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Effects of Partial Paralysis on the Swallowing Reflex in Conscious Humans

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The ability to swallow may be affected by administration of a small dose of muscle relaxant. To test the hypothesis that a subparalyzing dose of a muscle relaxant can impair swallowing, effects of partial paralysis produced by pancuronium on the swallowing reflex were investigated in eight conscious subjects. The swallowing reflex was induced by a bolus injection or a continuous infusion of distilled water into the mesopharynx. The swallowing function was assessed by electromyogram of suprahyoid muscles (EMG_{SH}), mesopharyngeal pressure (P_{meso}), and hypopharyngeal pressure (P_{hypo}). Peripheral muscle activity was simultaneously determined by train of four ratio (TOFR) of hypothenar muscles to electrical stimulation of ulnar nerve and by hand grip strength (HGS). Following control measurements, measurements during partial paralysis and after recovery from partial paralysis were performed after intravenous administration of pancuronium 0.02 mg/kg. Partial paralysis significantly depressed EMG_{SH} (bolus injection 44.1 ± 10.0%, continuous infusion 55.9 ± 10.2% of control value, $P < 0.01$). P_{meso} also significantly decreased (bolus injection 64.9 ± 6.7 to 47.8 ± 5.8 mmHg, $P < 0.01$; continuous infusion 63.4 ± 7.7 to 52.5 ± 5.8 mmHg, $P < 0.05$). The TOFR of peripheral muscles decreased to 81.4 ± 6.7% of control value ($P < 0.01$), and HGS was reduced from 44.6 ± 1.9 to 39.4 ± 2.0 kg ($P < 0.01$). In the bolus injection study, the decrease in P_{meso} was significantly greater than the decrease in HGS (73.7% *vs.* 88.3% of control value, $P < 0.05$), and the decrease in EMG_{SH} was significantly greater than that in TOFR (44.1% *vs.* 81.4% of control value, $P < 0.05$). After recovery of peripheral muscle activity, both EMG_{SH} and P_{meso} had completely recovered. Partial paralysis did not affect the latency of response and the pattern of swallowing after bolus injection, and the frequency of swallows elicited by continuous infusion was also unchanged. Our results suggest that 1) upper airway muscles are more sensitive than peripheral muscles to the effects of pancuronium; 2) both the elevation of the larynx and the propelling force during swallowing are affected by the administration of a small dose of pancuronium; and 3) partial paralysis does not affect the neural pathway of the swallowing reflex in the conscious state. (Key words: Deglutition. Neuromuscular blocking agents.)

ADMINISTRATION of a subparalyzing dose of a nondepolarizing muscle relaxant is often part of a rapid-sequence induction of anesthesia.[1–3] Although this practice is claimed to be safe in terms of maintaining adequate ventilation, the ability to overcome upper airway obstruction and to clear secretions are occasionally impaired.[4,5] Pavlin *et al.* have demonstrated that despite adequate ventilation, the function of upper airway muscles is greatly impaired during partial paralysis.[6] To prevent aspiration of pharyngeal contents into the respiratory tract, the swallowing reflex has an obvious protective value.[7] Despite the hazard that might be produced by inadequate swallowing, the effects of partial paralysis on the swallowing reflex have not been systematically examined. Thus, the present study was undertaken to characterize changes in the pattern of water-induced swallowing before and after achieving partial paralysis produced by pancuronium in conscious normal subjects.

Materials and Methods

Eight male volunteers aged 26–35 yr were studied while in the supine position. All were in good health and were free of neuromuscular and respiratory disorders. The protocol of the present study was approved by our Institutional Ethics Committee, and informed consent was obtained from each subject. All subjects had no oral intake for 4 h before the study. They received 0.5 mg atropine sulfate intramuscularly 30 min before the experiments.

After an intravenous catheter was inserted, a pair of surface electrodes was placed on the skin between the hyoid bone and the chin in the midline to record the electromyogram of the suprahyoid muscles (EMG_{SH}). The EMG signal was filtered, amplified, and integrated (Nihon Koden bioelectric amplifier AB-621G, integrator EI-601G). Three thin water-filled polyethylene catheters (1.35 mm ID) were inserted through the nares so that the tips of the two catheters lay in the mesopharynx (oropharynx) and the third in the hypopharynx 6 cm below the tip of the mesopharyngeal catheters. One of the mesopharyngeal catheters was used to induce the swallowing reflex by injection of distilled water. The remaining two catheters were connected to pressure transducers (Nihon Koden carrier amplifier AP-601G) to measure the changes in mesopharyngeal (P_{meso}) and the hypopharyngeal (P_{hypo}) pressure during swallowing. During recording, any obstruction of the catheters was readily detected by changes in the pressure tracings (such as baseline shift or slow response). The position of the mesopharyngeal catheters was checked before and after measurements by direct inspection. To assess the effects of pancuronium on the peripheral muscles, the left ulnar nerve was supramaximally

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TABLE 1. Effects of Partial Paralysis on Peripheral Muscle Function

	Control	Partial Paralysis	Recovery
TOFR (%)	100	81.4 ± 6.7*	100 ± 0
HGS (kg)	44.6 ± 1.9	39.4 ± 2.0*	44.5 ± 2.0

Values are means ± SE in eight subjects.
Control = control measurement before administration of pancuronium, partial paralysis = measurement at 3 min after administration of pancuronium; recovery = measurement at 50 min after administration of pancuronium; TOFR = train-of-four ratio; HGS = hand-grip strength.
* $P < 0.01$, significantly different from values at control.

stimulated at the wrist *via* surface electrode, and the train of four ratio (TOFR) was determined from the evoked EMG activity of the hypothenar muscles (Datex Anesthesia and Brain Activity Monitor). Hand grip strength (HGS) was measured using a hand grip dynamometer. Head lift (the ability of the subject to raise the head from the bed and sustain for 5 s) and tongue protrusion (the ability to protrude the tongue) were also tested.

The swallowing reflex was induced by a 0.5-ml bolus injection of distilled water at the end of expiration without the knowledge of the subject. At least three injections were performed in each subject with a 1-min interval between each trial. After completion of the bolus injection study, reflex swallowing was induced by continuous infusion of distilled water at the rate of 2.5 ml/min. The response to continuous infusion of water was determined by counting the number of swallows for 1 min (f) after the response became stable. After control measurements, pancuronium 0.02 mg/kg was intravenously administered. Measurements during partial paralysis were started at 3 min after administration of pancuronium. Finally, measurements after recovery were performed 50 min after induction of partial paralysis when the TOFR was completely returned to 100%.

In order to analyze changes in the pattern of swallows, four periods were defined in each swallowing act. These were the period from the injection of water to the onset of EMG_{SH} (latency, t_0), and the periods from the onset to the cessation of the raw EMG_{SH} (t_1), the peak of the P_{meso} (t_2), and the peak of the P_{hypo} (t_3).

Statistical analysis was performed using a two-way analysis of variance, Tukey's test, and Student's t test. All values were expressed as means ± standard error, and $P < 0.05$ was considered statistically significant.

Results

None of the subjects complained of difficulty in breathing throughout the course of the experiment. However, all eight subjects had blurred vision and had difficulty keeping their eyes open within 2 min after injection of pancuronium. Although five subjects complained of difficulty in swallowing and three had the feeling that their mandible had moved backward due to loss of jaw muscle tone with increasing paralysis, all subjects could perform both the head lift and tongue protrusion maneuvers. TOFR was reduced to 81.4 ± 6.7% of control ($P < 0.01$), and HGS also decreased significantly (table 1). These two parameters of peripheral muscles' activity had completely recovered at the time of the final measurements.

Bolus injection of 0.5 ml distilled water never failed to induce the swallowing reflex in all subjects. Representative recordings of pharyngeal pressures and EMG_{SH} before and during partial paralysis are illustrated in figure 1. After bolus injection of distilled water to the mesopharynx, a swallow was induced with a latency of approximately 0.4 s. The occurrence of swallowing was characterized by a gradual increase in EMG_{SH}, which was followed by an increase in P_{meso}. P_{hypo} reached its peak after a slight negative pressure that coincided with the increase in P_{meso}. This pattern of swallowing was consistently observed. However, peak values of all these parameters, especially the EMG_{SH}, decreased during partial paralysis. Results obtained from responses to bolus injection of water for all subjects are summarized in table 2. Both P_{meso} and EMG_{SH} were significantly decreased at 3 min after administration of pancuronium ($P < 0.01$), and these recovered 50 min after induction of partial paralysis. Change in P_{hypo} was not statistically significant. Periods t_0, t_1, t_2, and t_3 reflecting the pattern of swallowing were essentially unchanged during the course of the study, although the pattern was variable in each subject.

Continuous infusion of water invariably caused re-

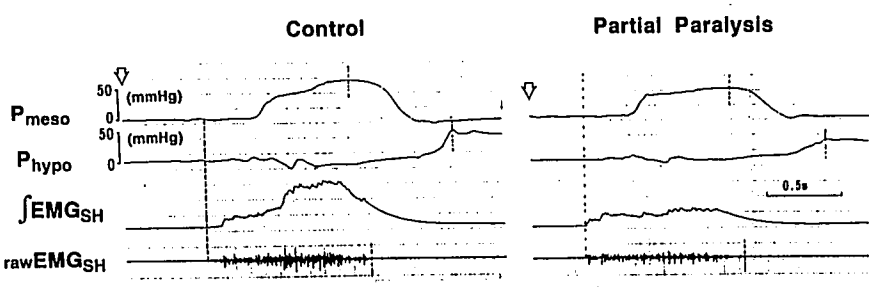

FIG. 1. Experimental records illustrating manometric and electromyographic changes during swallowing induced by bolus injection of distilled water. One half milliliter of water was injected into the mesopharynx, at the arrow. P_{meso} = mesopharyngeal pressure; P_{hypo} = hypopharyngeal pressure; $\int EMG_{SH}$ and raw EMG_{SH} = integrated and raw electromyogram activity of suprahyoid muscles, respectively. Recordings were done at a high paper speed (100 mm/s).

TABLE 2. Effects of Partial Paralysis on Swallowing Function in Response to Distilled Water Instillation

	Control	Partial Paralysis	Recovery
Bolus injection			
P_{meso} (mmHg)	64.9 ± 6.7	47.8 ± 5.8*	59.2 ± 5.2
P_{hypo} (mmHg)	41.1 ± 9.1	34.3 ± 8.7	36.5 ± 7.3
EMG_{SH} (%)	100	44.1 ± 10.0*	110.8 ± 7.6
t_0 (s)	0.34 ± 0.07	0.32 ± 0.05	0.29 ± 0.05
t_1 (s)	0.80 ± 0.07	0.80 ± 0.08	0.83 ± 0.07
t_2 (s)	0.63 ± 0.06	0.60 ± 0.06	0.59 ± 0.04
t_3 (s)	1.30 ± 0.19	1.20 ± 0.18	1.31 ± 0.18
Continuous infusion			
P_{meso} (mmHg)	63.4 ± 7.7	52.5 ± 5.8†	62.0 ± 5.8
P_{hypo} (mmHg)	46.1 ± 8.1	36.5 ± 7.0*	35.7 ± 7.3*
EMG_{SH} (%)	100	55.9 ± 10.2*	104.4 ± 4.2
f (1 per min)	8.5 ± 1.0	10.5 ± 1.3	9.4 ± 1.0

Values are means ± SE in eight subjects.

Control = control measurement before administration of pancuronium; partial paralysis = measurement at 3 min after administration of pancuronium; recovery = measurement at 50 min after administration of pancuronium; P_{meso} = mesopharyngeal pressure; P_{hypo} = hypopharyngeal pressure; EMG_{SH} = integrated electromyogram activity of suprahyoid muscles; t_0 = latency of response; t_1, t_2, and t_3 = periods from the onset of EMG_{SH} to the cessation of it, the peak of the P_{meso}, and the peak of the P_{hypo}, respectively; f = frequency of swallows during continuous infusion of distilled water.

* $P < 0.01$, significantly different from control.

† $P < 0.05$, significantly different from control.

peated swallowing in all subjects. Figure 2 shows the responses to continuous infusion of water in the same subject as in figure 1. Pharyngeal pressures and EMG_{SH} decreased during partial paralysis. P_{meso} and EMG_{SH} recovered while P_{hypo} progressively decreased when peripheral muscle activity had returned to the control value. Results of responses to continuous infusion of water for all subjects are summarized in table 2. P_{meso}, P_{hypo}, and EMG_{SH} were significantly reduced during partial paralysis. In addition, the reduction of P_{hypo} persisted 50 min after induction of partial paralysis. The frequency of swallows did not statistically change through the measurements.

During partial paralysis, the reduction of P_{meso} in the bolus injection study was significantly greater than that of HGS (73.7 *vs.* 88.3% of control value, $P < 0.05$). In the same way, reduction of EMG_{SH} in the bolus injection study was significantly greater than that of TOFR (44.1 *vs.* 81.4% of control value, $P < 0.05$) (fig. 3).

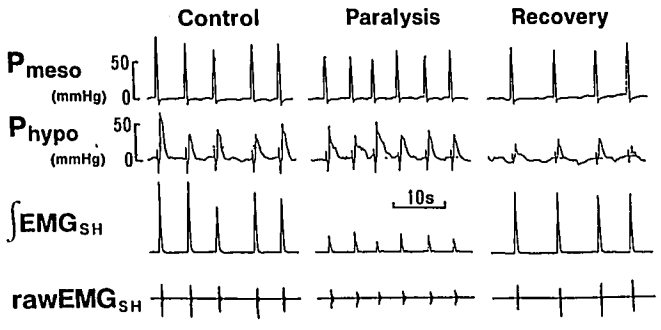

FIG. 2. Experimental records illustrating manometric and electromyographic responses to continuous infusion of water (2.5 ml/min) in the same subject shown in figure 1. P_{meso} = mesopharyngeal pressure; P_{hypo} = hypopharyngeal pressure; ∫ EMG_{SH} and raw EMG_{SH} = integrated and raw electromyogram activity of suprahyoid muscles, respectively. Recordings were done at a low paper speed (2.5 mm/s).

Discussion

The principal findings of this study are that 1) even a small dose of pancuronium 0.02 mg/kg significantly depressed EMG_{SH} and P_{meso} during swallowing; 2) although TOFR of peripheral muscles and HGS also decreased significantly, the decrease in P_{meso} was significantly greater than the decrease in HGS, and the decrease in EMG_{SH} was significantly greater than that in TOFR; and 3) partial paralysis did not affect the latency of response, the pattern of swallowing after bolus injection of distilled water, and the frequency of swallows elicited by continuous infusion of water. These results indicate that a small dose of pancuronium does not affect the sensitivity or synchrony of the swallowing reflex even though it reduces the magnitude of the forces associated with swallowing. This suggests that defense of the airway by clearance of pharyngeal secretions may be compromised, raising potential hazard of aspiration during partial paralysis.

Results from this study are in agreement with those from Pavlin *et al.*, who demonstrated that, despite adequate ventilation, function of upper airway muscles is greatly impaired during partial paralysis.[6] As shown in the figure 3, upper airway muscles are apparently more sensitive than peripheral muscles to pancuronium. Accordingly, the TOFR of peripheral muscles does not always reflect the extent of the depressant effects of muscle relaxant on upper airway muscles. Pavlin *et al.* concluded that head lift is the most sensitive assessment for muscular paralysis. In contrast to their conclusion, most subjects in the present study complained of difficulty in swallowing,

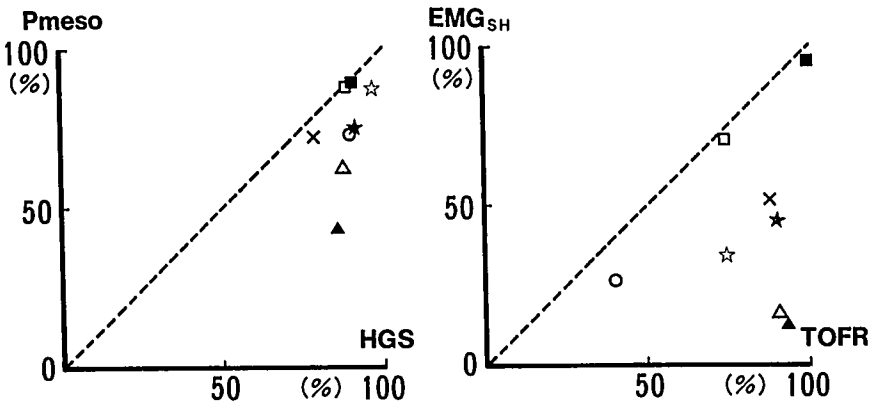

FIG. 3. Relationships between the hand-grip strength (HGS) and mesopharyngeal pressure (P_{meso}) and between the train-of-four ratio (TOFR) of peripheral muscles and the integrated electromyogram of suprahyoid muscles (EMG_{SH}). All values are expressed as percentages of control values. Each symbol represents an individual subject.

and both EMG_{SH} and pharyngeal pressures decreased significantly regardless of ability to maintain head lift, indicating that the head lift may not be the most sensitive indicator of neuromuscular blockade. Apparently, measurements of EMG_{SH} and pharyngeal pressure can be more sensitive indicators of neuromuscular blockade in terms of assessment of upper airway function.

The EMG_{SH} mainly represents the sum of the activities of bilateral mylohyoid, geniohyoid, genioglossus, and anterior belly of the digastric muscles, which are essential for elevation of the hyoid and the larynx during swallowing.[7] In the present study, EMG_{SH} was significantly depressed by a small dose of pancuronium, which indicates that elevation of the larynx was impaired. Because elevation of the larynx plays an important role both in the closure of the larynx and in opening the pharyngoesophageal junction during swallowing,[7,8] impairment of laryngeal elevation may predispose to aspiration of pharyngeal contents.

P_{meso} decreased significantly after administration of pancuronium, indicating that the propelling force during swallowing decreases with partial paralysis. It is interesting that P_{meso} in five subjects who experienced difficulty in swallowing was less than 75% of the control value, and in three subjects who did not experience dysphagia was greater than 85% of the control value (fig. 3). This supports that concept the decrease in P_{meso} accurately reflects impairment of swallowing.

P_{hypo} is mainly produced by the contraction of the cricopharyngeal muscle and the inferior pharyngeal constrictor and represents the pressure at the pharyngoesophageal junction. During swallowing, cessation of activities in these muscles is of more importance than their contractions,[7,9] implying that the decrease in P_{hypo} is not responsible for causing the impairment of swallowing. However, the reduction of P_{hypo} has the potential hazard of facilitating regurgitation of materials from the stomach, because the resting tone of the pharyngoesophageal junction is important in preventing regurgitation. Although the observed decrease in P_{hypo} might indicate the prolonged effects of pancuronium on the cricopharyngeal muscle and the inferior pharyngeal constrictor, it is likely that this observation was brought about by the technical failure of precise P_{hypo} recording. The tip of the side-holed polyethylene catheter placed in the hypopharynx might have rotated during the experiment, leading to erroneous measurement because the pressures recorded from anterior and posterior at the pharyngoesophageal junction are greater than those recorded from right and left.[9] Unless care is taken, the validity of the measuring P_{hypo} may be questionable, particularly during long term measurement.

Besides effects on the neuromuscular junction, muscle paralysis might affect the neural pathway of the swallowing reflex, including the afferent arc, the coordinating center, peripheral feedback, and the efferent arc. Sumi reported that gallamine-induced motor paralysis profoundly modified the pattern of the motor nerve fiber discharges during swallowing in the kitten, suggesting its effects on the neural pathway.[10] However, we did not find any changes in the latency of response, the pattern of swallowing, or the frequency of swallows during partial paralysis. This indicates that partial paralysis does not affect the neural pathway, at least, in conscious humans.

Our findings may have potentially important implications, in part during induction of or recovery from anesthesia. This study reproduces prevailing conditions after a small dose of muscle relaxant prior to rapid-sequence induction. The data suggest that such partially paralyzed patients may be in danger of aspirating pharyngeal contents into the respiratory tract. In addition, there is evidence that swallowing is considerably obtunded during sedation and/or analgesia.[11] Thus, during recovery from general anesthesia when the effects of residual anesthetics and residual muscle relaxant[12–14] are still present, impairment of the swallowing function may be augmented even more than that observed in the conscious state. Furthermore, it is worth noting that volatile anesthetics en-

hance the neuromuscular blocking properties of nondepolarizing muscle relaxants.[15,16] Thus, the effect of postoperative residual muscle paralysis[13–15] on upper airway muscles might be more prominent in the early postoperative periods.

In conclusion, our results suggest that 1) upper airway muscles are more sensitive to pancuronium than peripheral muscles; 2) both elevation of the larynx and the propelling force during swallowing is much disturbed by the administration of a small dose of pancuronium; and 3) partial paralysis does not affect the neural pathway of the swallowing reflex in the conscious state.

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