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A comparative in vitro study on the cerumenolytic effect of docusate sodium versus 2.5% sodium bicarbonate using UV–visible absorption spectroscopy

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ABSTRACT

Objective: To compare cerumenolytic effects of docusate sodium and of 2.5% sodium bicarbonate - *In vitro* study; observe characteristics of the solution, using ultraviolet–visible (UV/Vis) spectroscopy, and measurement of cholesterol levels.
Methods: Samples of human cerumen were mixed to form a relatively homogenous paste. Samples of about 500 mg were weighed and packed at the bottom of the test tubes. To each tube was added 1.5 ml of either docusate sodium or 2.5% sodium bicarbonate. Tubes were incubated at 36.4 °C in a water bath for 15, 30 or 60 min. Following incubation, the supernatant solution was pipetted into a cuvette. The cerumenolytic efficacy was defined as the absorbance (recorded at 350 nm and 400 nm) of the solutions. Results were the average of three replicates. A cholesterol level of each sample was then determined to confirm the result.
Results: Turbidity was much greater in tubes containing 2.5% sodium bicarbonate, indicating dissolution of cerumen. Mean difference of absorbance values measured at 350 nm and 400 nm after 15, 30, 60 min digestions were 1.93 [95%CI 1.49–2.38, p-value <0.001] and 1.81 [95%CI 1.21–2.41, p-value <0.001], respectively. Furthermore, levels of cholesterol were greater in tubes containing 2.5% sodium bicarbonate solution after digestion than in tubes containing docusate sodium; 11 mg/dl [95%CI 1.47–24.14, p-value = 0.083]
Conclusion: Both spectrophotometric and cholesterol level assessments suggest that 2.5% sodium bicarbonate has a higher cerumenolytic effect than docusate sodium. In other words, cerumen can be dissolved in 2.5% sodium bicarbonate much better than docusate sodium in a time-dependent manner.

1. Introduction

Cerumen impaction is one of the most common problems seen in any outpatient Department of Otorhinolaryngology. Cerumen builds up in the ear canal, causing a blocked, painful ear and hearing loss. There are several removal methods including mechanical technique and use of cerumenolytic agents.

The mechanical techniques of wax removal are classified into two categories including dry technique and wet technique (Aaron et al., 2018). For dry technique, the ear wax is removed under direct otoscope or microscope by otology instruments (such as an ear curette, an ear loop, and micro forceps); whereas, the wet technique is using of irrigation with body temperature water to wash the wax out of the ear canal. However, the evidence on the effectiveness of both mechanical techniques was equivocal (Clegg et al., 2010). Regarding using cerumenolytic agents, aim to the ear wax is soften that may self-administered remedies or easy to remove ear wax. Recently, there are many cerumenolytic agents including docusate sodium, sodium bicarbonate, olive oil, hydrogen peroxide and acetone that are often employed to soften the

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impacted cerumen but specific cerumenolytic agents are the most effective remains uncertain (Clegg et al., 2010; Bruton and Doree, 2003, 2009; Aaron et al., 2018). Thus, the choice of cerumenolytic agent depends on the experience and opinion of individual otolaryngologists in current practice. Sodium bicarbonate or docusate sodium in different concentrations are most often chosen because they are cheap and effective without serious adverse effects. However, most otolaryngologists recognize the inadequacy of comparative studies to date. Thus, we aimed to compare the efficacy of the most popular cerumenolytic agents using UV–visible absorption spectroscopy and the measurement of cholesterol levels. This could provide useful information for clinical practice in the future.

2. Materials and methods

A total of 18 g of cerumen was collected from healthy patients who come to the outpatient ENT clinic from August 1st, 2014 to December 31th, 2014. Samples were pooled and mixed, then stored at 4 °C. The sample pool was divided into 36 aliquots, each weighing 500 mg. Each aliquot was packed into the bottom of a tube that was 15 cm high with a diameter of 1.5 cm. Into each tube was added 1.5 ml of docusate sodium or of 2.5% sodium bicarbonate. Tubes were then incubated at 36.4 °C for 15 min. Two blanks were placed in a similar condition to calibrate the spectrophotometer. After 15 min, a micropipette was used to collect 0.8 ml from the top of the solution in each tube. This solution was then inserted into a cuvette to measure light absorbance at 350 and 400 nm in a spectrophotometer. Additional tubes were treated the same way but incubated for 30 or for 60 min. All procedures were repeated in triplicate (18 tubes). All solutions were then brought to the chemical laboratory to measure the quantity of cholesterol. Statistical data were analyzed using the mixed-effects REML regression in the program STATA version 10.0. This study was exempted by the local ethics committee in human research (HE571265).

3. Results

3.1. Characteristic changes of the dissolution

Greater turbidity was observed at all time points in tubes containing 2.5% sodium bicarbonate than in tubes containing docusate sodium (Fig. 1A-C). Turbidity of the top of the solution increased with time in tubes containing 2.5% sodium bicarbonate (Fig. 2A), but there was no apparent dissolving of cerumen in docusate sodium at any time point (Fig. 2B).

3.2. Spectrophotometric assessment

The optical density of dissolved cerumen in 2.5% sodium bicarbonate and docusate sodium was assessed by spectrophotometer at 15, 30 and 60 min. Optical density was greater in tubes containing 2.5% sodium bicarbonate than in those containing docusate sodium and increased through time (Table 1).

3.3. Cholesterol level

The cholesterol levels were measured in all samples after different digestion times. The cholesterol level of the dissolved cerumen solution was higher in tubes containing 2.5% sodium bicarbonate than in tubes containing docusate sodium. It can be inferred that 2.5% sodium bicarbonate has a greater cerumenolytic effect than docusate sodium (Table 2).

4. Discussion

Recently, many cerumenolytic agents are often used to soften the impacted cerumen; however, the superior efficacy of cerumenolytic agents is the lack of adequate data. In one in vitro study, the efficacy of six cerumenolytic agents (docusate sodium, sodium bicarbonate, olive oil, Earex, Cerumol, and acetone) was compared by observing the degree of cerumen disintegration following exposure to the agents for 15, 30, 60 and 120 min at 36.4 °C (Bellini et al., 1989). In that study, docusate sodium was the most effective in dissolving cerumen. The authors also commented that 60 min is an appropriate time to assess the efficacy of cerumenolytic agents due to a plateau effect of dissolution after 60 min. A more recent *in vivo* study by Singer et al. (2000) compared the efficacy of cerumenolytic agents, including docusate sodium and triethanolamine polypeptide, in the human external auditory canal by visualizing the tympanic membrane 15 min after applying 2 eardrops. If the tympanic membrane was still not completely visible, normal saline was irrigated into the ear canal for a second attempt. They concluded that docusate sodium was a better cerumenolytic agent than triethanolamine polypeptide. The mention of the efficacy of cerumenolytic agents in previous studies shows that docusate sodium seemed superiority efficacy that the other agents. However, another *in vivo* study by Bruton and Doree (2009) compared the efficacy of 11 cerumenolytic agents, including docusate sodium and sodium bicarbonate, in a similar way to the study by Singer et al. (2000). They found no statistical difference in efficacy among the cerumenolytic agents. The latest systematic review showed no evidence that oil-based cerumenolytic agents were not superior to water-based cerumenolytic agents (Aaron et al., 2018).

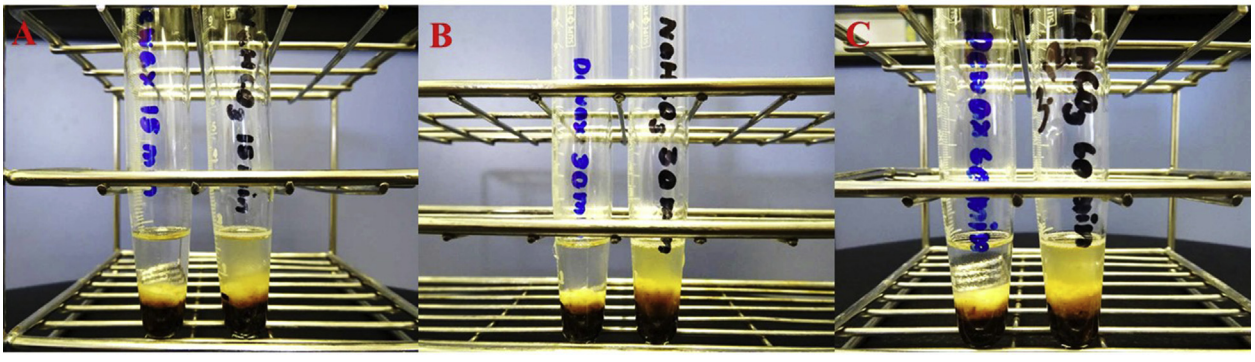

Fig. 1. Comparison of appearance of dissolved cerumen in 2.5% sodium bicarbonate (right-hand tube in each panel) and docusate sodium at 15 min (Figs. 1A), 30 min (Figs. 1B) and 60 min (Fig. 1C).

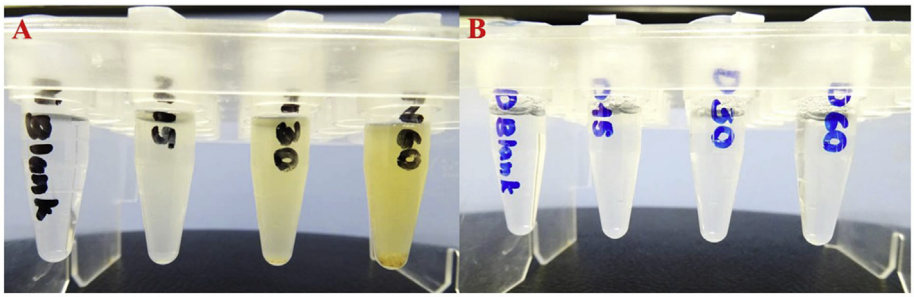

Fig. 2. The appearance of the top of the dissolved cerumen in 2.5% sodium bicarbonate (Fig. 2A) and docusate sodium (Fig. 2B) at 15, 30 and 60 min. The left-hand tube in each panel is the blank lacking cerumen.

Table 1
Optical density of dissolved cerumen solution.

Optical density	Time (minutes)	Dissolved cerumen	
		docusate sodium	2.5% sodium bicarbonate
350 nm	15	0.450	2.143
	30	0.276	2.544
	60	0.800	>3.00
	Mean difference	2.05 (95%CI: 1.70–2.41); p-value <0.001	
400 nm	15	0.329	1.657
	30	0.203	1.934
	60	0.619	>3.00
	Mean difference	1.81 (95%CI: 1.21–2.41); p-value <0.001	

Table 2
Cholesterol levels of dissolved cerumen solution.

Time (minutes)	Cholesterol levels (mg/dl)	
	docusate sodium	2.5% sodium bicarbonate
15	3.67	7.33
30	2.67	8.67
60	4.33	29
Mean difference	11.33 (95%CI: -1.47–24.14); p-value = 0.083	

Therefore, the superior efficacy of cerumenolytic agents still is controversy. Furthermore, several previous studies (Bellini et al., 1989; Singer et al., 2000; Bruton and Doree, 2009) have investigated the efficacy of cerumenolytic agents using subjective assessment of the results. Thus, we developed a more objective and quantitative approach using UV–visible absorption spectroscopy. The Beer-Lambert Law states (Beer, 1852) that absorbance of a sample is directly proportional to the concentration (c) and the path length (l) as in the equation below:

$$A = \varepsilon cl$$

Where A: Absorbance, ε: molar absorptivity (L mol^{-1} cm^{-1}), c: concentration (mol/L), l: path length.

According to the Beer-Lambert Law, greater absorbance indicates a higher concentration of dissolved cerumen in the solution. The mean difference in optical density of dissolved cerumen in 2.5% sodium bicarbonate when compare to docusate sodium measured at 350 nm and 400 nm after 15, 30, and 60 min digestion were 2.05 (95%CI: 1.70–2.41; p-value <0.001) and 1.81 (95%CI: 1.21–2.41; p-value <0.001), respectively. The statistically significant difference at both wavelengths implies that 2.5% sodium bicarbonate has greater efficacy in dissolving cerumen than does docusate sodium. Consistent with this, we observed greater turbidity of dissolved cerumen that indicated to superiority cerumenolytic efficacy in 2.5% sodium bicarbonate than in docusate sodium (Fig. 1A-C and Fig. 2A-B). Our result is different from Bellini et al. (1989) who found docusate sodium to be the most effective cerumenolytic agent. However, they measured the efficacy of agents only by assessing turbidity changes in the solutions; thus, bias could have occurred if turbidity did not differ much.

Measurement of components of cerumen in solution is the best method for assessing the efficacy of different agents to dissolve cerumen. The major components of cerumen are fatty acid and cholesterol (Okuda et al., 1991; Guest et al., 2004). Minor components include desquamated epithelium mixed with glandular secretion, dust and foreign bodies within the external auditory canal. Unfortunately, we cannot measure the fatty acid in our lab; therefore, we assayed the cholesterol levels. We found a greater quantity of cholesterol from dissolved cerumen in tubes containing 2.5% sodium bicarbonate relative to docusate sodium (11.33 mg/dl (95%CI: -1.47–24.14); p-value 0.083). Although this result did not reach statistical significance, it was consistent with our other results, showing that 2.5% sodium bicarbonate has a higher cerumenolytic effect than docusate sodium. However, there are several limitations in the present study. First, there is a lack of comparing with a control substance (e.g. saline) that will help to strongly support the efficacy of cerumenolytic agents. Second, although mixing of cerumen was attempted, the composition of cerumen may still vary that lead to be the confounding factor to cerumenolytic effect. The last limitation, the hydration of cerumen is a very important factor that facilitates to remove it. Thus, further study is needed to resolve these limitations and developed as clinical trials that will definitely support the superiority efficacy of cerumenolytic agents.

5. Conclusion

Both of the objective measurements that we employed (spectrophotometric and cholesterol level assessments) showed that 2.5% sodium bicarbonate has a greater cerumenolytic effect than does docusate sodium and that this effect increases with time. These results may be applied in clinical practice.

Conflicts of interest and source of funding

All authors have no personal financial or institutional interest in any of the materials and devices described in this article. We identify no conflict of interest. This work was supported by a grant from the Faculty of Medicine, Khon Kaen University, Thailand.

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