Title: Fentanyl-Oxygen Anesthesia in Septic Shock

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Fentanyl (50-100 ug/kg) oxygen anesthesia is an effective anesthetic technique in patients with valvular and coronary artery disease undergoing elective open heart operations because it minimizes alterations in cardiovascular dynamics. There are data that indicate that large doses of fentanyl do not change capacitance vessel volume or venous return in animals. These findings suggest that high doses of fentanyl plus oxygen may be a desirable anesthetic technique in patients with unstable circulatory dynamics secondary to sepsis. The primary objectives of this investigation were to determine the anesthetic requirements and circulatory effects of fentanyl oxygen anesthesia in patients in septic shock undergoing emergency exploratory abdominal operations. Additional objectives included evaluation of the cardiovascular consequences and effectiveness of naloxone antagonism of post-operative respiratory depression after fentanyl-oxygen anesthesia and operation.

A total of 18 patients in confirmed septic shock (systolic arterial blood pressure < 90 torr and positive gram negative blood cultures) about to undergo exploratory laparotomy served as the experimental subjects. All patients had been NPO for at least 48 hours and none were nauseated or vomiting. Three patients were intubated and were being mechanically ventilated. All subjects had central venous and central arterial catheterization prior to anesthesia. Following a 15 minute period of breathing 100% oxygen, stroke volume (SV), heart rate (HR), cardiac output($\dot{Q}_T$) systolic arterial blood pressure (SBP) and systemic vascular resistance (SVR) were determined using computer analysis of the central aortic pulse pressure curve. Fentanyl was then administered at 100-300 ug/min until the patients were unresponsive to verbal command and pinprick stimulation. Following an additional 250 ug of fentanyl succinylcholine (1.5 mg/kg) was given and those patients who were not already intubated had their tracheas intubated. Respirations were controlled to keep $PaCO_2$ between 30-35 torr. Additional fentanyl was administered throughout the operation in 150 to 250 ug increments when SBP > 120 torr, heart rate > 125 beats/min or other evidences of light anesthesia (tearing, sweating) were present. Patients were maintained paralyzed with increments (1-3 mg) of intravenous pancuronium. At the conclusion of operation 10 of the patients (< 40 years and without evidence of coronary artery disease) received naloxone (0.8 mg, IV) to antagonize fentanyl. Cardiovascular dynamics were recorded before administration of fentanyl, when patients became unresponsive but before intubation, 1 minute after intubation, 5 and 60 minutes following surgical stimulation, and immediately prior to and 15 minutes after administration of naloxone. $PaCO_2$ was utilized as a measure of adequacy of respiration after fentanyl antagonism and was measured before and every 15 minutes for 4 hours after naloxone.

Unresponsiveness was produced by an average of 10±3 ug/kg of fentanyl. A total of 16±4 ug/kg was required for the entire operation. Fentanyl produced a small decrease in heart rate and an increase in stroke volume but no significant change in any other cardiovascular variable measured, Table 1. There were no further changes in any measured variable until 60 minutes into the operation when SBP and $\dot{Q}_T$ became increased. Naloxone produced complete reversal of fentanyl unconsciousness in all patients within 2 minutes and allowed extubation in 4 minutes. No patient experienced pain during the 4 hour post-naloxone study period but all sustained significant increases in HR, SBP and SVR. Six of the 10 patients receiving naloxone maintained $PaCO_2$ between 35-48 torr for 4 hours after antagonism. The remaining 4 patients experienced increases of $PaCO_2$ > 55 torr and required one or more additional doses of naloxone postoperatively. There was no apparent relationship between dose of fentanyl administered and likelihood of renarcotization after naloxone administration. No patient remembered any aspect of their operative procedure.

The results of this study demonstrate that large doses of fentanyl and oxygen produce complete anesthesia but no cardiovascular depression in patients in septic shock with unstable circulatory dynamics undergoing abdominal operation. The data also indicate that naloxone is capable of rapidly and completely antagonizing anesthetic doses of fentanyl but renarcotization, requiring additional naloxone, can be a problem in the early post-narcotic reversal period.

TABLE 1

	Control	Fent	Post Intub	Surg 5 min	Stim 60 min	End Oper	Post Naloxone 5 mn	15 mn
HR	115	105*	102*	100*	98*	102*	128*	127*
SV	55	63*	65*	64*	66*	72#	54*	52*
$\dot{Q}_T$	6.2	6.6	6.5	6.4	7.1*	7.4*	6.9*	6.8*
SBP	83	81	84	85	98*	111#	126#	127#
SVR	11.5	11.7	11.7	11.8	12.4	12.6	15.8#	16.1#

*P < .05, #P < .01, Student's paired t-test when compared to control data.