Depression of the Swallowing Reflex during Sedation and/or Relative Analgesia Produced by Inhalation of 50% Nitrous Oxide in Oxygen

TAKASHI NISHINO, M.D.,* KAZUNORI TAKIZAWA, D.M.D.,† NOBUKO YOKOKAWA, M.D.,‡ KAZUAKI HIRAGA, M.D.‡

Swallowing results in reflex closure of the glottis, and has an obvious protective value against the aspiration of foreign materials into the respiratory tract. The protective pharyngeal and laryngeal reflexes, including the swallowing reflex, are depressed by deep general anesthesia.1–4 Perhaps swallowing reflex is also obtundated during sedation and/or relative analgesia (stage I of anesthesia). We, therefore, examined changes in activity of the swallowing reflex during sedation and/or relative analgesia produced by inhalation of 50% nitrous oxide (N₂O) in oxygen (O₂) by applying a new method which tests the swallowing response in a quantitative manner.

* Vice-director of Operation Theater.
† Clinical fellow.
‡ Staff Anesthesiologist.

Received from the Department of Anesthesiology, National Cancer Center Hospital, Tokyo, Japan. Accepted for publication June 29, 1987.

Address reprint requests to Dr. Nishino: Department of Anesthesiology, National Cancer Center Hospital, Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan.

Key words: Anesthetics, gases: nitrous oxide. Reflex: swallowing reflex.

MATERIALS AND METHODS

Ten male volunteers aged 28–39 yr were studied. All were physicians and were in good health. The protocol of the present study was approved by the Ethics Committee of the hospital. All subjects had no oral intake for 4 h before the study. Before the beginning of the experiment, a respiratory inductive plethysmography (RIP: Respiritrace™; Ambulatory Monitoring Inc., Airdsley, NY) was placed onto the subject and calibrated using the least squares method as described by Chadha et al.5 Then, each subject rested in the supine position for 10 min, during which time a multiple-purpose catheter having a diameter of 1.35 mm was inserted through the nasis so that the tip of the catheter lay in the epipharynx. Following the insertion of this nasal catheter, the subject was asked to breathe through his nose, and the subject’s mouth was sealed with a wide surgical adhesive.

The experiment was started while the subject was quietly breathing 100% O₂ through a tightly fitting nasal mask connected to a T-piece system. The swallowing reflex was induced by a bolus injection of a small amount of distilled water into the pharynx through the
nasal catheter without the knowledge of the subject. In each subject, four different volumes of distilled water (0.25, 0.5, 0.75, and 1.0 ml) were injected in random sequence during early expiration at intervals of about 90 s. Three injections were performed for each volume of distilled water. The swallowing act was identified by a submental electromyogram (EMG), a transient interruption of respiratory airflow, and visual observation of the characteristic laryngeal movements (fig. 1). Details of the recording technique for a submental EMG for the identification of the swallowing act are reported elsewhere. Submental EMG and RIP signals were recorded. The responses to injections of water were analyzed in terms of the number of swallows elicited and the latency of response. The number of swallows was counted for a period of 10 s immediately following the injection of water, and the latency of response was computed from the time of injection to the onset of the first swallowing act. When the injection of water failed to elicit swallowing, the latency of response was marked as 10 s although it was actually longer, or latency was infinite because the stimulus was below the threshold. After the above procedures were completed while breathing 100% O₂, the subject then breathed 50% N₂O in O₂ with a total gas flow of 16 l/min for a period of 10 min until equilibration with the inspired gas mixture could be assumed. Then, injections of distilled water were repeated in the same manner as described above, during which time inhalation of the mixture of N₂O in O₂ was continued. Administration of N₂O was then discontinued and 100% O₂ was substituted. During the entire procedure, the inspired concentrations of gas were monitored with an oxygen monitor (IL 402 oxygen alarm) inserted in the inspired line. The subject’s ECG was also monitored. All the necessary facilities for resuscitation were readily available. Statistical analysis was performed using Student’s t test.

RESULTS

During inhalation of 50% N₂O in O₂, all subjects were apathetic, amnesic, and well sedated. Although there was a considerable variation among subjects, similar responses to injections of water were observed in all subjects.

Figure 2 shows changes in the latency for initiation of the swallowing reflex in response to injections of different volumes of water during inhalation of 100% O₂ and during inhalation of 50% N₂O in O₂ for all subjects. As the volume of injected water was increased, there was a progressive shortening of the latency both during inhalation of 100% O₂ and during inhalation of 50% N₂O in O₂. However, the latency was longer during inhalation of 50% N₂O in O₂ than during inhalation of 100% O₂ at any corresponding volume of injected water.

Figure 3 shows the relationships between the volume of injected water and the number of swallows during inhalation of 100% O₂ and of 50% N₂O in O₂ for all subjects. Increases in the volume of injected water pro-
gressively increased the number of swallows both during inhalation of 100% O₂ and of 50% N₂O in O₂. However, the number of swallows during inhalation of 50% N₂O in O₂ was less than that during inhalation of 100% O₂ for any corresponding volume of injected water.

**DISCUSSION**

In experimental animals, the swallowing reflex can be readily elicited by electrical stimulation of the superior laryngeal nerve, and the effects of depressants on this reflex can be assessed by changes in the latency of responses, the number of swallows elicited, and thresholds of stimulus intensity. Nevertheless, this method cannot be easily applied to clinical studies of the swallowing reflex. We induced the swallowing reflex by injections of a small amount of water into the pharynx through a thin nasal catheter. Although, with this technique, the strength of stimulus may not be controlled as precisely as the electrical stimulation, the responses to injection of water were consistent and reproducible in repeated measurements. Also, the responses depended on the volume of injected water. These findings indicate that this method can be used for quantitative analysis of the swallowing reflex. Moreover, the injection of water into the pharynx provides more physiological stimulus than electrical stimulation. Our technique has many uses in evaluating the swallowing reflex in various clinical situations.

Our findings that inhalation of 50% N₂O in O₂ decreased the number of swallows and prolonged the latent period for initiation of the swallowing reflex in response to injection of water into the pharynx indicate that the swallowing reflex is considerably depressed during sedation and/or relative analgesia produced by administration of 50% N₂O in O₂. Our present data do not provide any dose-response relationship of N₂O concentrations to the swallowing reflex activity. However, in animals, increasing concentrations of N₂O exert progressive depression of the swallowing reflex. Therefore, perhaps, in humans, the higher the N₂O concentrations, the more the depression of the swallowing reflex.

Although there is no doubt that various protective airway reflexes including the swallowing reflex are depressed under deep anesthesia and coma, disagreement exists as to the efficiency of the protective airway reflexes during sedation and/or relative analgesia. Brock-Utne et al. demonstrated radiological evidence of pulmonary dye aspiration during neuroleptanalgesia in eight patients undergoing carotid angiography, indicating that the protective airway reflexes are depressed with neuroleptanalgesia. Similarly, Rubin et al. observed that two of ten healthy volunteers aspirated radio-opaque dye placed at the back of the tongue while breathing 50% N₂O in O₂. In contrast to these studies, Cleaton-Jones showed that, when 50% N₂O in O₂ was administered, no evidence of aspiration of radio-opaque dye was detected in 14 healthy volunteers, indicating that protective airway reflexes are intact during N₂O-O₂ sedation. However, in the latter study, 50% N₂O in O₂ with a total gas flow of 10 l/min was administered via a loosely fitting nasal mask for only 5 min before challenging laryngeal competence. Under these conditions, perhaps some contamination of the inspiratory N₂O concentration with air occurs, and the brain is not equilibrated with alveolar and arterial concentrations of N₂O, causing a significantly lower degree of sedation and/or analgesia.

Our results support the hypothesis of Pleasant that the pharyngeal protective reflexes might be obtunded during N₂O-O₂ sedation, and are additional evidence of incompetence of upper airway functions during sedation and/or relative analgesia. In this regard, accidental inhalation of radio-opaque dye may occur during sedation or light anesthesia, and is due in part to depression of the swallowing reflex.

It must be noted that all subjects in the present study were young and healthy males. Whether the response to injection of water into the pharynx would be similar with debilitated or elderly subjects is unknown. However, if protective airway reflexes are compromised with advancing age, depression of the swallowing reflex during sedation and/or relative analgesia may be
Hypocalcemia and Prolonged QT Interval Following Carotid Artery Surgery

EDWARD A. ZANE, M.D.* JAMES B. EISENKRAFT, M.D., † MOSHE HAIMOV, M.D.‡

Hypocalcemia is a complication of thyroidectomy, and is caused by the accidental removal of the parathyroid glands or by a compromise of their vascular supply. We describe a patient who, following right carotid endarterectomy, developed a prolonged QT interval due to acute hypocalcemia.

CASE REPORT

A 60-year-old (60-kg, 160-cm) woman was evaluated for headaches associated with a tingling sensation in the left hand. Bilateral carotid artery disease was found with a 90% stenosis of the right carotid bifurcation. The patient was scheduled to undergo a right carotid endarterectomy. She had essential hypertension for 10 yr and hypothyroidism for 8 yr. She had a lumbar laminectomy performed under uneventful general anesthesia 12 yr previously. She was taking levothyroxin 0.125 mg daily, captopril 12.5 mg qd, aspirin 325 mg qd, and calcium 500 mg tid as prophylaxis against postmenopausal osteoporosis. Three weeks prior to admission, the patient had reduced her calcium supplementation to 500 mg qd. Preoperative laboratory data revealed a hematocrit of 39%, hemoglobin 12.9 gm/dl, a normal clotting profile, normal serum electrolytes, calcium 9.6 mg/dl (normal range 8.5–11.0), phosphate 3.4 mg/dl (normal range 2.5–6.0), protein 6.3 g/dl (normal range 6.5–8.5), and albumin 4.8 g/dl (normal range 3.5–4.8). On admission, the chest radiograph showed a normalized heart and normal lung fields. The preoperative EKG showed a normal sinus rhythm with non-specific ST-T wave changes and a QT interval, corrected for heart rate (QTc), of 0.42 s (fig. 1A).

Morphine sulfate, 10 mg im, and diazepam, 5 mg po were given for premedication. Monitoring consisted of an automated blood pressure cuff, EKG, esophageal stethoscope and temperature probe, and mass spectrometer. Anesthesia was induced with thiopental 5 mg/kg, pancuronium 0.1 mg/kg, and lidocaine 1.0 mg/kg iv, and the trachea was intubated with an 8.0-mm ID cuffed endotracheal tube. Anesthesia was maintained with nitrous oxide 50% in oxygen and isoflurane 0.4–0.6% (end tidal). The intraoperative course was unremarkable except for the incidental surgical finding of the vagus nerve lying anterior in the right carotid sheath instead of in its usual postero-lateral position. Intraoperative arterial blood pressures ranged from 125–160 mmHg systolic over 80–100 mmHg diastolic, with a heart rate between 85–90 bpm. Normocapnea was maintained throughout the procedure, and the lowest esophageal temperature measured was 36.2°C. During the procedure, 1000 cc of crystalloid solution (Normosol®) was administered iv, and the estimated blood loss was 150 cc. Residual neuromuscular blockade was reversed with neostigmine 4 mg and glycopyrrrolate, 0.8 mg iv. No EKG changes were noted intraoperatively. The trachea was extubated in the operating room, and the patient was transferred to the recovery room in stable condition. There, she was mildly hypotensive (90–100/50–60 mmHg), and a postoperative EKG revealed slightly flattened T-waves as compared with the preoperative EKG and a prolonged QTc of 0.46 s (fig. 1B).

The hematocrit was 35%, potassium 3.9 mEq/l, and total calcium 7.5 mg/dl. The ionized calcium concentration was 0.67 mmol/l (normal range 1.12–1.32). Ionized calcium was measured using the NOVA 6...