Clinical practice guidelines for the diagnosis and management of acute otitis media (AOM) in children in Japan

Subcommittee of Clinical Practice Guideline for Diagnosis and Management of Acute Otitis Media in Children (Japan Otological Society, Japan Society for Pediatric Otorhinolaryngology, Japan Society for Infectious Diseases in Otolaryngology)

Received 11 July 2011; accepted 21 October 2011
Available online 23 December 2011

Abstract

Objective: To (1) indicate methods of diagnosis and testing for acute otitis media (AOM) in children (under 15 years of age); and (2) recommend methods of treatment in accordance with the evidence based consensus reached by the subcommittee on clinical practice guidelines for the diagnosis and management of AOM in children (subcommittee on clinical practice guidelines), in light of the causative bacteria of AOM in Japan and their susceptibility to antimicrobial agents.

Methods: We investigated the most recently detected bacteria causing childhood AOM in Japan as well as their antimicrobial susceptibility, developed clinical questions concerning the diagnosis, testing methods, and treatment of AOM, searched the literature published during 2000–2004, and issued the 2006 guidelines. In the 2009 guidelines we performed the same investigation with the addition of literature that was published during 2005–2008 and that was not included in the 2006 guidelines.

Results: We categorized AOM as mild, moderate, or severe on the basis of otoscopic findings and clinical symptoms, and presented a recommended treatment for each degree of severity.

Conclusion: Accurate assessment of otoscopic findings, as well as other signs and symptoms, is important for judging the degree of severity and selecting a method of treatment.

Keywords: Acute otitis media (AOM); Antimicrobial agent; Clinical practice guideline; Myringotomy; Multidrug-resistant bacteria; Recurrent otitis media (ROM)

1. Introduction

Acute otitis media (AOM) is a typical upper respiratory inflammation commonly affecting children and is mainly treated by otolaryngologists. Its exact frequency of occurrence in Japan is unknown, however. According to reports from Europe and the US, 62% of children aged less than one year and 83% of those up to the age of three have suffered from at least one bout of AOM [1]. Faden et al. [2] have reported that it affects 75% of children up to the age of one.

Some authors in Europe and the US do not recommend the use of antimicrobial agents for AOM. In the Netherlands, it has been proposed that antimicrobial agents are unnecessary in at least 90% of cases, and that patients should be observed for 3–4 days without antimicrobial agent administration [3,4]. Rosenfeld et al. have also reported observation as a management option [5–7], and more recent
studies have also found no significant difference in clinical outcome if antimicrobial agents are not given immediately but rather are prescribed if there is no improvement in symptoms after 48 or 72 h [8,9]. A Cochrane review that examined randomized controlled trials of antimicrobial agent administration versus placebo also found that antimicrobial agents had little effect on childhood AOM [10]. In addition, a double-blind randomized controlled trial of amoxicillin (AMPC) and a placebo found no significant difference in therapeutic efficacy between the two [11,12]. Dagan et al. [13,14] and Toltzis et al. [15], in a review and case-control study, advised that antimicrobial agent use would be reduced because the use of a wide variety of antimicrobial agent increases the survival of resistant Streptococcus pneumonia (S. pneumonia) in the nasopharynx, which can cause additional infections in middle-ear (ME) fluid.

In Japan, regular nationwide surveys are performed of the causative bacteria for AOM, acute sinusitis, acute tonsillitis, and peritonsillar abscess. These surveys have reported that multidrug-resistant bacteria are now being detected more frequently [16,17], which means that the recommendation to avoid administration of antimicrobial agents proposed in Europe and the US does not apply. In addition, the criteria and assessment levels used in conventional clinical assessment are not necessarily uniform even within Europe and the US [18]. Investigation and unified evaluation of the diagnosis and treatment of childhood AOM are therefore required, based on the actual situation in Japan. Based on this perspective, the Japan Otolaryngological Society (JOS), the Japan Society for Infectious Diseases in Otolaryngology (JSIDO), and the Japan Society for Pediatric Otorhinolaryngology (JSPO) produced 2006 clinical practice guidelines consistent with evidence-based medicine (EBM) [19] with the aim of supporting the diagnosis and treatment of childhood AOM [20–23], which was revised and published in 2009 [24].

This paper introduces extracts of the important parts of our 2009 edition of clinical practice guideline for diagnosis and management of AOM in children.

2. Users

The main users of these guidelines will be otolaryngologists who perform otological procedures including the accurate evaluation of otoscopic findings and myringotomy.

3. Subjects

The subjects of these guidelines are AOM patients aged <15 years who were free from AOM or otitis media with effusion (OME) within one month prior to onset, who do not have a tympanostomy tube inserted, who have no craniofacial abnormality, and who do not suffer from immunodeficiency. Patients with the following conditions are excluded as subjects: AOM with complications including facial palsy and inner ear disorder, elevated pinna with acute mastoiditis, and AOM with Gradenigo’s syndrome or similar findings. It can be difficult to distinguish between AOM and bullous myringitis, but the latter is not covered by these guidelines.

4. Gathering evidence

For the 2006 guidelines, PubMed and Japan Centra Revuo Medicina Web version 3 were used, and for the 2009 guidelines, PubMed, the Cochrane library, and Japan Centra Revuo Medicina Web version 4 were used.

5. Criteria for deciding recommendation grades

The method proposed by the Japan Stroke Society to indicate the level of evidence was used in the preparation of these guidelines, as shown below.

5.1. Level of evidence

Ia Meta-analysis (with homogeneity) of randomized controlled trials.

 Ib At least one randomized controlled trial.

IIa At least one well-designed, controlled study but without randomization.

IIb At least one well-designed, quasi-experimental study.

III At least one well-designed, non-experimental descriptive study (e.g., comparative studies, correlation studies, case studies).

IV Expert committee reports, opinions and/or experience of respected authorities.

Recommendation grades were determined based on the evidence obtained by the search policies described above and the anticipated degree of benefit or harm. During this process, reference was made to items according to the proposed grades outlined below. Five levels of recommendation grades were established, based on the US Preventive Services Task Force report (http://www.uspreventiveservicestaskforce.org/uspstf08/methods/proctab4.htm).

A: Strongly recommended: strong evidence is available, benefits substantially outweigh harms.

B: Recommended: fair evidence is available, benefits outweigh harms.

C: No recommendation made: fair evidence is available, but the balance of benefits and harms is close.

D: Recommended against: harms outweigh benefits.

E: Insufficient evidence to determine the balance of benefits and harms.

The specification of recommendation grades is one of the most important roles expected of clinical practice
guidelines, but there is great debate concerning the sort of factors that should be taken into account when determining recommendation grades. The subcommittee on clinical practice guidelines made overall judgments taking into consideration the factors below, with reference to the proposals of Fukui and Tango (guide to the preparation of clinical practice guidelines, 4th edition) [25] and of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group [26].

- Level of evidence.
- Quality of evidence.
- Consistency of evidence (supported by multiple studies).
- Directness (magnitude of clinical efficacy, external validity, indirect evidence, evaluation by surrogate outcomes).
- Clinical applicability.
- Evidence concerning harm or costs.

No Level I study reports on AOM in Japan were found. Accordingly, Grade A recommendations were determined based on the existence of at least one piece of Level I evidence from Europe or the US that was judged by the committee to be applicable to Japanese circumstances. The condition for determination of Grade B recommendations was the existence of at least one piece of Level II evidence demonstrating efficacy that was judged by the committee to be applicable to Japanese circumstances.

Opinions on these recommendations were solicited from the directors and executive committee members of the JOS, the JSIDO, and the JSPO before the final decision was made by the Subcommittee on clinical practice guidelines. The committee endeavored to maintain objectivity and transparency when deciding on recommendation grades, but it was not possible to guarantee this in every case.

A system will be put in place in the future for accepting comments and suggestions from users concerning the content of recommendations and recommendation grades, with a view to the future revision of these guidelines.

6. Pre-release review

Before these guidelines were released for general use, they were reviewed with reference to the Conference on Guideline Standardization (COGS) proposals concerning publication format [27] and the Appraisal of Guidelines for Research & Evaluation (AGREE) appraisal instrument for assessing content [28].

Before publication of the 2006 edition of the guidelines, opinions were solicited from the JOS, JSIDO, and JSPO, and pediatricians, and corrections were made where necessary. Otolaryngologists, regarded as the general users of the guidelines, were also surveyed regarding the utility of the guidelines in the clinical setting, and the results were reflected where appropriate.

7. Diagnosis and examinations

7.1. Clinical question 1: under what conditions is AOM diagnosed?

7.1.1. Recommendation

AOM is diagnosed when the following tympanic membrane findings are recognized, and thus, detailed inspection of the tympanic membrane is indispensable for its diagnosis (level of recommendation grade: B; hyperemia, protrusion, diminishment of the light reflex, thickening, bullar formation, cloudiness (turbidity), and perforation of the tympanic membrane, MEE, otorrhea, edema of middle-ear mucosa; references used to assess this recommendation level: Rosenfeld et al. [29] (Level IIb)).

Addendum

Otomicroscopic or otoendoscopic observation of the tympanic membrane is most desirable, but a recent modeling with a pneumatic otoscope is also acceptable.

7.1.2. Background

As AOM is acute inflammation of the middle-ear mucosa, confirmation by inspection of the findings of the tympanic membrane manifesting middle-ear inflammatory effusion and/or inflammatory change is indispensable for its diagnosis.

7.2. Clinical question 2: how is the severity of AOM assessed?

7.2.1. Recommendation

Severity of AOM is classified as mild, moderate and severe according to otoscopic findings and clinical manifestations (level of recommendation grade A).

References used to assess the recommendation level: Hotomi et al. [30,31] (Level IIa), Friedman et al. [32] (Level Ib), Biner et al. [33] (Level Ib).

Manifestations and findings and their scores used for classification of the severity of AOM (proposal from the Subcommittee on clinical practice guidelines)

- 3 points are automatically given below the age of 24 months.
- Otalgia is scored as 0, 1, or 2. 0: absent; 1: present; 2: present-continuous severe pain.
- Fever (axilla) is scored as 0, 1, or 2. 0: under 37.5 degrees centigrade (°C); 1: higher than 37.5 °C but under 38.5 °C; 2: higher than 38.5 °C.
- Crying and/or bad temper is scored as 0 or 1. 0: absent; 1: present.
7.3.1. Improvement of otoscopic examination

- Hyperemia of the tympanic membrane is scored as 0, 2, or 4. 0: absent; 2: present at the manubrium of malleus, or in a part of the eardrum; 4: present in the whole tympanic membrane.
- Protrusion of the tympanic membrane is scored as 0, 4, or 8. 0: absent; 4: present in a part of the tympanic membrane; 8: present in the whole tympanic membrane [34].
- Otorrhea is scored as 0, 4, or 8. 0: absent; 4: present but the tympanic membrane is visible; 8: present and obstructing visibility of the tympanic membrane.
- Condition of the light reflex of the tympanic membrane is scored as 0 or 4. 0: normal; 4: diminished or absent due to turbidity.

Classification of severity of AOM according to the total score

- Mild – ≤9
- Moderate – 10–15
- Severe – ≥16.

7.3.2. Background

For AOM, the treatment must be matched appropriately to the disease severity. In patients of younger age, there is often a discrepancy between the general condition and the tympanic membrane findings during the convalescent stage of AOM; that is, the general condition is often much improved even though the tympanic membrane findings are not [30,31]. Thus, a precise assessment of the tympanic membrane findings and thereby the severity of AOM will lead to a more appropriate choice of treatment [33].

7.3. Clinical question 3: is tympanometry useful to diagnose acute otitis media?

7.3.1. Recommendation

Tympanometry is recommended to identify the presence of MEE after the diagnosis of AOM is confirmed by a precise otoscopic finding (level of recommendation grade: B; references used to assess the recommendation level: Saeed et al. [35] (Level IIa)).

7.3.2. Background

Tymanometry is a reliable test to identify the presence of MEE in the tympanic cavity. Acoustic reflectometry, which has been recommended to identify the effusion in European countries and the US, is not recommended in Japan because it has not been available since 1994.

8. Treatment

The outcome of the treatment recommended by the present guidelines is defined by improvement of otoscopic findings such as hyperemia, protrusion, diminishment of the light reflex, thickening, bullar formation, cloudiness (turbidity), and perforation of the tympanic membrane, MEE, otorrhea, and edema of middle-ear mucosa at the time point of 3 weeks after onset. A score of 0 for the tympanic membrane and clinical manifestations except for age factor (under 24 months) is judged as cure of AOM.

A patient who has already received antimicrobial agents is, taking prescribed antimicrobial agents and their doses into consideration, also classified as having mild, moderate or severe AOM based on tympanic membrane findings, and clinical manifestations at the examination. In addition, the proposed algorithm in these guidelines should be adopted in consideration of the severity of AOM (Figs. 1–3).

8.1. Clinical question 1: is it reasonable not to administer antimicrobial agents for mild AOM?

8.1.1. Recommendation

Watchful waiting for 3 days without use of antimicrobial agents is recommended for mild AOM (level of recommendation grade: A; references used to assess the recommendation level: Damoiseaux et al., 2000 [4] (Level Ib), Glasziou et al., 2000 [36] (Level Ia), Little et al., 2006 [9] (Level IIa)).

---

![Fig. 1. Treatment algorithm of acute otitis media of mild grade (score 0–9).](image-url)
8.1.2. Background

It has been reported that most cases of AOM improve without use of antimicrobial agents [3,4,6,7,36,37]. However, as the incidence of AOM caused by multidrug-resistant bacteria is high in Japan, it is important for us to diagnose mild AOM precisely by the findings of the tympanic membrane, and to follow a child strictly when we do not use antimicrobial agents.

8.2. Clinical question 2: which antimicrobial agents should be used for AOM?

8.2.1. Recommendation

Recommended antimicrobial agents depending on bacterial resistance and the severity of AOM are as follows:

P.O.: amoxicillin (AMPC), clavulanate/amoxicillin (CVA/AMPC [1:14] formulation), cefditoren pivoxil (CDTR-PI); and DIV: ampicillin (ABPC), ceftriaxone (CTRX) (level of recommendation grade: A) (references used to assess the recommendation level: Ghaffar et al. [38,39] (Level Ib), Piglansky et al. [40] (Level Ib), Haiman et al. [41] (Level Ib).

8.2.2. Background

Currently in Japan: about 50–60% of S. pneumoniae and about 50–70% of Haemophilus influenzae strains are multidrug-resistant, and it is recommended that the above antimicrobial agents should be chosen corresponding to the severity of AOM based on the susceptibility against pathogens. This does not mean that other antimicrobial agents are not recommendable, but rather that the above antimicrobial agents are recommended in consideration of the current condition of drug sensitivity of bacteria in Japan.

Fig. 2. Treatment algorithm of acute otitis media of moderate grade (score 10–15).

Fig. 3. Treatment algorithm of acute otitis media of severe grade (score ≥16).
8.3. Clinical question 3: what are appropriate indications for myringotomy?

8.3.1. Recommendation

The indications should be considered depending on the severity of AOM (level of recommendation grade: I).

8.3.2. Background

In AOM, there is fluid accumulation due to inflammatory pathology in the middle ear, and therefore drainage of the inflammatory fluid by myringotomy would be efficient for early cure of the disease. However, currently there are only a limited number of studies about the clinical efficacy of myringotomy for the early cure of the disease.

8.4. Clinical question 4: risk factors deteriorating AOM

8.4.1. Recommendation

Since younger age and day-care attendance have an important role on deterioration of the disease, attention should be paid during the treatment (level of recommendation grade: A) (references used to assess the recommendation level: Ovetchkine and Cohen [42] (Level la)).

In cases of AOM associated with nasal disease, nasal treatments should be considered as complementary to the treatment of AOM (level of recommendation grade: I).

8.4.2. Background

It is requisite to treat AOM as an upper respiratory infection in considering the background of AOM being to be serious.

9. Recurrent otitis media (ROM)

9.1. Definition of ROM

The definition of ROM has yet to be standardized either in Japan or internationally, but in these guidelines it has been defined as three or more occurrences of AOM within the previous six months, or four or more within the previous 12 months, as generally used in comparatively recent studies [43–45].

9.2. Pathophysiology of and risk factors for ROM

The pathophysiology of ROM can be categorized into two types: recurrent simple AOM, and recurrent AOM occurring as an acute exacerbation in patients suffering from OME.

Proposed risk factors for ROM include young age, multidrug-resistant causative bacteria, immunity of the affected individual, and lifestyle and environmental factors. Genetic make-up has also been reported as a risk factor in young children aged <2 years [46]. In terms of causative bacteria, multidrug-resistant pneumococci are reportedly responsible in many cases [47], with incomplete elimination from the nasopharynx owing to reduced antimicrobial agent efficacy regarded as one cause of recurrence. The involvement of decreased immune response by the host to the causative bacteria is also important [48]. It has also been conjectured that there is a link between immunity received from the mother via breast milk and the onset of ROM, with the absence of breastfeeding constituting a strong risk factor for ROM [49]. Lifestyle and environmental risk factors include having siblings, attending daycare, and pacifier use [49].

9.3. Treatment of ROM

With the factors described above assumed to constitute risk factors for ROM, bacterial sensitivity tests must always be carried out prior to antimicrobial agent administration to counteract resistant causative bacteria, and an appropriate dose of antimicrobial agents must be selected. Recommended antimicrobial agents are listed in these guidelines.

Pneumococcal conjugate vaccine is used in Europe and the US to prevent ROM. In a double-blind randomized controlled trial of a 7-valent pneumococcal conjugate vaccine and pneumococcal polysaccharide vaccine in Holland, there was no significant reduction in the frequency of occurrence of ROM [50]. Although a Cochrane review accepts the utility of pneumococcal polysaccharide vaccine, it does not recommend the conjugate vaccine [51]. In a double-blind randomized controlled trial in the Czech Republic, however, 11-valent pneumococcal capsular polysaccharide vaccine conjugated to H. influenzae-derived protein D had a significant protective effect against AOM caused by pneumococci or non-typable H. influenza [52]. In Japan, 7-valent pneumococcal conjugate vaccine was approved for use in 2010. This vaccine covers 60.6% of pneumococcal serotypes isolated from the middle ears of childhood AOM patients in Japan and 87% of multidrug-resistant bacteria, and is anticipated to provide up to about 17% protection against all forms of AOM.

One form of treatment unique to Japan that has been proposed is the use of Chinese herbal medicines for their protective effect in boosting immunity, and Juzentaihoto has been reported as effective [53].

Adenoidectomy has not been shown to reduce the frequency of ROM as a surgical treatment in double-blind randomized controlled trials, nor is it regarded as having any preventive effect [54–56]. Myringotomy has not been shown to have any significant effect in reducing the frequency of occurrence of ROM in research on patients in Japan [57], but insertion of a tympanostomy tube for one year and short-term insertion for one month significantly reduce the frequency of occurrence [58,59]. As measures to deal with lifestyle and environmental factors, discontinuation of attendance of group daycare and breastfeeding are desirable.
References


