Title: FENTANYL VS SUFENTANIL: COMPARISON OF HEMODYNAMIC AND CATECHOLAMINE RESPONSES DURING CORONARY ARTERY (CABG) SURGERY

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Introduction: Sufentanil has been proposed as a superior narcotic anesthetic by virtue of its greater potency, higher therapeutic index, shorter duration of action and greater suppression of hemodynamic and catecholamine responses.[1] This hypothesis was tested by comparing fentanyl (F) and sufentanil (SF) in a prospective, randomized double-blind manner.

Methods: After obtaining written consent to the institutionally approved investigation, 12 patients scheduled for elective CABG, with ejection fractions $\geq$ 0.5, were randomized to receive either F or SF in two doses. The patients' received their usual antianginal medications, including beta-blockers, on the morning of surgery. Premedication with lorazepam 0.06 mg/kg P.O. and morphine 0.05 mg/kg I.M. was administered 90 min prior to surgery. A radial artery cannula, 2 large bore i.v. cannulae, and a pulmonary-artery catheter were inserted percutaneously under local anesthesia. Following mask oxygenation, pancuronium 25 µg/kg was administered followed by F 50 µg/kg or SF 15 µg/kg i.v. over 2 minutes. Narcotic (N) medications were diluted so that each patient received 1 ml N/kg. With the onset of rigidity, succinylcholine (S) 0.5 mg/kg was administered followed by a S infusion until the trachea was intubated. Metocurine 11 ± 5 mg was given for futher relaxation. The same dose of N was again administered over 2 min, immediately prior to skin incision. Heart rate, cardiac output, mean arterial (MAP), central venous, pulmonary arterial, and occlusion pressures were obtained, and cardiac index (CI) and systemic vascular resistance (SVR) were calculated. Hemodynamic measurements and blood for determination of plasma N, epinephrine (E) and norepinephrine (NE) levels were obtained prior to mask oxygenation (C), 2 min after the initial N dose (1), 2 min after intubation (2), 2 min after skin incision (3), 2 min after sternotomy (4), at the lowest rectal temperature during cardiopulmonary bypass (CPB) (5), after rewarming during CPB (6), after protamine administration (7), and after sternal closure (8). N levels were also determined 2 min after the second N dose (2a) and at the time of extubation (9). Arterial N concentrations and E and NE concentrations were determined by radioimmunoassay and radioenzymatic assay, respectively. Hypertension (MAP > 20% above C) was initially treated with 0.1 ml N/kg (F 5 µg/kg or SF 1.5 µg/kg) - up to 3 consecutive doses, then phentolamine 1 mg up to 3 doses and finally enflurane 0.5-3%. Hypotension and decreases in CI were treated at the anesthesiologist's discretion. Results are presented as the mean ± SEM. Data were analyzed by 2-group repeated measures analysis of variance.

Results: Age and chronic antianginal medications were similar in both groups. The dosage ratio utilized for F vs SF was 3.3 to 1 which produced a mean F vs SF plasma concentration ratio of 4.6 to 1 (see graph). SF produced unconsciousness more rapidly than F (71±3 sec vs 114±27 sec). SVR remained significally lower throughout the intraoperative period in the SF group, ($p<0.02$).

There was a statistically, though not clinically significant rise in SVR in the F group with incision, associated with an increase in MAP and a decrease in CI. One patient in each group developed clinically significant hypertension following sternotomy and required N plus phentolamine for control. Plasma E and NE did not change from control in either group in the pre-CPB period and were not significantly elevated when patients became hypertensive. F patients were extubated with plasma F concentrations averaging 2.0±0.5 ng/ml at 20±4 h after induction. SF patients were extubated at 23±1 h with a mean plasma SF concentration of 0.33±0.10 ng/ml, except one patient who was extubated with a plasma SF concentration of 0.4 ng/ml at 45 h. No patient had recall of any intraoperative events.

Discussion: The patients in both the F and SF groups experienced stable, uncomplicated anesthesia, except for the occurrence of a single hypertensive response to sternotomy in each group. It should be noted that the two hypertensive responses occurred within one hour of the administration of the total dose of F (100 µg/kg) or SF (30 µg/kg). This finding supports the conclusion that complete suppression of cardiovascular reflexes is not reliably produced by very high doses of F alone.[2] The same conclusion is also applicable to SF.

References:

1. deLange S, et al: Comparison of sufentanil-O_2 and fentanyl-O_2 for coronary artery surgery. Anesthesiology 56:112-118, 1982.

2. Wynands JE, et al: Blood pressure response and plasma fentanyl concentrations during high - and very high-dose fentanyl anesthesia for coronary artery surgery. Anesth Analg 61:521-525, 1983.