Efficacy of Naturopathic Extracts in the Management of Ear Pain Associated With Acute Otitis Media

E. Michael Sarrell, MD; Avigdor Mandelberg, MD; Herman Avner Cohen, MD

Objective: To determine the efficacy and tolerance of Otikon Otic Solution (Healthy-On Ltd, Petach-Tikva, Israel), a naturopathic herbal extract (containing Allium sativum, Verbascum thapsus, Calendula flores, and Hypericum perforatum in olive oil), compared with Anaesthetic (Vitamed Pharmaceutical Ltd, Benyamina, Israel) ear drops (containing ametocaine and phenazone in glycerin) in the management of ear pain associated with acute otitis media (AOM).

Design: Children between the ages of 6 and 18 years who experienced ear pain (otalgia) and who were diagnosed with eardrum problems associated with AOM were randomly assigned to be treated with Otikon or Anaesthetic ear drops, which were instilled into the external canal(s) of the affected ear(s). Ear pain was assessed using 2 visual analog scales: a linear scale and a color scale. Pain assessment took place throughout the course of 3 days. The mean score of pain reduction was used to measure outcome.

Setting: Primary pediatric community ambulatory centers.

Participants: One hundred three children aged 6 to 18 years who were diagnosed with otalgia associated with AOM.

Results: Each of the 2 treatment groups were comparable on the basis of age, sex, laterality of AOM, and the effectiveness of ameliorating symptoms of otalgia. The 2 groups were also comparable to each other in the initial ear pain score and in the scores at each application of Otikon or Anaesthetic drops. There was a statistically significant improvement in ear pain score throughout the course of the study period ($P= .007$).

Conclusions: Otikon, an ear drop formulation of naturopathic origin, is as effective as Anaesthetic ear drops and was proven appropriate for the management of AOM-associated ear pain.


According to the United States Department of Health and Human Services, otitis media is the most common condition for which children are seen in a physician’s office, with more than 31 million physician visits reported each year. The majority of children with acute otitis media (AOM) experience an earache. Acute otitis media is one of the most frequently diagnosed infections in the pediatric population, with a peak incidence in children aged between 6 and 18 months. By age 7 years, 93% of all children in the United States have had at least 1 diagnosed episode of AOM.

Adequately addressing reports of ear pain early in the course of AOM will improve the patient’s level of comfort and parental anxiety during the acute episode, as well as the healing process. Hoberman et al reported that topically applied ear drops were proven effective in the relief of ear pain within 30 minutes of treatment. A mixture of ametocaine and phenazone dissolved in dehydrated glycerine, Anaesthetic (Vitamed Pharmaceutical Ltd, Benyamina, Israel) ear drops are designed for instillation into the external auditory canal. The preparation has no known systemic effects, but it reputedly induces an analgesic effect on the tympanic membrane (TM). The mechanisms of action of topical ear drops have been postulated to be the following: (1) anesthetic action of ametocaine; (2) the anti-inflammatory and analgesic actions of phenazone; (3) hygroscopic activity of glycerin, which may result in decreased middle ear pressure via fluid osmosis through the TM; and (4) decompression of an edematous TM by osmotic properties.
PATIENTS AND METHODS

The study was conducted between January 1998 and October 1999. Children aged 6 to 18 years experiencing ear pain associated with AOM were eligible for enrollment. The study was conducted in a double-blind, randomized manner.

The study was approved by the Edith Wolfson Medical Center (Holon, Israel) Human Rights Committee. The diagnosis of AOM required the presence of middle ear effusion, ear pain, and at least one other indicator of acute inflammation. Indicators of acute inflammation were marked redness of the TM and/or distinct fullness or bulging of the TM. Determination of the presence of middle ear effusion was based on the presence of at least 2 of the following: decreased or absent TM mobility by pneumatic otoscopy, an “A” flat or “B” curve revealed in tympanogram images, visible bubbles or air fluid level behind the TM, or opacification of the TM other than that secondary to scarring.

Children were excluded from the study if any of the following conditions were present at the initial examination: prior use of any kind of ear drops or analgesic within the preceding 4 hours; known allergy to herbal medication, ametocaine, phenazone, glycerine, or acetaminophen; presence of otorhea, eardrum perforation or ventilation tube(s); known immune deficiency; past history of complication of AOM; history of treated or untreated ear disease in the 2 weeks prior to enrollment in the study; and inability to reliably use a visual analog pain scale.

INSTRUMENT FOR EAR PAIN ASSESSMENT

The first data point (TA0) was assessed at the diagnosis of AOM. After installation of the Otikon or Anaesthetic ear drops, the patients and parents, under the guidance of the physician, recorded the pain scores at 15 and 30 minutes (TA15, TA30, respectively). At day 2 and day 3, patients and parents used the pain evaluation scale at home. Telephone interviews with the parents were then conducted 24 and 48 hours after the treatment period. The frame of reference for each data point was the time before the first ear drops were installed (at TA0 [1-day evaluation], TA10 [2-day evaluation], and TA30 [3-day evaluation]).

A total of 110 children were enrolled in the study. Seven children were excluded: 5 due to noncompliance (those who could not be reached by telephone for the interview or those who forgot to take the medication), and the 2 additional children were overcome by the smell of the ear drops. One hundred three children completed the study. Sixty-one children (59.3%) received Otikon, and 42 children (40.7%) received Anaesthetic ear drops. Fifty-four children (32.4%) were girls. Of those, 22 (40.7%) received Anaesthetic ear drops, and 32 (59.3%) received Otikon. Forty-nine of the participating children (47.6%) were boys. Of those, 20 (40.8%) received Anaesthetic ear drops, and 29 (59.2%) received Otikon. The median age of the girls was 8.1 years, and the median age of the boys was 8.3 years (Table). Evaluation of laterality of AOM revealed that 67 (65%) of the participants had unilateral ear infections; 34 (50.7%) of them received Anaesthetic, and 33 (49.3%) received Otikon ear drops. Of the 36 patients who had view or those who forgot to take the medication), and the 2 additional children were overcome by the smell of the ear drops. One hundred three children completed the study. Sixty-one children (59.3%) received Otikon, and 42 children (40.7%) received Anaesthetic ear drops. Fifty-four children (32.4%) were girls. Of those, 22 (40.7%) received Anaesthetic ear drops, and 32 (59.3%) received Otikon. Forty-nine of the participating children (47.6%) were boys. Of those, 20 (40.8%) received Anaesthetic ear drops, and 29 (59.2%) received Otikon. The median age of the girls was 8.1 years, and the median age of the boys was 8.3 years (Table). Evaluation of laterality of AOM revealed that 67 (65%) of the participants had unilateral ear infections; 34 (50.7%) of them received Anaesthetic, and 33 (49.3%) received Otikon ear drops. Of the 36 patients who had

The use of herbal medicine is widespread and growing, with an increasing number of herbal products available in conjunction with, or as replacement for, conventional medicine. The clinical purpose of the present study was to compare the efficacy of Otikon (Healthy-On Ltd, Petach-Tikva, Israel), a naturopathic herbal extract (consisting of \textit{Allium sativum}, \textit{Verbasum thapsus}, \textit{Calendula flores}, and \textit{Hypericum perforatum} in olive oil), with Anaesthetic ear drops in the management of ear pain associated with AOM.

RESULTS

On entering the study, all children were treated with acetaminophen (a single dose of 15 mg/kg), and parents were instructed not to use any analgesic for the remainder of the study.

The Observational Scale of Behavioral Distress (the Pain-O-Meter) was used to assess ear pain. On one side of the Pain-O-Meter is a linear scale (1-10) and a color scale (ranging from blue to red). The color scale begins with blue, indicating no pain, and darkens to the color red, indicating the elevated level of pain experienced. On the reverse side of the card is the face scale, which is composed of 5 facial representations ranging from a broad smile, indicating no pain, to a sad and crying child, indicating the worst possible pain.

The parents and children were educated in the use of the pain scale. Eligibility for study participation required a \textit{T}0 score of 3 or more out of 10. Measurements of both the facial and linear scales were recorded separately for each time evaluation, and then averaged to determine an overall ear pain score.

Success was determined if, after 48 hours, the child had a reduction in ear pain of at least 75%, if there was improvement in the child’s appearance, and if there was improvement in activity level and quality of sleep as reported by patients and parents.

STUDY DESIGN

Informed consent was obtained from one of the parents of each child, and the children were randomly assigned to 1 of 2 treatment groups. Group A was administered 5 drops of Otikon, and group B was given 5 drops of Anaesthetic ear drops, applied to the affected ear canal 3 times daily.

ANALYSIS

Survey responses were analyzed using SPSS for Windows (Statistical Product and Services Solutions 9.01b; SPSS Inc, Chicago, Ill). Data are reported using the chi\textsuperscript{2} test or the Fisher exact test. Comparisons for abnormal distribution of continuous data were assessed using the repeated-measures analysis and paired \textit{t} test. A 2-tailed test with a \textit{P} value of .05 was used to define statistical significance for differences observed between groups, and to calculate confidence intervals around differences in sample means and odds ratios.

©2001 American Medical Association. All rights reserved.
bilateral AOM, 8 (22.2%) received Anaesthetic and 28 (77.8%) received Otikon ear drops. No adverse events were documented.

The main emphasis of this study was based on the evaluation of the severity of pain experienced by patients in each of the groups. The pain was graded on a scale from 1 to 10, with 1 signifying no pain, and 10 signifying excruciating pain. The mean pain score was evaluated for 3 days. The reduction in the pain score was apparent in both groups (Figure). The difference in the mean pain levels between the 2 groups was not statistically significant, although there was less pain at T150 in the group receiving the Otikon (P = .007) (Figure).

Comparison of the ear pain evaluation between the 2 groups revealed a reduced score on repeated measurements in the Otikon groups. All children with AOM were effectively treated with Otikon or Anaesthetic ear drops, and we observed no complications secondary to abstention from the use of systemic antibiotics.

**COMMENT**

Ear pain is a common problem associated with AOM that frequently leads to a child’s requiring medical evaluation. Pain may result from receptor stimulation via various mechanisms, such as stretch and pressure, or from a release of toxic products of inflammation. The pain may originate from the TM, the periostium of the mastoid, or the mucoperiostium. The responses to pain may vary, depending on the source of pain and the mechanism of relief. Anaesthetic ear drops, which are sold over the counter, have analgesic, anesthetic, and hygroscopic properties. Otikon solution, produced from herbal extract in an olive oil base, has analgesic, anti-inflammatory, hygroscopic, and occlusive effects, as well as anti-infective properties.

Self-reporting is considered the most reliable means of pain measurement, since pain is subjective and related to many variables. Children are limited in their ability to accurately describe their pain experience. The Pain-O-Meter provides a desirable tool in the measurement of pain. Although the younger children were not able to use the numerical symbols to quantify pain, they understood the concepts of “more” or “less,” and “higher” or “lower,” and they applied them to the facial representations. A possible limitation of the Pain-O-Meter is that the color may reflect only anger and fear and not the intensity of pain.

The ear pain evaluation comparing the 2 groups showed that topically applied drops of the herbal extract (Otikon) seem to provide the analgesic equivalent of Anesthetic ear drops.

The complete absorption rate of acetaminophen ranges from 23 to 60 minutes. It is possible that in both treatment groups, at 30-minute pain evaluations, pain reduction may have been influenced by the onset of analgesia induced by acetaminophen.

Although AOM is often a mild, self-limiting infection, most clinicians recommend use of antibiotics to avoid suppurative complication, to prevent progression to chronic otitis media, and to reduce the risk of mastoiditis, meningitis, and bacteremia. Diagnostic criteria for AOM used by practicing physicians in the United States and in other countries are inconclusive, and the rates of misdiagnosis are uncertain.

Antibiotic treatment of AOM in older children is controversial. There is little evidence that routine use of antimicrobials is necessary or more effective than selective use in preventing mastoiditis and meningitis.

All the children participating in this study recovered without requiring systemic antibiotic treatment, and no complications were observed during the study period.

Decreased use of antimicrobial agents might delay the development of antimicrobial resistance in both the individual child and the community. Naturopathic herbal extract medications may offer significant benefits in the management of ear pain associated with AOM. Primary care physicians should be aware that a least one tenth of their patients may have tried one or more forms of alternative or complementary medicine. Herbal extracts have the potential to meet all the requirements of an appropriate medication that could be used routinely in the pediatric population. They have been shown to stimulate the immune response, serve as an antioxidant, and have anti-inflammatory properties.
inflammatory effects. They are of natural origin and well absorbed, with good penetration to the tissue surrounding the TM; furthermore, they work via local enhancement of anti-inflammatory and immunological activity.

Shaparenko et al19 described the possible bactericidal and immunologic abilities of plant extracts in the treatment of AOM. These herbal extracts were well tolerated, had a long half-life, and were easy to administer. There were no documented major adverse effects.

We are aware that the relatively small sample size and the fact that the study did not include a control group are possible limitations. Furthermore, the lack of standardization of herbal products may be a disadvantage to interpretation of the study results. Additional studies on the efficacy and safety of herbal products are required.

This study suggests that an ear solution of herbal extracts applied in the affected ear canal may reduce the ear pain associated with AOM, and that it is at least as effective as Anaesthetic ear drops. In children older than 6 years, initial antibiotic treatment at the diagnosis of AOM may be withheld; however, if at follow-up no improvement is observed, antimicrobial treatment should be initiated. In this way, we may be able to avoid the development of allergies, staggering costs, risk of overtreatment, and increasing bacterial resistance to antibiotics. Larger studies on the efficacy of herbal extract ear drops in reducing otalgia associated with AOM are necessary.

Accepted for publication February 27, 2001.
This work was supported by David Naker, MPharm, from Healthy-On, who created and supplied the herbal extract, naturopathic ear drops, Otikon.
We also thank Dorit Karsh, MA, from the Department of Epidemiology and Statistics, Section of Information and Statistics at Klalit Health Maintenance Organization, for assistance with statistical analysis. We thank the following investigators for enrolling their patients: Monica Finkelstein, MD, Katusa Karlnosca, MD, and Routh Senhav, MD.

Corresponding author: E. Michael Sarrell, MD, Hairis 7 Moshav Gan-Haim, 44910 Israel (e-mail: sarrell@netvision.net.il).

REFERENCES