The role of bacteriotherapy in the prevention of adenoidectomy

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Abstract. - OBJECTIVE: Adenoidectomy is a surgical procedure with potential adverse events. Effective nonsurgical therapy could reduce patient risk and harm. The aim of this study was to evaluate the role of bacteriotherapy to reduce the necessity of adenoid surgery.

PATIENTS AND METHODS: This experimental study was conducted as an open study in 44 children (30 males and 14 females, mean age 4.9 years) who were candidates for adenoidectomy and tympanocentesis as treatment for adenoidal hypertrophy and otitis media with effusion. Twenty-two children were treated with *Streptococcus salivarius* 24SMB and *Streptococcus oralis* 89a nasal spray, administered as 2 puffs per nostril twice a day for a week for 3 months (study group). The other half of the children was treated with hypertonic saline nasal lavage on the same schedule (control group). Tympanometry and adenoid size assessment were evaluated throughout the intervention period.

RESULTS: In the study group, 6/22 children required surgery, compared to 20/22 children in the study group (p<0.0001). The clinical change in the treated children was a significant reduction of adenoid size (p<0.0001) and improvement of middle ear effusion measured with tympanometry (p<0.0001).

CONCLUSIONS: Bacteriotherapy with *Streptococcus salivarius* 24SMB and *Streptococcus oralis* 89a nasal spray could significantly reduce the need for adenoid surgery.

Key Words

Adenoidectomy, Bacteriotherapy, Streptococcus salivarius 24SMB, Streptococcus oralis 89a, Nasal spray, Children.

Introduction

Adenoidectomy with or without tonsillectomy is a long practiced and one of the most frequently performed surgical procedures in children worldwide. At present, this surgical procedure has

well defined indications: an obstructive state in the upper airways or severe recurrent infections. Restrictions on this treatment option derive from the possibility of serious adverse events, including death. Another concern with adenoidectomy is frequency of the need for revision surgery¹⁻³. The combination of potentially serious risk factors and concern about the lasting effectiveness of surgery lend the adenoidectomy decision a profound clinical and social importance. The possibility of avoiding adenoidectomy thus deserves thoughtful consideration. Since recurrent severe infections - including recurrent otitis media with effusion (OME) - and clinically relevant adenoid hypertrophy are the present indications for adenoidectomy^{4,5}, effective action against these causal factors could reduce the requirement for surgery. Recurrent infections represent a trigger for immune response in lymphoid tissue, including adenoids. Repeated respiratory infections and repeated local immune response enlarge the adenoids and are at the base of adenoid hypertrophy.

A new approach to prevent and potentially treat respiratory infections, including otitis, is manipulation of the respiratory microbiome⁶. The upper airway microbiome has been shown to inhibit the growth of pathogens resident in the rhinopharynx. Bacteriotherapy, the administration of "good" bacteria, could prevent the onset of respiratory infections (due to "bad" bacteria) and consequently avoid antibiotic resistance⁷⁻⁹. It has been reported that a mixture of Streptococcus salivarius 24SMB and Streptococcus oralis 89a (intranasally administered as spray, Rinogermina, DMG, Rome, Italy) is able to colonize the respiratory tract 10 and to be an effective preventive agent in children suffering from recurrent OME^{11,12}. Drawing on this theoretical framework and prior research, the current experiment tested

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the hypothesis that the apparent need for surgery could be reduced in a group of children waiting for adenoidectomy and tympanocentesis, by administering bacteriotherapy as treatment for already established disease-state indications for surgery.

Patients and Methods

Patients

The present study was open and included 44 children (30 males and 14 females) aged 3 to 6 years (mean age 4.9) suffering from adenoid hypertrophy and OME who were candidates for adenoidectomy and tympanocentesis in the period from October 2016 to February 2017. All of the children had grade 4 adenoid hypertrophy, assessed and recorded with fibre-optic endoscopy, and type B tympanometry. The study was specifically approved by the Ethical Committee of our hospital. The children were randomly (1:1) treated with bacteriotherapy (study group) or with hypertonic nasal lavage (control group). Bacteriotherapy (Streptococcus salivarius 24SMB and Streptococcus oralis 89a) or nasal lavage was prescribed as 2 puffs per nostril twice a day for 7 days in each of 3 consecutive months. The suspension consisted of a minimum of 10⁹ colony-forming units per dose. Fibre-optic endoscopy (Karl Storz) and tympanometry (Madsen Zodiac 901) were performed before and after the course of treatment. Adenoid size was measured according to validated criteria ⁴. The statistical analysis was made by chi-square test or Fisher's exact test, in case of expected frequencies lower than 5. Statistical significance was set at p < 0.05, and the analyses were performed using GraphPad Prism software (GraphPad Software Inc., La Jolla, CA, USA).

Results

After treatment, 6/22 (27.3%) children in the study group still required surgery, compared to 20/22 (90.9%) children in the control group (p <0.0001) (Figure 1). Adenoid hypertrophy was grade 4 in all children at baseline. After treatment, adenoid hypertrophy was grade 4 in 6 children (27.3%), grade 3 in 11 children (50%) and grade 2 in 5 children (22.7%) in the study group while in the control group adenoid hypertrophy was grade 4 in 20 children (90.1%) and grade 3 in 2 children (9.9%) (p < 0.0001) (Figure 2). All children had a type B tympanometry at baseline; after treatment 36 (81.8%) ears showed type C and no subjects had bilateral type B in the study group, whereas only 3 children (7.3%) had a type C and one (0.9%) had a type AS tympanogram in the control group (p < 0.0001) (Figure 3). No adverse effects were reported, and all children tolerated bacteriotherapy.

Discussion

Avoiding adenoidectomy is a particularly intriguing goal for the otolaryngologist and the pediatrician. Respiratory infections, including OME, may more frequently occur in the presence of some microbiota patterns ¹²⁻¹⁴. Bacteriotherapy

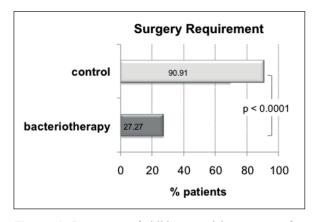


Figure 1. Percentage of children requiring surgery after treatment period in the study group (Bacteriotherapy, dark grey) and in the control group (light grey).

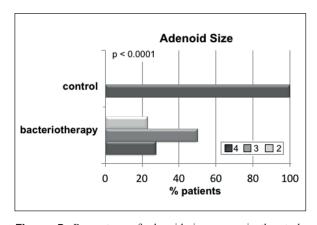


Figure 2. Percentage of adenoid size scores in the study group (Bacteriotherapy, dark grey) and in the control group (light grey).

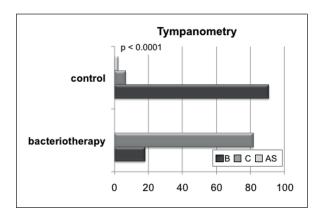


Figure 3. Percentage of tympanogram scores in the study group (Bacteriotherapy, dark grey) and in the control group (light grey).

- the administration of "good" bacteria - presents an interesting alternative to current treatments 9,15. This study showed that Streptococcus salivarius 24SMB and Streptococcus oralis 89a nasal spray could reduce the need for adenoidectomy, as the adenoid size clinically diminished in a significant number of treated children. In addition, treated children experienced improved tympanometry. This preliminary study suggests that Streptococcus salivarius 24SMB and Streptococcus oralis 89a nasal spray might be a reliable option for preventing unneeded surgery. No adverse effects were reported, and all children tolerated bacteriotherapy. The present study has some limitations: i) it had a limited number of participants. ii) it did not have a true placebo group, and iii) no cultural investigations were performed. Further research with larger study groups is necessary to confirm these preliminary results.

Conclusions

This preliminary study suggests that *Streptococcus salivarius* 24SMB and *Streptococcus oralis* 89a nasal spray might be a reliable option to prevent adenoid surgery in children suffering from adenoid hypertrophy and OME.

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Conflict of Interests

The authors declare that they have no conflict of interest.

References

- Sunnergren O, Odhagen E, Stalfors J. Incidence of second surgery following pediatric adenotonsillar surgery: a population-based cohort study. Eur Arch Otorhinolaryngol 2017; 274: 2945-2951.
- LEE CH, CHANG WH, Ko JY, YEH TH, HSU WC, KANG KT. Revision adenoidectomy in children: a population-based cohort study in Taiwan. Eur Arch Otorhinolaryngol 2017; 274: 3627-3635.
- Lou Z. Adenoid hypertrophy in children and allergic rhinitis. Eur Arch Otorhinolaryngol 2018; 275: 831-832.
- 4) VAN DEN AARDWEG MT, SCHILDER AG, HERKERT E, BOONACKER CW, ROVERS MM. Adenoidectomy for recurrent or chronic nasal symptoms in children. Cochrane Database Syst Rev 2010: CD008282.
- MIKALS SJ, BRIGGER MT. Adenoidectomy as an adjuvant to primary tympanostomy tube placement: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg 2014; 140: 95-101.
- MAROM T, MARCHISIO P, TAMIR SO, TORRETTA S, GAVRIEL H, ESPOSITO S. Complementary and alternative medicine treatment options for otitis media: a systematic review. Medicine (Baltimore) 2016; 95: e2695.
- GAO Z, KANG Y, YU J, REN L. Human pharyngeal microbiome may play a protective role in respiratory tract infections. Genomics Proteomics Bioinformatics 2014; 12: 144-150.
- MARCHISIO P, NAZZARI É, TORRETTA S, ESPOSITO S, PRINCIPI N. Medical prevention of recurrent acute otitis media: an updated overview. Expert Rev Anti Infect Ther 2014; 12: 611-620.
- CAMPANELLA V, SYED J, SANTACROCE L, SAINI R, BALLINI A, INCHINGOLO F. Oral probiotics influence oral and respiratory tract infections in pediatric population: a randomized double-blinded placebo-controlled pilot study. Eur Rev Med Pharmacol Sci 2018; 22: 8034-8041.
- 10) SANTAGATI M, SCILLATO M, MUSCARIDOLA N, METOLDO V, LA MANTIA I, STEFANI S. Colonization, safety, and tolerability study of the Streptococcus salivarius 24SMBc nasal spray for its application in upper respiratory tract infections. Eur J Clin Microbiol Infect Dis 2015; 34: 2075-2080.
- 11) MARCHISIO P, SANTAGATI M, SCILLATO M, BAGGI E, FATTIZZO M, ROSAZZA C, STEFANI S, ESPOSITO S, PRINCIPI N. Streptococcus salivarius 24SMB administered by nasal spray for the prevention of acute otitis media in otitis-prone children. Eur J Clin Microbiol Infect Dis 2015; 34: 2377-2383.
- 12) LA MANTIA I, VARRICCHIO A, CIPRANDI G. Bacteriotherapy with streptococcus salivarius 24SMB and streptococcus oralis 89a nasal spray for preventing recurrent acute otitis media in children: a real-life clinical experience. Int J Gen Med 2017; 10: 171-175.

- 13) Bernstein JM, Faden HF, Dryja DM, Wactawski-Wende J. Micro-ecology of the nasopharyngeal bacterial flora in otitis-prone and non-otitis-prone children. Acta Otolaryngol 1993; 113: 88-92.
- 14) COHEN R, MARTIN E, DE LA ROCQUE F, THOLLOT F, PECQUET S, WERNER A, BOUCHERAT M, VARON E, BINGEN E, LEVY C. Probiotics and prebiotics in preventing episodes of acute otitis media in high-risk children: a randomized, double-blind, placebo-controlled study. Pediatr Infect Dis J 2013; 32: 810-814.
- 15) MARCHISIO P, CLAUT L, ROGNONI A, ESPOSITO S, PASSALI D, BELLUSSI L, DRAGO L, POZZI G, MANNELLI S, SCHITO G, PRINCIPI N. Differences in nasopharyngeal bacterial flora in children with nonsevere recurrent acute otitis media and chronic otitis media with effusion: implications for management. Pediatr Infect Dis J 2003; 22: 262-268.