TITLE: PHARMACOKINETIC COMPARISON OF SUFENTANIL AND FENTANYL DURING ANESTHESIA FOR CARDIAC SURGERY

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INTRODUCTION. The previous comparison of fentanyl (F) 100 ug/kg with sufentanil (S) 20 ug/kg had shown that there was still about a 20% break through hypertension at sternotomy. The purpose of this investigation was to study the pharmacokinetics of a higher dose of S (25 ug/kg) and F (100 ug/kg) and compare the hemodynamics at various serum concentrations.

MATERIALS AND METHODS. Forty patients (ASA III EF≥.4) who were to undergo coronary artery bypass procedures of multiple grafts gave their informed consent to randomly receive either 25 ug/kg of S or 100 ug/kg of F. The patients were on propranolol and/or calcium antagonists which they received together with lorazepam 0.05 mg/kg orally 1.5 hrs before surgery. The patients vessels were cannulated with two IV's, an arterial and a Swan Ganz catheter under local anesthesia. At induction after pre-oxygenation, 15 ug/kg of S or 50 ug/kg of F was injected into the side port of the Swan Ganz catheter together with muscle relaxant(s) over 1.5 minutes. After loss of consciousness and 1.5 minutes of mask ventilation with 100% O_2, the trachea was sprayed with 160 mg of lidocaine and the patient intubated. A second dose of 10 ug/kg of S or 50 ug/kg of F was administered just before sternotomy. Complete hemodynamic profiles were performed when the patient was awake and 15 times during surgery, including 1, 2, and 5 minutes after the major stress events. Blood was obtained for analysis of serum concentrations of either S (13 patients) or F (12 patients) from the arterial cannula 10 times during the procedure. The serum was analysed by gas-liquid chromatography and checked by radioimmunoassay. Coefficient of variation was 12%. Serum concentrations were fit by non-linear least-squares regression (NONLIN) and pharmacokinetic parameters were calculated. Correlation of the serum concentrations to the calculated hemodynamic effects was assessed. EEG was analyzed by both Walsh and Fourier transformations of the power spectrum.

RESULTS. Rapid induction as judged clinically and by EEG was achieved by both drugs. The dose of F to S was administered in a ratio of 4:1, and this was reflected in the serum concentrations (Fig. 1). S concentrations declined more rapidly during this initial period; the distribution half-life being S=14.8±8.0 min compared to F=29.6±6.3 min ($p \leq .01$). The effective therapeutic concentration of both drugs was difficult to ascertain as there was nearly a fourfold interpatient variability in drug concentration. At sternotomy, no patients were hypertensive with serum concentrations above 40 ng/ml for F or 15 ng/ml for S. However, a few normotensive patients had serum concentrations below these values. The concentrations of S adequate for induction fell more rapidly than F prior to chest incision, (S 38.05 ng/ml to 3.19 ng/ml; F 62.2 ng/ml to 15.5 ng/ml), with the patients showing some activity out of the delta band on EEG. Redosing both groups (F 50 ug/kg, S 10 ug/kg) 2 mins prior to chest incision resulted in serum concentration of S=20.72 ng/ml and F=45.40 ng/ml at sternotomy. No significant differences in systolic pressure, heart rate, or cardiac output were found at this time.

DISCUSSION. The results show that clinically the two drugs are similar, achieving anesthetic concentrations rapidly. However S declines more rapidly before bypass and judicious timing of the second dose around the time of chest incision and sternotomy would be important to achieve a therapeutic concentration at this point. From analysis of clinical response and serum concentrations, it appears that the two doses of S used at induction and prior to sternotomy maintained a blood pressure and heart rate (Fig. 2) within normal ranges compared to F at serum concentrations compatible with their known potency ratios.

CONCLUSION. To maintain serum concentrations in the range thought adequate for stable hemodynamics at sternotomy, additional doses of both narcotics are necessary. The timing of the S dose may be more critical due to its more rapid initial decline.

Fig. 1

MEAN INTRA-OPERATIVE FENTANYL AND SUFENTANIL DRUG CONCENTRATION

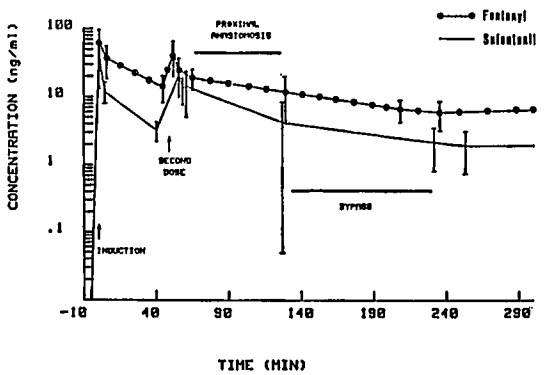

Fig. 2

INTRA-OPERATIVE HEMODYNAMIC EPISODES

		Hypertensive Episodes	Tachycardic Episodes	Hypotensive Episodes	Bradycardic Episodes
Episodes/Observations	Sufentanil	17/189	23/190	4/189	10/190
	Fentanyl	12/241	21/241	11/241	1/241
Episodes Expressed as % of Observation	Sufentanil	9.0	12.1	2.1	5.3
	Fentanyl	5.0	8.7	4.6	0.4

Hypertensive Episodes: SAP > 150 mmHg
Tachycardic Episodes: HR > 90 bpm
Hypotensive Episodes: SAP < 95 mmHg
Bradycardic Episodes: HR < 50 bpm