformity. To reduce this risk, we only operated on patients that were disease-free for at least one year pre-operatively.

Limitations of the study

A single surgeon's experience and small numbers limit this study. We will continue to follow-up patients to monitor for disease recurrence longer-term.

Conclusion

This case series demonstrates that using L-shaped costal cartilage grafts can be a reliable, reproducible approach in augmentation rhinoplasty for disparate indications including for saddle-nose deformity secondary to inflammatory disease, trauma and for cosmetic reasons, in the hands of a low-volume operator. Long-term follow-up showed good outcomes and ongoing high patient satisfaction. Careful patient selection, pre-operative planning and meticulous execution are required.

Ethical considerations

Informed consent was obtained from all individual participants for whom identifying information is included in this article.

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INDEX COPERNICUS INTERNATIONAL

ORIGINAL ARTICLE

Bacteriotherapy for preventing recurrent upper respiratory infections in children: a real-world experience

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ABSTRACT:

Background: Recurrent upper respiratory infections (RURI) constitute a social problem for both their pharmaco-economic impact and the burden for the family. Bacteriotherapy could be an interesting preventive option.

Objective: The aim of this study was to evaluate the preventive effects of RURI in children.

Design: The study was designed as spontaneous and was conducted in real-life setting. Globally, 80 children (40 males, mean age 5.26 (2.52) years) with RURI were enrolled. Children were treated with *Streptococcus salivarius 24SMB* and *Streptococcus oralis 89a*: nasal spray 2 puffs per nostril twice/day for a week for 3 monthly courses. Number of URI, and school and work absences were evaluated and compared with the past year.

Results: Bacteriotherapy significantly halved the mean number of URI episodes being 5.98 (2.30) in the past year and 2.75 (2.43) after the treatment ($p<0.0001$). Bacteriotherapy also induced an over 35% reduction both in the number of school days and in the number of working days missed per month from 4.50 (2.81) to 2.80 (3.42) and from 2.33 (2.36) to 1.48 (2.16), respectively ($p<0.0001$).

Conclusions: This real-life study provides the first evidence that *Streptococcus salivarius 24SMB* and *Streptococcus oralis 89a* nasal spray could be effective in preventing RURI in children..

KEYWORDS: recurrent upper respiratory infections, bacteriotherapy, *Streptococcus salivarius 24SMB, Streptococcus oralis 89a*, nasal spray, children

INTRODUCTION

Upper respiratory infections (URI) during infancy and childhood are a relevant issue (1,2). As many children suffer from recurrent URI (RURI), it determines a relevant impact on pharmaco-economy and is a burden for both the family and the society (2,3). So, RURI represents a challenge for both the paediatrician and the otolaryngologist.

Many factors may be involved in promoting and/or causing RURI, including early age (for a relative immaturity of the immune system), early attendance at nursery school, air and home pollution, passive smoking, low socio-economic level, and atopy (2). In addition, viral infections may increase the probability of contracting frequent RI because of the high number of circulating viruses and numerous sub-types (3). Usually, viral infections are predominant, but bacterial over-infections may also frequently appear.

In common practice, the diagnosis of URI is usually based on a clinical ground, such as consideration of the clinical history, and the presence of typical signs and symptoms. As punctually pointed out by guidelines, treatment includes anti-inflammatory drugs and antibiotics prescribed on an empiric basis (3,4). On the other hand, anti-inflammatory agents may have relevant side effects, mainly in children. In addition, antibiotic overuse is frequently associated with the outgrowth of multi-resistant microbes. Actually, effective RURI preven-

Tab. I. Demographic and clinical characteristics of studied population (No. 80).

	WHOLE POPULATION (NO. 80)
Age at the beginning of treatment [yrs mean (SD)]	5.26 (2.52)
Preschool aged children (<6 yrs) [(No. (%)]	57 (71.25)
Male-to-female ratio (m/f)*	1.0 (40/40)
Days of treatment [median (LQ-UQ)]	89 (69-92)
[mean (SD)]	88.59 (32.54)
Follow-up duration [median (LQ-UQ)]	122.00 (94.00-156.50)
[mean (SD)]	132.00 (40.90)
Siblings [No. (%)]	44 (55.00)
Exposure to passive smoking [No. (%)]	15 (18.75)
Allergy [No. (%)]	6 (7.50)

Tab. II. Decrease in the number of URI, in the number of school days missed per month and in the number of working days missed per month after treatment with Rinogermina.

		>6 URI EPISODES/YR	<6 URI EPISODES/YR	P VALUE
Number of URI after treatment	Mean (SD)	5.8 (2.2)	2.0 (2.8)	<0.0001
	Median (LQ-UQ)	6.0 (4.5-7.0)	2.0 (1.0-4.0)	
Number of school days missed per month after treatment	Mean (SD)	2.2 (3.6)	1.4 (2.5)	<0.0001
	Median (LQ-UQ)	3.0 (1.5- 4.5)	1.0 (0-3.0)	
Number of working days missed per month after treatment	Mean (SD)	1.5 (1.9)	0.5 (1.6)	<0.0001
	Median (LQ-UQ)	2.0 (0-3.0)	0 (0-1.5)	
		0 (0-1.5)	0.5 (1.6)	

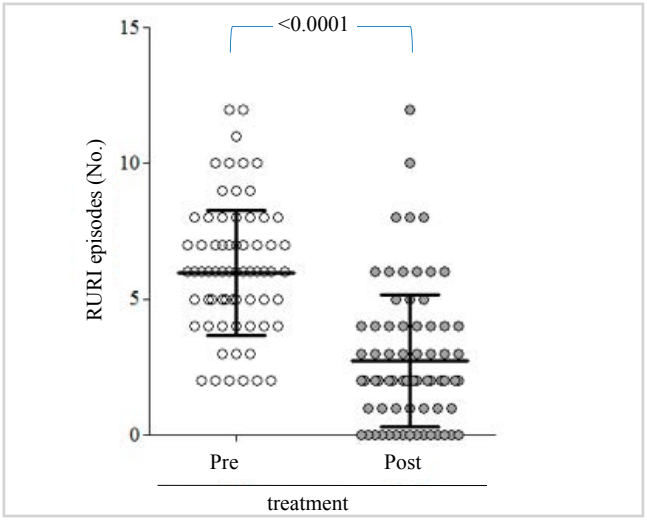

Fig. 1. Number of URI episodes in the past year before and after treatment with Rinogermina. Horizontal bars represent mean values with standard deviation. Each point represents an individual patient.

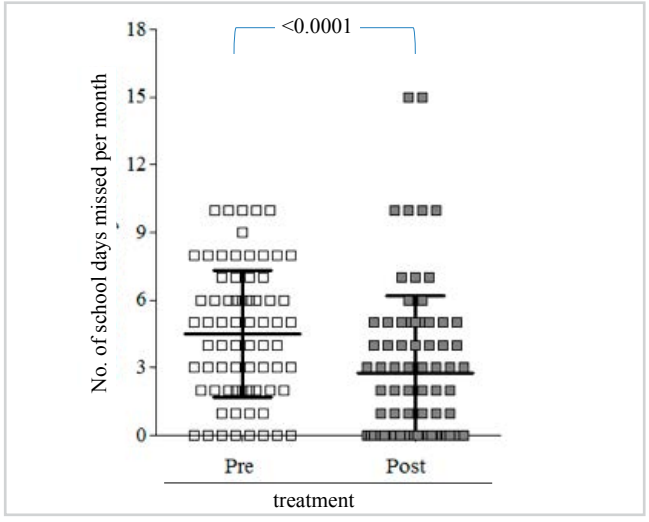

Fig. 2. Number of school days missed per month before and after treatment with Rinogermina. Horizontal bars represent mean values with standard deviation. Each point represents an individual patient.

tion might significantly affect risk of complications, medical costs, and social and family impact. On the other hand, many past attempts of prevention were tried, but they were usually expensive, long-lasting, and seldom fruitless or accompanied by adverse events. Therefore, preventing RURI using alternative ways might represent an interesting and stimulating issue. In this regard, an intriguing topic has been highlighted by the investigation of the upper airways microbiome (5). The physiological nasopharyngeal microbiome does physiologically inhibit the growth of local pathogens. So, it has been hypothesized that the administration of ‚good' bacteria could exert preventive effects on infections as it might wipe out pathogens. Some years ago, it was demonstrated that an α-haemolytic strain, obtained from healthy children (*Streptococcus salivarius 24SMB*), administered by nasal spray, had the capability to reduce the risk of new episodes of acute otitis media (AOM) in otitis-prone children (6). The results were promising, so a further study was successful in demonstrating that *Streptococcus salivarius 24SMB* associated with *Streptococcus oralis89a* administered as nasal spray in children suffering from recurrent AOM was effective in preventing recurrent otitis in a real-life setting (7). However, no clinical study evaluated the capacity of this combined Bacteriotherapy in children with RURI. Therefore, the present real-world study aimed to evaluate the po-

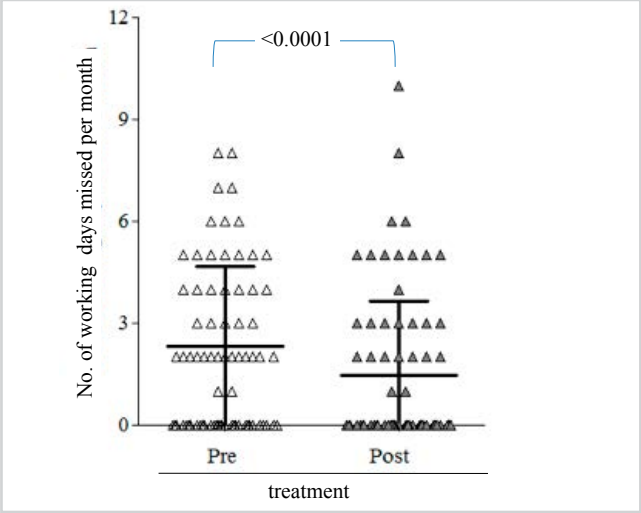

Fig. 3 Number of working days missed per month before and after treatment with Rinogermina. Horizontal bars represent mean values with standard deviation. Each point represents an individual patient.

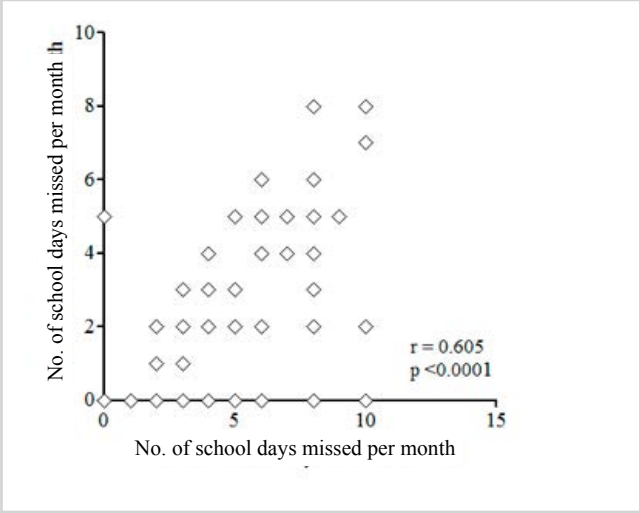

Fig. 5 Correlation between the number of school days missed per month and the number of working days missed per month.

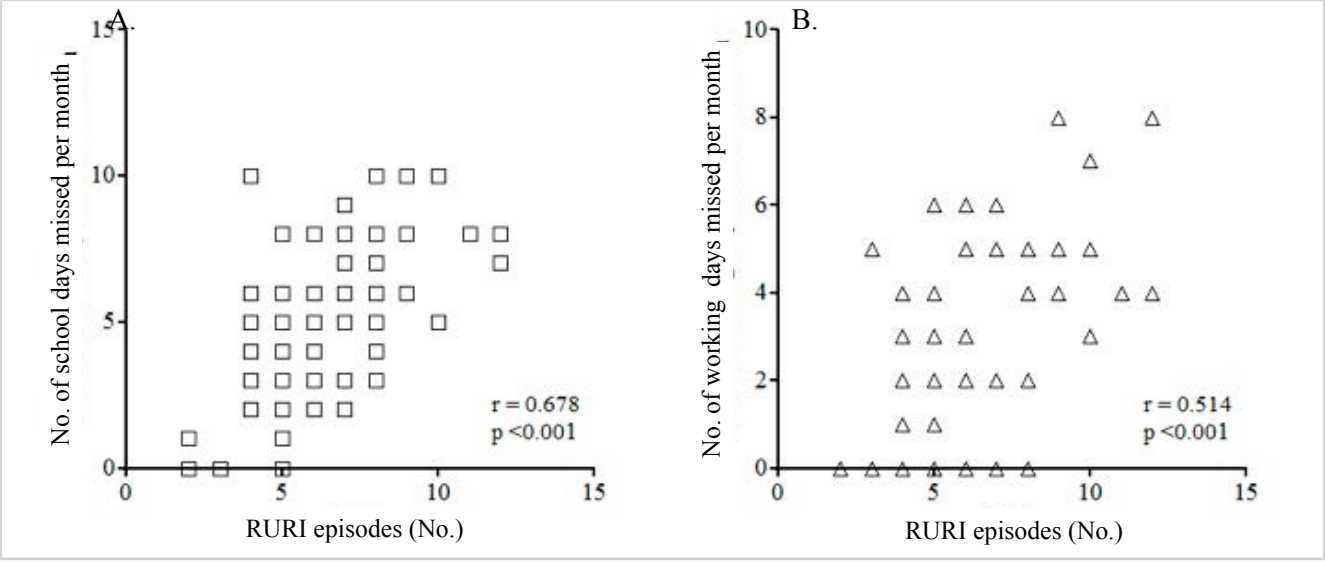

Fig. 4. Correlation between the number of URI episodes and the number of school days missed per month (panel A) or the number of working days missed per month (panel B).

ssible preventive effect of this Bacteriotherapy in a cohort of children suffering from RURI.

MATERIALS AND METHODS

Population and eligibility criteria

Globally, 80 children [40 males, mean age 5.26 (2.52) years] with RURI were enrolled in the study. Inclusion criteria were: i) age ranging between 3 and 14 years, ii) both genders, iii) documented history of RURI in the past year, iv) written informed consent by parents. Exclusion criteria were: i) severe allergic symptoms (able to interfere the assessment of treatments), ii) congenital or acquired immunodeficiency, iii) craniofacial abnormalities, iv) sleep apnoea, v) Down syndrome, vi) chronic disease (including metabolic disorders, cystic fibrosis, cancer, etc.), vii) clinically relevant passive smoking,

and viii) previous (last 3 months) or current administration of drugs able to interfere with the study (e.g., immunomodulant, homeopathic therapy, or systemic corticosteroids for at least 2 consecutive weeks).

Study design

The current study was designed as retrospective and observational. Children with URI were initially visited by primary care paediatricians who sent them to the otolaryngologists for thorough management. Children were treated with a commercially available class IIa medical device nasal spray containing *Streptococcus salivarius 24SMB* and *Streptococcus oralis 89a* (Rinogermina nasal spray, DMG, Rome, Italy). It was administered in 2 puffs per nostril twice/day for 7 days. The suspension consisted of a minimum of 109 colony forming unit per dose. This course was usually administered for 3 consecutive months. As Bacteriotherapy has a preventive activity, the course usually started in early autumn.

The evaluated parameters were: the number of URI, and the number of days of school or work (for parents) absence in the past. These variables were evaluated in the past year and at follow-up re-evaluation. In addition, siblings' presence, and passive smoking were evaluated.

Safety

Safety and tolerability were evaluated on the basis of the number and type of adverse events recorded according to the rules of good clinical practice.

Study procedures

The investigators diagnosed URI on the basis of the symptoms reported by the parents, as previously defined (8). RI diagnosis was made when at least 2 symptoms or fever (axillary temperature >38°C), in addition to one other symptom, were present for at least 48 hours. The symptoms taken into consideration for this diagnostic purpose were: mucopurulent rhinorrhoea, stuffy or dripping nose or both, sore-throat, cough (dry or productive), otalgia (earache), fever, and mucopurulent secretion. RURI diagnosis was performed based on history, such as patient's recall of symptoms.

The children were examined at study entry, and at follow-up re-evaluation (in the summer). The study started in September 2016 and ended in June 2017.

All assessed parameters were regularly recorded in a daily diary card.

Statistical analysis

Demographic and clinical characteristics are described using means with SDs for normally-distributed continuous data (i.e. age) or medians with lower and upper quartiles for not normally-distributed. Any statistically significant difference in mean values or in median values of each continuous variable (URI number, number of school days or working days missed per month between pre- and posttreatment with Rinogermina or between patients with more or less frequent URI episodes was evaluated with the Wilcoxon signed-rank test or with Mann–Whitney U test, respectively.

Correlations were evaluated with Spearman rank-order correlation coefficient. We labelled the strength of the association as follows: for absolute values of r, 0 to 0.19 is regarded as very weak, 0.2 to 0.39 as weak, 0.40 to 0.59 as moderate, 0.6 to 0.79 as strong, and 0.8 to 1 as a very strong correlation (9).

Statistical significance was set at $p < 0.05$, and the analyses were performed using GraphPad Prism software, GraphPad Software Inc, CA, USA

RESULTS

All treatments were well tolerated and no clinically relevant side effect was observed.

Analysis of the whole population

The present study analysed the reports of 80 outpatients. Demographic and clinical characteristics are reported in Table I.

Bacteriotherapy significantly halved the mean number of URI episodes being 5.98 (2.30) [median: 6 (4.25-7)] in the past year and 2.75 (2.43) [median: 2 (1-4)] after the treatment ($p<0.0001$, Figure 1). Bacteriotherapy also induced an over 35% reduction both in the number of school days and in the number of working days missed per month from 4.50 (2.81) [median: 5.0 (2.0-6.0)] to 2.80 (3.42) [median: 2.0 (0.0 – 5)] and from 2.33 (2.36) [median: 2.0 (0.0-4.75)] to 1.48 (2.16) [median: 0.0 (0.0 – 2.0)], respectively ($p<0.0001$, Figure 2 and 3).

The number of URI episodes strongly correlated with the number of school days missed per month ($r = 0.678$, $p<0.001$, Figure 4A). Similarly, a moderate correlation was detected between the number of URI episodes and the number of working days missed per month ($r = 0.514$, $p<0.001$, Figure 4B). As expected, the number of school days missed per month strongly correlated with the number of working days missed per month ($r = 0.601$, $p<0.0001$, Figure 5).

No correlations were found between changes in the number of URI episodes after Bacteriotherapy and the age at the beginning of treatment (r = 0.076, p = 0.50, not shown).

Moreover, sibling presence and allergy did not affect any result. Passive smoking was significantly associated only with school absence (p=0.02).

Comparison between patients with high or low number of URI episodes in the year preceding treatment

Patients were subdivided in two sub-groups on the basis of the number of URI episodes in the year preceding the study: > 6 or < 6.

The reduction in the number of URI episodes after treatment and in the number of school days or working days missed per month was higher for patients with a high number of URI episodes (i.e. >6 episodes) in the year preceding treatment than in those with a low number of URI episodes (i.e. <6 episodes) in the year preceding treatment (p<0.001, each comparison) as reported in Table II.

DISCUSSION

RURI represents a demanding challenge for both the ENT specialist and the paediatrician. The therapy is suggested by guidelines that limit antibiotic prescription to more demanding infections. However, in the clinical practice, antibiotics are frequently prescribed, ignoring guidelines precepts. In addition, prevention of RURI is even more debated. In this regard, a very recent placebo-controlled study investigated the potential preventive effect of a 12-month treatment with azithromycin (5mg/Kg/d) 3 d/wk in children with RRS (10,11). Actually, azithromycin prophylaxis reduced the number of ARS episodes, the medication score, and respiratory symptoms. However, this preventive proposal is very long-lasting and could easily induce the occurrence of resistance to macrolides. Macrolides resistance is an emerging problem in many European countries, including Italy (12). So, it seems better to consider alternative ways. Bacteriotherapy, such as the use of ‚good' bacteria, may be a promising preventive strategy. In fact, the rationale is based on the demonstration that some non-pathogenic strains may protect from bacterial infections. Indeed, the current study, conducted in a real-life setting, shows that *Streptococcus salivarius 24SMB* and *Streptococcus oralis 89a* nasal spray may be a reliable option in RURI prevention. Off note, no side effects were reported, so the compound was safe and well tolerated by all treated children. The main outcomes of the current study provided evidence that Bacteriotherapy significantly diminished the number of URI and consistently, school and work absences. Notably, Bacteriotherapy was more effective in children with frequent RURI, such as >6/year. This issue underlines the clinical relevance of the present findings.

However, this study has some limitations: i) to be an open study, ii) to be without a control-placebo group, iii) to be based only on clinical outcomes without cultural investigations, and iv) data concerning the past year were retrospectively collected by parents' queries. Thus, further studies should be conducted to correctly define the unmet needs.

In conclusion, the current real-life study demonstrated that *Streptococcus salivarius 24SMB* and *Streptococcus oralis 89a* nasal spray could be effective in preventing RURI in children.

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