Title: Fentanyl-Oxygen Anesthesia for Coronary Artery Surgery: Plasma Catecholamine and Cortisol Responses

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High dose fentanyl (50-100 ug/kg) oxygen anesthesia has been suggested as an alternative to morphine or halothane anesthesia in patients undergoing valvular or coronary artery bypass open-heart operations. Advantages of this technique include absence of cardiovascular stimulation or depression. The hormonal effects of fentanyl-oxygen before and during surgical stimulation have not been carefully studied. In this investigation we measured the catecholamine and cortisol responses to fentanyl-oxygen anesthesia before and at numerous intervals during operation in 18 patients undergoing coronary artery revascularization procedures.

All patients were ASA class III and scheduled to undergo elective coronary artery bypass operations. Each had central venous and central arterial catheters implanted via percutaneous extremity vessel catheterization prior to anesthesia. Following a 15 minute period of breathing 100% oxygen, a 10 ml venous blood sample was obtained and heart rate (HR), cardiac output ($\dot{Q}_T$), mean arterial blood pressure $\overline{BP}$ and peripheral vascular resistance (SVR) were determined using computer analysis of the central aortic pulse pressure curve. Fentanyl was then administered at 200 ug/min, until the patients were unresponsive to verbal command and pinprick stimulation. Succinylcholine (1.5 mg/kg) was then given and the patients were intubated and had their respirations controlled to keep $PaCO_2$ between 30-35 torr. Additional fentanyl was then administered until each patient had received 75 ug/kg. Following this, the surgical procedure began. Additional blood samples were obtained and cardiovascular dynamics recorded immediately following intubation, before and 10 minutes following initial surgical stimulation, immediately before cardiopulmonary bypass, and 15 and 60 minutes after beginning bypass. Venous blood samples were assayed for plasma cortisol via a radio-immunoassay technique. Plasma epinephrine, norepinephrine and dopamine were measured via radioenzymatic assay. Unresponsiveness was produced by an average of 1.7 mg (25 ug/kg) of fentanyl. Fentanyl (25 ug/kg) did not significantly alter $\dot{Q}_T$ or SVR but resulted in small decreases in $\overline{BP}$ and HR. Additional fentanyl (up to 75 ug/kg), intubation, surgical stimulation, pre-bypass manipulations and cardiopulmonary bypass did not further alter any cardiovascular variable measured except $\overline{BP}$ which was somewhat further reduced during bypass (the heart was cooled and stopped during bypass so that HR was not obtainable during this interval), Table 1. Plasma cortisol, epinephrine and norepinephrine concentrations were unchanged by endotracheal intubation, Table 1. Plasma concentrations of the above hormones were significantly decreased by further administration of fentanyl (up to 75 ug/kg) and remained lower than control pre-anesthetic levels until bypass. Fifteen minutes of bypass resulted in marked increases in plasma epinephrine and norepinephrine which were further increased after 60 minutes of bypass. Plasma cortisol was further decreased after 15 minutes of bypass but increased to pre-anesthetic concentrations following 60 minutes of extracorporeal circulation. Plasma dopamine concentrations remained unchanged when compared to pre-anesthetic values until bypass when they became markedly increased.

These data demonstrate that anesthetic doses of fentanyl and oxygen produce minimal changes in cardiovascular dynamics and complete anesthesia in patients with coronary artery disease. In addition, our findings indicate that high dose fentanyl-oxygen anesthesia prevents increases in and actaully decreases plasma concentrations of the "stress responding hormones" during operation up until cardiopulmonary bypass. The results suggest that fentanyl and oxygen is a unique anesthetic technique because it produces "stress free" anesthesia in patients with coronary artery disease (at least up until bypass). However, as with most, if not all anesthetic techniques so far studied, cardiopulmonary bypass produces increases in most of the "stress responding hormones."

Table 1

	Control	Following Intub	Fentanyl (75/ug/kg)	Surg Stim	Pre-Bypass Period	Bypass 15 mn	Bypass 60 mn
HR (bts/mn)	73	66*	65*	64*	65*	-	-
$\dot{Q}_T$ (l/min)	4.6	4.5	4.6	4.5	4.4	4.3	4.2
$\overline{BP}$ (torr)	106	98*	96*	97*	95*	80#	80#
SVR (PRU)	25.6	24.8	24.9	25.0	25.2	24.3	27.4
Epinephrine (pg/ml)	44	36	23*	29*	28*	126#	200#
Norepinephrine (pg/ml)	203	198	149#	158#	142#	345#	656#
Dopamine (pg/ml)	59	66	63	72	68	91*	156#
Cortisol (ug%)	7.4	7.2	5.5*	5.9*	5.6*	4.4#	8.1

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