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Effects of menthol on the triggering of the swallowing reflex in elderly patients with dysphagia

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Aims
To investigate the effect of menthol on swallowing reflex sensitivity in elderly patients with dysphagia.

Methods and results
The swallowing reflex sensitivity of institutionalized elderly patients was evaluated as a latent time of swallowing reflex (LTSR), induced by the injection of 1 ml solution into the pharynx. LTSR was significantly shortened in a concentration-dependent manner, from 13.8 s [95% confidence interval (CI) 11.1, 16.5] by distilled water to 9.4 s (95% CI 7.1. 11.8) by 10^{-2} M menthol.

Conclusion
Using menthol with elderly patients with dysphagia may improve the sensitivity of their swallowing reflex, resulting in prevention of aspiration pneumonia.

Introduction

Morbidity and mortality from aspiration pneumonia continues to be a major health problem in the elderly [1]. Dysphagia, such as delayed triggering of the swallowing reflex, an important respiratory defence mechanism, predisposes to aspiration pneumonia. Triggering of the swallowing reflex could be accelerated if swallowed material was cooled down, even in dysphagic patients [2]. Moreover, it has been clinically accepted that there are dysphagic patients who benefit from a therapeutic procedure known as thermal stimulation, a technique consisting of a brief, light touch with a cooled laryngeal mirror to the anterior faucial pillars followed by the application of small amounts of iced fluid [3]. This suggests that repeated cold stimulation restores sensitivity to trigger the swallowing reflex in dysphagic patients. In 2002, two groups independently cloned and characterized the cold receptor as a member of a transient receptor potential (TRP) superfamily, named TRPM8 [4, 5]. TRPM8 could be activated not only by

cooling with an activation temperature <25–28 °C and but also by menthol, a chemical agent found in mint. Therefore, we examined the effect of menthol in elderly patients with dysphagia.

Patients and methods

The elderly patients were recruited from institutionalized patients located near Sendai, Japan. This long-term care facility is for older patients with a physical handicap or mental deterioration. Residents are highly dependent on their caregivers for assistance with the activities of daily life. From residents in the nursing home, we selected patients who fed themselves or needed help eating and had had a stable condition for a minimum of the last 2 months. We excluded patients who had either a feeding tube or percutaneus endoscopic gastrostomy. We assessed the latent time of swallowing reflex (LTSR) in 42 patients who met the criterion and had given informed consent. Written informed consent was obtained from all study patients. A detailed explanation of the study was given to each patient. When patients lacked the ability to understand the study, or the capacity to consent, their family was asked on their behalf. This protocol was approved by the Institutional Review Board of the Tohoku University Ethics Committee (no. 2004-379).

The swallowing reflex was induced by a bolus injection of 1 ml distilled water into the pharynx through a nasal catheter (8 Fr). The subjects were unaware of the actual injection. Swallowing was identified by submental electromyographic (EMG) activity and visual observation of characteristic laryngeal movement. EMG activity was recorded from surface electrodes on the chin. The swallowing reflex was evaluated by the latency of response, timed from the injection to the onset of swallowing [6]. The mean LTSR was 10.1 s [95% confidence interval (CI) 7.1, 13.2] for the 42 patients. The ultimate goal of the study was to develop a medicine for dysphagia. We focused on patients with mild to moderate dysphagia due to the potential risk of aspiration in patients with very severe dysphagia. We excluded patients with a LTSR of >20 s and <5 s, resulting in the selection of 14 patients.

Menthol (L-menthol; Sigma-Aldrich, St Louis, MO, USA) was dissolved in distilled water using a sonicator. Various concentrations (10^{-4}–10^{-2} M) of menthol and distilled water at room temperature were injected in a double-blind, randomized manner at 2-min intervals. After completing all the dosages of the menthol prepared, we changed the catheter to a two-lumen indwelling catheter (7 Fr). One lumen was used to inject cold water and the other to measure the temperature of the injected water at the larynx by a miniature thermocouple (MT-29/2; Physitemp, Clifton, NJ, USA). The cold distilled water was then placed on a bed of ice until just before the application and then injected. Statistical analysis was conducted using SPSS version 9.0J (SPSS Inc., Chicago, IL, USA). The comparisons among groups were done by one-way ANOVA with posthoc application of Fisher's least-significant-difference test. $P < 0.05$ was taken as significant.

Results

For the 14 patients who completed the study, the mean age was 88 ± 3 (SD) years (range 81–95). The mean LTSR induced by distilled water at room temperature was 13.8 s (95% CI 11.1, 16.5). The LTSR was significantly shortened in a concentration-dependent manner by the menthol (Figure 1). The mean LTSRs induced by 10^{-4} M, 10^{-3} M and 10^{-2} M menthol were 9.4 s (95% CI 7.1, 11.8), 6.1 s (95% CI 4.7, 7.6) and 3.9 s (95% CI 2.8, 5.0), respectively. The cold water also significantly shortened the LTSR and the effect was comparable to that of 10^{-4} M menthol. The mean LTSR induced by distilled water at room temperature was 8.1 s (95% CI 6.4, 9.7). The temperature of the injected cold water at the outlet of the catheter was 23.5 ± 1.2 °C (mean ± SD). There were no harmful effects or unpleasant feelings exhibited by patients during or after the study.

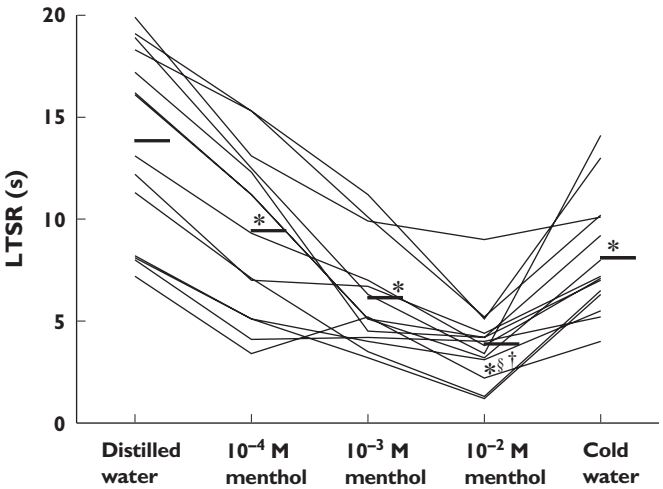

Figure 1

Latent time of swallowing reflex (LTSR) induced by distilled water at room temperature and ice cold water, and 10^{-4} M, 10^{-3} M and 10^{-2} M menthol in each subject ($N = 14$). *$P < 0.0005$ *vs.* distilled water at room temperature (distilled water); §$P = 0.0013$ *vs.* 10^{-2} menthol; †$P = 0.0001$ *vs.* distilled ice cold water.

Discussion

The study showed that menthol has an effect similar to that of cold temperature on triggering the swallowing reflex, suggesting the involvement of TRPM8 in the neural afferent of the swallowing reflex. The menthol dosage used was lower than that used to induce cold hyperalgesia by applying to the surface of the skin [7], but higher than that used to activate *in vitro* TRPM8 channel [4, 5]. Very recently, another cold receptor, TRPA1, was cloned and characterized [8]. TRPA1 is activated by noxious cold temperature (<18 °C) and by pungent compounds such as cinnamaldehyde and mustard oil, but not by menthol. Further studies are needed to elucidate the possible involvement of TRPA1 in the swallowing reflex.

Our results suggest that menthol stimulation as well as cold stimulation restores sensitivity to the triggering of the swallowing reflex in dysphagic patients. The addition of menthol to liquids or food may stimulate the swallowing reflex and help to prevent aspiration pneumonia in the elderly with dysphagia. The physiotherapy for dysphagia, known as thermal stimulation of reflex, requires considerable effort by physiotherapists or caregivers. Therefore, an alternative pharmacotherapy is needed. We have previously shown that the lozenge containing capsacin, an agonist of receptor for hot temperature (TRPV1), could improve the swallowing reflex in the dysphagic elderly [9]. Hence, letting a lozenge containing menthol dissolve in the mouth before meals in the dysphagic elderly may improve the sensitivity of the swallowing reflex. Since applying the lozenge is much easier than the procedure of thermal stimulation, evaluation of the efficacy of the menthol lozenge is warranted to prevent aspiration pneumonia in elderly dysphagic patients.

Another important defence reflex from aspiration pneumonia is cough reflex. Interestingly, menthol is known to lower cough reflex sensitivity [10]. The swallowing and cough reflexes are not always impaired simultaneously [11]. There are patients whose swallowing reflex is impaired but whose cough reflex is hypersensitive rather than impaired. Menthol may be a remedy for such patients.

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