

Efficacy of Large-Particle Nasal Nebulizer-Delivered Medication Therapy to Prevent Revision Surgery for the Treatment of Nasal Polyps – a Pilot Study

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Abstract:

Objective: Surgical failure rates for the treatment of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) are well documented in the literature, with 10-12% of patients needing revision surgery within 3 years.¹ Corticosteroids and antibiotics have been used both pre- and post-surgery in an attempt to reduce the development of nasal polyps, however, major limitations exist in delivering them effectively.^{1,2} A patented large-particle nasal nebulizer device (LPNN)(NasoNeb-Medinvent) has been shown to consistently deliver medication to more nasal sub-sites than other topical delivery methods, however it is unclear whether LPNN therapy would prevent CRSwNP revision surgery.³⁻⁵ The objective of this study was to determine whether LPNN therapy is effective in preventing revision surgery in post-surgical patients with CRSwNP.

Methods: A convenience sample of 130 charts from a local otolaryngologist's office was reviewed for inclusion criteria for both the treatment (patients prescribed LPNN therapy) and the control group (patients not prescribed LPNN therapy). The 64 charts meeting inclusion criteria—32 in the treatment group and 32 in the control group—were evaluated for need for revision surgery within 4 years. Inclusion criteria comprised patients aged 18-65, diagnosed with CRSwNP, who had undergone surgery in the previous 4 years for the removal of nasal polyps. Patients were excluded if they had active malignant disease or other immunocompromising conditions.

Results: The treatment group showed 1/32 (3.1%) as needing revision surgery within 4 years whereas the control group had 5/32 (15.6%) needing revision surgery (p=0.022). The absolute risk reduction was 12.5% and number needed to treat was 8. The most common LPNN prescription treatments were mometasone 0.6mg BID (n=13), and mometasone 0.6mg/mupirocin 5mg BID (n=8). The average number of yearly refills for the treatment group was 3.8.

Conclusion: According to our pilot data, using LPNN therapy post-surgery to prevent revision surgery showed statistically significant efficacy.

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Introduction:

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) is a condition affecting 2-4% of the population in which inflammation in the nasal passages and sinuses causes congestion, blockage, nasal discharge, facial pain/pressure and/or a reduction or loss of smell.^{1,6} It can significantly reduce quality of life and represents a significant financial burden on society.⁶⁻⁸ In 1996, total direct healthcare costs related to diagnosis of sinusitis were estimated to be in excess of \$3 billion (\$4.59 billion in 2016 dollars).⁷ Patients with CRSwNP frequently require functional endoscopic sinus surgery (FESS) to remove polyps, and, according to current literature, revision surgery is indicated in approximately 10-12% of patients within 3 years, a number which rises to 20% over the course of a lifetime.^{1,6} Antibiotics and corticosteroids applied topically or orally have been used to prevent recurrence of polyps after surgery.^{1,2} However, topical delivery methods often leave areas of the nasal and sinus passages untreated, and courses of oral antibiotics or corticosteroids can have undesired side effects including drug interactions, diarrhea, bone density reduction, fluid retention, hyperglycemia and others.^{1,5}

A patented large-particle nasal nebulizer device (LPNN)(NasoNeb-Medinvent), available since 2009, has been demonstrated to consistently deliver medication to more nasal sub-sites than other topical delivery methods such as spray bottles, metered dose inhalers, powered irrigators, atomizers, or modified pulmonary nebulizers.^{3,5,9} Standard respiratory nebulizers create very small medication particles to bypass the nasal and sinus passages and deliver treatment to the lungs, whereas LPNN devices have been designed to produce larger medication particulates that are intended to be filtered out of the air stream into the nasal and sinus passages where they can act topically.⁵ Combining this more robust delivery method with medications that reduce inflammation could be a promising medical management option to prevent revision surgery. However, LPNN has not been studied in the context of preventing revision surgery in CRSwNP patients.

Objective:

The objective of this pilot study was to determine if treatment with an LPNN device is an effective treatment option post-FESS to prevent revision surgery for the treatment of CRSwNP.

Methods:

A literature-based, retrospective analysis of the epidemiology, incidence, prevalence, outcomes, and treatment costs of patients with CRSwNP was performed to create a model projecting expected outcomes of patients divided into two groups: post-FESS patients prescribed LPNN therapy (treatment group), and post-FESS patients who were not prescribed LPNN therapy (control group). A retrospective, convenience-sampled chart review was also conducted with the cooperation of a local otolaryngology (ENT) specialist's office on 130 charts. Inclusion criteria for the chart review were patients aged 18-65, diagnosed with CRSwNP, who had at least a 4 year history since their initial FESS for the removal of nasal polyps. While the most recent meta-analysis of CRSwNP cases reported revision surgery rates at 3 years, a 4 year time frame was utilized in this study to account for treatment delays due to lack of physician or appointment availability for either evaluation or surgery. Patients who had active malignant disease or other immunocompromising conditions were excluded from the chart review. Patients who met

inclusion criteria were then separated into two cohorts: those who were prescribed LPNN therapy and those who weren't. A total of 64 charts were included with 32 patients in the treatment group and 32 patients in the control group. Within the limits of this pilot study, the patients were not matched across groups.

The primary outcome was the difference in revision surgery rates between the treatment group and the control group. This relationship was examined using a one-tailed, 2 sample t-test with $p \leq 0.05$. Data analysis was performed using SPSS v23.

Secondary outcomes included absolute risk reduction, number needed to treat, most common steroid \pm antibiotic therapy in the treatment group, average number of refills for steroid medication in the treatment group, average number of office visits for both groups, and average age of patients in both groups.

Results:

130 charts were reviewed; of these, 32 met inclusion criteria for the treatment group and 32 met inclusion criteria for the control group (Table 1). The average age of patients was 48.5 years for the treatment group and 42.0 for the control group, which was shown to be statistically significant ($p=0.0058$). The treatment group showed 1/32 (3.1%) needing revision surgery within 4 years, whereas the control group had 5/32 (15.6%) needing revision surgery within the same time frame. A one-tailed t-test showed these results to be statistically significant ($p = 0.022$). The absolute risk reduction (ARR) for the treatment group was 12.5%, and the number needed to treat (NNT) was 8. Of the 32 patients who received LPNN therapy, the most common prescription treatment was mometasone 0.6mg BID ($n=13$), and mometasone 0.6mg/mupirocin 5mg BID ($n=8$). The average number of yearly refills for the treatment group was 3.8. The average number of office visits per year was 6.4 for the treatment group and 6.8 for the control group, which was shown to be non-significant ($p=0.22$).

Discussion

Our pilot findings suggest that LPNN-delivered steroid therapy is effective at reducing revision surgery rates within the first 4 years. A recent meta-analysis found that the average rate of revision surgery for CRSwNP patients was 11.8% within 3 years.¹ The control group in this pilot study displayed a 15.6% revision rate at 4 years (5/32), whereas the treatment group displayed a significantly lower rate of 3.1% (1/32) at 4 years.

While efficacy is an important endpoint, cost-effectiveness of LPNN therapy will be of particular interest to payors within the healthcare industry as they consider covering this method of treatment.

Preliminary investigation into costs of surgery and LPNN treatment show current costs of surgery to be \$24,248-\$26,098, whereas 4 years of LPNN-delivered steroid therapy as used by patients in this study would cost \$2,325-\$2,888.^{10,11} Based on an NNT of 8, treating 8 people with 4 years of LPNN-delivered steroid therapy would cost \$18,604-\$23,103 and would theoretically prevent 1 revision surgery (Figure 1). The ratio of LPNN cost to revision surgery avoided would thus be 0.767-0.885. This does not take into account additional costs of surgery such as lost productivity, complications, and post-surgical pain

control. This finding suggests that LPNN therapy may indeed be cost-effective, and that further prospective research is warranted to determine the extent of LPNN cost-effectiveness.

Number of office visits per year will also be of interest to payors. Our pilot data indicates that the treatment group required 6.4 office visits per year over 4 years compared to 6.8 for the control group, a difference which was shown to be non-significant ($p=0.22$). This indicates that LPNN-treated patients do not require more follow-up visits for treatment of CRSwNP vs non-LPNN-treated patients.

While the most common LPNN-delivered medication therapies were mometasone 0.6mg with or without mupirocin 5mg delivered BID, there was a wide variety of prescribed medications including multiple commercially available injection solutions mixed with normal saline, or compounded capsules containing multiple ingredients which were intended to be opened and the powder mixed with normal saline. According to the prescription records at the ENT office, patients also had control over how concentrated the medications were by varying the amount of normal saline they mix in with the active ingredients for delivery.

Limitations

Performing the chart review at a single ENT office limited the number of charts available for review that met inclusion criteria, which limited the sample size for this study. It also limited the availability of data on prior surgeries or treatment that may have happened at another medical office.

Researchers used convenience sampling in reviewing charts chronologically to find patients with sufficient medical history for the chart review. Patients were also not able to be matched across groups. The paper-based nature of the charts at the ENT office made it somewhat difficult to gather pertinent data, and data gathered from patient-completed intake or medical history forms may have been incomplete or affected by recall bias.

Limitations also existed when determining the number of patients in the treatment group who were compliant with LPNN therapy. Currently, few insurance companies cover the LPNN device itself, and its MSRP of \$279.95 may have been a deterrent for patients seeking to utilize LPNN therapy as prescribed. There is also some variability in insurance coverage for medications used in LPNN therapy, and many compounded medications are not covered at all.¹²⁻¹⁴ These costs may have significant effects on compliance rates for patients receiving LPNN therapy.

This pilot study is intended to lay the groundwork and explore limitations that will need to be overcome in future prospective research on this subject.

Conclusion

Our pilot data indicates that LPNN-delivered corticosteroid therapy may be effective in reducing rates of revision surgery in patients with CRSwNP within a 4 year window. The calculated NNT of 8 along with estimates of costs of surgery and LPNN therapy raise interesting questions as to the cost-effectiveness of LPNN therapy for post-FESS patients. The data and conclusions in this study are intended to be

probabilistic estimations of efficacy to inform decision makers until such a time as a full-scale primary data study can be performed.

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