Review #1

Comments for Editorial Office (Sheet A)

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Manuscript No.: 2000-0 147 Date Sent: 
Reviewer: .08686 1 Date Due: 

Decision Editor: 

Title: The Ceruminolytic Effects of Ducosate Sodium: A Randomized Trial

Format: Brief Report

Please rate the following measures of desirability for publication in Annals as: NA (not applicable) or 1 (lowest) to 5 (best).

Measures

3 Originality of concept
5 Abstract accurately reflects all essential aspects of study (including all major results and limitations)
4 Quality of the study methodology and design
4 Conclusions supported by results
3 Limitations are addressed
5 Composition is clear, organized, and complete
2 Scientific importance of the results
3 Overall desirability for publication in Annals

If accepted for publication, should this article be accompanied by an editorial? C Yes xxO No

If yes, by whom?

Comments for Editor Only:

Simple but well-done, well-written study about a topic that is of practical importance to EPs. This is not great science, however.
General Comments:

In general, well-done study presented in concise, easily understood format. Well-written. The abstract needs a few more details, outlined below. Study would have been strengthened with a control group, i.e., irrigation with 100 ml NS only. This would have broadened the study to examine the utility of adding a ceruminolytic to the cerumen removal protocol.

Specific Comments:

Refer to:

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<th>Page</th>
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</table>
| 13   | Table 2   | The 3rd row, “All Patients Completely visualized ears after irrigation....” needs clarification to ensure that reader understands you are grouping those visualized with ceruminolytic only plus those visualized with ceruminolytic after irrigation. I suggest, “All Patients Completely visualized ears after solvent with or without irrigation”.

Instructions to Annals Staff

Additional biostats review needed? ☑️ Yes ☐ No
Comments below for decision editor? ☑️ Yes ☐ No
Comments below for authors? ☑️ Yes ☐ No
Additional comments for Staff only:

Instructions/Questions for Biostatistical Reviewer

None.

Comments for Decision Editor

See also Comments for Authors.
**Comments for Authors**

**General Comments**

**Items that Must be Addressed by Authors**

1. The results are presented largely in the form of $P$ values. They should instead be given as point and interval estimates of effect magnitude, *e.g.* the difference in proportions and the confidence interval on that difference, or the number needed to treat and its CI [1]

2. Hypothesis testing is neither appropriate nor effective for establishing the equivalence of two randomized groups [2]. Therefore, recommend removing the $P$ values in Table 1.

3. The inter-observer agreement reported in the Methods sections of Abstract and the text is actually a result and should be reported in the respective Results sections.

4. The power calculation is not completely described, since the baseline proportion is not given.

5. Table 2. Replace the $P$ values with the difference in proportions and its CI.

**Other Suggestions to Improve the Manuscript**

None.

**References**


**CONSORT compliance checklist:**

Title, Abstract, Introduction provide:

1. Title identifies study as RCT  
   
   _Met _Not met, acceptable x_Not met, not acceptable  
   Remarks: Add “controlled” to the title

2. Structured abstract  
   
   x_Met _Not met, acceptable _Not met, not acceptable  
   Remarks:

3. Prospective hypothesis, planned subgroups  
   
   x_Met _Not met, acceptable _Not met, not acceptable
Methods -- Protocol describes:

1. Study pop, incl/excl criteria
   - Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

2. Planned interventions
   - Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

3. Outcome measures, min important difference
   __Met     x__Not met, acceptable     __Not met, not acceptable

   Remarks: The minimum clinically important difference was not defined.

4. Methods for statistics
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

5. Prospective stopping rule
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

Methods -- Assignment describes:

1. Unit of randomization
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

2. Allocation method
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

3. Allocation blinding and timing
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

4. Generation vs execution of assignment
   x__Met     __Not met, acceptable     __Not met, not acceptable

   Remarks:

Methods -- blinding describes:
1. Mechanism
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

2. Success in subjects, physicians, outcome assessors
   __Met     __Not met, acceptable     x__Not met, not acceptable
   Remarks: Not described

Results -- Flow diagram describes:
1. Subject flow thru project
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

Results -- Analysis provides:
1. Point and interval estimate of effect size
   __Met     __Not met, acceptable     x__Not met, not acceptable
   Remarks:

2. Results in absolute numbers
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

3. Data and detail sufficient for analysis
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

4. Prognostic variables and adjustment if any
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

5. Deviations from protocol
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

Comment provides:
1. Interpretation of findings, sources of bias
   x__Met     __Not met, acceptable     __Not met, not acceptable
   Remarks:

2. Interpretation in light of all available evidence
   x__Met     __Not met, acceptable     __Not met, not acceptable
**Title:** The Ceruminolytic Effects of Ducosate Sodium: A Randomized Trial

**Format:** Brief Report

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<td>2</td>
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</tbody>
</table>

If accepted for publication, should this article be accompanied by an editorial? C Yes ~No

If yes, by whom?

**Comments for Editor Only:**

The article is a rather straightforward study that points out a method to remove cerumen that is known to some practitioners and me but certainly not all. The study itself has small numbers, particularly as it relates to the...
number of children included. I think it should be shortened and submitted as a letter to the editor.

**Annals of Emergency Medicine**

Manuscript No.: 2000-0 147

Reviewer:

**General Comments:**

This is a prospective, randomized, controlled study that reviewed the use of solvents to loosen and remove cerumen. This study has a very small number of enrollees and it’s even smaller for the number of children, less than five years of age.

Within the study itself on Page 6, the authors state that the patient had the material placed in their ear canal and if the TM was not completely visualized, the physician irrigated the ear with up to 100cc of lukewarm normal saline. However, there is no mention in the study of how much irrigant was used per patient and this could make a significant difference in interpreting the results. For example, if the majority of patients cleared with the solvent and less than 20cc of irrigant while the other agent required 90 to 100cc of irrigant for a majority of the patients, one could conclude that there was a difference between agents used in the study.

The number of patients per study arm limit the conclusions which can be drawn from the study. The authors identified several other limitations in this study: it was a convenient sample; the solvents not only had different appearances but, once the physician looked into the ear canal or at the material that drained from the canal, the physician could guess which agent was used. The authors also note that there were not enough cases in the study to detect any study group differences in the rate of adverse events. It is difficult to draw any distinction between the patients under five years of age due to the small number of children in each treatment arm.

While this is a great practical tip there are several problems that should be addressed if possible: the amount of irrigant used per patient and an analysis based on this and have a larger study group.
Review #4

Comments for Editorial Office (Sheet A)

(These materials are confidential and should not be copied or used in any way other than for the specific purpose of peer review of this Journal)

Manuscript No.: 2000-0 147 Date Sent: 
Reviewer: 147536 Date Due: 

Decision Editor:

Title: The Ceruminolytic Effects of Docusate Sodium: A Randomized Trial

Format: Brief Report

Please rate the following measures of desirability for publication in Annals as:
NA (not applicable) or 1 (lowest) to 5 (best).

Does the case warrant publication on the basis of any of these criteria:

4 Originality of Concept
3 Abstract accurately reflects all essential aspects of study (including all major results and limitations)
4 Quality of the study methodology and design
5 Conclusions supported by results
3 Limitations are addressed
5 Composition is clear, organized, and complete
3 Scientific importance of the results
4 Overall desirability for publication in Annals

If accepted for publication, should this article be accompanied by an editorial? 0 Yes 0 No

If yes, by whom?

Comments for Editor Only:

This is a well-written study with clear objectives and end-points. The methodology is solid and the
conclusions are justified by the results. The findings may well change clinical practice for a common and bothersome obstacle to evaluation of ear problems. I think it is perfect for a brief report. Minimal changes are suggested.
General Comments: This is a well designed, well-written study investigating the cerumenolytic efficacy of
docusate sodium (colace) compared to the more commonly employed triethanolamine (cerumenex) I
must admit that I was not familiar with the use of docusate sodium to solubilize cerumen but the authors
make a compelling case for its use. I usually use irrigation with syringe and butterfly administration set
(sans needle and most of tubing), and it is well tolerated and effective. However it can be time consuming
and labor intensive. I wonder if the use of a cerumen solvent enhances the effects of irrigation or whether
it detracts from its effectiveness, since the cerumen seems to be ejected in a well-formed pellet after
irrigation. Solubilizing the pellet could conceivably result in less effective irrigation. A third limb of your
study could have compared either agent to irrigation alone. Still, I am anxious to try docusate sodium with
my next problematic otic visualization.

Was it necessary for the same physician to both instill the agent and determine the degree of
visualization? Since there was visible difference in the appearance of the agents, this potential bias could
have been avoided if the person determining the endpoint measurement was in fact truly blinded to the
results. You do address this concern in your discussion.

Specific Comments:
Refer to:  I
Page 2 (abstract) Results
in the Objective section of the
abstract. Should be TP for consistency. Presume it was an oversight.
4 I Discuss death as possible complication of both techniques although the
stated reference suggests that
“there have even been rare deaths
manuscript overstates the risk of death;
6 1
8 l&2
TM was visualized
10 2
but I am concerned about the use in
excluded, Is it really true that it doesn’t
bacteria, specifically presumably
Use CX to indicate triethanolamine rather than TP as established earlier
irrigation can cause cardiac depression. Would be better to state that
associated with syringe irrigation”. I think the way it is stated in the
specifically, what type of device was used for irrigation
Would specifically report whether any perforations were present after
Certainly colace would not need to be sterile for use as a stool softener,
clearing an occluded ear canal when a TM perforation cannot be
need to be sterile? Do you know whether colace is easily colonized by
antibiotic resistant bacteria common in hospital settings? Is single dose
administration possible either commercially or as prepared steriley by hospital pharmacy?
Comments for Editorial Office (Sheet A)
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Manuscript No.: 2000-0 147  Date Sent: 
Reviewer: 421574 Date Due: 
Decision Editor: 

Title: The Ceruminolytic Effects of Ducosate Sodium: A Randomized Trial  

Format: Brief Report  

Please rate the following measures of desirability for publication in Annals as: 
NA (not applicable) or 1 (lowest) to 5 (best).

Measures
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___ Scientific importance of the results
___ Overall desirability for publication in Annals

If accepted for publication, should this article be accompanied by an editorial? C Yes C No

If yes, by whom?

Comments for Editor Only:
This study addresses a common ED problem with a RCT design. However the sample size is a major concern. This undermines the credibility of the results particularly in children <5 years (9 vs 4 subjects).

Recommendation: I like the hypothesis and approach however the small number of subjects when taken into account with the broad age range and subsequent stratification of the cohort is a very serious limitation. Therefore I recommend rejection but with strong encouragement to resubmit after studying more subjects.
General Comments:
1. This addresses a common Emergency Department problem. However I am concerned with your sample size particularly because you studied patients of all ages and you subsequently stratified the results by presenting the outcome in children less than 5 and for all subjects.
2. I am uncertain as to how many children less than five years of age were studied. On page 8, line 2 you state that there were 20; but in Table 1 you indicate that there were 13. If indeed there are 13 subjects with only 4 in the TP group, such a small sample size is of concern.
3. You have shown a difference for all patients and for patients less than 5. However, you have not analyzed for patients greater than 5. The number of subjects, outcomes and p-value for this subset should be included in Table 2. Assuming that the numbers of children less than 5 in this table are correct, then my calculations for tympanic membrane visualization in subjects greater than 5 are 78% and 57% for DS and TP respectively. A p-value for this subset is necessary.

Specific Comments:

Refer to:

4. Page 2, line 15: In addition to the mean age, provide the range.
5. Page 2, line 18: Should “CX” be “TP”?
6. Page 2, last line: State how many children less than 5 years old were in each group.
7. Page 6, para 1: State how the saline irrigation was performed — ear syringe or some other device?
8. Page 6, para 1: How many physicians were involved with this study? How many patients did each physician assess? Were there differences amongst individual physicians regarding success rate of each cerumenolytic?
9. Page 6, para 2: Please provide more detail regarding the assessment of inter-observer agreement. State whether the subset of 20 was actually a subset within the
50 studied patients. State whether the physicians who were assessed for inter-
observer agreement were the same physicians who were involved in the study. Also
state what was actually done — agreement prior to instillation of cerumenolytic,
agreement after instillation of cerumenolytic, or both.
10. Page 8, para 1: Clearly state whether any patient had both ears studied.
11. Page 8, line 2: Is + 18 a S.D. or a S.E.? Also provide the range in addition to the
mean.
12. Page 10, second last paragraph. This paragraph discusses limitations of your
study. The small number of children less than 5 years of age should be included as a
limitation.
13. Page 10, second last line: “Ideal” is a bit too strong since it was effective in 82% of
patients. Perhaps the term “well-suited” would be more appropriate.
14. Page 14: The study profile is not complex. Thus this figure could be deleted.