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Pediatricians' attitudes in management of acute otitis media and ear pain in Turkey

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ABSTRACT

Objectives: Acute otitis media (AOM) is predominantly a disease of childhood and one of the common reasons for prescribing antibiotics. Ear pain is the main symptom of AOM, with the result that parents frequently seek immediate medical assistance for their children. Antibiotic therapy for AOM does not provide symptomatic relief in the first 24 hours, and analgesics are commonly recommended for relieving the pain associated with AOM. The aims of the present study were to assess pediatricians' attitudes toward AOM and ear pain management in Turkey.

Methods: This multicenter descriptive questionnaire study was conducted in 20 centers from different geographic locations in Turkey, with 977 pediatricians, between June 2015 and December 2016. The questionnaire comprised 20 questions focusing on the pediatricians' sociodemographic variables, experiences, and treatment related to AOM and ear pain.

Results: Of the pediatricians, 58.2% were residents, 36.5% were specialists, and 4.3% were lecturers. Most participants were working in a university hospital (54.8%) or education and research hospital (32.2%). In general daily practice, the AOM diagnosis rates were between 6% and 20% in outpatient clinics, and 52.3% of the participants stated the patients complained about ear pain in pediatric clinics. The watchful waiting (WW) rate, as opposed to immediate antibiotic treatment, was 39.8% for all the pediatricians. The pediatric residents used the WW strategy less than the specialists and lecturers did ($p = 0.004$). The rates of the WW strategy were higher in outpatient clinics where AOM was commonly diagnosed ($p < 0.001$). The most common antibiotic

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prescribed for AOM was amoxicillin clavulanate (76.7%). The mean recommended treatment period for AOM was 9.3 ± 2.2 days. The choices for systemic ear pain treatment were acetaminophen (26.8%), ibuprofen (29.4%), and alternating between ibuprofen and acetaminophen (43.9%). Moreover, 34.6% of the participants recommended topical agents for otalgia. Topical agents were more commonly recommended by the pediatric residents than specialists or lecturers ($p < 0.001$). Finally, 58.3% of pediatricians had experiences of the parents' usage of a variety of herbal and folk remedies, such as breast milk or olive oil, for their children's ear pain.
Conclusion: Amoxicillin clavulanate was the most frequently prescribed antibiotic for AOM. WW was approved by the pediatricians, and having more AOM patients was a significant factor in the physicians' choice of WW; nevertheless, the WW rate was poor. Implementation of educational intervention strategies will help pediatricians in improving their compliance with evidence-based guidelines for AOM treatment. Otalgia is taken seriously by parents and pediatricians, and otalgia treatment seems to be well accepted in Turkey for providing symptomatic relief and enhancing the patients' quality of life.

Abbreviations

AOM Acute otitis media
WW Watchful waiting
A.B and A.K Ayşe Büyükcam and Ateş Kara
SPSS software (version 20.0, SPSS, Inc, Armonk, NY, USA) Statistical Package for the Social Science software (version 20.0, Statistical Package for the Social Science, Incorporated,Armonk, New York, United States of America
S.pneumoniae *Streptococcus pneumonia*
H. influenza *Haemophilus influenza*
M. catarrhalis *Moraxella catarrhalis*

1. Introduction

Acute otitis media (AOM) is one of the most common infectious diseases of childhood, with a varied clinical spectrum ranging from self-limiting to serious complications, such as mastoiditis, meningitis, and sigmoid sinus thrombosis [1–3]. AOM is also a common reason for antibiotic prescriptions in this age group [2,4]. It is characterized by the presence of the rapid onset of signs and symptoms of inflammation in the middle ear space, often following an upper respiratory viral infection with an eustachian tube dysfunction, causing illness and sometimes hearing loss [3–6]. The peak incidence of AOM is between 6 and 15 months, and 50–85% of children have had AOM by the age of 3 years [7].

AOM is the most common cause of ear pain in the pediatric population, and parents frequently seek medical assistance for their children [8]. Ear pain is an emergency condition encountered by parents and pediatricians. However, antibiotic therapy does not provide symptomatic relief for otalgia in the first 24 h; thus, analgesics are recommended for relieving the pain associated with AOM at the beginning of the treatment in almost all guidelines, including that of the American Academy of Pediatrics [4].

The infectious causes of AOM may be bacterial or viral [6]. However, with no treatment, approximately 60% of children recover spontaneously from AOM within 24 h, while approximately 80% of children do so within 3 days [9]. The main reason for treating AOM with antibiotics is to prevent complications. In addition, appropriate and effective AOM treatment has significant effects on child health, healthcare costs, and the development of antimicrobial resistance [10]. However, the compliance with the treatment guidelines for AOM is poor, and there are limited data on the knowledge, attitudes, and management concerning AOM in many countries, including Turkey [6]. Assessment of physicians, including pediatricians' knowledge and attitudes to AOM, with a focus on treatment approaches, is extremely important for understanding the reasons for the barriers between the guidelines and practice [11]. Addressing these knowledge gaps is extremely important when it comes to planning a fundamental intervention strategy [11]. The aim of the present study was to evaluate pediatricians' attitudes concerning the management of AOM including ear pain in relation to their adherence to the AOM treatment guidelines in Turkey.

2. Material and methods

2.1. Study design

This multicenter, descriptive survey of pediatricians' attitudes toward the management of otitis media and ear pain was conducted in 20 centers from different geographic locations in Turkey, with 977 pediatricians, between 1 June 2015 and 30 December 2016. The survey was developed via the consensus of the study authors (A.B. and A.K.) as an anonymous, self-completion questionnaire. Uncomplicated AOM was evaluated, and the questionnaire was piloted by a sample of 20 pediatricians at Hacetttepe İhsan Dogramacı Children's Hospital. The questionnaire was sent via post to 20 pediatric centers in Turkey that agreed to respond to the survey, covering 1100 pediatricians at the centers. Each center was contacted at least three times by phone to ensure the maximum participation on the pediatricians' part. The details of this observational study, as well as the purpose of the research, assurance of participants' privacy, and voluntary nature of participation, were clarified with the centers by phone before beginning the survey. The study was conducted according to Good Clinical Practice and the Declaration of Helsinki, and informed consent was obtained from all the study participants.

2.2. Questionnaire

Twenty questions, grouped into two sections, were included in the questionnaire. In the first section, the questions concerned the pediatricians' general characteristics, including age, gender, workplace (university hospitals, state hospitals, education and research hospitals, private hospitals, or private offices), working years, the participants' and participants' child(ren)' otitis experiences, otalgia pain scores according to the participants, and the frequency of children with AOM and/or otalgia seen each day as primary visits or colleague referrals in the care setting.

In the second section, the questions focused on the treatment approach, including how pediatricians would manage an AOM episode in children, treatment options (immediate antibiotic administration or watchful waiting [WW]), first and second antibiotic choices, treatment duration for otitis media, treatment choice for otalgia (systemic analgesic, topical drops, or alternative treatments like the external application of heat or cold and home remedies), and participants' experiences concerning parents' alternative treatments of their children with AOM and/or otalgia, such as oil drops and human milk.

2.3. Definitions

- **AOM:** The rapid onset of signs and symptoms of inflammation in the middle ear area [4];

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- **Initial antibiotic therapy:** Treatment of AOM with antibiotics prescribed at the time of diagnosis with the intent of starting antibiotic therapy as soon as possible after the encounter [4];
- **Initial observation (watchful waiting):** Initial management of AOM limited to symptomatic relief, with commencement of antibiotic therapy only if the child's condition worsens at any time or does not show clinical improvement within 48–72 h of diagnosis; a mechanism must be in place to ensure follow-up and initiation of antibiotics if the child fails observation [4];
- **University hospital:** The university hospitals in Turkey are tertiary-care hospitals. These hospitals treat outpatients and inpatients, as well as medical student and resident training is provided by lecturers. The durations of medical education for medical students and pediatricians in Turkey are 6 and 4 years, respectively.
- **Education and research hospital:** The education and research hospitals in Turkey are tertiary-care hospitals. These hospitals treat outpatients and inpatients, and only resident education is provided by lecturers.
- **State hospital:** The state hospitals in Turkey are secondary-care hospitals. They treat outpatients and inpatients. The state hospitals do not provide training for medical faculty students or residents.

2.4. Statistical analyses

All data were analyzed using SPSS software (version 20.0, SPSS Inc., Armonk, NY, USA). Continuous variables were described as the mean ± standard deviation and compared using the Student's *t*-test if the variables were normally distributed or the Mann–Whitney U test if the variables were not normally distributed. Normal distribution was determined by histograms and the Kolmogorov–Smirnov test. Categorical variables were described using absolute numbers and percentages and compared using the Chi-square or Fisher's exact test. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

3.1. Study population and characteristics

This was a multicenter descriptive survey of pediatricians. The survey results were based on the responses of 977 pediatricians, for an overall response rate of 89%. The participating pediatricians were from Ankara, İstanbul, İzmir, Bursa, Konya, Eskişehir, Van, Erzurum, Diyarbakır, Ordu, Rize, and Kırklareli, which were considered to represent a larger part of the Turkish population (44.2%, according to the Turkish Statistical Institute, Population of Provinces by Year (2016) [12]. In addition, according to the Health Education and Human Resources Status Report in Turkey-2014 the number of pediatric specialists is 4601 for all of Turkey [13].

The mean age of the participating pediatricians was 32.29 ± 6.9 years, and the median age was 30 years (range: 23–62 years). The female-to-male ratio was 1.8:1. The mean working years of pediatricians was 8.6 ± 7.3 years. Of the participants, 58.2% (n = 566) were pediatric residents, 36.5% (n = 355) were pediatric specialists, and 4.3% (n = 52) were lecturers (assistant professors, associate professors, or professors of pediatrics). Among the surveyed pediatricians, including residents, specialists, and lecturers, 54.8% (n = 531) were from university hospitals, 32% (n = 313) were from education and research hospitals, 9.7% (n = 95) were from state hospitals, and 3.3% (n = 32) were from private hospitals. Similarly, when we excluded resident responders, most of the participants were working in a university hospital (34%) or education and research hospital (36%).

In general daily practice, the AOM diagnosis rates of participants were frequently between 6% and 20% (n = 402) each day in the centers' outpatient pediatric clinics (Fig. 1). In addition, the AOM diagnosis rates of the university hospitals and education and research hospitals were between 6% and 20%, while they were 21–40% in the state hospitals (p = 0.001). Of the participants, 52.3% (n = 508) stated that they encountered ear pain “often,” 13% (n = 126) “very often,” 20.5% (n = 199) “rarely,” and 14.3% (n = 139) “very rarely” in outpatient pediatric clinics in a day (Fig. 2).

Overall, 42% (n = 394) of participants had suffered at least one episode of AOM in their lives, and 50.2% (n = 479) had no children. Moreover, 27.7% (n = 271) of participating pediatricians' child(ren) had experienced ear pain previously. When we asked to score the pain level of ear pain in otitis media on a scale of 1–10 in the pediatricians' daily practice, 61.4% (n = 586) scored ear pain at ≥ 7 points.

3.2. Management of AOM treatment and antibiotic prescription practices

The WW rather than immediate antibiotic treatment rate of the pediatricians was 39.8% (n = 389). However, when we asked about the frequency of WW as primary management, 8.7% (n = 85) and 1.4% (n = 14) of participants stated that they used it “often” and “very often,” respectively.

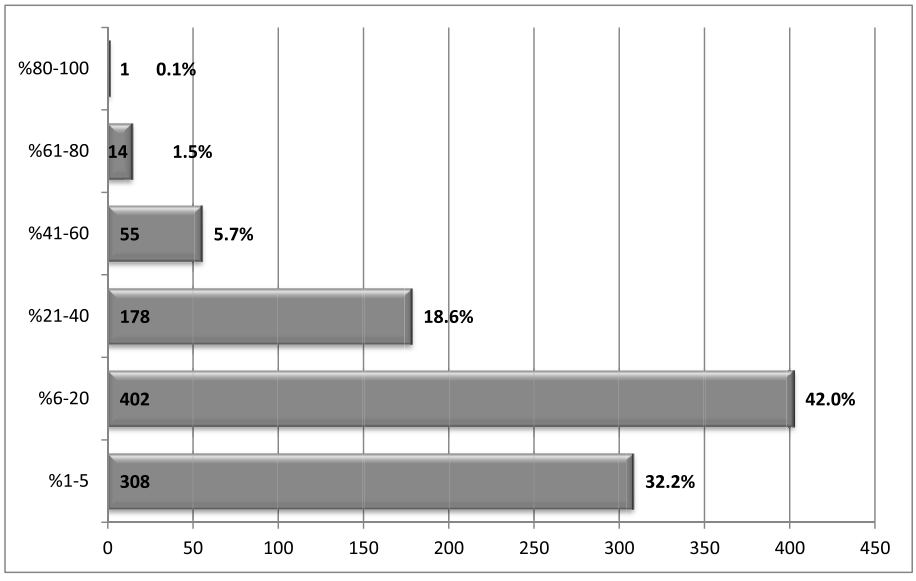


Fig. 1. Frequency of acute otitis media (AOM) diagnosis rates in outpatient pediatric clinics.

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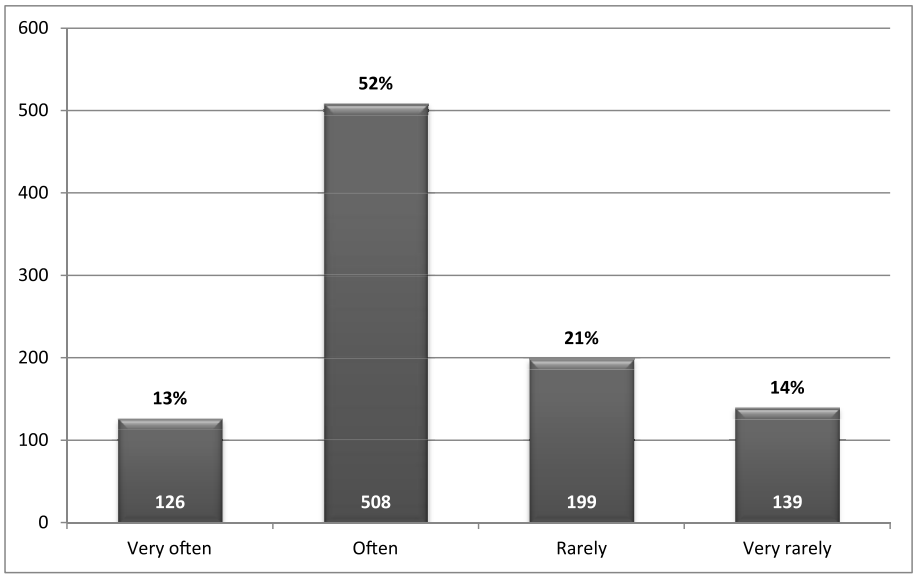


Fig. 2. Frequency of encountering ear pain in pediatric outpatient clinics.

The pediatric residents (37.3%, $n = 201$) preferred to treat AOM primarily with a WW strategy less frequently than the specialists (48.4%, $n = 164$) and lecturers (46.2%, $n = 24$) did ($p = 0.004$). In addition, the rates of adopting a WW strategy were higher in outpatient clinics where there were augmented AOM diagnosis rates and it was commonly diagnosed ($p = 0.001$).

The participants stating that they encountered ear pain "very often" (47.5%) implemented WW more than the "often" (45.9%), "rarely" (34%), and "very rarely" (32.6%) groups did ($p = 0.003$). The participants that had children performed WW more often than the group that had no children did ($p = 0.031$). There were no differences in the WW strategy in terms of the workplace groups ($p = 0.622$) or whether the participants had suffered at least one episode of AOM in their lives ($p = 0.084$).

Most of the participating pediatricians (76.7%, $n = 749$) preferred to prescribe amoxicillin clavulanate, followed by amoxicillin (12.6%, $n = 123$) and ampicillin–sulbactam (2.3%, $n = 122$) as the first-line choice of antibiotic therapy for AOM. The highest percentage (15.4%) of amoxicillin prescribing was reported in university hospitals among the workplace groups. The most common second-line choices were cephalosporins (74.6%, $n = 283$) and macrolides (7.2%, $n = 54$) among the pediatricians that initially preferred amoxicillin clavulanate. Cefuroxime (26.8%, $n = 76$), cefdinir (23.6%, $n = 67$), and cefuroxime axetil (19%, $n = 54$) were the most commonly prescribed antibiotics in the cephalosporin group. The factors of participants' having a child or suffering at least one episode of AOM in their lives did not affect the first-line choice ($p = 0.106$, $p = 0.672$).

The duration of the recommended AOM treatment varied between 3 and 21 days without an age range. The mean recommended AOM treatment period was 9.3 ± 2.2 days. Most of the antibiotic prescriptions (85.7%, $n = 819$) were for 7- to 10-day treatments.

3.3. Management of otalgia treatment and experience of alternative treatments

Approximately 97.1% ($n = 949$) of the participating pediatricians recommended analgesic treatment for otalgia, while 2% ($n = 20$) did not. The choices of oral medications were acetaminophen (26.8%, $n = 246$), ibuprofen (29.4%, $n = 270$), and alternating between ibuprofen and acetaminophen (43.9%, $n = 403$). The pediatric residents (47.5%, $n = 248$) preferred to prescribe alternating treatments more than specialists (42%, $n = 144$) or lecturers (20%, $n = 10$) did ($p = 0.001$). The participants from state (61.3%) and private hospitals (61.3%) indicated that they mostly used alternating treatments for otalgia. The participants that stated they encountered ear pain "very often" preferred an alternating treatment (54.8%) more than the "often" (45%), "rarely" (34.2%), and "very rarely" (43.7%) groups did.

Among the pediatricians who recommended analgesic treatment, 34.8% ($n = 325$) also suggested topical analgesics for otalgia (Table 1). The most common reason for disapprobation of topical treatment in responders was the assessment of topicals as ineffective (Table 2).

Topical agents were more commonly recommended by the pediatric residents than they were by the specialists and lecturers ($p = 0.001$). The participants that suggested topical agents (mean age = 30.7 ± 6 years) were more likely to be younger than the pediatricians who did not (mean age = 33 ± 7.2 years). Among the workplace groups, the participants from private hospitals recommended using topical drugs more commonly (54.8%) than the other groups did ($p = 0.045$).

Based on their knowledge, only a minority of participants (9.2%, $n = 90$) indicated a preference for alternative approaches to otalgia treatment, including the external application of heat or cold. Approximately 58.3% ($n = 565$) of participating pediatricians had experiences with the parents' usage of a variety of herbal folk remedies and other topical agents, such as breast milk or olive oil, for their children's ear pain (Fig. 3).

Table 1
Participants' treatment preferences for otalgia.

	Pediatric resident	Pediatric specialist	Lecturer
	n (%)	*n* (%)	*n* (%)
Systemic Treatment			
Acetaminophen	137 (26.2)	85 (24.8)	23 (46.0)
Ibuprofen	137 (26.2)	114 (33.2)	17 (34.0)
Alternating	248 (47.5)	144 (42.0)	10 (20.0)
Total	**522 (100)**	**343 (100)**	**50 (100)**
Topical Treatment			
Yes	233 (42.2)	90 (25.6)	9 (17.6)
No	308 (55.8)	249 (70.7)	41 (80.4)
Other	11 (2)	13 (3.7)	1 (2)
Total	**552 (100)**	**352 (100)**	**51 (100)**

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Table 2
Reasons for disapproval of topical analgesic treatment for otalgia.

Reasons	*n*	%
Topical analgesic treatment is ineffective or controversial	51	37.2
I do have limited or no experience with this	20	14.6
Systemic analgesic treatment is adequate or efficacious	23	16.8
There are side effects/complications	14	10.2
It should be used only for the otitis externa	16	11.7
Topical analgesic treatment is not necessary/insignificant	13	9.5
Total	137	100

4. Discussion

The objectives of this study were to identify the pediatricians' attitudes and management of otitis media and ear pain in Turkey. To our knowledge, few studies have compared the attitudes of pediatricians concerning AOM in children [6,10,14,15]. Furthermore, our study is one of the few studies to evaluate not only antibiotic prescriptions, but also ear pain management [15]. The 977 participating pediatricians were from the major cities, representing a large segment of the Turkish population. The questionnaire response rate was high. Our findings likely provide an accurate picture of pediatricians' attitudes toward otitis media and ear pain management in Turkey.

In our study, we only discussed cases of simple, uncomplicated AOM as the diagnosis. The treatment could be more controversial in complicated AOM cases.

Our findings showed that amoxicillin clavulanate remained the most widely administered first-line antibiotic for AOM; this was followed by amoxicillin among the participating pediatricians that preferred amoxicillin clavulanate as the first treatment, regardless of age and out of line with the AOM treatment guidelines. There could be several possible explanations for this. Amoxicillin clavulanate is an effective broad-spectrum agent for all the main bacterial pathogens, namely *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*. AOM is usually diagnosed clinically rather than by microbiological diagnostic tests [16]. The antibiotic susceptibility of the major AOM bacterial pathogens continues to change, but the data on middle ear pathogens for antibiotic resistance is unsatisfactory, as tympanocentesis is not generally performed in studies of children with uncomplicated AOM [17]. The impossibility of clinically distinguishing *S. pneumoniae* from nontypeable *H. influenzae* and *M. catarrhalis* in AOM and the fear of serious complications, such as mastoiditis, or skepticism about the clinical guidelines regarding the first-line recommended treatment may affect the pediatricians' first-line antibiotic choice [6]. In our study, the highest percentage (15.4%) of amoxicillin prescription was observed in university hospitals. This finding concerning the workplace groups may be related to the better and more frequent training of pediatricians at university hospitals, contributing to broader knowledge on the appropriate approach to AOM treatment. We think that specific educational programs may be one of the effective solution for increasing the implementation of AOM treatment guidelines, as some studies have revealed that training programs, clinical decision support, and performance feedback could change physicians' adherence to AOM treatment [15,18,19].

This study was conceived in 2015–2016, when the AOM treatment guidelines recommended not only antibiotic therapy as the first treatment option, but also a 24- to 48-h period of WW “without administration of antibiotics in children > 6 months age without severe diseases” as an alternative option for AOM in childhood. Most children with AOM spontaneously remit without complications [20]. In our study, the pediatricians' percentage of WW adoption rather than immediate antibiotic treatment was 39.8%, but in terms of the frequencies, it was interesting to find that 8.7% and 1.4% of the participants stated that they used WW as the primary treatment “often” and “very often,” respectively, whereas the rates of the WW strategy increased where the diagnosis rates of AOM were higher and it was commonly diagnosed ($p = 0.001$). The participants' greater approval of WW with increased AOM practice was a significant factor, but overall, the use of WW was poor. In addition, there was no effect on the WW adoption of the participants who had suffered at least one episode of AOM in their lives or not. It may be that the potentially increased risk of mastoiditis was a factor, as different methodologies have been used to calculate the incidence of mastoiditis when WW is implemented, with conflicting results, which may have negatively influenced the adherence rate [10,21]. Other possible factors are the effect of parent/caregiver education combined with shared decision making, as well as parents' satisfaction and anxiety. Following up the children at home and timely re-evaluation are necessary in WW, and parents' anxiety sometimes does not permit WW treatment. In addition, parents' satisfaction may be influenced by personal beliefs and preconceptions about observation, as well as insufficient knowledge. Most parents prefer using antibiotics over observation [6,21]; however, spending more time with parents to adequately explain observation, so that they feel involved in

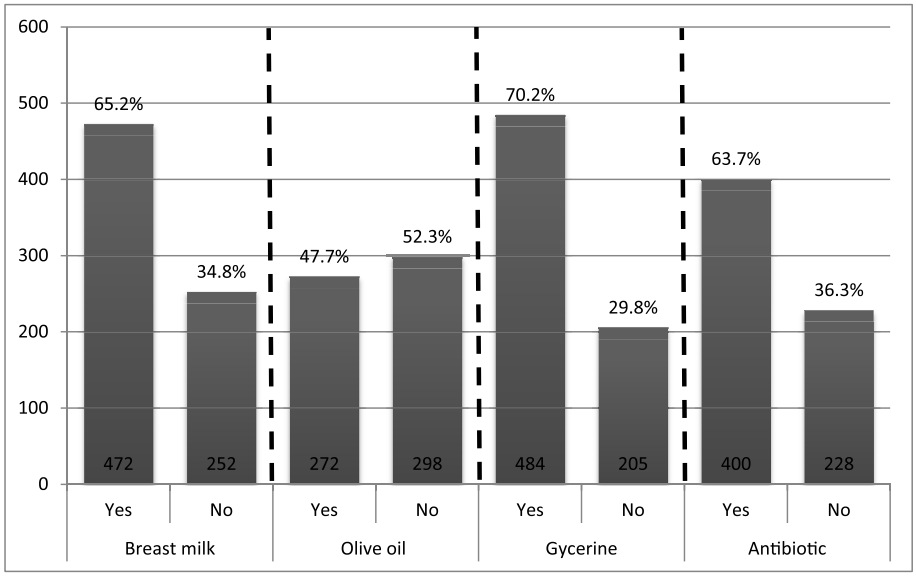


Fig. 3. Participants' experience concerning parents' topical administrations of remedies for ear pain in their children.

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the decision making, would provide them with confidence in and satisfaction with their doctors' choice of WW, making this approach more acceptable to them [18,22].

Middle ear pain is the main symptom of AOM [17,23]. Poorly controlled pain results in patients' anxiety, and parents frequently seek medical assistance or alternative treatments for their children [24]. Pain control should be actively performed, regardless of whether the initial treatment includes immediate antibiotics [24]. Antibiotic therapy for AOM does not provide symptomatic relief in the first 24 h; thus, analgesics are the cornerstone of AOM-associated otalgia treatment in children, and relief of pain due to AOM at the beginning of treatment is recommended [17,23]. In addition, it seems that otalgia is taken seriously by both pediatricians and parents in Turkey in our study.

There are many options for otalgia treatment, including oral, topical, and homeopathic agents, but there is much debate concerning its management and limited data on the effectiveness of pain remedies, especially in terms of topical and homeopathic agents [17,24]. Acetaminophen and ibuprofen as a choice of monotherapy seem more effective than a placebo in otalgia, but high-quality evidence is absent in the literature, despite the AOM treatment guideline recommendations [24]. Alternating between ibuprofen and acetaminophen (43.9%) was the most common preference in our study. In practice, ibuprofen and acetaminophen are frequently alternated in the treatment of fever or pain in children, although evidence is lacking concerning both the safety and efficacy of this usage [25]. The concomitant use of acetaminophen and ibuprofen in children (0–12 years) may be associated with an increased risk of acute kidney injury [25].

Some studies have advocated that both anesthetic and naturopathic topical drops help in relieving ear pain without systemic side effects, but it is unclear whether the effect of topical drops is a result of their pharmacological effects, the natural course of the illness, the placebo effect of receiving treatment, or the soothing effect of any liquid in the ear [26]. There are insufficient data to make any conclusions about the effectiveness of ear drops in this regard [17]. Home remedies, distraction, external application of heat or cold, and oil drops in the external auditory canal may have some benefit, but high-quality evidence does not exist to support their use [17]. Additional well-designed trials are needed, and the clinicians should select drugs for otalgia based on their benefits and risks.

Our study had some limitations. It was a descriptive, rather than a cross-sectional study. We did not ask about complicated AOM in the survey, as the treatment decisions in such cases may be more complex and controversial for clinicians. In addition, the survey was evaluated by pediatricians according to their statements, without any direct evaluation of their actual prescriptions.

5. Conclusions

Our series is one of the large-scale studies assessing pediatricians' attitudes toward and management of AOM and ear pain. Pediatricians adopt different therapeutic approaches for AOM and ear pain in Turkey. Awareness of the pediatricians' antibiotic prescription patterns is becoming important due to antibiotic resistance. Our study highlights the importance of selecting WW and administering empirically selected antibiotics in certain conditions, and this point will help in preventing the medical, economic, and social problems associated with unnecessary prescriptions. The implementation of educational intervention strategies will help pediatricians in improving their compliance with evidence-based guidelines for AOM treatment.

Otalgia treatment seems to be used commonly in Turkey. However, pediatricians must be careful in alternating between ibuprofen and acetaminophen due to growing evidence of adverse events resulting from such treatment. More high-quality studies are needed for assessing the safety of alternating antipyretic therapies and other analgesics, such as eardrops.

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Conflicts of interest

The authors have indicated they have no potential conflicts of interest to disclose.

Clinical trial registration

None.

Contributors' statements

Dr. Büyükcam and Prof.Dr. Kara conceptualized and designed the study, coordinated and supervised data collection, collected data in their hospital, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Bedir, Dr. Gülhan, Dr. Özdemir, Dr. Sütçü, Dr. Düzgöl, Dr. Arslan, Dr. Tekin, Prof. Dr. Çelebi, Dr. Kukul, Dr. Bayhan, Dr. Köşker, Dr. Karbuz, Dr. Çelik, Dr. Kocabay Sütçü, Dr. Metin, Dr. Karakaşlılar, Dr. Dağlı, Dr. Sertan Kara, Dr. Albayrak, Dr.Kanık,Prof. Dr.Tezer, Associate Prof. Dr.Aslınur Parlakay, Prof. Dr.Ergin Çiftci, Prof.Dr. Ayper Somer, Associate Prof.Dr.İlker Devrim, Prof.Dr.Zafer Kurugöl, Prof.Dr.Ener Çağrı Dinleyici, Dr.Pınar Atla collected data in their hospital, carried out the initial analyses of their hospital survey data and drafting the article.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ijporl.2018.01.011.

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