Inhibition of Progressing Primary Esophageal Peristalsis by Pharyngeal Water Stimulation in Humans

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Background & Aims: **Sensory impulses initiated from the pharynx exert differing effects on the deglutitive apparatus. They have an inhibitory effect on the lower esophageal sphincter but an excitatory effect on the upper esophageal sphincter. The aim of this study was to systematically investigate the effect of pharyngeal sensory impulses evoked by water stimulation on the progressing esophageal peristalsis.** ***Methods:*** **Sixteen healthy young volunteers were studied in the supine position. The presence of normal peristalsis was verified. Esophageal peristalsis was recorded 3, 6, 9, 12, 15, and 18 cm above the lower esophageal sphincter. Pharyngeal stimulation was performed by injecting a predetermined threshold volume into the pharynx 2 cm above the upper esophageal sphincter, directed posteriorly. The injections were timed to coincide with the arrival of the peristaltic wave induced by dry swallows at respective recording sites.** ***Results:*** **Injection of the threshold volume (0.5 ± 0.1 mL) stopped the progression of peristalsis at both the striated and smooth muscle esophagus. Topical pharyngeal anesthesia blocked this inhibitory effect ($P < 0.01$).** ***Conclusions:*** **Sensory impulses initiated from the pharynx evoked by water injection inhibit the progression of primary esophageal peristalsis. Although the clinical significance of these findings is not determined, they may explain the mechanism of some of the failed esophageal peristalsis.**

Sensory impulses initiated from the pharynx exert differing effects on the deglutitive apparatus. They have an inhibitory effect on the lower esophageal sphincter (LES), resulting in its complete or, less commonly, partial relaxation.[1] On the upper esophageal sphincter (UES), they exert an excitatory effect, resulting in an increase in its resting tone.[1–3] However, the effect of these sensory impulses on the esophageal body motor function is not known. A preliminary study in our laboratory suggested an inhibitory effect on esophageal peristalsis. The aim of the present study was to systematically investigate the effect of pharyngeal sensory impulses evoked by water stimulation on the progressing esophageal peristalsis.

Materials and Methods

We studied 16 healthy young volunteers (5 female and 11 male; age, 32 ± 2 years; age range, 19–44 years). The studies were performed with the subjects in the supine position. The study protocols were approved by the Human Research Review Committee of The Medical College of Wisconsin, and the subjects gave informed written consent before their studies.

The UES, esophageal body, LES, and gastric pressure phenomena were recorded concurrently using two sleeve assemblies, which were passed through each nostril and positioned so that the LES sleeve device (6 × 0.5 × 0.4 cm; Dentsleeve, Adelaide, Australia) straddled the LES and the UES sleeve device (6 × 0.5 × 0.3 cm; Dentsleeve) straddled the UES. With this arrangement, the esophageal body pressure phenomena were recorded at the top of the LES sleeve 3, 6, 9, 12, 15, and 18 cm proximal to the LES. The upper sleeve assembly also incorporated an injection port located 2 cm proximal to the sleeve device. This manometric assembly was positioned so that the injection port faced posteriorly. The subjects were monitored for 10 minutes after the positioning of the two manometric assemblies.

Subsequently, the presence of normal peristalsis was confirmed for each subject by monitoring 10 dry swallows before pharyngeal stimulation; only subjects with normally progressing esophageal peristalsis during dry swallows were studied.

To study the effect of pharyngeal water stimulation on the progression of esophageal primary peristalsis, subjects were asked to swallow on command, and their pharynx was stimulated by injections of minute amounts of water. Water injections were timed to coincide with complete UES relaxation or arrival of the peristaltic pressure wave at each recording site.

Pharyngeal water stimulation was initiated by a rapid pulse injection of 0.1 mL of water directed toward the posterior pharyngeal wall. The volume of injected water was increased by 0.1-mL increments until either the progression of the peristaltic wave was halted or an irrepressible swallow occurred.

Abbreviations used in this paper: UES, upper esophageal sphincter.

0016-5085/96/$3.00

Table 1. Effect of Pharyngeal Water Stimulation on the Amplitude of the Peristaltic Pressure Wave

	Sites of pressure wave above LES coincident with pharyngeal water injection				
	18 cm	15 cm	12 cm	9 cm	6 cm
Amplitude (*mm Hg*)					
Before injection	79 ± 4	63 ± 4	72 ± 6	72 ± 6	72 ± 6
After injection	56 ± 6[a]	50 ± 5[a]	47 ± 7[a]	59 ± 8[a]	36 ± 6[a]
Percent decrease	29 ± 6	18 ± 8	33 ± 10	13 ± 5	49 ± 9

NOTE. Pharyngeal water injection significantly reduced the amplitude of the developing pressure wave in both the striated and smooth muscle portions of the esophagus.
[a]$P < 0.05$.

Each volume was repeated three times for each recording site, and the subjects withheld swallowing after water injection for as long as they could. Occurrence of the swallow was judged by typical deglutitive UES and LES relaxation, by subject's signal using a handheld marker, and by observer's marks on the polygraph paper. Each swallow tested by pharyngeal stimulation was performed 25–30 seconds after a control swallow and was followed 25–30 seconds later by a second control swallow. Subsequently, the pharyngeal mucosa of each subject was anesthetized by the application of 4% topical lidocaine spray (Roxan Laboratories Inc., Columbus, OH), and the test was repeated 5 and 20 minutes afterward. Inhibition of progressing peristalsis after each pharyngeal water injection was accepted when the pressure wave was completely eliminated after the injection. Frequency of inhibition after each water injection was determined as a percentage of the trials for each site.

To correlate the effect of pharyngeal water stimulation on progressing esophageal peristalsis with its effect on respiration, the above protocol was repeated in 5 additional subjects while the respiration was monitored by a pneumobelt wrapped around the subject's chest.[4] The output signal induced by the respiratory chest wall movement was recorded on the same polygraph paper used for recording esophageal peristalsis.

We measured the threshold volume for inhibition of peristalsis in each subject and determined the presence or absence of development of a new peristaltic pressure wave after each inhibited peristalsis. We also determined the effect of pharyngeal water injection on the amplitude of the pressure wave at whose onset the water was injected into the pharynx. In subjects in whom respiration was monitored, duration of deglutitive apnea, the presence or absence of apnea induced by water injection, and the respiratory rate for the 10-second period immediately after pharyngeal water injection were determined and compared with the period before water injection. Statistical analysis was performed using analysis of variance with repeated measures and χ^2 tests, when appropriate. Data are presented as mean ± SE unless otherwise stated.

Results

At a threshold volume of 0.5 ± 0.1 mL, progression of primary esophageal peristalsis induced by dry swallows was inhibited in all volunteers except in 2 subjects, in whom the mere injection of 0.1 mL of water resulted in a pharyngeal swallow. Therefore, the inhibitory effect of pharyngeal water stimulation on the progression of primary peristalsis could not be evaluated in these 2 subjects. The level of peristaltic inhibition was dependent on the extent to which peristalsis had progressed before the development of pharyngeal water injection; specifically, water injected before the development of complete UES relaxation did not induce inhibition. Likewise, when the peristaltic wave reached the most distal site, it did not inhibit the development of the pressure wave even if the water was injected coincidently with the onset of the pressure-wave upstroke. However, it frequently resulted in the reduction of the amplitude of the pressure wave at this site compared with dry swallows before and after water injection. As a rule, at all recording levels, the pressure wave coincident with the water injection was not inhibited, but the peristaltic wave inhibition occurred at the next recording site.

The uninhibited pressure wave had a significantly lower amplitude than its counterparts induced by swallows before and after pharyngeal water injection ($P < 0.05$). The attenuating effect was observed in both the striated and the smooth muscle portion of the esophagus. Although there was a trend for a larger reduction in the amplitude of the pressure wave in the distal esophagus compared with the proximal esophagus, the difference did not reach statistical significance ($P = 0.06$) (Table 1).

Figure 1 shows the inhibition of progressing primary peristalsis at various segments of the esophagus that were induced by pharyngeal water injection. This inhibition occurred in both the proximal striated muscle portion and the distal smooth muscle portion of the esophagus. This inhibitory effect was significantly reduced by the application of topical pharyngeal anesthesia (Figure 2). However, the effect of topical anesthesia was reversible (Figure 3).

Analysis of concurrent recordings of esophageal peri-

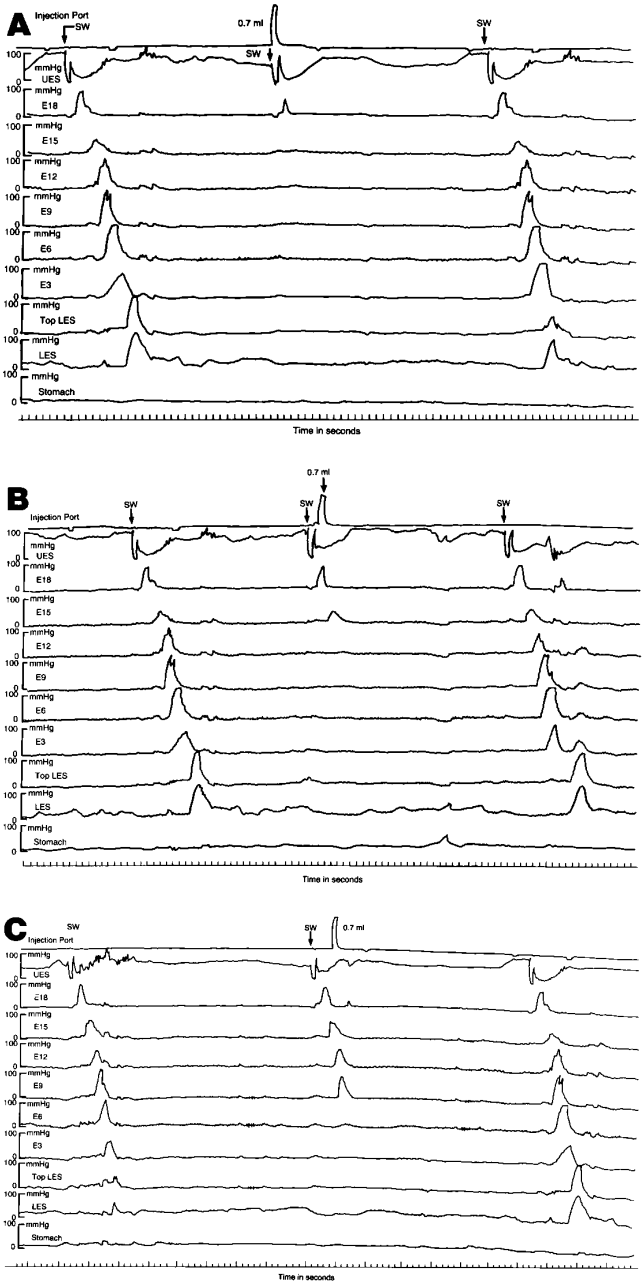

Figure 1. Examples of inhibition of progressing primary esophageal peristalsis in the (*A* and *B*) proximal striated and (*C*) distal smooth muscle esophagus by pharyngeal water stimulation. (*A*) Rapid injection of 0.7 mL room-temperature water into the pharynx immediately after UES relaxation and arrival of peristaltic wave at the site 18 cm above LES inhibited the progression of peristalsis to the sites below. (*B*) Similar injection when the peristaltic wave had reached the site 15 cm above the LES inhibited its progression to the more distal sites. (*C*) Rapid pulse injection of 0.7 mL room-temperature water into the pharynx when the peristaltic wave was 9 cm above the LES resulted in its inhibition in the smooth muscle portion in the distal 6 cm of the esophagus. Note that these inhibitions were not followed by another peristaltic pressure wave. Each inhibition trial is preceded and followed by a normal peristaltic pressure wave induced by a dry swallow. SW, swallow.

stalsis and respiration showed that inhibition of esophageal peristalsis by pharyngeal water injection was associated with a small but significant decrease in the respiratory rate (18 ± 0.1 vs. 15 ± 0.2/min; $P < 0.05$) at all levels. This decrease in respiratory rate lasted for an average of 11 ± 3 seconds and was frequently reset to the preinjection rate after a swallow. Comparison of the respiratory rate in the periods before and after swallows that were not challenged by pharyngeal water stimulation did not show any significant difference. The duration of deglutitive apnea for swallows that were followed by pharyngeal water injection was similar to that of spontaneous swallows. There was no detectable apnea besides the deglutitive apnea identified after pharyngeal water stimulation.

In 5 subjects, we also determined the threshold volume for inducing isolated LES relaxation. The threshold volumes for induction of LES relaxation and inhibition of progressing primary esophageal peristalsis were similar.

Discussion

In this study, we determined the effect of pharyngeal sensory impulses induced by water stimulation on the progressing esophageal peristalsis. Our study findings show that abrupt injection of minute amounts of water toward the posterior pharyngeal wall results in the inhibition of a swallow-induced progressing peristaltic wave

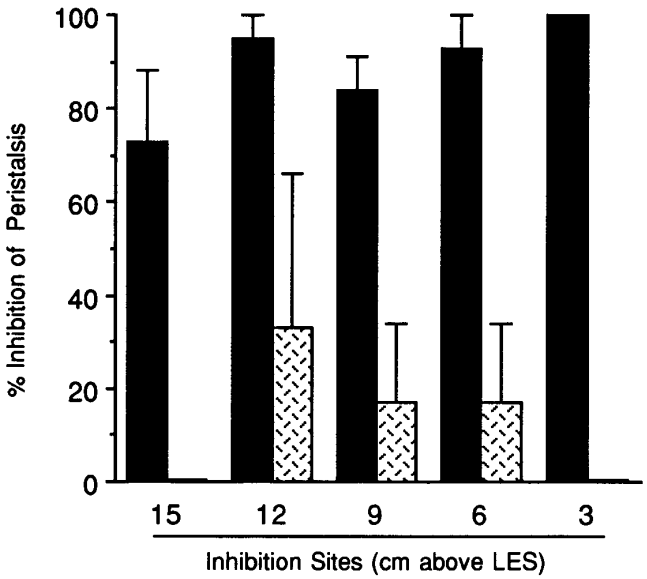

Figure 2. Effect of topical pharyngeal anesthesia on the inhibition of progressing primary esophageal peristalsis by pharyngeal water stimulation. Pharyngeal water stimulation at a threshold volume inhibited the progression of the peristalsis in both the striated and smooth muscle portions of the esophagus. Topical pharyngeal anesthesia significantly reduced this inhibitory effect ($P < 0.01$). ■, Before anesthesia; ⊠, after anesthesia.

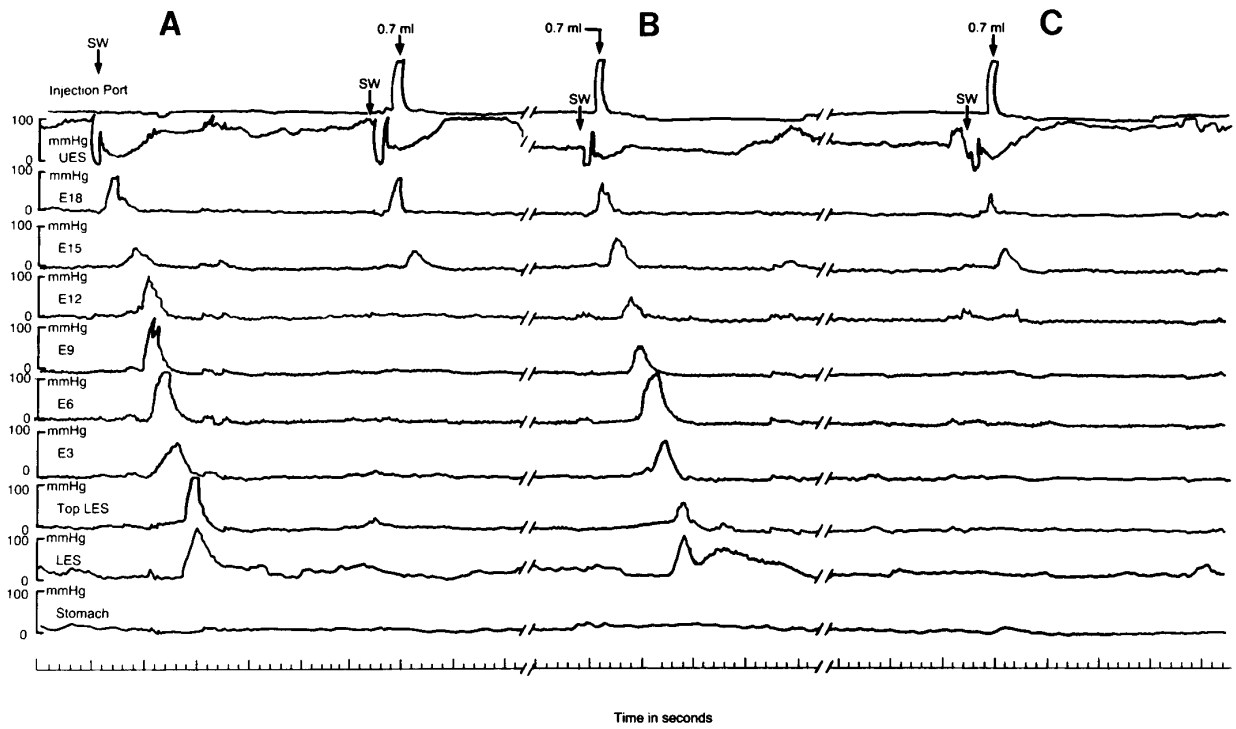

Figure 3. An example of the effect of pharyngeal topical anesthesia on the inhibition of progressing esophageal peristalsis by pharyngeal water stimulation. (*A*) Inhibition of progressing esophageal peristalsis by pharyngeal water stimulation before application of topical pharyngeal anesthesia. (*B*) Five minutes after topical anesthesia, injection of the same volume of water into the pharynx did not result in inhibition of progressing esophageal peristalsis. (*C*) Twenty minutes after topical pharyngeal anesthesia, the inhibitory effect of pharyngeal water injection has returned. SW, swallow.

in both the striated and smooth muscle portions of the esophagus.

Previous studies have shown that minute amounts of water injected into the pharynx induce isolated LES relaxation in humans.[1] Findings of the present study support the notion that pharyngeal water stimulation results in a generalized inhibition of the contractile activity of the esophageal body and the LES. Mechanisms of this inhibitory effect are not currently known. However, it may be postulated that it is mediated centrally through the brain stem swallowing center.

Our study findings concur with previous reports that the inhibitory effect of the swallowing centers on the deglutitive apparatus could be uncoupled from its excitatory effect by pharyngeal water stimulation.[1] This technique may be useful in further delineating the complex mechanism of deglutitive peristalsis.

Various factors are known to affect esophageal peristalsis. Sensory feedback, such as that originating from the presence of a bolus, is known to increase the amplitude of the peristaltic pressure wave[5,6] and reduce the rate of failed peristalsis.[5,6] A swallow occurring in close temporal proximity to a previous swallow tends to either inhibit or attenuate the preceding peristaltic pressure wave.[7–9] This inhibitory effect may occur in both the striated and smooth muscle portions of the esophagus, as shown by Vanek and Diamant.[10] However, the peristaltic wave generated by the second swallow progresses uninterrupted, although it may be attenuated. The latter study confirms the presence of a central inhibition that precedes the stimulation of the deglutitive esophageal peristalsis. The inhibitory effect of pharyngeal stimulation on progressing esophageal peristalsis described in the current study is different from that of the above mentioned studies by not inducing a second peristaltic wave after the inhibition of the original peristalsis. Whether this finding is another manifestation of deglutitive inhibition, or simply shows the isolated stimulation of inhibitory function of the brainstem swallowing center through an unrelated pathway, or yet suggests the presence of a different inhibitory pathway is not clear at this time.

Considering the fact that pharyngeal stimulation induces a centrally mediated contraction of the cricopharyngeus striated muscle[1–3] while inhibiting the proximal esophageal striated muscle layer, these findings suggest that pharyngeal water stimulation seems to have a dual effect on the brain stem neurons: an inhibitory effect on one group of neurons and an excitatory effect on the other group. The findings also suggest the possibility that the excitatory effect of the pharyngeal stimulation

on the cricopharyngeus muscle may not be mediated through the deglutitive pathways.

Previous studies have shown the existence of a close coordination between deglutition and respiration.[4,11–13] Earlier studies have documented the effect of alterations of the respiratory function on the coordination of deglutition with the phases of respiration.[4] On the other hand, pharyngeal water stimulation in a feline model has been shown to inhibit the activities of the inspiratory neurons while increasing the activities of expiratory neurons.[14] Our finding of the association of inhibition of esophageal peristalsis by pharyngeal water stimulation with a reduction in the respiratory rate is another example of the close central coordination of the deglutitive and respiratory functions.

In conclusion, sensory impulses initiated from the pharynx by water injection inhibit the progression of primary esophageal peristalsis. Although the clinical significance of these findings is not currently determined, it is conceivable that they explain the mechanism of some of the failed esophageal peristalsis.

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Received July 19, 1995. Accepted September 25, 1995.

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Supported in part by National Institutes of Health grants RO1-DC00669 and RO1-DK25731 and by a Merit Review Grant from the Department of Veterans Affairs. Dr. Trifan's research fellowship was supported in part by an Astra Merck research fellowship grant.