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Original Paper

Effects of Arterial Oxygen Saturation on Gag Reflex in Humans

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Abstract

The gag reflex is known to be induced by oro-pharyngeal stimulation. Its physiological role is presumably to expel a bolus interrupting the upper airway. The present study used 27 healthy subjects to investigate how changes in arterial oxygen saturation (SpO_2) influences the gag reflex. The gag reflex was elicited by compression of the lingual root in 25 subjects, however, two subjects did not respond. After recording the gag reflex under normal ventilation (control), eight subjects inhaled air containing 30% oxygen for three minutes. Compression of the lingual root was started five seconds after the inhalation. Seventeen subjects were asked to hold their breaths for 30 seconds and the gag reflex was induced five seconds later. SpO_2 was significantly increased in those inhaling 30% oxygen and was significantly decreased in those who held their breath. Inhalation of 30% oxygen caused prolonged latency of the gag reflex and attenuation of integral abdominal muscle activity corresponding to the gag reflex. In contrast, latency of the gag reflex was shortened and integral abdominal muscle activity was augmented during decrease of SpO_2. These results suggested that induction of the gag reflex was modified by input from chemoreceptive afferents integrated in the medulla oblongata.

Introduction

Retching and/or expulsion induced by irritation of the oropharyngeal mucosa are known as the gag reflex. The gag reflex is considered to be a protective response that prevents noxious materials from entering the pharynx and larynx, or trachea [1][2]. It is also induced when a large bolus blocks the oropharyngeal region causing suffocation. It is also elicited by electrical stimulation of the pharyngeal branch of the glossopharyngeal nerve or the superior laryngeal branch of the vagus nerve in animal experiments [3][4]. These nerves enter the medulla oblongata and connect to secondary neurons in the nucleus of the tractus solitarii (NTS).

We know by experience that the gag reflex is induced when chewed food intercepts the airway when swallowed. Furthermore, vomiting or the gag reflex occurs when oxygen concentrations become lower at high altitude, a condition known as mountain sickness. In an animal experiment, Fukuda and Koga [5] reported that hypercapnia and/or hypoxia promotes transition retching to expulsion when the abdominal vagal afferent nerve was electrically stimulated in decerebrated dogs. It is known that oxygen and carbon dioxide concentrations are monitored by chemoreceptors in the carotid sinus and aortic arch. Information

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of blood gases as well as afferent gag reflex activities are sent to secondary NTS neurons in the medulla oblongata via the vagus and glossopharyngeal nerves. From these findings, it is possible that oxygen and carbon dioxide concentrations could affect induction of the gag reflex. The gag reflex, which is induced during endoscopic examinations or clinical oral care, may be due to oxygen concentration. Arterial oxygen saturation (SpO_2) can be non-invasively recorded in humans and reflects arterial oxygen concentration. In the present study, how the gag reflex is influenced by changes in SpO_2 was investigated in healthy subjects.

Methods

Twenty-seven male subjects participated in this study. None had a clinical history of respiratory, cardiovascular, or neuromuscular disorders. All of them gave their informed consents to be enrolled in the study. All experimental procedures were performed in accordance with guidelines set forth by the Ethics Committee of Kawasaki Medical School.

All subjects were seated in comfortable chairs and asked to relax their muscles in a silent room regulated to a temperature of ∼26 ℃ with normal humidity. Temperature of the airflow through the nasal cavity was continuously recorded using a thermosensor (TR-762T, Nihon Kohden). SpO_2 at the left index finger was measured using a standard pulse oxymeter (OLV-3000, Nihon Kohden). Two cutaneous bipolar disposable Ag/ AgCl electrodes were used to record surface electromyograms of the digastric and abdominal muscles. Myoelectrical activities were amplified by biophysical amplifiers (AB621G, Nihon Kohden). Each subject was instructed to compress the lingual root strongly enough to induce the gag reflex. Before starting the experiments, each subject was asked to practice inducing the gag reflex at least 3 times. Induction of the gag reflex was identified by a characteristic firing pattern of digastric and abdominal muscle activities. Examiner's visual observation and subjects' self assessments were also used to identify the gag reflex.

After recording control gag reflex patterns, air containing 30% oxygen generated by an oxygen generator (MS-100, National) was inhaled for 3 min by 8 subjects (group 1). Compression of the lingual root to induce the gag reflex was started 5 sec after the inhalation. The remaining 19 subjects were asked to hold their breaths for 30-sec after control recordings were taken (group 2). Compression of the lingual root for inducing the gag reflex was started 5 sec later. Latency of the gag reflex, duration and interval activities of the abdominal muscles were measured. Latency of the gag reflex was defined as the interval from tongue compression to onset of abdominal muscle activity associated with the gag reflex. Digastric muscle activity was not employed for measuring latency of the gag reflex, because this muscle was active during insertion of the tongue depressor.

All data were converted to digital data using an analog-to-digital converter (Power Lab, AD Instruments) stored in a computer (Macintosh Powerbook G3, Apple), and analyzed using a software program (Chart ver 5.0, AD Instruments). All numerical values are represented as means ± SD. Statistical analysis was performed using paired t-test, and significance was taken as $p<0.05$.

Results

Twenty-five of 27 subjects showed the gag reflex after lingual root compression under normal ventilation. Two subjects could not induce gag reflex. The latency of the gag reflex was 4.38 ± 3.46 sec (n=25). In eight subjects (group 1), SpO_2 was 97.5 ± 0.7 % under normal ventilation, and significantly increased to 98.1 ± 0.8 % just after 30% oxygen inhalation ($p<0.01$, Table 1). In the remaining 17 subjects (group 2),

SpO_2 was 98.8 ± 0.7 % under normal ventilation, and significantly decreased to 96.6 ± 1.9 % after holding the breath for 30-sec ($p<0.01$, Table 1).

Table 1 SpO2 change by inhalation of 30% oxygen and holding the breath

	Age	SpO_2(%)		
		control	30% oxygen	holding the breath
Group1	22.4±0.7	97.5±0.7	98.1±0.8**	—
Group2	21.5±1.0	98.8±0.7	—	96.6±1.9**

**$p<0.01$, significant difference compared with the values of control

Effects of increased SpO_2 on the gag reflex.

Typical gag responses before (A) and after increased SpO_2 (B) are shown in Fig. 1. Just after the onset of lingual root compression (arrows in Fig.1), changes in nasal temperature ceased, indicating pulmonary ventilation was interrupted. Subsequently, the abdominal muscle showed a prolonged burst of activity corresponding to the gag reflex ("G" in Fig.1). The digastric muscle showed bursts of activity similar to those of the abdominal muscle. Periodic changes of nasal cavity temperature reappeared after the gag reflex, indicating ventilation was resumed. After oxygen inhalation, latency of the gag reflex was elongated, and abdominal muscle activity was attenuated (Fig. 1B). Latency of the gag reflex before inhalation of 30% oxygen was 3.93 ± 2.69 sec and was significantly elongated after inhalation to 6.84 ± 5.84 sec. (Fig. 2A, n=8, $p<0.05$). Durations of abdominal muscle activities before and after inhalation were 1.47 ± 0.10 and 0.92 ± 0.65 sec, respectively. Integral abdominal muscle activity was 0.36 ± 0.45 mV・sec under normal ventilation, and significantly decreased to 0.16 ± 0.23 mV・sec after inhalation (Fig.2B, $p<0.05$).

Effects of decreased SpO_2 on the gag reflex.

Typical gag responses reflecting the effects of holding the breath are shown in Fig.3. After holding the breath, activities of the digastric and abdominal muscles corresponding to the gag reflex increased compared with the control (Fig.3B). Latency of the gag reflex was 4.59 ± 3.83 sec under normal conditions, and was significantly shortened to 3.02 ± 2.09 sec after holding the breath (Fig.4A, n=17, $p<0.05$). Durations of abdominal muscle activities before and after holding the breath were 0.98 ± 0.36 and 1.32 ± 0.42 sec, respectively. Integral abdominal muscle activity at the gag reflex was 0.38 ± 0.27 mV・sec during normal ventilation, and was significantly increased to 0.48 ± 0.35 mV・sec after holding the breath (Fig.4B, $p<0.05$).

Discussion

It is well known that irritation of the oropharyngeal mucosa induces a gag reflex. The major force of the gag reflex is reported to be produced by simultaneous contraction of the diaphragm and abdominal muscle. Similarly, these muscles synchronously contract during vomiting, which is composed of retching and expulsion. The expulsion phase corresponds to the gag reflex. In this study, a prolonged burst of abdominal muscle activity was found just after the onset of lingual root compression. The digastric muscle activity followed the burst activity of abdominal muscle, indicating that the mouth was opened. Further, subjects complained about the experience of inducing the gag reflex by compressing the lingual root. Thus,

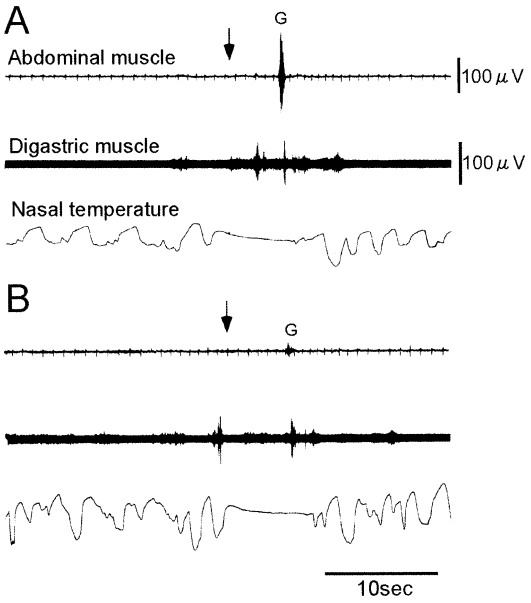

Fig. 1 Abdominal muscle, digastric muscle and nasal temperature recordings on the gag reflex. (A) Control conditions normal ventilation. (B) After inhalation of 30% oxygen. A, B Were obtained in a single subject. The onset of lingual root oppression is indicated by arrows. G; gag reflex. These explanations also apply to Fig. 3.

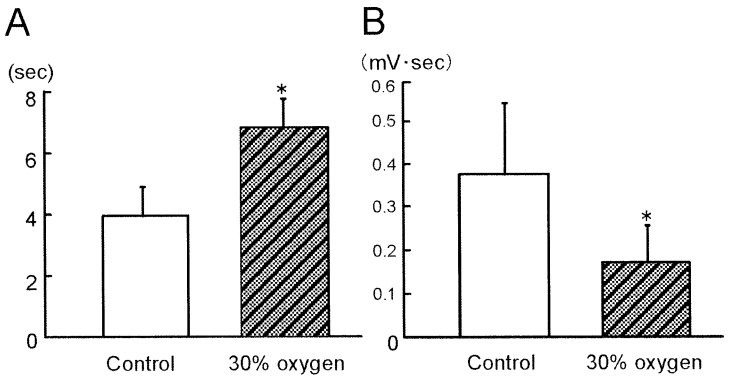

Fig. 2 Influence of oxygen inhalation on gag reflex. (A) Latency of gag reflex. (B) Integral abdominal muscle activity at gag reflex. The values shown are mean ± SEM. $^{*}p < 0.05$, significant difference compared with the values of control.

abdominal burst and ensuing digastric activities were considered to be indicators of the gag reflex.

In the present study, 25 subjects were able to induce the gag reflex, while two subjects could not. It was reported that the gag reflex was absent in 37% of 140 healthy subjects [1], and no significant differences were found with respect to age [6]. Thus, the threshold of the gag reflex seems to be rather different from person-to-person.

Increase of SpO_2 caused a prolonged latency of the gag reflex and decreased integral abdominal muscle activity corresponding to the gag reflex in this study. In contrast, latency of the gag reflex was shortened and integral abdominal muscle activity was increased with a decrease in SpO_2. It is known that oxygen and carbon dioxide concentrations are monitored by chemoreceptors of the carotid sinus and aortic arch. Afferent fibers of chemoreceptors make synaptic connections to secondary neurons of NTS [7][8]. The glossopharyngeal nerve, which presumably was stimulated in this study, similarly enters the NTS. The results of this study suggested that induction of the gag reflex was modified by input from chemoreceptive afferents. Fukuda and Koga [5] found that retching induced by stimulation of abdominal vagal afferents was

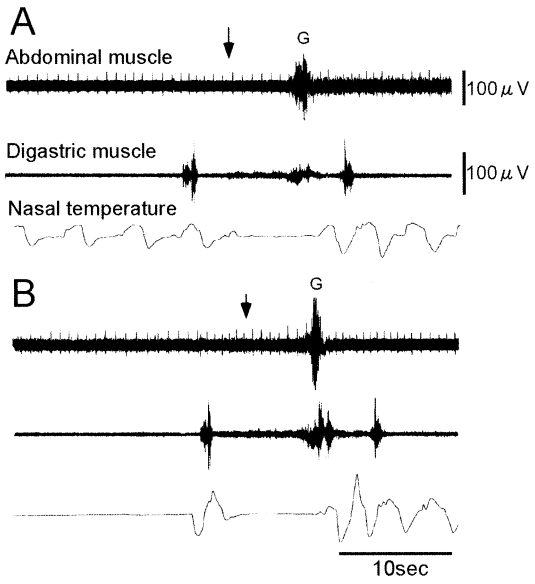

Fig. 3 Abdominal muscle, digastric muscle and nasal temperature recordings on the gag reflex. (A) Control conditions normal ventilation (B) After holding the breath A, B were obtained in a single subject.

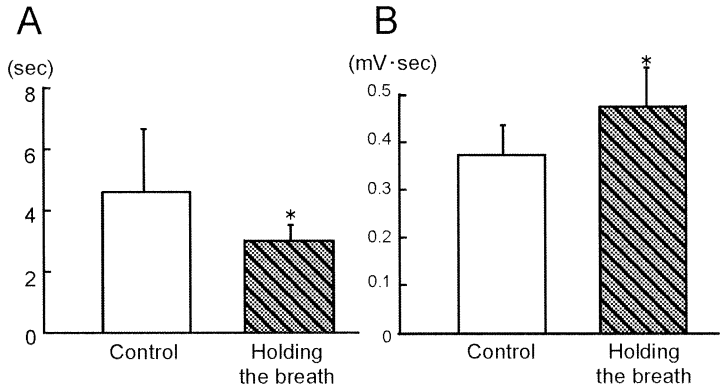

Fig. 4 Influence of holding the breath on gag reflex. (A) Latency of gag reflex. (B) Integral abdominal muscle activity at gag reflex. The values shown are mean ± SEM. $^*p < 0.05$, significant difference compared with the values of control.

switched to expulsion by hypercapnia and/or hypoxia in dogs. They further reported that this switching was enhanced by stimulation of the sinus nerve, which is composed of afferent fibers of chemoreceptors [9]. It may be explained by similar mechanisms that hypoxia in mountain sickness induces nausea, retching and expulsion.

Stimulation of the superior laryngeal nerve (SLN) or glossopharyngeal nerves causes swallowing reflex. These afferents make synaptic connections to secondary neurons of NTS [10][11], similar to those for the gag reflex. It has been reported that some interaction of inputs from primary afferents in the elicitation of swallowing occurs at the level of the NTS [12]. Also, swallowing induced by continuous infusion of distilled water is inhibited by increased arterial partial pressure of carbon dioxide [13]. We recently found that an increase of SpO_2 promoted frequency of swallowing and shortened latency of the first swallow (in submission). These findings and the results of this study indicate that the swallowing reflex seems to be promoted by an increase of SpO_2, although the gag reflex seems to be inhibited. Ingested foods are sent from the oral cavity to the stomach via the pharynx and esophagus by swallowing. On the other hand, the gag reflex exerts forces to transport stomach contents in the opposite direction. Liquids or a small

bolus can be easily swallowed, but it is difficult to swallow a large bolus, especially when they occlude the upper airway. From experience we know that the gag reflex is often elicited when this occurs. Our recent study indicated that low voltage electrical stimulation of the SLN induced the swallowing reflex, and high frequency stimulation at a higher voltage induced the gag reflex in rats. Thus, it appears that afferent activities of the SLN influence the switching of the swallowing and the gag reflexes. Furthermore, it is possible that a decrease of SpO_2 due to obstruction of the upper airway promoted the switching.

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