

Randomized, Placebo-Controlled Evaluation of Cerumenex and Murine Earwax Removal Products

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Objective: To evaluate the efficacy of 2 ceruminolytic products, Cerumenex Eardrops (Purdue Frederick Company, Norwalk, Conn) and Murine Ear Drops (Abbott Laboratories, Abbott Park, Ill), in subjects with partial or complete occlusion of the ear canal due to cerumen.

Design: Randomized, subject- and observer-blind, placebo-controlled, clinical trial.

Setting: Corporate research clinic.

Participants: From among 230 volunteers screened, 74 subjects (age, 22-66 [mean, 45] years) were enrolled in the study. Participants had baseline occlusion levels of mild (n=10), moderate (n=26), or complete (n=38) impairment of tympanic membrane visualization.

Interventions: Subjects were randomly assigned to 1 of 3 treatments: Cerumenex (10% triethanolamine polypeptide oleate-condensate), Murine (6.5% carbamide peroxide), and a placebo, BSS Sterile Irrigating Solution (Alcon Laboratories Inc, Ft Worth, Tex). The test medication was instilled into 1 occluded ear for up to two 15-

minute applications. Following the treatment, the subject's ear was irrigated with 50 mL of lukewarm water delivered at low pressure via a WaterPik irrigator equipped with a Grossan irrigator tip.

Main Outcome Measure: The degree of occlusion, measured against a previously established 4-point scale, was assessed and recorded at baseline and after each instillation and irrigation procedure.

Results: Neither Cerumenex nor Murine was superior to saline placebo. By the end of treatment, 29.2%, 15.4%, and 41.7% of subjects treated with Cerumenex, Murine, and placebo, respectively, experienced resolution of cerumen occlusion. These values were not statistically significantly different from one another.

Conclusion: The currently marketed ceruminolytic products, Cerumenex and Murine, are no more effective than a saline placebo in removing earwax.

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EXCESSIVE EARWAX IN THE external auditory canal is a common problem in clinical practice. Accumulated earwax can cause discomfort, temporary hearing loss, occasional cough or vertigo, and can promote infection.¹ It can also impede proper otologic examination, hearing and balance testing, and the effective use of hearing aids.

While in many instances earwax can be removed mechanically, specialized instruments such as operating microscopes, suction, and/or flushing equipment may not be available in a primary care setting. Training in the use of specialized equipment is required; mechanical removal is potentially damaging to the ear structures if conducted incorrectly.^{2,3} Ceruminolytic agents that soften and/or loosen earwax from the tympanic membrane can facilitate the removal process. However, these products may also be irritating and/or ineffective.⁴ Varying levels of effectiveness of ceruminolytic agents have been reported.³⁻⁷ Dif-

ferences in effectiveness can perhaps be attributed to differences in treatment regimen, including the duration of treatment and the volume and pressure of irrigation following application of the softening agent. These variations in study design prevent valid comparisons between products. Therefore, in an effort to evaluate the effectiveness of currently available ceruminolytic agents, we compared representative prescription and over-the-counter products with a placebo in a controlled clinical setting.

METHODS

This was a randomized, observer- and subject-blind, placebo-controlled, 1-day trial in volunteers with excessive or impacted cerumen. Volunteers were enrolled over a 2-month period (July-September 2001) at a single corporate site (sponsor's research clinic). Ethics review board approval of the protocol, informed consent form, and other study documentation were obtained prior to initiation of the study. Study participants were company (sponsor) employees and were recruited via an intracompany advertise-

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Table 1. Degree of Occlusion Scale

Score	Degree of Occlusion
0	No occlusion: no effective impairment of tympanic membrane visualization due to cerumen
1	Mild occlusion: slight impairment of tympanic membrane visualization due to cerumen
2	Moderate occlusion: significant impairment of tympanic membrane visualization due to cerumen
3	Complete occlusion: complete impairment of tympanic membrane visualization due to cerumen

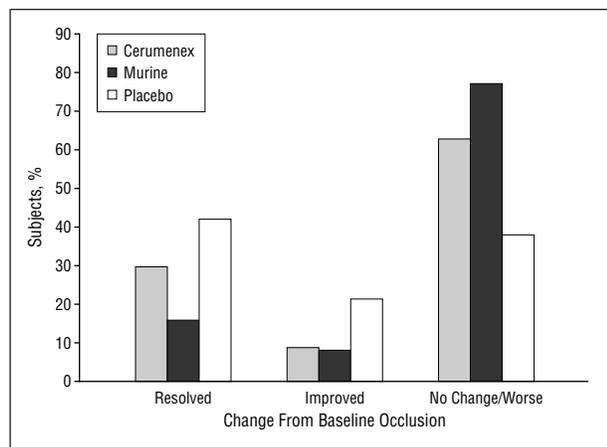
Table 2. Efficacy Outcome at End of Treatment*

Degree of Occlusion at End of Treatment	Cerumenex (n = 24)	Murine (n = 26)	Placebo (n = 24)	P Value†	P Value‡
No occlusion	7 (29)	4 (15)	10 (42)	.37	.06
Mild, moderate, or complete occlusion	17 (71)	22 (85)	14 (58)		

*Data are numbers (percentages) of patients unless otherwise specified. See the "Methods" section for a description of Cerumenex, Murine, and placebo products.

†Cerumenex vs placebo (χ^2 test of independence).

‡Murine vs placebo (Fisher exact test).



Change from baseline occlusion. Proportion of subjects experiencing resolution, improvement, or no change/worsening. See the "Methods" section for a description of Cerumenex, Murine, and placebo products.

ment to participate in an earwax removal study. The clinical investigator (P.S.R) was an independent physician, who provided consulting services to the sponsor.

Of 230 volunteers screened, 74 qualified for enrollment. Signed written informed consent was obtained from all subjects in advance of any study procedures. Standardized data forms were used to collect demographic information, medical history, current medications, and baseline occlusion status, as well as to document posttreatment outcomes and any complications. Potential subjects were excluded if they had ear anomalies, diabetes, allergies to study medications, were pregnant or nursing, or had instilled anything other than water in their ear in the previous 72 hours. Subjects were required to be 18 years or older and to have mild, moderate, or complete cerumen occlusion, as measured against a previously established 4-point scale (**Table 1**).

Pretreatment occlusion was assessed at baseline; treatment effect was assessed after each application and irrigation

step. Efficacy was based on the posttreatment level of occlusion. Otologic signs and symptoms were also assessed. All clinical assessments were performed by a qualified specialist. To maintain masking of the clinical assessor and subject, test articles were stored out of view and were administered by clinic staff who did not perform clinical assessments.

Summary statistics (mean \pm SD and number of subjects) for demographic and baseline characteristics were calculated, and either a χ^2 test of independence or a 2-sample *t* test was used to assess differences between treatments for each demographic characteristic. Descriptive statistics were calculated for (1) the proportion of subjects in each degree of occlusion category at the end of treatment by baseline severity and (2) the proportion of subjects who obtained resolution of their occlusion relative to the subjects who did not obtain resolution. Because this was planned as a descriptive study, no power calculations were made prior to study initiation. Analyses that were performed were done post hoc.

A total of 74 subjects ranging in age from 22 to 66 years (mean age, 45 years) were enrolled into the study. Baseline occlusion levels were mild ($n=10$), moderate ($n=26$), or complete ($n=38$). There were 51 men and 23 women (male-female ratio, 2.2:1). No statistically significant differences between demographic factors (age and sex) or between baseline degree of occlusion levels were observed between treatment groups.

Subjects were randomly assigned to 1 of 3 treatments: Cerumenex Eardrops (10% triethanolamine polypeptide oleate condensate; Purdue Frederick Company, Norwalk, Conn), Murine Ear Drops (6.5% carbamide peroxide; Abbott Laboratories, Abbott Park, Ill), or placebo (BSS Sterile Irrigating Solution, a saline preparation containing 0.64% sodium chloride and physiologic concentrations of multiple electrolytes; Alcon Laboratories Inc, Fort Worth, Tex). Subjects were asked to lie on their side with the study ear facing upward during treatment. Treatment consisted of up to two 15-minute applications of a ceruminolytic agent or placebo. Each application was followed by a standardized irrigation procedure using a WaterPik Oral Jet Irrigator (WaterPik Technologies, Inc, Fort Collins, Colo), modified with a Grossan tip (Hydro Med, Inc, Sherman Oaks, Calif). Irrigation consisted of 50 mL of lukewarm water delivered into the ear canal at the lowest pressure setting in compliance with manufacturer instructions for otic use. Occlusion level was reassessed after each application of medication or placebo and after each irrigation procedure. If the ear canal was cleared of cerumen after a single application and irrigation, the second application was not conducted.

RESULTS

Results demonstrated that neither Cerumenex nor Murine was superior to placebo in resolving the occlusion due to cerumen. By the end of treatment, 29.2%, 15.4%, and 41.7% of subjects treated with Cerumenex, Murine, and placebo, respectively, experienced resolution of cerumen occlusion and/or impaction. While placebo appeared to be more effective than both ceruminolytics, the difference between Cerumenex and placebo was not statistically significant ($P=.37$) and was marginally nonsignificant for Murine compared with placebo ($P=.06$) (**Table 2**). The change from baseline degree of occlusion to a resolved, improved, or unchanged/worsened condition is depicted in the **Figure**.

Overall, most subjects (90.5%) required 2 applications, whereas 9.5% had successful treatment outcomes after only 1 application and rinse. Results after a single

application showed that no 1 test article appeared more effective than the others in removing occlusions. Of 24 occlusions treated with Cerumenex, 2 (8%) cleared after 1 treatment; of 26 occlusions treated with Murine, 3 (12%) cleared after 1 treatment; and of 24 occlusions treated with placebo, 2 (8%) cleared after 1 treatment.

Undesirable complications were minimal with all 3 test articles. A total of 6 subjects reported adverse events related (n=5) or not related (n=1) to test article. These events are presented in **Table 3**.

COMMENT

Currently marketed ceruminolytic products primarily act by softening earwax to facilitate its removal with irrigation, rather than by dissolution.⁴ Items used to aid earwax removal include household agents such as water and olive oil, stool softeners, and chemicals such as hydrogen peroxide, carbamide peroxide, and surfactants. These agents have been evaluated under a variety of circumstances, and wide ranges in level of effectiveness have been reported.

We used a 4-point degree of occlusion scale and found it helpful in differentiating between the severity of occlusions before, during, and after treatment, which allowed us to compare the effectiveness of the test articles. Because full visualization of the tympanic membrane is the ultimate goal of many cerumen removal procedures, the scale was based on the assessor's ability to visualize the tympanic membrane, rather than on the amount of cerumen present or removed. We found the scale, with its qualitative descriptions of occlusion levels, to be effective, particularly in differentiating between complete, mild or moderate, and no occlusion. The distinction between mild and moderate levels of occlusion, however, is more subjective. Introduction of a quantitative cutoff between mild and moderate occlusion levels may improve interinvestigator reliability of degree of occlusion scale assessments.

It is generally accepted that cerumen removal is a commonly performed, time-consuming procedure that carries added risk if mechanical means or lengthy irrigation procedures are required.^{2,4,8} In the present study, per manufacturer's recommendations, the pressure generated by the WaterPik irrigator was controlled by both the speed setting (lowest speed) and the special Grossan tip attachment. Use of the WaterPik for ear irrigation under other conditions is not advised because introducing undue force can be harmful to ear structures. The senior author (P.S.R.) directed a study on the effect of oral jet irrigation on the tympanic membrane in fresh cadavers.⁹ The study concluded that oral jet irrigators were a safe method of cerumen removal but that only the lowest settings should be used.

In the present study, we compared the effectiveness of 2 marketed ceruminolytic products, Cerumenex Ear Drops and Murine Ear Drops, with a saline placebo, BSS Sterile Irrigating Solution, in a controlled clinical setting, in which duration of treatment and method of irrigation were held constant. Randomization addressed potential issues of selection bias, while masking and placebo-control allowed for unbiased assessment of assigned treatments. Limiting the duration of treatment and controlling the irrigation procedure ensured consistent application of treatments and allowed for reliable comparisons between prod-

Table 3. Frequency and Incidence of Adverse Events*

Adverse Event	Cerumenex (n = 24)	Murine (n = 26)	Placebo (n = 24)
Related			
Ear pruritis	1 (4)	2 (8)	0
Ear discomfort	0	0	1 (4)
Contact dermatitis	1 (4)	0	0
Not related			
Vertigo	1 (4)	0	0

*Data are numbers (percentages) of patients. See the "Methods" section for a description of Cerumenex, Murine, and placebo products.

ucts. The study design also replicated actual use of a ceruminolytic product in an outpatient clinic setting. While we did not test all marketed ceruminolytics, the products selected for comparison were representative of available ceruminolytic agents, both prescription and over the counter. The results of this study demonstrated that neither Cerumenex nor Murine is more effective than a saline placebo in facilitating the removal of cerumen in a controlled clinical setting. Although we do not know why there was a higher incidence of success in the saline arm of this study, one may speculate that an aqueous solution such as saline may be more effective in softening the cerumen because it produces swelling of the epithelial components of a cerumen impaction, loosening and separating these components from each other.¹⁰ Further assessment of the ceruminolytic properties of saline might potentially be done using comparators such as pure water or no pretreatment in a controlled clinical setting.

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As required by editorial policy, an independent statistician, William Frawley, PhD, Department of Statistics, University of Texas Southwestern Medical Center, Dallas, reviewed the data, and his analysis confirmed the statistical evaluation.

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REFERENCES

1. Spiro SR. A cost-effectiveness analysis of earwax softeners. *Nurse Pract.* 1997; 22:28-31.
2. Grossan M. Cerumen removal. *Ear Nose Throat J.* 1998;77:541-548.
3. Singer AJ, Sauris E, Vicecellio AW. Ceruminolytic effects of docusate sodium: a randomized controlled trial. *Ann Emerg Med.* 2000;36:228-232.
4. Robinson AC, Hawke M. The efficacy of ceruminolytics: everything old is new again. *J Otolaryngol.* 1989;18:263-267.
5. Carr MM, Smith RL. Ceruminolytic efficacy in adults versus children. *J Otolaryngol.* 2001;30:154-156.
6. Andaz C, Whittet HB. An in vitro study to determine efficacy of different wax-dispersing agents. *ORL J Otorhinolaryngol Relat Spec.* 1993;55:97-99.
7. Dirr JP, Nimer H, O'Kane MJ, Meyer J. Clinical observations on ceruminolysis with a new pharmacologic agent. *J Med Soc NJ.* 1959;56:504-506.
8. Sharp JF, Wilson JA, Ross L, Barr-Hamilton RM. Ear wax removal: a survey of current practice. *BMJ.* 1990;301:1251-1253.
9. Dinsdale RC, Roland PS, Manning SC, Meyerhoff WL. Catastrophic otologic injury from oral jet irrigation of the external auditory canal. *Laryngoscope.* 1991; 101:75-78.
10. Robinson AC, Hawke M, Mackay A, Ekem JK, Stratis M. The mechanism of ceruminolysis. *J Otolaryngol.* 1989;18:268-273.