The rhinotopic protocol for chronic refractory rhinosinusitis: how we do it

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Dear Editor,

In the hands of experienced surgeons, the majority of chronic rhinosinusitis patients who undergo endoscopic sinus surgery (ESS) experience significant improvement in symptoms in the first 12 months postoperatively; however, this does not seem to be long-lasting. Three-year outcome analysis indicates that the beneficial effect dissipates over time and that the symptoms continue to worsen in 5–25% of the patients, despite maximal medical therapy.[1–3] Possible contributing risk factors include atopy, immune deficiency, disrupted mucociliary transport, foreign bodies in the sinus cavities, non-compliant patient, error in diagnosis, primary mucosal disease (such as sarcoidosis, cystic fibrosis, ciliary dyskinesia), residual or obstructive sinus disease (residual uncinate process, retained agger nasi or Haller cells, missed maxillary sinus ostia, lateralised middle turbinate, scarred frontal sinus, incomplete ethmoidectomy, etc.), resistant organisms, mucosal biofilm and/or underlying osteitis.[4,5] The management of these patients has proven to be challenging, and has traditionally included control of the predisposing factor(s), oral antibiotics, nasal and/or systemic corticosteroids and/or saline pressure hydrotherapy.[6,7] Nasal endoscopy of patients who have persistent symptoms often shows patent sinus antrostomies but inflamed or polypoid mucosa, with and without crusts and mucopurulence (Figs 1 and 2). For those patients, who as labelled as having refractory chronic rhinosinusitis, topical therapy offers one effective alternative.

Methods

We describe our experience with the rhinotopic protocol, which consists of 6 weeks of saline pressure hydrotherapy, regular sinus debridement, along with topically aerosolised mometasone and an antibiotic chosen based on naso-endoscopic guided swab culture from the ethmoid/maxillary cavities. The aerosols are self-administered twice daily using a vibrating mesh nebuliser (VMN; Aerogen LTD, Galway, Ireland), which creates an aerosol mist by rapidly vibrating a mesh with hundreds of 4 to 8 μm holes, and allows a fast and uniform delivery of small aerosolised medication particles to the sinuses (Fig. 3). The patients are instructed to practice hydrotherapy, consisting of twice daily normal saline rinses using the NeilMed® Sinus Rinse (Santa Rosa, CA, USA), before starting the nebulised treatment. No oral antibiotics are given throughout the duration of nebulised therapy. Weekly follow up is carried out in the clinic, for a period of 6 weeks, at which time a thorough endoscopic debridement of any sinus crusts and/or mucous is performed, followed by direct aerosolisation of the same antibiotic and corticosteroid directly in the sinus cavities, using a mucosal atomising device.

One month after completion of treatment, a repeat naso-endoscopic swab culture is obtained from the ethmoid/maxillary sinus cavities to check on any persistent sinus bacteriology. All patients are followed 1 month, 2 months and 6 months (or longer) after the completion of therapy, and the clinical response to treatment as monitored using the Lund-Kennedy (LK) symptoms score and the LK endoscopic appearance score.[8]

Ethical considerations

The protocol was approved by the Liberty Institutional Review Board (DeLand, Florida), and all patients were consented prior to the beginning of the management plan.

Results

We have used the above rhinotopic protocol to treat 20 patients with refractory chronic rhinosinusitis who have failed ESS and standard medical therapy. We consider

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Fig. 1. The vibrating mesh nebuliser (VMN) provides a fine aerosol mist and a uniform delivery of small aerosolised medication particles to the sinuses.

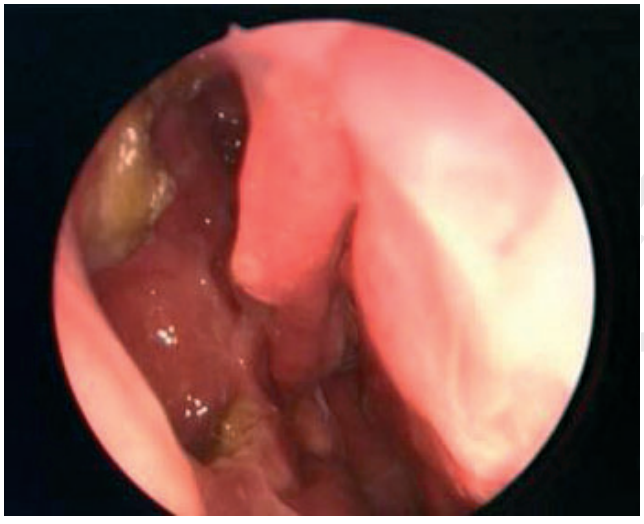

Fig. 2. Patent maxillary antrostomy with crusting and infected secretions in the maxillary and ethmoid sinuses.

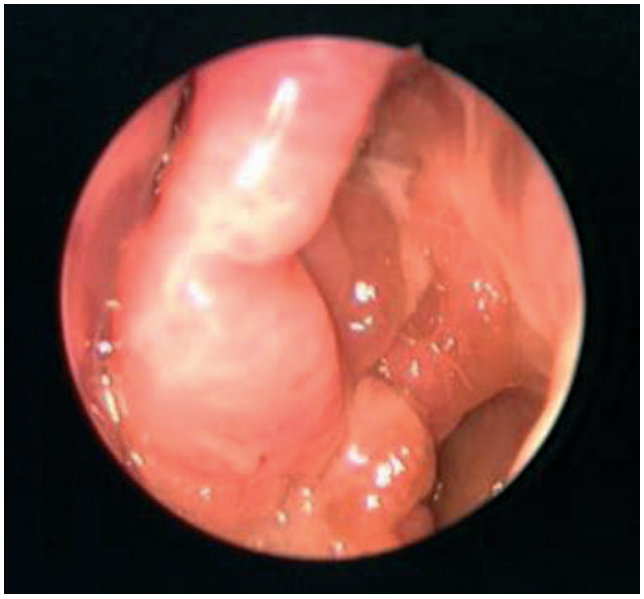

Fig. 3. Patent maxillary antrostomy with polypoid changes of the ethmoid sinuses.

medical therapy a failure if the patient suffers from persistent sinusitis symptoms despite three or more repeated courses of different oral antibiotics, nasal corticosteroids sprays and nasal saline rinses lasting at least 3 weeks each, within a 6 month-period, along with oral corticosteroids when indicated (such as case of significant polyposis or Samter's triad).

There were 12 women and 8 men, ranging in age from 13 to 76 years (mean 48 years). Allergy workup (allergen-specific IgE antibody) upon enrolment was positive in 4/20 patients, and all four patients received anti-allergy treatment. Two patients had Samter's disease (polyposis, asthma and aspirin intolerance) and both received leukotriene inhibitors. Swab aerobic and anaerobic cultures taken from the ethmoid/maxillary sinus cavities under endoscopic guidance. The most commonly cultured aerobic bacteria were *Staphylococcus aureus* ($n = 8$, 36%) and *Pseudomonas aeruginosa* ($n = 6$, 27%). No anaerobes were recovered. The nebulised antibiotics included tobramycin (in 72% of cases), vancomycin and levofloxacin. The mean pre- and post-treatment LK symptom and LK endoscopic appearance scores showed a statistically significant improvement (Student's T-test P value < 0.001) (Fig. 4). All six LK symptoms were improved, including nasal congestion and obstruction, headache, facial pain, alteration in the sense of smell, nasal discharge and sneezing. Repeat swab culture performed 1 month after completion of treatment revealed no growth in 65% of the cases, normal respiratory flora in 25% and persistent pathogenic organisms in 10%.

Discussion

The clinical effectiveness of nebulised antibiotics to the sinuses in treating refractory post-ESS sinusitis has been demonstrated in numerous studies.[7,9] The fundamental principles that determine efficiency of deposition of aerosolised particles in the paranasal sinuses are: the size of the sinus ostium, the pressure/rate of flow of aerosol and the particle size, with small particle nebulisation reported as more successful.[7] We have elected to aerosolise both antibiotics and corticosteroids, as we believe that there is an intricate association between infection

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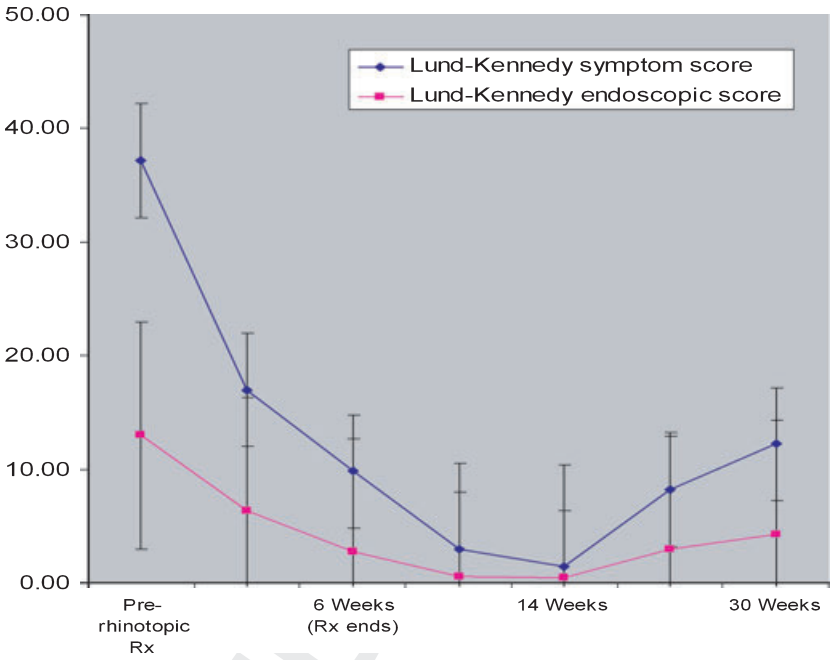

Fig. 4. Absolute change is Lund-Kennedy symptom score and endoscopic appearance score after rhinotopic therapy.

and inflammation in chronic refractory rhinosinusitis, and we found that rhinotopic therapy provides sustained symptom relief in the majority of our patients. Other treatment alternatives have been described in the literature, including intravenous antibiotics, on the premise that osteitis might be the underlying culprit; or mucolytics, bacterial lyates, baby shampoo and other methods that have the potential to disrupt bacterial biofilms formation. Biofilms are a complex organised community of germs that adhere to the mucosal surface, inducing inflammatory modulation at the local level and playing a significant role in the aetiology of refractory chronic sinusitis. Their extracellular polymeric encasement provides them with means to evade mucociliary clearance and resist oral antibiotics. We suspect that it is possible that the rhinotopic therapy protocol disrupts biofilms formation, through a combination of pressure saline hydrotherapy and by reaching supra-MIC antibiotic levels inside the biofilm, long enough until bacteria are eradicated (something that is difficult to achieve with oral antibiotics alone). Current investigation is being carried out at our institution to quantify the impact of this therapy on biofilms counts. What is not yet clear either is whether long-term application of antibiotics aerosols can cause resistance to antibiotics and that will also require further investigation.

Rhinotopic therapy is a promising treatment modality that has the potential to restore sinus health and mucosal homeostasis in the majority of patients with refractory post-ESS sinusitis. Further studies at multiple institutions with larger samples and longer follow up are needed.

Keypoints

- Medical treatment of patients who failed to improve after sinus surgery is challenging and requires stepwise approach management.
- A multi-modality approach to treat refractory chronic rhinosinusitis is described. The rhinotopic protocol consists of topically delivered antibiotics and corticosteroids, nasal debridement and nasal pressure hydrotherapy.
- This protocol was successfully used to treat 20 patients with refractory chronic rhinosinusitis. The Lund-Kennedy symptom and endoscopic scores showed a sustained and statistically significant improvement with treatment. Post-therapy swab culture cleared the pathogenic organisms in 90% of the cases.
- When treating refractory chronic rhinosinusitis, the rhinotopic protocol offers a safe alternative to prolonged intravenous antibiotics, and it has potential to change the threshold for revision sinus surgery in those patients who show no evidence of residual or obstructive disease.

Acknowledgement

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Conflict of interest

None to declare.

References

1 Bhattacharyya N. (2004) Clinical outcomes after revision endoscopic sinus surgery. *Arch. Otolaryngol. Head Neck Surg.* **130,** 975–978

2 Young J., Frenkiel S., Tewfik M. *et al.* (2007) Long-term outcome analysis of endoscopic sinus surgery for chronic Rhinosinusitis. *Am. J. Rhinol.* **21,** 743–747

3 Poetker D.M. & Smith T.L. (2007) Adult chronic rhinosinusitis: surgical outcomes and the role of endoscopic sinus surgery. *Curr. Opin. Otolaryngol. Head Neck Surg.* **15,** 6–9

4 Lund V.J. & Scadding G.K. (1991) Immunologic aspects of chronic sinusitis. *J. Otolaryngol.* **20,** 379–381

5 Ferguson B.J., Otto B.A. & Pant H. (2009) When surgery, antibiotics, and steroids fail to resolve chronic rhinosinusitis. *Immunol. Allergy Clin. North Am.* **29,** 719–732

6 Palmer J.N. & Kennedy D.W. (2003) Medical management in functional endoscopic sinus surgery failures. *Curr. Opin. Otolaryngol. Head Neck Surg.* **11,** 6–12

7 Desrosiers M.Y. & Salas-Prato M. (2001) Treatment of chronic rhinosinusitis refractory to other treatments with topical antibiotic therapy delivered by means of a large-particle nebulizer: results of a controlled trial. *Otolaryngol. Head Neck Surg.* **125,** 265–269

8 Lund V.J. & Kennedy D.W. (1997) Staging for rhinosinusitis. *Otolaryngol. Head Neck Surg.* **117,** S35–S40

9 Vauhgan W.C. & Calvalho G. (2002) Use of nebulized antibiotics for acute infections in chronic sinusitis. *Otolaryngol. Head Neck Surg.* **127,** 558–568

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