

Integrative versus Conventional Therapy of Chronic Otitis Media with Effusion and Adenoid Hypertrophy in Children: A Prospective Observational Study

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Keywords

Chronic otitis media with effusion · Adenoid hypertrophy · Impaired hearing · Pneumatization · Integrative medicine · Conventional medicine · Surgical intervention · Antibiotics · Analgesics

Summary

Background: Chronic otitis media with effusion (COME) and adenoid hypertrophy (AH) are common entities in the pediatric population. The conventional treatment approach (conventional medicine; COM) involved mainly surgery after a period of close observation. In this study, we aimed to introduce an integrative, non-invasive approach (integrative medicine; IM) for COME, AH, and associated episodes of recurrent acute otitis media, and compared outcomes with conventional treatment. **Methods:** We conducted a prospective, non-randomized study in an integrative primary care pediatric practice and a conventional pediatric otolaryngological clinic, where treatment modality was determined by patient preference. Out of a total 101 patients aged 1–8 years, integrative therapy was chosen by 46, and conventional treatment by 55. All patients had COME and AH diagnosed by an otolaryngologist and had moderate to severe hearing impairment. COM treatment was based on close observation over time, nasal decongestants and surgical intervention. In contrast, the IM involved a complex personalized approach with non-invasive interventions, non-allopathic medications, diet and patient education. **Results:** The number of surgical interventions (adenoidectomy, pressure-equalization tube insertion, myringotomy) was significantly less in the IM cohort (1 of 28 vs. 15 of 35 in the COM group, $p < 0.001$). The frequency of antibiotic use was significantly less in the IM group ($p < 0.001$). The frequency of analgesic use was also significantly less in the IM group ($p = 0.029$). Improvement in tympanometric measures (normal A-type curve) was higher in IM patients compared to expected spontaneous remission during the observation period. Improvement in audiometric measures (intact hearing) of IM patients was also higher than expected compared to spontaneous remission during the observation period. **Conclusion:** Compared to conventional treatment, integrative treatment of patients with COME and AH showed significantly lower invasive surgical intervention rates and significantly decreased antibiotic and analgesic use. The integrative treatment was effective, safe and well tolerated.

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Schlüsselwörter

Chronische Otitis media mit serösem Erguss · Adenoide Hypertrophie · Hörverlust · Pneumatisation · Integrative Medizin · Konventionelle Medizin · Chirurgische Intervention · Antibiotika · Analgetika

Zusammenfassung

Hintergrund: Chronische Otitis media mit serösem Erguss (COME) und adenoide Hypertrophie (AH) sind häufige Erkrankungsbilder im Kindesalter. Die konventionelle Standardtherapie führt nach einer Beobachtungszeit (watchful waiting) in der Regel häufig zu operativen Maßnahmen. In dieser Studie stellen wir einen integrativen, nichtinvasiv orientierten Behandlungsansatz (integrative medicine; IM) für COME, AH und assoziierte Episoden von rezidivierender akuter Otitis media vor und vergleichen dessen Ergebnisse mit der konventionellen Behandlung (conventional medicine; COM). **Methoden:** Wir gestalteten eine prospektive, nichtrandomisierte Studie in einer integrativmedizinischen pädiatrischen Praxis und in einer konventionellen pädiatrisch-otolaryngologischen Krankenhaus-Fachambulanz; die Patienten wählten die Therapieform selbst. Von insgesamt 101 Patienten im Alter von 1–8 Jahren wählten 46 Patienten eine integrative, 55 eine konventionelle Therapie. Die Diagnose der COME und AH aller Patienten war durch einen Hals-Nasen-Ohren-Facharzt gestellt. Der Hörverlust war mittel- oder schwergradig. Die COM basierte auf Zuwarten unter Beobachtung, abschwellenden nasalen Maßnahmen und chirurgischen Interventionen. Im Gegensatz dazu wurde die IM als ein personalisierter, komplex-systemischer Ansatz durchgeführt, die nichtinvasive Maßnahmen, nichtallopathische Medikation, Diät und Patientenedukation umfasste. **Ergebnisse:** Die Anzahl chirurgischer Interventionen (Adenoidektomie, PET-Insertion, Myringotomie) war signifikant geringer unter IM (IM: $n = 1$ von 28; COM: $n = 15$ von 35; $p < 0,001$). Die Häufigkeit antibiotischer Therapien war in der IM-Gruppe signifikant niedriger ($p < 0,001$). Die Häufigkeit analgetischer Therapien war in der IM-Gruppe signifikant niedriger ($p = 0,029$). Während des Beobachtungszeitraums verbesserten sich die tympanometrischen (normale A-Typ-Kurve) sowie die audiometrischen Messungen (intaktes Hörvermögen) in der mit IM behandelten Patientengruppe stärker als die potenzielle Spontanremission. **Schlussfolgerung:** In der Behandlung von COME und AH zeigte ein IM-Ansatz im Vergleich zu COM signifikant niedrigere Raten an chirurgischen Interventionen, Antibiotika- und Analgetikaeinsatz. Die IM-Behandlung war wirksam, sicher und wurde gut vertragen.

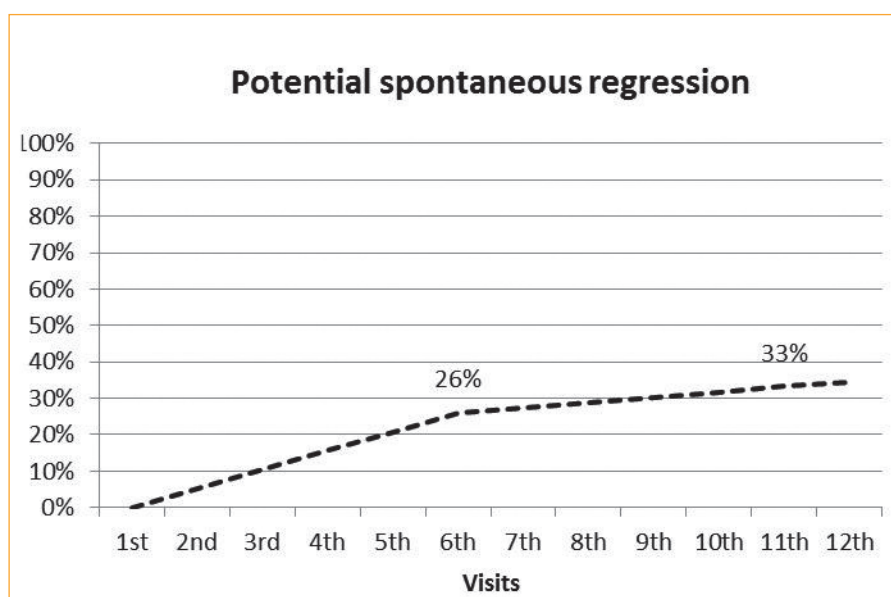


Fig. 1. Expected spontaneous regression rates in chronic otitis media. The dots mark historical data, the pecked curve indicates assumed values.

Introduction

Chronic otitis media with effusion (COME) and adenoid hypertrophy (AH) are common entities in the pediatric population with a bimodal age distribution peaking at years 2 and 5. Children with this condition frequently present with impaired hearing to the pediatric otolaryngological clinic. The disease course typically shows symptoms fluctuating with time [1].

While the diagnosis is usually based upon clinical presentation and an abnormal audiometry or/and tympanometry, endoscopy may also be involved in the diagnostic evaluation.

In general, otitis media of unknown duration has a rate of spontaneous remission of 28% by 3 months rising to 42% in 6 months. In contrast, COME has a lower rate, with 26% resolving in 6 months and only 30–33% by 1 year after diagnosis (fig. 1.) [2, 3]. The longer that COME persists, the lower is the rate for spontaneous remission [4, 5]. Prognosis also depends on age at presentation, with more remission occurring in children younger than 2 or older than 6 [6]. Children between the ages 2 and 6 years tend to have more AH and, therefore, may need surgery more frequently [7].

Eustachian tube rehabilitation therapy was originally introduced in the 1980s. COME and early retraction pockets are the usual indications [8]. Enhancing muscle strength in the muscles keeping the Eustachian tubes open is the key objective. Randomized controlled trials evaluating the use of nasal balloons for autoinflation revealed a clear benefit [9]. This technique appears safe, simple and effective [10–13]. Autoinflation and external thermal interventions are also widespread and are extensively used in Hungary.

Integrative medicine is used by several primary care physicians to treat upper respiratory or ear infections. However, it has not been formally investigated in the complex setting of chronic otitis media. Integrative medicine often involves the use of anthroposophic medications that are safe and usually well tolerated [14, 15].

Specifically, extracts such as *Cydonia fructus glycerinum* and *citrus lemon fructus* have been used in clinical practice for decades [16]. Preparations containing these substances are readily available in the European Union. Their most common indications include rhinitis and specifically allergic rhinitis. This indication is based on their decongestant, adstringent and immunomodulatory, i.e. anti-inflammatory and anti-allergic, properties [17–19]. Their efficacy was graded as moderate (GRADE classification) and their application was found to be generally safe [20].

In this study, we hypothesized that using a personalized therapeutic plan in the treatment of COME, AH and associated episodes of recurrent acute otitis media, the integrative medicine approach could reduce the need for surgical interventions, and antibiotic and analgesic use. Additionally, we hypothesized that an integrative approach would represent a safe and effective alternative to conventional treatment.

Material and Methods

Study Design

We conducted a Good Experimental Practice(GEP)-conform, prospective observational study with non-randomized group assignment and descriptive comparison of outcomes. Groups were non-randomized as patients self-selected under real-world conditions to be included either in the integrative or the conventional therapy arm. The study was conducted in our integrative pediatric practice Clinic (integrative medicine, IM) and a conventional pediatric otolaryngological clinic (conventional medicine, COM) in Hungary.

Ethics Committee approval was granted and the study was performed according to the Declaration of Helsinki. Written informed consent in accordance with local legal requirements was obtained from parents of all patients before study entry.

Patients, Clinical Characteristics

Between 1 September 2013 and 30 June 2014 we recruited all outpatients presenting with COME and AH to the pediatric practice (IM, n = 46) or otolar-

Table 1. Primary outcome variables

| Variable | |
|--|--|
| No. of invasive surgical interventions | count |
| No. of acute infection episodes needing antibiotic therapy | no. during observation period (local and systemic) |
| No. of acute infection episodes needing analgesic therapy | no. during observation period (local and systemic) |
| Tympanometric measurement with evaluation of worse ear | A-type curve: normal pressure C- or D-type curve: under- or overpressure B-type curve: low admittance |
| Audiometric measurement with evaluation of worse ear | normal hearing: -10 to -20 dB slight hearing loss: -30 to -40 dB middle hearing loss: -50 to -60 dB severe hearing loss: ≥ 60 dB |

Table 2. Secondary outcome variables

| Variable | |
|---|--|
| Frequency of acute otitis media during observation | number |
| Parents' report on treatment outcome | |
| nasal congestion | subjective scale: 1 = none, 2 = moderate, 3 = severe |
| hearing | subjective scale: 1 = good, 2 = moderate, 3 = bad |
| Adherence to therapy | subjective scale: 1 = good, 2 = moderate, 3 = bad |
| Median time of follow-ups | days |
| Mean no. of days counted from first visit in follow-up period | days |
| Participation at visits | no. of patients, % |

ngological clinic (COM, n = 55), who were willing to participate in the study (n = 101). Patients self-selected in terms of group assignment and were included either in the integrative or the conventional therapy arm. Per definition, chronic otitis media was diagnosed when symptoms had persisted for at least 3 months. AH was diagnosed by a pediatric otolaryngologist.

Additional inclusion criteria were baseline age of 1–8 years, and moderate (30–40 dB on the less affected ear) or severe (over 40 dB on the less affected ear) hearing loss with abnormal findings in tympanometry at least once during the first 3 visits. Children with anatomical abnormalities (e.g. cleft palate), congenital syndromes (e.g. Down's syndrome), concurrent illnesses requiring continuous medical treatment (e.g. cystic fibrosis) and previous otolaryngological surgical interventions were excluded. Patients lost to follow-up completing less than 3 monthly visits after diagnosis were also excluded from statistical evaluation as they did not fulfill required eligibility criteria.

Baseline parameters included age, type of delivery (cesarean section vs. vaginal), prior number of antibiotic treatments per year, prior number of analgesic treatments per year, prior number of acute otitis media per year, prior indication of adenoidectomy by an otolaryngologist. All patients were followed up by monthly visits over a period lasting at least 1 year to a maximum of 400 days. Data collection was also stopped at the day of surgical intervention if performed. Each initial visit lasted about 40 min, while about 20 min was usual for follow-up visits.

Treatments: COM Group

In both groups, the primary aim of therapy was to minimize hearing loss through improvement of nasal breathing, better pneumatization of Eustachian tubes and size reduction of AH. Primary outcome variables for both groups are detailed in table 1. Secondary outcome variables for both groups are detailed in table 2.

In the COM group, treatment was performed according to the Hungarian guidelines released in 2008 [21] and updated in 2010 [22]. Based on these

guidelines, adenoidectomy was the standard surgical intervention. These guidelines differ from the German guidelines updated in 2012 [23, 24] and the guidelines of the American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) and their updates [25–27]. According to the latter guidelines, active surveillance or 'watchful waiting' is recommended for at least 3 months with monthly audiometry to assess hearing. Antibiotics, decongestants, antihistamines and steroids are not recommended as a routine treatment for COME. Otherwise healthy children with COME persisting over 4 months are considered for surgery if hearing loss exceeds 40 dB. Tympanostomy with a pressure-equalization tube (PET) insertion is recommended for children younger than 4 years of age. Myringotomy alone or adenoidectomy as initial procedures are not recommended. Adenoidectomy plus myringotomy with or without tube insertion is recommended if tympanostomy proves to be ineffective. It is also the preferred initial surgical modality for children over 4 years. We emphasize that the COM treatment of the study followed Hungarian guidelines rather than international recommendations in treating the patients.

Treatments: IM Group

Treatment for the IM group was based on a complex personalized, non-invasive therapeutic system approach as characterized below. It included the use of local nasal preparations, non-allopathic medications, facilitation of pneumatization, external thermal interventions, parent and patient education and anti-allergic medications and/or diet if an allergic condition was present (table 3).

Local Nasal Preparations

Patients were prescribed nasal spray containing Cydonia fruct. glycerinum extract (APC 3.0): 9% volume with citrus lemon fruit 2% volume in 1% NaCl solvent 4–5 times a day on both sides. The horizontal application of the nasal spray was a key feature in the application to reach the adenoid and the meatus of the Eustachian tube more successfully.

Table 3. Therapeutic elements of integrative method for chronic otitis media

| Therapeutic elements of IM |
|--|
| Local nasal preparations |
| Constitutional non-allopathic medication |
| Facilitation of pneumatization |
| External warmth (thermal) interventions |
| Anti-allergic therapy and/or diet in case of allergy |
| Parents and patient education |
| IM = integrative medicine. |

Constitutional Non-Allopathic Medications

Berberis/Quarz Glob. WALA (10 g containing Berberis vulgaris e fructibus ferm, 33c Dil. D2 0.1 g (HAB, Vs. 33c); Quarz Dil. D19 aquos. 0.1 g, sucrose) 3 × 5 globuli per day as oral application over 3–6 months as described in [28]. In our study, no other non-allopathic medications were used.

Facilitation of Pneumatization (Table 4)

Passive Techniques without Pressure

Chewing and swallowing were encouraged to intensify the function of peritubular muscles with hard to chew food [29] or chewing gum for several minutes 4–5 times per day [30]. Singing, piping, and yawning were encouraged to allow the soft palate to move upward, the tongue to flatten, the pharynx to dilate, and the hyoid bone to move downward. The Eustachian tubes open at the acme of the yawn.

Exercises to contract the velopharyngeal sphincter involved: (i) tongue movements such as sweeping the palate and moving the tongue backward; (ii) soft palate movements such as contraction of the soft palate, i.e. first stage of swallowing and induced yawning; (iii) protraction and side-to-side movements of the jaw; and (iv) combined movements of the tongue and soft palate, to which jaw movements are then added.

Nasal valve exercises included acquiring awareness to nostril dilation and working against resistance (the parent's thumb and forefinger). Diaphragmatic function can be improved by exercises against pressure from the parent's hand placed on the epigastric region.

Pressure Exercises

Low-pressure exercises (0–circa 50 mm Hg) included snuffing out a candle, and rolling along a ping-pong ball, and letting a feather fly with 1 opened and 1 pinched nostril. Middle-pressure exercises (circa 50–100 mm Hg) used blowing of party noise makers with well-cleaned noses. High-pressure exercises involving autoinsufflation with strictly cleaned noses used balloon techniques (OTO-BAR, Otovent, Piszé orrballon, Hungary), the Valsalva maneuver, and the Misurya maneuver.

External Warmth (Thermal) Interventions

Local interventions used infrared light or a warming cap (OTO-THERM fülmelegítő gyógyszapka) [31] 2–3 times a week for a few minutes on the ears. Systemic interventions included measures such as avoiding areas on the patient's body getting cold, and warm (ca. 40–45 °C) foot baths in fresh 1–1.5% NaCl and Zingiber officinale pulvis.

Anti-Allergic Therapy and/or Diet in Case of Allergy

Consumption of rough cow milk and dairy products was generally restricted to 150 ml/day [29]. In case of IgE or IgG positivity to beta-lactoglobulin, albumin or casein, a complete dairy-free diet was undertaken. No conventional anti-allergic treatment was used.

Parental and Patient Education

Since prior data have shown that such education may enhance compliance and treatment efficacy [32], we undertook a detailed education program with

Table 4. Techniques for facilitation of pneumatization

| Used facilitation techniques of pneumatization |
|--|
| Passive techniques without pressure |
| Low-pressure exercises (0–circa 50 mm Hg) |
| Middle-pressure exercises (circa 50–100 mm Hg) |
| High-pressure autoinsufflation exercises (circa 100–150 mm Hg) |
| Balloon techniques |
| Valsalva maneuver |
| Misurya maneuver |

anatomical and physiological-functional illustrations, videos [33], brochures, feed-back sessions, and detailed instructions on all interventional measures, as well as nasal hygiene, and the proper nose-blowing technique.

Statistical Analysis

Statistical evaluation for small datasets was performed using t-test, Shapiro-Wilk test of normality, Mann-Whitney test, Independent Samples Median test, Chi-Squared test, and 2-sided Fischer's exact test as appropriate. Comparison of the 2 groups and expected versus actual remissions were performed using IBM SPSS Statistics 22 software and Microsoft Excel. For all analyses, $p \leq 0.05$ was considered significant.

We used Shapiro-Wilk to test variables for normal distribution. We found that within the groups none of the variables had normal distribution with the single exception of baseline age. Accordingly, we used methods appropriate for non-normal distributions such as the Mann-Whitney test and Fisher's exact test.

Results

Baseline characteristics for both groups are detailed in table 5. 101 patients aged 1–8 years were recruited in the study, with 46 selecting integrative therapy and 55 conventional treatments. We had to exclude patients, who did not fulfill eligibility criteria. In the IM group, for 17 of the 18 excluded patients, the reason given was the excessive distance from their home to the praxis; 1 patient had to be excluded because of a central hearing disorder. In the COM group, 16 were excluded for missing at least 3 follow-ups, and 4 as no abnormal finding in tympanometry was found during at least 1 of the first 3 visits.

Primary Outcomes

The number of invasive surgical interventions (adenoidectomy + PET insertion + myringotomy) was significantly less in the IM patient group (1 of 28, 3.6%) compared to the COM group (15 of 35, 42.9%; odds ratio (OR) 20.250, 95% confidence interval (CI) 2.467–166.229). The difference was statistically significant using the Fisher's exact test, $p < 0.001$ (fig. 2). Similarly, the frequency of antibiotic use was less in the IM group (5 of 28, 17.9%) compared to the COM group (29 of 35, 82.9%; OR 22.233, 95% CI 6.018–82.147). The difference was statistically significant using the Fisher's exact test, $p < 0.001$ (fig. 3). Frequency of analgesic or antipyretic medication was also less in the IM group (6 of 28, 21.4%) compared to the COM group (18 of 35, 51.4%; OR 3.882, 95% CI 1.267–11.898). The difference was statistically significant using Fisher's exact test, $p = 0.020$ (fig. 4).

Table 5. Baseline parameters in the IM versus COM therapy groups

| Baseline parameter | IM group | COM group | p value ^a |
|---|-----------|-----------|----------------------|
| Mean baseline age, months | 56 | 38 | < 0.001 |
| Tympanometry: abnormal findings ^b , % | 100 | 85 | 0.058 |
| Audiometry: hearing loss | | n.p. | n.p. |
| Light, % | 50 | | |
| Moderate, % | 32 | | |
| Severe, % | 11 | | |
| Data missing, % | 7 | | |
| Parents' initial report on nasal obstruction ^c , % | 96 | 93 | 1.000 |
| Parents' initial self-report on hearing ^c , % | 86 | 54 | 0.049 |
| Prior no. of acute otitis media/year | 1.6 | 0.5 | < 0.001 |
| Prior no. of antibiotic treatments/year | 1.57 | 1.33 | 0.833 |
| Prior no. of analgesic treatments/year | 1.36 | 1.48 | 0.817 |
| Adenoidectomy at baseline, n (%) | 7/28 (25) | 7/35 (20) | 0.763 |
| Rate of cesarean section, % | 14 | 25 | n.p. |

^aReflect differences detected on the 2-sided Fisher's exact test and Mann-Whitney test; p < 0.05 considered statistically significant.
^bB+C+D type curves, found at least twice during the first 3 visits.
^cAbnormal = 2 and 3 on subjective scale of 1–3.
 IM = integrative medicine; COM = conventional medicine; n.p. = not performed.

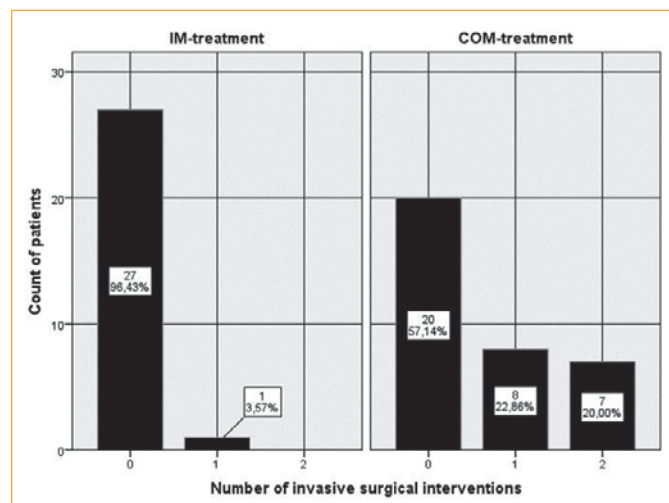


Fig. 2. Number of surgical interventions performed in the 2 groups during the observational period. In the integrative medicine (IM) group, the rate was significantly lower.

Improvement in tympanometric measurement (A-type curve with normal pressure, see also table 2) was higher in IM patients compared to expected spontaneous remission during the observation period (fig. 5). Improvement in audiometric measurement (intact hearing, see also table 2) was higher in IM patients compared to expected spontaneous remission during the observation period (fig. 6).

Secondary Outcomes

The frequency of acute otitis media during the observation period did not significantly differ between the IM and the COM groups (Mann-Whitney test p = 0.256) (fig. 7). Objective outcomes as measured by audiometry correlated well with subjective outcomes as reported by parents on most of the visits. A strong and

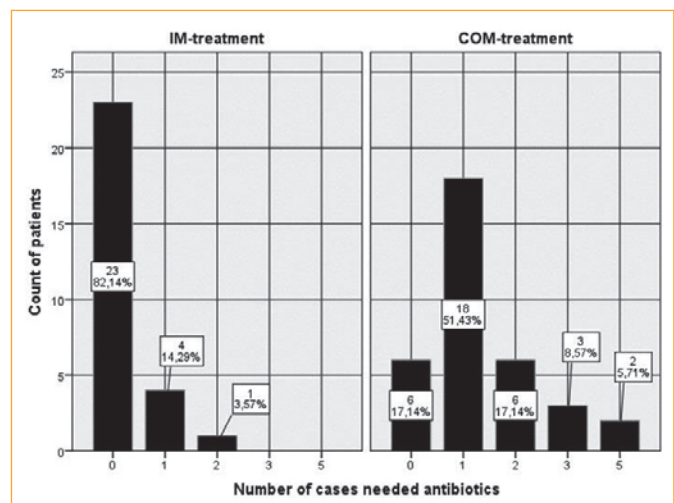


Fig. 3. Antibiotic use in the 2 groups during the observational period. In the integrative medicine (IM) group, the use was significantly lower.

statistically significant correlation was reflected by a Spearman's Rho of 0.54–1.00 (from p < 0.001 to p = 0.01). On follow-up visits 4 and 5, this correlation was less marked with a Spearman's Rho of 0.33–0.36 and were not significant.

Adherence to prescribed therapies was not significantly different (using a self-reported subjective scale of 1 = good, 2 = intermediate, 3 = bad; Pearson Chi-Squared test p = 0.181). Median duration of follow-up did not differ significantly (IM 40 days, COM 32 days, Independent Samples Median test p = 0.843). The mean number of days counted from the first visit to the follow-up period is described in table 6. Number of follow-ups during the observation period differed significantly between the 2 groups (Mann-Whitney test p < 0.001) (fig. 8).

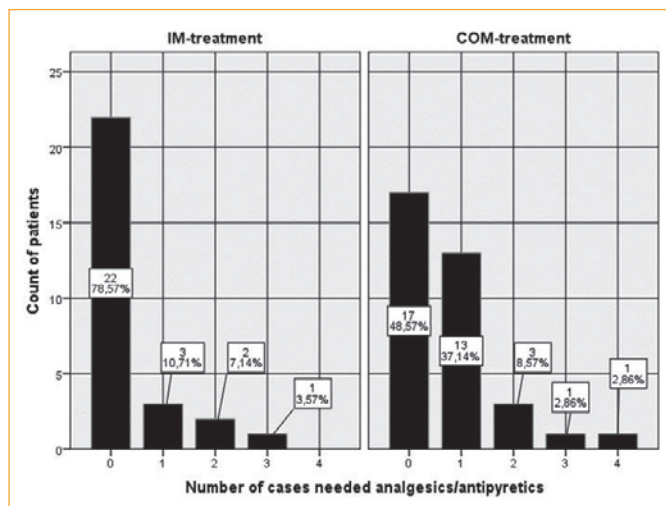


Fig. 4. Analgesic/antipyretic use in the 2 groups during the observational period. In the integrative medicine (IM) group, the use was significantly lower.

Regarding adverse reactions, 2% of the patients in the IM group reported adverse effects. All adverse reactions were described as mild. No adverse effect report was collected for the COM group. The expected rate of adverse reactions using historical data would have been 6–10%.

Discussion

Main Findings

The main findings of this study confirmed our hypothesis that an integrative approach in the treatment of COME and AH is effective in improving hearing loss. It also has the potential to minimize medication use and the number of surgical interventions.

The 2 arms of the study represented 2 different therapeutic settings with a different routine and a different general approach (attitude) by both medical personnel and patients. In fact, in our population both the IM and the COM approaches provided effective therapies. However, while the integrative approach required more efforts in terms of creating and adhering to a more complex treatment plan, requiring multiple non-conventional treatments and more intense patient education, it also induced less adverse reactions than could be expected from conventional therapy considering historical data.

In addition, the integrative approach had the additional benefit of creating more opportunity for personalization and more active parental participation with the caveat that such a proactive approach may not be suitable for all parents and patients [34], although this was not the case in our study.

Additional Findings

We should emphasize the fact that the overall frequency of invasive interventions in our conventional treatment group was higher than reported previously [35, 36]. This could be partly explained by

the differences between Hungarian and international guidelines detailed in the Materials and Methods section. Specifically, according to Hungarian guidelines [21, 22], adenoidectomy is the preferred surgical intervention and it is often performed if nasal decongestants do not provide adequate relief in symptoms. Thus, these regional differences need to be considered when trying to generalize our findings to populations in other countries.

A further finding in our study was a different rate of cesarean section in the obstetric history of patients in 2 groups. This might mirror the different attitude of parents to surgical interventions in each group. Some patients may be more inclined toward surgical interventions when so prompted, while others may tend to adopt a more conservative approach when this option is given to them [37, 38]. We argue that the parents of the patients more inclined to accept the option of cesarean section may have been less likely to use a more conservative approach with IM.

Strengths and Limitations

Our study has several strengths and limitations. We were able to evaluate several objective and subjective variables in a real-world clinical setting. Due to a long follow-up period and a relatively good adherence to follow-up visits, we were in the position to closely observe the clinical course and were well placed to distinguish between fluctuations in symptomatology compared to true remission.

In terms of selection bias, we evaluated many baseline parameters and these were similar between groups in terms of: (i) pathological tympanometry findings (B+C+D type curves), (ii) indication of adenoidectomy prior to first visit, (iii) prior number of antibiotic or analgesic treatments per year, and (iv) parents' report on the degree of nasal congestion. However, several important parameters were statistically different between the groups at baseline. Age at presentation, although mostly remaining in the typical range between 2 and 6 years, was nevertheless significantly different between the groups. An important factor in this age difference might have been that parents who opted for integrative treatment might have had the tendency to avoid interventions even before the study due perhaps to a more conservative attitude. Prior number of acute otitis media episodes was also higher in the IM group, presumably for similar reasons. Parents' reports on hearing loss were also more striking in the IM group at baseline. There was also a higher occurrence of cesarean section in the medical history of the COM group patients compared to the IM group (25% vs. 14%), although both groups had a lower rate than previously reported in the Hungarian population (35%).

From these differences in baseline characteristics it is clear that the IM group had a disadvantage from the start due to higher age, longer prior symptom duration, and more previous otitis episodes at baseline. This situation tended to diminish the detection of any true benefit from IM as compared to the COM arm. As the IM group was generally disadvantaged, any confounding by baseline imbalances would have worked against the IM group. This natural disadvantage [4–7] and the clear differences in baseline characteristics together made any beneficial baseline confounding so unlikely that no fur-

Table 6. Mean number of days counted from the first visit during the follow-up period (with 95% CI)

| Treatment | Visit | | | | | | | | | | |
|-----------|---------------|---------------|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| | 2nd | 3rd | 4th | 5th | 6th | 7th | 8th | 9t | 10th | 11th | 12th |
| IM | 30 (26–35) | 63 (54–72) | 102 (88–115) | 137 (121–152) | 177 (168–187) | 213 (206–220) | 246 (236–255) | 276 (267–285) | 312 (302–322) | 351 (340–362) | 393 (379–408) |
| COM | 27 (19–34) | 53 (43–62) | 86 (71–100) | 125 (103–146) | 172 (156–189) | 195 (178–212) | 252 (216–288) | 281 (250–311) | 316 (293–338) | 342 (314–371) | 386 (371–401) |
| Total | 29 (24–33) | 58 (52–64) | 93 (84–103) | 131 (119–143) | 175 (167–184) | 206 (198–214) | 248 (237–259) | 278 (267–288) | 313 (303–324) | 348 (337–359) | 391 (381–401) |

CI = confidence interval; IM = integrative medicine; COM = conventional medicine.

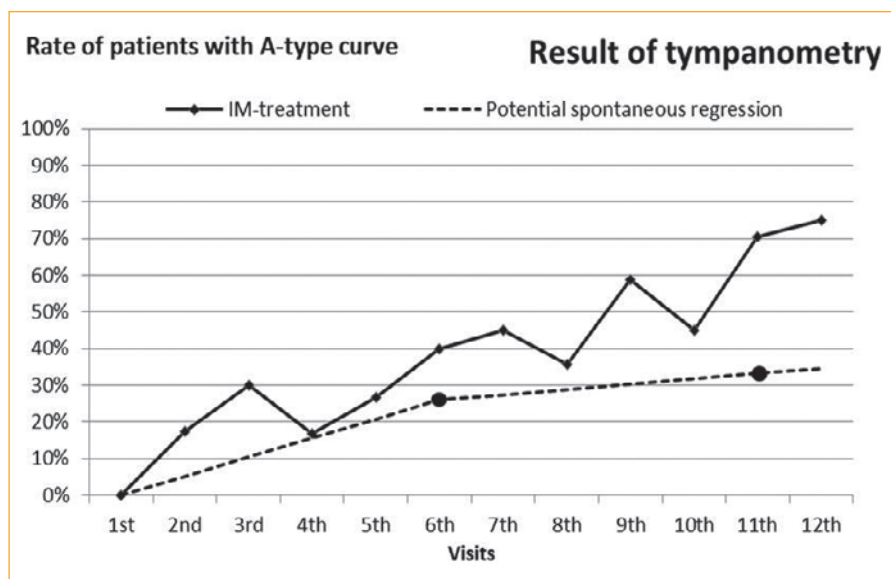


Fig. 5. Improvement in tympanometry in the integrative medicine (IM) group was higher than expected spontaneous regression.

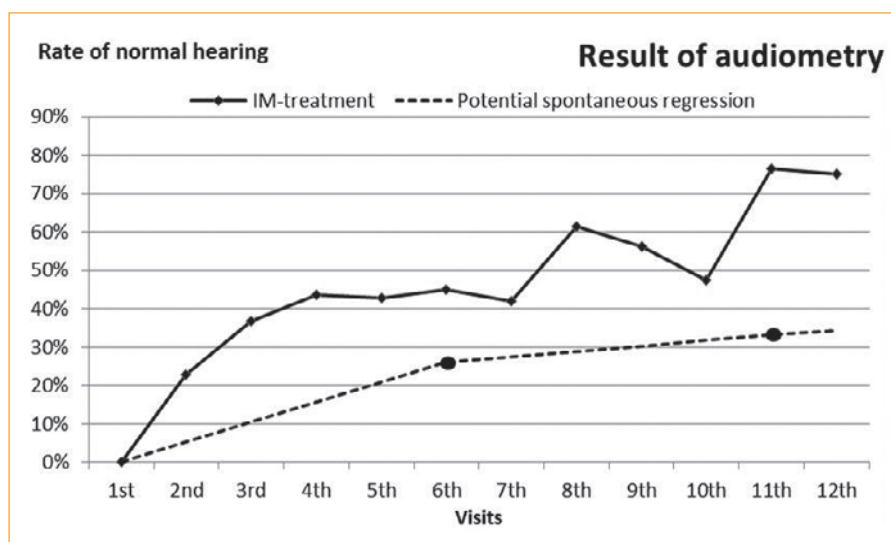


Fig. 6. Improvement in hearing in the integrative medicine (IM) group was higher than expected spontaneous regression.

ther measures were needed to exclude them. Adherence to therapy was similar in the 2 groups; the number of follow-ups was higher in the IM group, although relatively good in both groups, further reducing confounding effects of miscellaneous factors.

In terms of attrition bias, a number of patients had to be excluded from both groups due to non-appearance at follow-up visits. In fact, this was the reason for nearly all of the patients being excluded. In the IM group, 18 patients were excluded due to non-

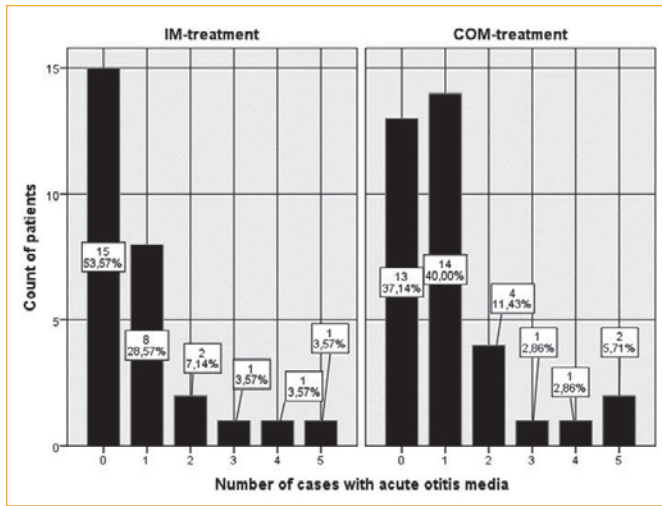


Fig. 7. The number of acute otitis media episodes in the 2 groups during the observational period. The number of episodes was not significantly different between the groups.

completion of the minimum number (3) of visits; the number of exclusions in the COM group for this indication was similar ($n = 20$). The exclusion of these patients is unlikely to result in an attrition bias as there were no statistically significant differences between the groups in terms of clinical characteristics of the excluded patients. Specifically, baseline age (IM group: Mann-Whitney test $p = 0.620$; COM group $p = 0.759$), the number of prior surgical interventions (IM group: Fisher's exact test $p = 1.000$; COM group $p = 1.000$) and the grading of baseline symptoms were all similar. These patients also tended to have similar findings on tympanometric and audiometric evaluations (tympanometric findings IM group: Fisher's exact test $p = 0.642$, COM group $p = 0.068$; audiometric findings IM group: Fisher's exact test $p = 0.163$). In addition, all exclusions occurred within the first 3 months of the observation period. This meant overall that prognostic factors for spontaneous remission and treatment outcomes were similar in the 2 groups for both the excluded and the included patients.

Dropouts during the observational period occurred in both groups mainly due to surgical interventions. Dropout rates were widely different, amounting to only 1 of 28 (4%) after the seventh visit in the IM group, while reaching 14 of 35 (40%) after a mean of 5.64 visits in the COM group. After surgery, data collection was difficult as patients no longer presented for follow-up in our clinic. This represented the single reason for dropping out. Overall, the attrition bias could be estimated as moderate and was unlikely to affect the main findings of the study.

A detection bias was also present as the COM group had inadequate audiometry and tympanometry data, so we needed historical data to create a base for comparison for IM group measurements (expected/potential spontaneous remission). A further observation/reporting bias was possible as audiometry was measured on the worse ear as reported by the parent, a subjective judgment.

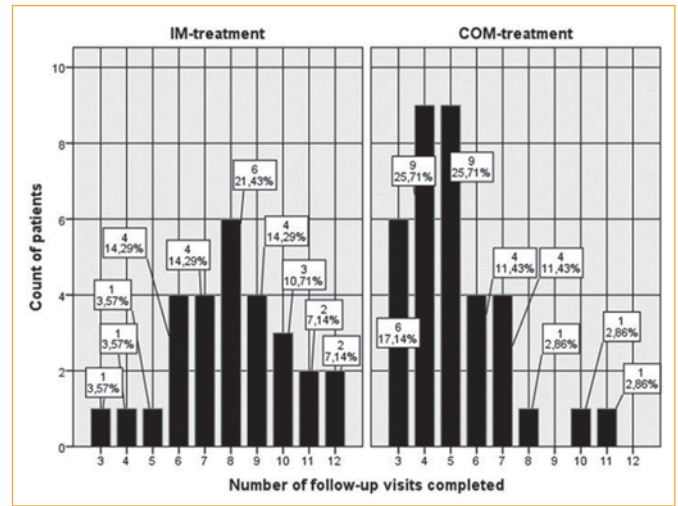


Fig. 8. The number of follow-up appointments kept during the observational period was significantly different in the 2 groups, Mann-Whitney test; $p < 0.001$.

Interpretation and Comparison to Previously Published Work
 This study provides a useful addition to previous data reporting a beneficial effect of integrative measures in treating upper respiratory tract infections in children [34, 39]. Complementary and alternative methods (CAM) are encouraging in this context, although data are insufficient to draw definitive conclusions [40, 41]. There is some research showing that CAM seems to reduce the need for antibiotic and analgesic use [42-46]. However, ours is the first study to introduce a complex IM method in the treatment of chronic otitis media and the first work to evaluate the effectiveness of such a treatment plan with objective outcome measures.

Implications for Practice and Research
 With the caveats mentioned above regarding the generalizability of our present research due to differences in guideline-related practices, our findings seem to suggest the benefit from using alternative treatments during the watchful waiting period that in many cases might eliminate for the need of surgery altogether. These treatments may also obviate the need for antibiotics and analgesics.

As we introduced a quite complex treatment plan with a large number of potentially beneficial components, our study is far too small to distinguish between the individual contributions by each of these components to the total benefit seen in our patients.

Further research is needed with sufficient statistical power to clarify this issue. Some of the examples for potential research is the evaluation of different local nasal preparations or other non-allopathic medications [28], and the individual assessments of pneumatication techniques, external thermal interventions under various climatic and seasonal conditions, anti-allergic therapy and the efficacy of different parent and patient education techniques.

Conclusion
 The complex integrative system approach was effective in reducing hearing loss while also lowering the need for surgical inter-

vention and the use of analgesics and antibiotics in our pediatric patients suffering from COME and AH and associated episodes of recurrent acute otitis media. The integrative approach was safe and well tolerated. Further research is needed to evaluate the efficacy of such treatment.

Dedication

Present scientific contribution is dedicated to the 650th anniversary of the foundation of the University of Pécs, Hungary.

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