TITLE: PULMONARY RETENTION OF SUFENTANIL IN THE LUNGS

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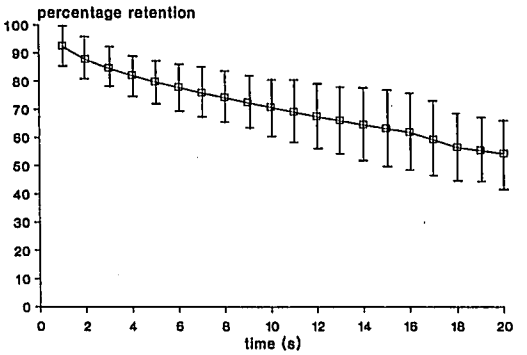
Introduction. Significant first-pass pulmonary uptake has been demonstrated for lidocaine[1], meperidine[2,3], fentanyl[3,4] and alfentanil[4,5]. We have investigated the uptake of sufentanil in the lungs of patients undergoing cardiac surgery.

Methods. The study protocol was approved by the local ethics committee. Ten patients scheduled for elective coronary artery surgery were studied after giving informed consent. Patients with poor left ventricular function, valvular dysfunction, pulmonary disease, or hypersensitivity to iodine were excluded from the study. Premedication was with lorazepam 4-5 mg orally. In the operating room a radial artery was cannulated and a pulmonary artery catheter inserted. Patients received indocyanine green (ICG) 22 mg and sufentanil (SUF) 43 µg, injected in 1 s via the atrial port of the pulmonary artery catheter. Using a fraction collector arterial blood samples were collected at 1 s intervals for 60 s after drug injection. In each sample the ICG and the SUF concentrations were measured. ICG was measured by spectrophotometry at 805 nm. SUF concentration was measured by radioimmunoassay. Pulmonary extraction and retention ratios of SUF were calculated for each time t as: $extraction_{t,SUF}$ (%) = $(1-(C_{t,SUF}/dose_{SUF}) / (C_{t,ICG}/dose_{ICG})) \times 100$ and $retention_{t,SUF}$ (%) = $(1 - (AUC_{t,SUF}/AUC_{t,ICG})) \times 100$, where AUC_t = area under the concentration-time curve up to time t. Results are expressed as mean (SD).

Results. Peak extraction after injection of SUF was 93.7(9.3)%. After 16.1(3.0) s there was net release of SUF from the lungs. After 95% passage of ICG 61.1(13.7)% of the SUF dose was still retained in the lungs. The figure shows the percentage of SUF dose retained in the lungs relative to the time of injection.



Discussion. After SUF there is significant first-pass retention in the lungs. Retention is significantly higher than that of alfentanil, reported earlier[5]. This difference can be explained by the greater lipophilicity of SUF.

References

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2. Br J Clin Pharmacol 25:235-241, 1988
3. Anesthesiology 67:466-472, 1987
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5. Anesthesiology 71:A227, 1989

TITLE: ESMOLOL/N2O/RELAXANT - A NEW EFFECTIVE ANESTHETIC MAINTENANCE TECHNIQUE

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The use of esmolol (ESM) during anesthesia is mainly for the control of hypertension and tachycardia that are associated with the stress of anesthesia and surgery. However, beta blockers are also known to affect the central nervous system and produce stress-reduction and anxiolysis. We have used ESM as a substitute for commonly used anesthetic agents, and report its hemodynamic, hormonal, analgetic and amnestic properties.

After obtaining institutional approval and informed consent fifteen ASA 1-2 patients (Age 38+8y) undergoing general surgery (mostly thyroid and breast) were premedicated with oral diazepam .15mg/kg. On arrival to the OR 2mg/kg of ESM were administered IV over 2min, followed by an infusion of 0.3mg/kg/min througout the operation. Five min after the start of the ESM drip, induction with sodium pentothal 5mg/kg and vecuronium 1mg was followed by succynilcholine 1.5mg/kg, endotracheal intubation, and anesthetic maintenance with 67% N2O and vecuronium.

Blood samples for norepinephrine(NE), epinephrine (E), cortisol(CORT), prolactine(PROL), were taken before (0), 10min, 60min and 24h after the start of ESM. At the end of the operation ESM and N2O were discontinued and muscle paralysis reversed. Another group of 7 patients was maintained with N2O/n/fentanyl/relaxant during the procedure and served as a control group (CONT).

Blood pressure (BP) and heart rate (HR) were similar in the two groups throughout the procedure except that following intubation mean BP in the ESM group (134±18mmHg) was lower (p<.0001) than CONT (181±29). NE and E levels were unchanged within and between groups. CORT increased at 60min in the ESM group, and was higher than CONT. PROL increased in both groups at 60min (table). All hormone values were unchanged from baseline at 24h.

TABLE:

	PROL(ng/ml)		CORT(mcg%)		NE(pg/ml)	
	0	60	0	60	0	60
ESM	43±94	141±95*	14±7	42±6*#	120±48	153±89
CONT	10± 5	125±79*	21±10	30±16	102±17	127±31

*p<.015 compared to 0 ; #p<.032 compared to CONT

All patients woke up and obeyed oral commands 5-10min following cessation of ESM. Two out of the 7 patients in the CONT group needed naloxone for full recovery. Mean time from arrival to recovery and demand of analgesia was 22+21min in the ESM, not different than CONT. An interview 24h potoperatively revealed no recall in any patient.

Our results show that ESM may replace commonly used anesthetic agents. Its use is associated with stable hemodynamics, low hormonal stress response, immediate recovery, normal analgetic demand and no recall. All these combined with its ultra short half life, make it an extremely promising anesthetic option. The mechanism by which ESM exerts its central effects remain to be elucidated.

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