TITLE: NITROUS OXIDE STIMULATES EXPIRATORY MUSCLES IN DOGS

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Nitrous oxide (N_2O) is often a part of anesthetic techniques that employ spontaneous breathing because it causes little or no respiratory depression. However, the effects of N_2O on the pattern of respiratory muscle activation are unknown. We measured the electrical activity of the primary respiratory muscles in pentobarbital-anesthetized dogs before, during, and after the administration of N_2O.

Chronic electromyogram (EMG) electrodes were implanted in the triangularis sterni (TS), transversus abdominis (TA), costal diaphragm (COS), crural diaphragm (CRU) and parasternal intercostal (PS) muscles of 5 mongrel dogs (8 to 13 kg). After at least 3 weeks, the dogs were anesthetized with sodium pentobarbital (25 mg/kg iv) and placed supine. Gas flow through an endotracheal tube was integrated to measure tidal volume. EMG measurements were quantified as the peak moving average of the rectified, integrated signal. Measurements were obtained during quiet breathing of 30% O_2 in 70% N_2, after at least 5 min of breathing 30% O_2 in 70% N_2O, then 5 min after washout of N_2O. Each dog was studied twice on separate days, and mean values were calculated. Statistical comparisons were made with Student t tests.

The dogs always exhibited phasic expiratory electrical activity in the TS and TA, and phasic inspiratory electrical activity in the PS, COS, and CRU. N_2O significantly increased expiratory activity in the TS and TA, decreased inspiratory activity in the PS, and did not change COS or CRU (Table). N_2O significantly increased breathing frequency (from 13±2 to 17±3 min^{-1} [M±SE]) but did not change tidal volume (191±17 to 205±23 ml). The $PaCO_2$ tended to decrease with N_2O, but not significantly (from 45±1 to 43±1 mmHg), while the PaO_2 was significantly increased (from 125±4 to 146±3 mmHg). These values returned to near baseline after removal of N_2O.

Pentobarbital-anesthetized dogs, like anesthetized human subjects, demonstrate phasic expiratory muscle activity. N_2O accentuated this activity, while diminishing the activity of a rib cage inspiratory muscle (PS) and having no effect on diaphragmatic activity. Thus, the effects of N_2O on respiration were caused by a selective activation of the expiratory muscles and changes in respiratory timing (as evidenced by increased breathing frequency).

Table.–Peak integrated EMG activities during and after N_2O.

	Inspiratory activity			Expiratory activity	
	COS	CRU	PS	TS	TA
During	1.01±0.06	1.03±0.11	0.67±0.08*	1.41±0.15*	1.81±0.29*
After	0.99±0.03	1.04±0.05	0.83±0.07*	0.97±0.14	1.05±0.09

Values are fractions of the values before N_2O. *Significant difference ($P < 0.05$) from value before N_2O.

Supported by HL-04664, GM-40909, and GM-08288.

A1173

TITLE: ANTAGONISM OF THE POSTOPERATIVE RESPIRATORY DEPRESSION CAUSED BY LARGE DOSES OF MORPHINE

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Nalmefene, 0.5 µg/kg, antagonized the respiratory depression in patients who received large doses of the short acting fentanyl as a component of balanced anesthesia.[1] In the present study the effect of nalmefene on the postanesthetic respiratory depression, caused by large doses of the long acting morphine (Mσ), has been investigated.

Thirty-one ASA classification I and II patients, scheduled for total abdominal hysterectomy, signed informed consent to participate in this open label study, approved by our Institutional Review Board. Premedication consisted of 0.2 mg glycopyrolate and 0.1 mg/kg Mσ i.m. Anesthesia was induced with 3 to 5 mg/kg thiopental and maintained with N_2O - O_2 (Fi O_2 = 30 to 35%), containing 0.1 to 0.3% isoflurane, and with 5 mg increments of Mσ. Relaxation was maintained with vecuronium. Patients were mechanically ventilated (RR 10/min; RMV 10 ml/kg). At the end of surgery, after antagonism of the residual neuromuscular block, 30 patients, whose RR was < 16 were divided into 3 groups of 10 each and given i.v. 0.25 (group 1), 0.5 (group 2) or 1.0 µg/kg (group 3) nalmefene. If the RR was < 16/min 5 min after nalmefene or at any time during the next 4 hr, the initial dose was repeated up to 3 times. RR, HR, BP, nausea, vomiting and pain intensity were observed for 24 h and O_2 saturation for 2 h after nalmefene.

The mean and SEM of the total doses of Mσ were 31.05 ± 1.02, 34.3 ± 1.01 and 35.8 ± 1.2 mg and the mg/kg/hour doses were 0.18 ± 0.02, 0.17 ± 0.02 and 0.19 ± 0.01 in group 1, 2, and 3 respectively. At the end of anesthesia, RR were 5.5 ± 1.1 in group 1, 7.5 ± 1.4 in group 2 and 3.3 ± 1.4 in group 3. Five min after the injection of the initial dose, RR increased to 13.8 ± 1.9, 18.1 ± 2.5 and 18.3 ± 1.8 in group 1, 2 and 3. In the ensuing 24 hours the mean RR remained above 16 in all groups. However, 4, 5 and 4 patients required one additional dose of nalmefene at 5 min, 2, 1 and 1 patients at 10 min in group 1, 2 and 3 respectively. Only 1 patient in group 1 required a third dose at 15 min. This same patient was given 0.2 mg naloxone at 234 min when her RR was 8. O_2 satuation was satisfactory in all patients. There were no significant changes in HR or BP. Four, 3 and 2 patients in group 1, 2 and 3 respectively had pain requiring analgesics during the first 8 h. Four patients in group 2, and 3 in group 3, were nauseated, one of these in group 3 vomited.

Nalmefene, 0.25, 0.5 or 1.0 µg/kg, antagonized and prevented the recurrence of respiratory depression caused by large doses of Mσ, without apparent antagonism of residual Mσ analgesia. The only difference between the effect of the 3 doses was that mean RR only became > 16 at 10 min with the 0.25 µg/kg dose.

Reference

1. Anesth. Analg. 68: S195, 1989