

TITLE: FENTANYL-MIDAZOLAM ANESTHESIA FOR CARDIAC SURGERY AND POSTOPERATIVE CARE: COMPARISON OF BOLUS VS. COMBINED INFUSION TECHNIQUES.

AUTHORS: R.N. Sladen, M.B.ChB., J.Z. Berend, B.S., J. Lu, M.D., L. Hodgins, M.D., R. Yevak, M.D.

AFFILIATION: Anesth. Service, VA Med. Ctr., Dept. Anesthesiology, Duke Univ. Med. Ctr., Durham, North Carolina 27710

Introduction: Established bolus techniques with fentanyl and midazolam (FENT-MIDAZ) combine analgesia and hypnosis and provide excellent anesthesia in the operating room (OR) but do not guarantee smooth, effective postoperative sedation in the intensive care unit (ICU). We hypothesized that a continuous FENT-MIDAZ infusion would allow anesthesia to be continued into the ICU to provide more controlled sedation and hemodynamic stability, without prolonged narcosis when discontinued.

Methods: After institutional approval and consent, 22 male patients undergoing cardiac surgery, (CABG, n=17; AVR, n=3), were prospectively randomized to receive FENT-MIDAZ by bolus (Group I, n=11) or infusion (Group II, n=11). Patients for reoperation, with CHF, liver or kidney disease, or who had intraoperative complications were excluded. Group I patients were induced with FENT 25-50 µg/kg and MIDAZ 25-125 µg/kg. Anesthesia was maintained by boluses of FENT 3-6 µg/kg and MIDAZ 25 µg/kg pm in the OR, and FENT 100-200 µg and MIDAZ 1-2 mg pm in the ICU. In Group II patients, Harvard mini-infuser 900 devices (Bard Inc.) were used to provide continuous FENT-MIDAZ infusions with pm boluses. FENT infusion rate was adjusted between 0.025-0.075 µg/kg/min; boluses of 2.0 µg/kg were added pm. A dose of 12-20 µg/kg was given prior to skin incision. MIDAZ infusion rate was adjusted between 0.25-3.0 µg/kg/min; boluses of 15 µg/kg were added pm. A dose of 50 - 120 µg/kg was given prior to skin incision. Infusion rates were reduced by 50% during cardiopulmonary bypass. In the ICU, infusion rates of FENT and MIDAZ were adjusted between 0.02-0.05 and 0.25-1.0 µg/kg/min respectively. In both groups, muscle relaxation was provided with vecuronium. Sedation was discontinued at 2200 hrs on the operative day to allow ventilatory weaning and extubation the next morning.

Hemodynamic perturbation was defined as a 20% change from preinduction systolic blood pressure (SBP) in the OR and from admission SBP in the ICU. Patient demographics, drug dosages, time to first response, and duration of intubation were analyzed by unpaired t-test. Incidence of hypotension and hypertension in the OR and ICU and agitation in the ICU was analyzed by contingency tables.

Results: There were no significant differences in age, weight, BSA or ejection fraction between the two groups. Drug dosage data are summarized in Table 1. Time to response and duration of intubation after admission to the ICU are summarized in Table 2. One patient in Group I required reexploration for bleeding and is excluded from ICU data; one patient in each group required prolonged mechanical ventilation for atelectasis and are excluded from intubation data. There were no significant differences between the two groups in hypotension and hypertension in the OR, and in hypotension in the ICU. However, 10 patients in Group I were hypertensive in the ICU, compared with 3 in Group II (χ^2 8.9, $p < 0.005$). Five patients in Group I became agitated in the ICU, compared with 0 in Group II (χ^2 4.7, $p < 0.05$).

Discussion: FENT-MIDAZ provided equivalent anesthetic control in the OR whether given by bolus or combined infusion technique. However, in the ICU, combined infusion provided superior sedation, with significantly fewer episodes of hypertension and agitation than intermittent boluses. This was achieved without prolonging the duration of intubation. Combined continuous infusion of FENT-MIDAZ allows precise control of the depth and duration of anesthesia to be extended into the ICU after cardiac surgery.

Table 1	FENT-OR (µg/kg)	MIDAZ-OR (mg/kg)	FENT-ICU (µg/kg)	MIDAZ-ICU (mg/kg)
Bolus (I)	54.43 ±10.7	0.17 ±0.05	7.21 ±4.20	0.08 ±0.07
Infusion (II)	52.47 ±16.0	0.30 ±0.08	20.99 ±8.35	0.27 ±0.16
p	NS	<0.0001	<0.0002	<0.005

Table 2	Response Time (hr)	Intubation Time (hr)
Bolus (I)	4.70 ±2.73	17.02 ±2.72
Infusion (II)	7.09 ±4.73	19.73 ±3.42
p	NS	NS

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TITLE: TRACHEAL O₂ AT LOW FLOW (<8 ml/kg/min) OXYGENATES AND REMOVES CO₂ DURING APNEA

AUTHORS: CF Mackenzie, G Barnas, S Nesbitt.
Dept. of Anesthesiology University of Maryland,
Baltimore, MD 21201.

Tracheal insufflation of O₂ (TRIO) is similar to apneic oxygenation but TRIO, given during apnea, results in some CO₂ excretion and requires no denitrogenation for efficacy⁽¹⁾. TRIO is suggested as a temporizing technique for oxygenation of patients difficult to intubate and, by cricothyroidotomy, for ventilation of mass casualties when conventional techniques are not available or feasible⁽²⁾. We determined the minimum flow (V_{min}) of TRIO (desirable to minimize field O₂ supplies) necessary to maintain PaO₂ above 50 mmHg for 30 min during apnea and examined whether CO₂ excretion could be improved by superimposing oscillations on V_{min} TRIO. **Methods** Nine dogs, mean weight 12 kg, were anesthetized (pentobarbital 30 mg/kg then thiamylal 3 mg/kg/hr) and paralyzed (pancuronium 4 mg then 0.1 mg/kg/hr) and tracheally intubated with a 1.5 mm TRIO catheter outside a 9 mm cuffed tube. Arterial and pulmonary artery (PA) catheters and a pulse oximeter monitored pressure and O₂ saturation (SaO₂). Serial arterial (ABG) and mixed venous blood gases and SaO₂ were monitored. Room air conventional mechanical ventilation (CMV) returned ABG to baseline values between interventions as progressively lower TRIO flows, delivered within 1 cm of the carina, were used to establish V_{min}. In 6 dogs the duration of survival at V_{min} until

systolic BP fell <50mmHg was established before CMV was reinstated. The effects on ABG and airway gases sampled by mass spectrometry were compared (paired t-test) in 6 dogs after 5 min with and without oscillation (1000 cycles/min) of V_{min} TRIO by a piston pump. **Results** V_{min} for 30 min was 91 ± SE 5 ml/min. PaO₂ was unchanged from baseline values on CMV but PA pressure and PaCO₂ (mmHg) rose ($p < 0.05$) from 17 ± SE 0.7 to 28 ± 1.9 and 35 ± 1.1 to 172 ± 20.8 respectively. In all dogs PaCO₂ was higher ($p < 0.05$) than PvCO₂ throughout TRIO. The average duration of V_{min} TRIO beyond 30 min was 97 min (range 45-140). All animals were resuscitated without O₂ or inotropes by CMV. Addition of oscillation to TRIO decreased PaO₂ and PaCO₂, lowered airway O₂ and CO₂ but increased N₂. **Discussion** The Haldane effect probably accounts for higher PaCO₂ during TRIO. PaCO₂ rose at 2.4 mmHg/min between 10 - 60 min TRIO. Slutsky⁽¹⁾ predicts an alveolar ventilation of 500 ml/min for such a CO₂ rise during TRIO indicating that other mechanisms of CO₂ excretion were operative. One factor may be increased gas mixing due to cardiogenic oscillations which are especially important during extreme hypoventilation⁽³⁾. Another factor is the sevenfold increase in CO₂ diffusion gradient from alveoli to mouth. Oscillation of V_{min} TRIO enhanced gas mixing causing ambient gas to dilute O₂ between the carina and alveoli and impaired the efficacy of oxygenation. V_{min} TRIO sustains life for up to 2 hours sufficient for subsequent resuscitation by CMV. **Supported by DAMD 17-88-C8136. References** 1) Anesthesiol 63:278-286, 1985. 2) Amer Rev Resp Dis 138:175-193, 1988. 3) J Appl Phys 60:965-971, 1986.