ORIGINAL ARTICLE

A Prospective Study of the Effect of Gastroesophageal Reflux Disease Treatment on Children With Otitis Media

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Objectives: To demonstrate improvements in validated quality-of-life measures for otitis media and gastroesophageal reflux disease (GERD) and an objective score for pediatric reflux obtained by fiberoptic laryngoscopy after treatment with antireflux precautions and therapy in children diagnosed as having either recurrent acute otitis media or otitis media with effusion and GERD.

Design: Prospective, before-and-after intervention study.

Setting: Hospital-based pediatric otolaryngology practice.

Participants: Population-based sample of 47 patients (mean age, 19.5 months).

Intervention: Standard antireflux therapy for 2 consecutive 12-week periods.

Main Outcome Measures: Otitis Media 6-Item quality-of-life survey, Infant GERD Questionnaire–Revised, GERD Symptom Questionnaire for Young Children, Pediatric Reflux Finding Score, and speech awareness threshold.

Results: Follow-up data were available for 37 patients. Mean (SD) change scores for Otitis Media 6-Item quality-of-life survey were 1.6 (1.1) at visit 2 and 1.5 (1.1) at visit 3 ($P<.001$ and $P=.004$, respectively). Change scores were significantly improved for Infant GERD Questionnaire–Revised and GERD Symptom Questionnaire for Young Children at visit 2 and for Infant GERD Questionnaire–Revised at visit 3. Mean (SD) change scores for the Pediatric Reflux Finding Score were 6.4 (4.9) at visit 2 and 8.0 (7.2) at visit 3 ($P<.001$ and $P=.03$, respectively). Hearing loss was significantly improved following therapy, as were laryngeal findings of reflux on fiberoptic laryngoscopy. Otitis media was considered by the examining physician to be clinically improved in 28 of 37 children (76%; 95% confidence interval, 60%-87%) at visit 2 and in 6 of 10 children (60%; 95% confidence interval, 31%-83%) at visit 3. Nine children (19.1%) required myringotomy tube placement.

Conclusions: Children with otitis media with effusion or recurrent acute otitis media and GERD have improved quality of life following treatment with antireflux therapy. Control of gastroesophageal reflux may play a role in the management of otitis media and avoidance of tympanostomy.

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OTITIS MEDIA WITH EFFUSION (OME) is a multifactorial condition and the most common cause of hearing impairment in children.[1] Recurrent acute otitis media (RAOM) is another highly prevalent childhood condition; it accounts for frequent antibiotic use and missed productivity and may have serious infectious sequelae. Otitis media with effusion and RAOM may manifest independently or may coexist in a patient.

Gastroesophageal reflux disease (GERD) may account for a wide variety of symptoms in the pediatric population.[2] Reflux of gastric contents beyond the esophagus into the oropharynx, larynx, tracheobronchial tree, and nasopharynx leads to extraesophageal manifestations of GERD. These may include hoarseness, laryngomalacia, vocal cord granulomas, chronic cough or congestion, recurrent bronchitis or pneumonia, reactive airway disease, chronic sore throat, globus pharyngeus, and sinusitis.[3]

Because OME, RAOM, and GERD are so prevalent among children, the possibility of controlling these conditions with a single therapy is of particular interest. We hypothesized that children with OME and/or RAOM have significant patho-

logic gastroesophageal reflux as an inciting event and that empiric treatment with antireflux therapy will improve their quality of life (QOL) with regard to ear disease and GERD. Our objectives for this study were to demonstrate subjective improvement on validated QOL surveys for otitis media and GERD after antireflux therapy, as well as objective improvement on audiometry and fiberoptic laryngoscopy (FOL). We believe this to be the first prospective study of the QOL effect of antireflux therapy on otologic disease in young children.

METHODS

This study was designed as a prospective, before-and-after intervention evaluation of children with otitis media and GERD. The study was approved by the institutional review boards of the Long Island College Hospital and the State University of New York–Downstate Medical Center.

PATIENTS

Children aged 6 months to 7 years were recruited from the pediatric otolaryngology clinics at the Long Island College Hospital and the State University of New York–Downstate Medical Center. Criteria for inclusion were (1) 3 episodes of acute otitis media in the past 6 months, or 4 in the past 12 months, or 3 months of bilateral middle ear effusion and (2) symptomatic GERD as determined by routine office history and physical examination, including FOL. Criteria for exclusion were the presence of immunodeficiency; craniofacial syndrome, including cleft lip or palate; cystic fibrosis; sickle cell disease; treatment with antireflux medications during the 6 weeks prior to the initial visit; allergy to ranitidine hydrochloride, nizatidine, or lansoprazole; or inability of the parent or caregiver to read or understand English. Informed consent was obtained from the parent or caregiver at the time of the first patient visit and a convenience sample was recruited.

STUDY DESIGN

Children were assessed on the initial visit by the physician with respect to the number of episodes of acute otitis media, the number of courses of antibiotics, duration of OME, audiometric findings, history of speech delay and GERD symptoms, and physical examination findings. The parent or caregiver completed both the Otitis Media 6-Item quality-of-life survey (OM6) and either the Infant Gastroesophageal Reflux Questionnaire–Revised (I-GERQ-R) or the GERD Symptom Questionnaire for Young Children (GSQ-YC) at the initial visit. The severity of GERD-related laryngeal findings shown on FOL was recorded using the Pediatric Reflux Finding Score (Ped-RFS). The examining physician was masked to the results of the questionnaires. Parents and caregivers were instructed on antireflux precautions, antireflux therapy was prescribed, and children were followed up at 8- to 12-week intervals for 2 visits. Antireflux precautions included avoiding chocolate, acidic or fruit juices, tomatoes, and fatty or greasy foods; not eating before bedtime; and elevating the head of the bed. In addition, the parents and caregivers were instructed to avoid smoking near the child. Children received the proton pump inhibitor lansoprazole (15 mg/d in the morning) with ranitidine hydrochloride (4 mg/kg/d at bedtime) or nizatidine (5 mg/kg/d at bedtime).

At each follow-up visit, the parent or caregiver again completed the OM6 and either the I-GERQ-R or the GSQ-YC, and the physician completed a follow-up data sheet documenting the interval number of episodes of acute otitis media, number of antibiotics, presence of OME, audiometric findings, speech concerns, GERD symptoms, and physical examination findings, including the Ped-RFS by FOL. Children who improved while taking antireflux medications remained on the therapy until the conclusion of the study. Children in whom otitis media had not improved were withdrawn from the study for placement of tympanostomy tubes. *Improvement* was defined as improvement in middle ear effusion and/or audiometric testing and 1 or fewer additional episodes of otitis media between the study visits. Adherence to antireflux medications and precautions was assessed by direct questioning.

OUTCOME ASSESSMENTS

The OM6 for chronic and recurrent otitis media consists of 6 items representing domains reported by the parent or caregiver.[4] Responses for the items are scored from 1 to 7, with 1 indicating no problem and 7 reflecting the greatest problem. Individual scores are totaled and divided by 6 to produce a severity score from 1.0 to 7.0. A change score is obtained by subtracting the follow-up survey scores from the initial survey score. A positive change score indicates clinical improvement; a negative change score indicates clinical deterioration. Change scores of 0.5, 1.0, and 1.5 reflect small, moderate, and large levels of clinical change, respectively. The OM6 has been validated only for English-language use.

Children younger than 18 months at the time of enrollment were assessed using the I-GERQ-R.[5] The I-GERQ-R consists of 12 items designed to assess the response of GERD symptoms to treatment throughout a defined period. It is based on a 1-week recall period. Response choices range from 2 to 5 categories, with higher scores indicating greater symptom burden. Total scores range from 0 to 42 points. The I-GERQ-R is validated for use in children aged 6 to 18 months and has been validated in several languages.

Children older than 18 months at the time of enrollment were assessed using the GSQ-YC.[6] The GSQ-YC is an open-ended, 6-question instrument based on a 1-week recall period. It is validated for use in children aged 1 to 4 years. Symptoms assessed are abdominal/belly pain, burping/belching, choking when eating, difficulty swallowing, refusal to eat, and vomiting/regurgitation. The severity of each symptom is rated on a scale of 1 to 7, then multiplied by the number of times the symptoms occurred in the previous 7 days to produce an individual symptom score. A composite symptom score is recorded as the sum of all individual symptom scores; there is no upper limit.

Fiberoptic laryngoscopy is a routine procedure performed under topical anesthesia. The Reflux Finding Score is a scale that can be used to assess the severity of extraesophageal reflux findings on FOL.[7] Investigators at the Montreal Children's Hospital, Montreal, Quebec, Canada, have developed the Ped-RFS for use as an evaluative tool during flexible FOL. The Ped-RFS is currently undergoing validation by correlation with 24-hour pH probe results by the group at the Montreal Children's Hospital and we were granted permission to use the Ped-RFS for our study. The Ped-RFS consists of 10 items scored as 0 (absent), 2 (mild), and 4 (severe), which are recorded by the examining physician at the time of FOL. The items are thick endolaryngeal mucus, cobblestoning, lingual tonsil enlargement, laryngeal erythema, diffuse laryngeal edema, ventricular edema, true vocal fold edema, posterior commissure hypertrophy or edema, granuloma/granulation tissue, and laryngomalacia.

Audiometric testing was performed by a licensed pediatric audiologist in a soundproof booth using an audiometer (model

GSI-16; Grason-Stadler, Eden Prairie, Minnesota). Air conduction testing was performed by visual reinforcement audiometry. Single frequency (226 Hz) tympanometric measurements of static admittance (measured in milliohms) and gradient (measured in decapascals) were recorded for each ear. Both the pure-tone average (the average hearing sensitivity at 500, 1000, and 2000 Hz) and the speech awareness threshold (the minimal hearing level at which the child discerns speech stimuli at least 50% of the time) were determined. *Hearing loss* was defined as a pure-tone average greater than 25 dB.

STATISTICAL DESIGN AND ANALYSIS

Sample size estimation was based on the expected change in OM6 and I-GERQ-R scores after treatment with Power Analysis Software (nQuery Advisor Version 5.0; Statistical Solutions, Saugus, Massachusetts), using the paired 2-tailed *t* test. In a study by Rosenfeld et al[8] of 248 children undergoing tympanostomy tube insertion for treatment of otitis media, the mean (SD) OM6 change score was 1.4 (1.3). In a study by Kleinman et al[5] of 185 infants with GERD, the mean (SD) I-GERQ-R change score was 5.7 (8.4) for the infants with improvement. Based on a mean (SD) change score of 1.4 (1.3), a significance level of .05, and a power of 90%, 12 children would be needed for our study. A similar calculation using the values obtained for the I-GERQ-R yielded a required sample size of 25. To account for dropouts and to compensate for change scores not as large as expected, the sample size was increased.

Comparisons of initial and follow-up OM6, I-GERQ-R, GSQ-YC, and Ped-RFS scores and speech awareness threshold at each visit were performed using a paired 2-sided Wilcoxon signed rank test. Spearman rank correlations were used to measure association among OM6, I-GERQ-R, GSQ-YC, and Ped-RFS scores at each visit. The proportions of children improved at each visit after antireflux therapy were calculated, along with the corresponding 95% Agresti-Coull confidence intervals. The 2-sided Mann-Whitney test was used to test the difference in OM6, I-GERQ-R, GSC-YC, and Ped-RFS change scores between children whose condition improved and those whose condition did not improve at visit 2. The exact 2-sided binomial test was used to compare middle ear status (no effusion vs effusion in 1 or both ears), hearing loss (none vs pure-tone average >25 dB), and tympanometry results (A vs B or C for 1 or both ears) between visits 1 and 2. The Fisher exact test was used to determine whether any of the following predictors were associated with improvement of otitis media: sex, diagnosis (OME vs RAOM vs both), family history of otitis media, exposure to cigarette smoke, daycare attendance, history of allergies, pacifier use, history of breastfeeding, adenoid hypertrophy, and insurance (commercial vs public assistance or none). All analyses were conducted with SAS software version 9.2 (SAS Institute, Inc, Cary, North Carolina). $P<.05$ was considered statistically significant.

RESULTS

A total of 47 patients (29 male [61.7%] and 38 white [80.9%]) met inclusion criteria. Mean (SD) age was 19.5 (14.7) months. Presenting diagnosis was RAOM for 14 (29.8%), OME for 18 (38.3%), and both for 15 (31.9%) of the children. The most common GERD symptoms were congestion (22 [46.8%]), irritability (21 [44.7%]), cough (19 [40.4%]), regurgitation (13 [27.7%]), and vomiting (10 [21.3%]). Middle ear effusion was present in 43 children (91.5%), 30 of 36 (83.3%) had type B tympanograms, and 31 of 36 (86.1%) had hearing loss. Additional characteristics are presented in **Table 1**. Thirty-seven patients returned for visit 2 and 10 patients returned for visit 3. The median (SD) duration to each follow-up was 12.0 (7.6) weeks and 12.5 (4.6) weeks, respectively. Adherence to prescribed measures at visit 2 was reported by 44 parents or caregivers (93.6%).

Table 1. Baseline Characteristics of 47 Study Patients[a]

Characteristic	No.	Mean (SD) [Range]
Age, mo	. . .	19.5 (14.7) [4.0-74.0]
Sex		
Male	29 (61.7)	. . .
Female	18 (38.3)	. . .
Ethnicity		
White	38 (80.9)	. . .
Black	8 (17.0)	. . .
Hispanic	1 (2.1)	. . .
AOM episodes in past 6 mo	47	3.1 (2.1) [0-6.0]
AOM episodes in past 12 mo	47	4.7 (3.4) [0-12.0]
Lifetime No. of antibiotics	29	6.5 (3.8) [0-12.0]
Diagnosis		
RAOM	14 (29.8)	. . .
OME	18 (38.3)	. . .
Both	15 (31.9)	. . .
GERD symptoms		
Regurgitation	13 (27.7)	. . .
Vomiting	10 (21.3)	. . .
Irritability	21 (44.7)	. . .
Congestion	22 (46.8)	. . .
Cough	19 (40.4)	. . .
Hoarseness	5 (10.6)	. . .
Arching	4 (8.5)	. . .
Stridor	2 (4.3)	. . .
Passive smoking	1/34 (2.9)	. . .
Allergies	14/42 (33.3)	. . .
Pacifier use	9/35 (25.7)	. . .
Breastfeeding	12/37 (32.4)	. . .
Daycare attendance	16/36 (44.4)	. . .
Family history	6/32 (18.8)	. . .
Adenoid hypertrophy	14/45 (31.1)	. . .
Middle ear effusion	43 (91.5)	. . .
Tympanogram		
Type A	3/36 (8.3)	. . .
Type B	30/36 (83.3)	. . .
Type C	3/36 (8.3)	. . .
Hearing loss[b]	31/36 (86.1)	. . .

Abbreviations: AOM, acute otitis media; GERD, gastroesophageal reflux disease; OME, otitis media with effusion; RAOM, recurrent acute otitis media.
[a] Data are given as number (percentage) unless otherwise indicated.
[b] Pure-tone average >25 dB.

Significant improvements were found for all of the assessment tool scores at visit 2 and for most at visit 3 (**Table 2**). Mean (SD) change scores for the OM6 were 1.6 (1.1) at visit 2 and 1.5 (1.1) at visit 3 ($P<.001$ and $P=.004$, respectively), indicating a large level of clinical change. Mean (SD) change scores for the I-GERQ-R were 7.4 (7.8) at visit 2 and 12.6 (4.6) at visit 3 ($P<.001$ and $P=.008$, respectively) and for the GSQ-YC were 33.8 (23.0) at visit 2 and 22.0 (11.3) at visit 3 ($P=.001$ and $P=.50$, respectively). Mean (SD) change scores for the Ped-RFS were 6.4 (4.9) at visit 2 and 8.0 (7.2) at visit 3 ($P<.001$ and $P=.03$, respectively). The mean (SD) speech awareness threshold was 9.4 (16.7) dB lower at visit 2 and 10.0 (14.7) dB lower at visit 3 ($P=.04$ and $P=.38$, respectively). The

Table 2. Scores of Assessment Tools at Each Visit

Assessment Tool, Visits	No. of Visits	Score, Mean (SD)	No. of Change Scores	Change Score, Mean (SD)[a]	*P* Value[b]
OM6					
1	47	3.5 (1.1)	. . .	. . .	. . .
2	37	2.1 (1.0)	37	1.6 (1.1)	<.001[c]
3	10	2.3 (0.9)	10	1.5 (1.1)	.004[c]
I-GERQ-R					
1	30	15.9 (6.4)	. . .	. . .	. . .
2	25	9.8 (7.1)	25	7.4 (7.8)	<.001[c]
3	8	6.8 (2.1)	8	12.6 (4.6)	.008[c]
GSQ-YC					
1	17	44.4 (31.7)	. . .	. . .	. . .
2	12	12.8 (12.1)	12	33.8 (23.0)	.001[c]
3	2	9.5 (13.4)	2	22.0 (11.3)	.50
Ped-RFS					
1	46	8.8 (3.7)	. . .	. . .	. . .
2	28	2.8 (2.8)	27	6.4 (4.9)	<.001[c]
3	7	3.1 (3.8)	7	8.0 (7.2)	.03[c]
SAT, dB					
1	34	30.9 (12.3)	. . .	. . .	. . .
2	25	24.2 (11.2)	18	9.4 (16.7)	.04[c]
3	5	24.0 (12.4)	4	10.0 (14.7)	.38

Abbreviations: GSQ-YC, Gastrointestinal Reflux Symptom Questionnaire for Young Children; I-GERQ-R, Infant Gastrointestinal Reflux Questionnaire–Revised; OM6, Otitis Media 6-item quality-of-life survey; Ped-RFS, Pediatric Reflux Finding Score; SAT, speech awareness threshold.
[a] Baseline score minus follow-up score. Positive values indicate improvement.
[b] Two-sided Wilcoxon signed rank test.
[c] $P < .05$.

Table 3. Middle Ear Status, Hearing Loss, and Tympanometry at Visits 1 and 2

Variable	No.[a]	Visits, No. (%) 1	Visits, No. (%) 2	*P* Value[b]
Middle ear effusion	37			
Absent		4 (10.8)	21 (56.8)	<.001
Present in 1 or both ears		33 (89.2)	16 (43.2)	
Hearing loss	20			
Absent		3 (15.0)	13 (65.0)	.01
Present[c]		17 (85.0)	7 (35.0)	
Tympanometry	24			
A		3 (12.5)	10 (41.7)	.04
B/C in 1 or both ears		21 (87.5)	14 (58.3)	

[a] Patients with data for both visits.
[b] Exact 2-sided binomial test.
[c] Pure-tone average >25 dB.

small sample size at visit 3 may account for the inability to obtain statistically significant results for the GSQ-YC and speech awareness threshold.

There was moderate and significant correlation between the OM6 and the I-GERQ-R (r=0.442, n=25, *P*=.03) and the OM6 and the Ped-RFS (r=0.459, n=28, *P*=.01) at visit 2. However, correlations between the OM6 and the I-GERQ-R were not significant at the other visits. There was no significant correlation between OM6 and GSQ-YC at any visit. Correlations between Ped-RFS and either I-GERQ-R or GSQ-YC were also not significant at any visit.

Otitis media was considered by the examining physician to be clinically improved in 28 of 37 children (76%; 95% confidence interval, 60%-87%) at visit 2 and in 6 of 10 children (60%; 95% confidence interval, 31%-83%) at visit 3. Improvement of otitis media at visit 2 was associated with significant improvements in the scores for the OM6 (*P*=.04), I-GERQ-R (*P*=.03), and Ped-RFS (*P*=.003), but not for the GSQ-YC (*P*=.83). Since only 9 patients did not exhibit clinical improvement, power of these tests is lacking, and only 2 unimproved patients had GSQ-YC scores determined at visit 2. There were also significant improvements in middle ear status, hearing loss, and tympanometry at visit 2 (**Table 3**). The sample size at visit 3 was too small to conduct comparable analyses. Nine children (19.1%) required tympanostomy tube insertion and were withdrawn from the study.

Bivariate analysis of potential predictors of improvement in otitis media demonstrated that only daycare attendance (*P*=.02) and a family history of otitis media (*P*=.02) were significantly associated with improvement (**Table 4**). The sample size was too small to allow regression analysis to assess confounding effects of other potential covariates.

COMMENT

Gastroesophageal reflux disease is a common physiologic occurrence in infants and decreases in frequency during the first year of life.[9] Pediatric middle ear disease often coexists with GERD.[10] The size and shape of the immature eustachian tube may contribute to an increase in reflux of nasopharyngeal contents into the middle ear.

The functional derangement of OME is believed to involve metaplasia of the middle ear epithelium with a proliferation of goblet cells and mucous glands, leading to hypersecretion, mucociliary dysfunction, and

middle ear effusion with concomitant conductive hearing loss. An analogous process may be implicated in other disorders, such as pediatric sinusitis. In that disease, improvement with empiric antireflux therapy has been demonstrated in up to 85% of children studied,[11] with a decrease in the number of necessary surgical procedures.[12]

Because GERD and OME are 2 of the most prevalent diseases in young children, a number of investigators have taken preliminary steps to demonstrate a causative link between the diseases. Of particular interest has been the presence of gastric enzymes in the middle ear space. Studies on rats with repeated middle ear exposure to pepsin have demonstrated impaired eustachian tube function[13] as well as impaired mucociliary clearance of middle ear contents.[14] In a study by Tasker et al,[1] middle ear effusions were sampled from 54 children aged 2 to 8 years who underwent myringotomy. More than 80% of the children were found to have pepsin concentrations of up to 1000-fold greater than serum levels, suggesting a contributory role of GERD in OME.[1] Subsequent studies of middle ear fluid in children aged 1 to 7 years with RAOM or OME demonstrated the presence of pepsin in 73% to 77% of effusions.[15-17]

One study of 31 children with OME showed middle ear pepsin/pepsinogen to be present in concentrations up to 231 times higher than serum levels from the same children.[18] A correlation was also identified between the concentration of the enzyme and the number of reflux episodes using 24-hour pH-probe monitoring.[18]

A recent prospective study by O'Reilly et al[19] found that pepsin was detectable in the middle ear cleft of 20% of 509 patients with OME undergoing tympanostomy, compared with 1.4% of controls undergoing cochlear implantation. *Helicobacter pylori*, which is a known pathogen for several inflammatory gastric disorders, also has been postulated as a factor in the development of otitis media. In a study by Yilmaz et al,[20] *H pylori* was identified by reverse transcription–polymerase chain reaction in 67% of middle ear effusions in a study of 18 children with OME. Additional research is necessary to determine the significance of these findings.

Although basic science studies suggest that GERD has a role in the pathogenesis of OME, there have been few clinical studies evaluating GERD in patients with otitis media. A small study of 32 patients found a higher incidence of conductive hearing loss and physical findings of middle ear dysfunction in children with GERD vs in those without, although statistical significance was not demonstrated.[21] In a series of 21 adults with chronic secretory otitis media or eustachian tube dysfunction, empiric therapy with a proton pump inhibitor produced resolution of symptoms in all participants from 2 to 16 weeks.[3] A majority of these patients had GERD confirmed by upper gastrointestinal endoscopy, 24-hour dual-probe esophageal pH monitoring, and/or esophageal manometry. More severe cases of GERD were believed to correspond with more severe manifestations of otologic disease, as measured by duration of therapy to achieve symptom relief, maintenance dose needed to remain symptom-free, and objective examination findings.[3]

Table 4. Bivariate Analysis of Potential Predictors of Improvement of Otitis Media at Visit 2

Covariate	No.	Improved, No. (%)	*P* Value[a]
Sex			
Male	25	17 (68.0)	.22
Female	12	11 (91.7)	
Diagnosis			
RAOM	13	8 (61.5)	.06
OME	13	9 (69.2)	
Both	11	11 (100.0)	
Insurance			
Commercial	24	18 (75.0)	>.99
Public assistance or none	13	10 (76.9)	
Passive smoking			
Yes	0	. . .	. . .
No	25	18 (72.0)	
Family history of otitis media			
Yes	6	2 (33.3)	.02[b]
No	18	16 (88.9)	
Daycare attendance			
Yes	11	11 (100.0)	.02[b]
No	16	9 (56.3)	
Allergies			
Yes	10	7 (70.0)	.68
No	22	17 (77.3)	
Pacifier use			
Yes	7	4 (57.1)	.34
No	19	15 (79.0)	
Breastfeeding			
Yes	9	5 (55.6)	.17
No	19	16 (84.2)	
Adenoid hypertrophy			
Yes	10	6 (60.0)	.19
No	25	21 (84.0)	

Abbreviations: OME, otitis media with effusion; RAOM, recurrent acute otitis media.
[a] Fisher exact test.
[b] $P < .05$.

An ideal method to assess the presence and severity of GERD, especially extraesophageal GERD, has not yet been determined. Fiberoptic laryngoscopy is commonly used for this purpose in adults, yet the use of airway endoscopy in children with GERD has been less well studied. The criterion standard for diagnosis of GERD in adults and children is 24-hour dual-probe pH monitoring, yet the proper administration of the test and interpretation of results remain the subject of debate.[22] Testing using the pH probe is also invasive, as it often requires sedation for placement and needs to stay in place for 24 hours. Therefore, alternative means of assessment are often sought.

Carr et al[7] studied a group of 77 children (mean age, 4.2 years) to determine the usefulness of direct laryngoscopy in identifying laryngopharyngeal manifestations of GERD using a qualitative rating scale. The highest correlation was found for lingual tonsil hypertrophy, postglottic edema and erythema, and arytenoid edema and erythema.[7] While the patients in that study underwent direct laryngoscopy under general anesthesia, laryngeal appearance can be readily assessed by flexible FOL

in the office setting via noninvasive means. At the time of the study by Carr et al, there was no validated measure of FOL findings to assess GERD in children. As with any physical examination tool, FOL is subject to observer bias and serves only as an approximation of the severity of reflux. Once the Ped-RFS is validated for this purpose it may prove to be a useful tool for the assessment of GERD in children.

Health-related QOL research is reliant on the principle that disease-specific measures are necessary to evaluate treatment benefits. Outcomes assessment has been shown to be a useful means of reporting patient QOL among young children who may be otherwise unable to express their symptoms. The OM6 has been shown to have good test-retest reliability and responsiveness, and has been validated for use in children aged 6 months to 12 years.[4] The OM6 has been used to show that tympanostomy tubes produce large short-term improvements in QOL for most children.[8] The I-GERQ-R was validated by a multinational 3-week observational study of caregivers of infants aged 18 months and younger.[5] The I-GERQ-R was found to have high internal consistency reliability, test-retest reliability, construct validity, and correlation with caregiver- and physician-rated severity of disease. The GSQ-YC has been validated for use with older children[6] and was included in the study reported here to provide a means of QOL assessment of this age group.

Potential limitations of this prospective study include the absence of a control group and the lack of randomization. The lack of control for observer bias may have yielded results that inaccurately represented the presence of reflux. The before-and-after study design may not account for resolution of otitis media based on natural disease course. Some degree of bias was eliminated by masking the examining physician to survey results. Also, incomplete follow-up, especially for the second follow-up visit, reduces the potential to detect a significant improvement after a longer course of antireflux therapy. Improvement in symptoms during antireflux therapy may have partially accounted for the high attrition rate, although this remains uncertain. The study population was heterogeneous in age, which may confound conclusions about the relationship of GERD with otitis media and the effects of therapy. A study population limited to very young children may yield more widely applicable results, as that population accounts for the majority of OME and RAOM cases. Further study, such as a randomized, controlled, double-blind trial of the effect of antireflux therapy on children with OME, may provide additional support for a causative link between otitis media and GERD. The optimal pharmacologic agent and dosing for antireflux therapy in the prevention of OME and RAOM also remain to be determined.

CONCLUSIONS

To our knowledge, this is the first prospective study of the effect of antireflux therapy on the QOL of children with otitis media. We found that validated measures of the disease burden of otitis media and GERD showed significant improvement with antireflux therapy. Hearing loss demonstrated on audiometric testing was significantly improved following therapy, as were laryngeal findings of reflux on FOL, although a validated scale for assessment is lacking. We conclude that reduction of gastroesophageal reflux may play a role in the prevention of otitis media, although additional high-quality clinical trials are warranted.

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Author Contributions: Drs McCoul, Goldstein, and Goldsmith had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* McCoul, Goldstein, and Goldsmith. *Acquisition of data:* McCoul, Goldstein, Koliskor, Jackson, and Goldsmith. *Analysis and interpretation of data:* McCoul, Goldstein, and Weedon. *Drafting of the manuscript:* McCoul. *Critical revision of the manuscript for important intellectual content:* Goldstein, Koliskor, Weedon, Jackson, and Goldsmith. *Statistical analysis:* Weedon. *Study supervision:* Goldstein.
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Correction

Error in Table. In the article titled "Sensorineural Hearing Loss in a Pediatric Population: Association of Congenital Cytomegalovirus Infection With Intracranial Abnormalities" published in the October issue of the *Archives* (2010;136[10]:999-1004), there was an error in Table 3. The column subheading "CMV-Negative (n=7)" should have read "CMV-Negative (n=87)."