Title: ARE PLASMA SUFENTANIL LEVELS DECREASED BY BLOOD CONSERVATION DEVICES?

Authors: JG Stone MD, MC Damask MD, and HJ Khambatta MD

Affiliation: Department of Anesthesiology, Columbia University, College of Physicians and Surgeons, New York City 10032

Introduction. To conserve blood during open heart surgery, cell savers and hemoconcentrators are used. Cell savers retrieve and filter shed blood from the operative field and then wash and separate reconcentrated erythrocytes from a supernate by centrifugation. Hemoconcentrators are in-line extracorporeal devices which employ ultrafiltration across a semipermeable membrane to withdraw plasma water from a diluted perfusate during cardiopulmonary bypass. Both supernate and ultrafiltrate are discarded, and thus both devices are capable of extracting intravenous anesthetics while processing blood. This study was undertaken to quantitate that phenomenon, using sufentanil as a marker.

Methods. With IRB approval, 20 patients were anesthetized with sufentanil, 30 mcg/kg, and diazepam, 0.1 mg/kg, infused over 3 minutes. They were paralyzed, intubated, and ventilated with 100% oxygen. No additional sufentanil was administered; but if supplemental anesthetics were needed, morphine, diazepam or droperidol were given. The cell saver was in use from the beginning of surgery until the last unit of autologous blood was infused. All patients underwent hypothermic cardiopulmonary bypass with a membrane oxygenator and 2 liters of bloodless prime. Excessive hemodilution during bypass was prevented either by centrifuging extracorporeal perfusate in the cell saver or by connecting a hemoconcentrator in parallel to the bypass circuit. Perfusate was pumped through the hemoconcentrators at 200 ml/min, and a transmembrane pressure gradient of 200-300 torr was applied across the device to draw off an ultrafiltrate. After patients were weaned from bypass, the perfusate remaining in the extracorporeal circuit was hemoconcentrated prior to autotransfusion with either a cell saver or a hemoconcentrator. At the completion of the operation, the total combined volume of the cell saver supernate was measured and an aliquot stored at -70°C for subsequent sufentanil analysis. The same was done with the hemoconcentrator ultrafiltrate. A 5 ml blood sample was drawn prior to induction, at the time of incision, shortly before bypass, on bypass (when flow stabilized), after weaning from bypass, and following the reinfusion of the last unit of autologous erythrocytes. The plasma was separated and stored frozen until drug analysis. The concentrations of sufentanil in plasma, supernate and ultrafiltrate were determined by radioimmunoassay (1). The percentage of the total dose contained in the plasma at the time of sampling was calculated.

Results. Patients received 2.3 ± 0.2 mg (mean ± sem) of sufentanil as a total dose. Cell savers were used in 19 cases, hemoconcentrators in 8, and both in 7. The cell saver reconstituted 1001 ± 105 ml of autologous erythrocytes to a hematocrit of 53 ± 1%. In the process, 7860 ± 810 ml of supernate, containing 0.32 ± 0.02 ng/ml of sufentanil, were discarded. Thus, 2.5 mcg, or approximately 0.1% of the total given dose of sufentanil, was removed by the cell saver. Bypass lasted 148 ± 10 min, and the hemoconcentrators extracted 1650 ± 250 ml of ultrafiltrate. A Bentley CPB-7000 Blood Processor (Baxter, Irvine, CA) was used in 3 cases, and its ultrafiltrate was also found to contain approximately 0.1% of the given dose of sufentanil. In contrast, no drug was detected in the ultrafiltrate from the William Harvey H-4200 Hemo-Concentrator (Bard, Santa Ana, CA) used in the other five patients.

Plasma sufentanil levels are listed below.

Sample	time (min)	ng/ml	% of dose
Control	0	0	0
Incision	30	8.5 ± 0.3*	1.3
Pre-bypass	96	4.9 ± 0.4*	0.8
On bypass	111	2.5 ± 0.3*	0.6
Off bypass	253	1.5 ± 0.1*	0.3
Study end	346	1.4 ± 0.1	0.3

* significantly different from preceding

Discussion. Sufentanil's pharmacokinetics are best described by a triexponential distribution and elimination curve with half-lives of 84 sec, 18 min and 2.7 hrs (2). Our data confirm that after an intravenous injection the drug rapidly leaves the plasma compartment and is virtually unavailable for extraction by the time cell savers or hemoconcentrators become operational. Thus these devices should not be able to alter the depth of sufentanil anesthesia or the level of other intravenous anesthetics with similar kinetics.

References

1. Michiels M, Hendriks R, Heykants JJ: Radioimmunoassay of the new opiate analgesics alfentanil and sufentanil. J Pharm Pharmacol 35:86-93, 1983

2. Bovill JG, Sebel PS, Blackburn CL, Oei-Lim V, Heykants JJ: The pharmacokinetics of sufentanil in surgical patients. ANESTHESIOLOGY 61:502-506, 1985