Characterization of the pharyngo-UES contractile reflex in humans

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Shaker, Reza, Junlong Ren, Pengyan Xie, Ivan M. Lang, Eytan Bardan, and Zhumei Sui. Characterization of the pharyngo-UES contractile reflex in humans. Am. J. Physiol. 273 (Gastrointest. Liver Physiol. 36): G854–G858, 1997.—Preliminary human studies suggest the presence of an upper esophageal sphincter (UES) contractile reflex triggered by pharyngeal water stimulation. The purposes of this study were to further characterize this reflex and determine the threshold volume for its activation. We studied 10 healthy young volunteers by manometric technique before and after topical pharyngeal anesthesia. UES pressure responses to various volumes and temperatures of water injected into the pharynx were elucidated. At a threshold volume, rapid-pulse and slow continuous pharyngeal water injection resulted in significant augmentation of UES pressure in all volunteers. Threshold volume for inducing UES contraction averaged 0.1 ± 0.01 ml for rapid-pulse injection and was significantly smaller than that for slow continuous injection (1.0 ± 0.2 ml). UES pressure increase duration averaged 16 ± 4 s. Augmentation of UES resting tone by injection of water with three different temperatures was similar. This augmentation was abolished after topical anesthesia. Conclusions were that stimulation of the human pharynx by injection of minute amounts of water results in a significant increase in resting UES pressure: the pharyngo-UES contractile reflex. The magnitude of pressure increase due to activation of this reflex is not volume or temperature dependent. Loss of pharyngeal sensation abolishes this reflex.

upper esophageal sphincter: airway protection

During earlier studies aimed at determining the threshold volume for triggering a pharyngeal/reflexive swallow (6), it was noted that subthreshold volumes for triggering a pharyngeal swallow resulted in augmentation of upper esophageal sphincter (UES) resting pressure. Subsequent works in a feline model (3) confirmed the presence of a contractile reflex triggered by pharyngeal mechanical stimulation that resulted in contraction of the cricopharyngeus muscle. However, the presence of this contractile reflex in humans and the threshold volume for its triggering have not been systematically studied. For this reason, the present study was undertaken to further characterize this reflex in young healthy humans.

METHODS

Ten healthy volunteers, aged 33 ± 2 yr (range: 22–39 yr; 3 women, 7 men) were studied. The study was approved by the Human Research Review Committee of the Medical College of Wisconsin, and subjects gave informed consent before the study began. Each subject was studied before as well as after application of 4% Aquase xylocaine (Roxane Laboratory, Columbus, OH) to the pharynx, applied by a spraying device. Topical anesthesia was confirmed by abolition of the gag reflex.

A UES sleeve catheter (Dentsleeve, Adelaide, Australia) that incorporated a sleeve device (6 × 0.5 × 0.3 cm) and side-hole manometric ports at its proximal and distal ends for manometric positioning was used to monitor the UES resting pressure and its response to pharyngeal water stimulation. The sleeve assembly also had additional recording sites 4.5 cm distal and 3 cm proximal to the sleeve. After application of 2% xylocaine to the more patent nostril, the manometric assembly was introduced through the nose and positioned within the UES such that the manometric port immediately proximal to the sleeve was positioned 2 cm above the UES high-pressure zone. After manometric positioning, this port was used only for water injection and, similar to the other pharyngeal ports, was otherwise not perfused.

The nonperfused injection port, the esophageal tips, and the sleeve sensor were connected to pressure transducers in line with a pneumohydraulic pump (Arndorfer Medical Specialties, Greendale, WI). With this arrangement, the onset and offset of water injection and UES pressure were recorded on chart paper run at a speed of 25 mm/s, providing an equivalent of 40 ms for each millimeter distance of pen movement.

For pharyngeal stimulation, two modes of fluid delivery into the pharynx were tested: rapid-pulse and slow continuous injection. For pulse injection, we started with 0.05 ml, followed by 0.1 ml of water, and then increased the volume by 0.1-ml increments until an irrepressible swallow occurred. Slow continuous infusion was performed at a rate of 5.5 ml/min by using a Harvard infusion pump (model N0975; Harvard Apparatus, Dover, MA) until an irrepressible swallow occurred. Each injection was started immediately after the UES pressure returned to baseline after a swallow, and subjects withheld swallowing as long as they could. For both rapid and slow injection, liquid temperatures of 0, 37, and 60°C were tested with subjects in the supine position. Swallowing was monitored by submental surface electromyograph and the distinctive UES relaxation response during swallowing.

After the sleeve was positioned, each subject was monitored for 10 min for adaptation, and we then determined in each subject the consistent change in UES pressure in response to various volumes of pharyngeal water injection (3 of 3 injections). For comparison of UES pressure before the injection with that after the injection, the average end-expiratory pressure for a 10-s period before the injection was used. We measured the maximum UES pressure after pharyngeal water injection, excluding the 3-s interval before deglutitive relaxation, if a swallow occurred. This was done to avoid the commonly seen pressure increase that is registered by the sleeve during the oral excursion of the UES immediately before its swallow-induced relaxation. Also determined in each subject was the smallest volume that consistently
Fig. 1. Effect of pharyngeal water injection on upper esophageal sphincter (UES) resting pressure. A: rapid-pulse injection of 0.2 ml of room-temperature water resulted in augmentation of UES pressure from 55 to 137 mmHg. As seen, this augmentation persisted for 22 s until it returned to baseline after a dry swallow (DS). Esop., esophageal; EMG, electromyogram. B: slow continuous infusion of room-temperature water also resulted in an increase of preinfusion pressure of 80 to 200 mmHg measured 3 s before a swallow occurred.
triggered a pharyngeal swallow on rapid-pulse injection as well as on slow continuous injection.

Statistical analysis was performed by using one-way or two-way analysis of variance as appropriate. Values are presented as means ± SE unless otherwise stated.

RESULTS

At a threshold volume, rapid-pulse as well as slow continuous pharyngeal water injection resulted in augmentation of UES pressure in all volunteers (Fig. 1). The threshold volume for inducing UES pressure increase averaged 0.1 ± 0.01 ml. The threshold volume for 2 of 10 volunteers was 0.05 ml, in 7 volunteers it was 0.1 ml, and in 1 volunteer it was 0.2 ml. Further increase in the volume of injected water above the threshold volume did not result in any significant additional increase in the UES pressure (Fig. 2). Similarly, slow continuous injection of water into the pharynx resulted in augmentation of UES resting pressure. The threshold volume for slow continuous injection (1.0 ± 0.2 ml) was significantly larger than that of rapid-pulse injection (P < 0.05). The magnitude of this augmentation was comparable to that induced by rapid-pulse injection (Fig. 2). The magnitude of UES pressure following rapid-pulse injection of threshold volumes of water into the pharynx averaged 76 ± 5 mmHg compared with the baseline preinjection value of 45 ± 2 mmHg (61 ± 13% increase). For slow continuous injection, it was 81 ± 6 mmHg compared with the baseline of 46 ± 2 mmHg (63 ± 9.0%).

In all, 120 rapid water injections for 0.05-, 0.1-, 0.2-, 0.3-, and 0.4-ml volumes were performed. In 17 instances, and in 7 volunteers, the UES pressure increase induced by water injection returned to baseline preinjection value before a swallow occurred. The duration of UES augmentation in these instances averaged 9.0 ± 3.0 s (range 4–45 s). In the remaining 103 instances, the UES pressure increase persisted until a swallow occurred. In these instances, the duration for UES pressure increase averaged 16 ± 4 s (range2–40 s). For slow continuous injection, there was no return of the pressure to baseline before the occurrence of a swallow.

The effect of temperature of injected volumes on the UES pressure is shown in Fig. 3. Augmentation of UES resting tone by injection of water with three different temperatures was similar.

In all subjects, rapid-pulse injection of 0.5 ± 0.1 ml of water into the pharynx resulted in an irrepressible swallow. This threshold volume was significantly larger than the threshold volume that induced UES pressure augmentation (P < 0.01).

DISCUSSION

In this study we determined the effect of pharyngeal stimulation by water injection on the resting tone of the
UES. The study findings confirm the presence of a pharyngo-UES contractile reflex in humans. The afferent arm of this reflex most probably includes the pharyngeal mechanoreceptors and the glossopharyngeal nerve, although the contribution of the superior laryngeal nerve cannot be excluded. The efferent arm is undoubtedly the vagus nerve. The central pathway for this reflex is not currently known, but is probably different from those of deglutition because the contractile response to the stimulation of this reflex is the opposite of the relaxation response of the UES to a volitional, subconscious, or reflexive/pharyngeal swallow.

Except for the UES, pharyngeal water stimulation induces an inhibitory effect on the deglutitive apparatus; on the lower esophageal sphincter, its effect is complete or partial inhibition of the basal tone (9), and these inhibitions may be associated with gastroesophageal reflux (4, 10). Pharyngeal water stimulation is also

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Fig. 4. Example of effect of topical pharyngeal anesthesia on UES pressure response to pharyngeal water injection during 0.2-ml rapid-pulse injection (A) and 5.5 ml/min continuous water infusion (B). As seen, pharyngeal water injection by both modes did not result in any change in resting UES pressure after pharyngeal topical anesthesia.
capable of inhibiting the crura of the diaphragm (4). On
the esophageal body, pharyngeal water stimulation
inhibits the progression of the primary peristalsis (8),
resulting in a halt in bolus transport (1). On the
contrary, we found in this study that the effect of
pharyngeal water stimulation on the UES is stimula-
tory, resulting in a significant increase in the resting
UES pressure. It is conceivable that this contractile
response of the UES may counteract the inhibitory
effect of pharyngeal water stimulation on the rest of
the deglutitive apparatus, thus preventing pharyngeal
reflux of gastric and/or esophageal content. In addition,
it may be postulated that this reflex may be activated
during gastroesophageal reflux events by contact of regurgitated
material with pharyngeal mucosa, thus inducing an augmenta-
tion of UES resting pressure and possibly preventing
further entry of refluxate into the pharynx. In this
regard, the pharyngo-UES contractile reflex may be
considered one of the airway-protective mechanisms
against aspiration of gastric content.

It is known that stimulation of the pharynx by
various stimuli results in contraction of the diaphragm
as well as of the intercostal muscles, resulting in
inhalation: the aspiration reflex (5, 7). Increase or
decrease in ambient pressure of the pharynx results in
stimulation of rapidly adapting receptors of pharyngeal
mucosa. These discharges have been recorded by single
fibre recording from the glossopharyngeal as well as
the superior laryngeal nerves (2). Although in this
study the effect of pharyngeal stimulation on respira-
ition was not determined, during previous studies on its
effect on esophageal peristalsis (7, 8), which were done
with similar methodology, respiration was monitored
and showed only a reduction of respiratory rate without
evidence for induction of apnea or inhalation reflex.
The pharyngo-UES contractile reflex is an example of
digestive tract reflexes originating from the pharynx in
humans. This same reflex has been documented in
felines (3).

In the feline model, the afferent arc of this reflex was
found to be the glossopharyngeus nerve because sever-
ance of this nerve abolished the reflex (3). The efferent
arc was the cricopharyngeal branch to the pharyn-
geo-oesophageal nerve. Contraction of the cricopharyngeal
muscle induced by pharyngeal mechanical stimulation
was short lived, indicating that the reflex was being
mediated through rapidly adjusting mechanoreceptors.

The duration of reflex contraction of UES after
pharyngeal water injection in humans determined in
this study is significantly longer than that found in the
feline model. Commonly, it was long enough until a
spontaneous swallow occurred. However, it needs to be
considered that in feline studies we used pressure
application and a light touch that had a distinct
beginning and end. In the present study, although the
onset and completion of water injection were distinct,
the injected volume stayed in the pharynx until it was
cleared by a swallow. This dwelling of the injected
water and its continuous stimulation of the pharynx
may account for the longer duration of UES contraction
and indicate that responsible receptors in the pharynx
stimulated by this technique are slowly adjusting.
These slowly adapting receptors recruited for stimula-
tion of the pharyngo-UES contractile reflex in humans
seem to be different from those reported in the litera-
ture as responsible for the aspiration reflex (2, 5), which
consists of rapidly adapting receptors.

In summary, stimulation of the pharynx in humans
by injection of minute amounts of water results in a
significant increase in resting UES pressure: the phary-
ngo-UES contractile reflex. Threshold volume for
stimulation of the pharyngo-UES contractile reflex is
significantly lower than that for a pharyngeal swallow.
The degree of pressure increase due to activation of this
reflex in normal young humans is not volume or
temperature dependent. Loss of pharyngeal sensation
abolishes this reflex.

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