TITLE: NONUNIFORMITY OF ALFENTANIL PHARMACOKINETICS IN HEALTHY ADULTS

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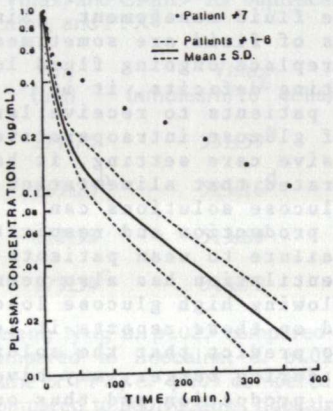
Introduction: Alfentanil is a new, short acting narcotic structurally related to fentanyl. Alfentanil by infusion has been used for induction and maintenance of general anesthesia. A previous study reported its kinetics in patients undergoing a variety of procedures with different anesthetics [1]. We investigated the kinetics of alfentanil 200 µg/kg given as a bolus for anesthetic induction in healthy young females undergoing infertility procedures, finding one apparently normal patient with markedly reduced clearance.

Methods: The investigation was approved by the institutional Committee on Studies Involving Human Beings, and informed consent was obtained from each patient. Seven females, ASA Status I, undergoing tubal reanastomosis or lysis of pelvic adhesions were studied. No premedication was given. After d-tubocurarine 3 mg and oxygen by mask for three minutes, a bolus of alfentanil 200 µg/kg was injected rapidly. Succinylcholine 1.5 mg/kg was given followed by tracheal intubation one minute later. Enflurane (0.2% to 1.5% inspired), N_2O (70%) and d-tubocurarine were used for maintenance of anesthesia, with no additional narcotic or sedative. Blood was sampled prior to induction and 1, 2, 3, 5, 7, 10, 15, 25, 40, 60, 120, 180, 240, 300, and 360 minutes after the dose from a catheter positioned in the superior vena cava. Plasma concentrations were determined in duplicate by radioimmunoassay method. Nonlinear regression analysis* was used to fit the data to a sum of exponentials, and standard equations were used to derive the model parameters. Data are presented as mean ± SD.

Results: The mean age of patients was 30.3 ± 6.0 yrs, and the median duration of anesthesia was 4.7 hr (range: 2.5 to 5.5 hr). Pharmacokinetics of alfentanil was best described by a two-compartment open model: $C_p(t) = Ae^{-\alpha t} + Be^{-\beta t}$. The addition of a third exponential term generally yielded coefficients with low confidence and not significantly different from zero. There was an initial rapid decline in concentration followed by an elimination phase. Model parameters are listed in the table. Late secondary peaks in plasma concentration were not consistently seen. One patient (#7) had a much slower Cl_E (1.65 ml/kg/min) and $t_{\frac{1}{2}\beta}$ (151 min), with smaller V_D (0.347 l/kg). The figure compares the best-fit line for the other six patients with the data points of #7. Review of this patient's record revealed use of enflurane 0.5 - 1.0%



† Kinetics of Alfentanil 200 µg/kg, N = 7

Cl_I	Cl_E	V_C	V_D	$t_{\frac{1}{2}\alpha}$	$t_{\frac{1}{2}\beta}$
(ml/kg/min)		(l/kg)	(l/kg)	(min)	(min)
8.83	5.02	0.188	0.513	8.2	10
±4.28	±1.90	±0.022	±0.098	±3.4	±2

inspired, intraoperative nasopharyngeal temperature 35.0 -36.5 °C, stable hemodynamics, duration of anesthesia of 4.7 hr, and normal physical exam and laboratory tests.

Discussion: Our results for Cl_E, V_D and $t_{\frac{1}{2}\beta}$ agree with those from other human studies [1,2]. Compared to fentanyl, V_D and $t_{\frac{1}{2}\beta}$ are [3] of considerably smaller magnitude. Though our patient population, procedure and anesthesia were controlled, one patient demonstrated markedly slower clearance of alfentanil. This suggests decreased hepatic extraction or flow because the renal excretion of alfentanil is only 1 percent. This finding has important implications for alfentanil infusion regimens. Patient #7 would have a steady-state plasma concentration three times that predicted from the clearance data of the group.

References: 1) Bovill JG, Sebel PS, Blackburn CL, et al: Kinetics of alfentanil and sufentanil: a comparison. Anesthesiology 55: A174, 1981. 2) Schuttler J, Stoeckel H: Alfentanil (R 39209) ein neues Kurzwirkendes opioid. Anaesthesist 31: 10-14, 1982. 3) McClain, DA, Hug CC Jr.: Intravenous fentanyl kinetics. Clin Pharm Ther 28: 106-114, 1980.

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† $Cl_{I,E}$: intercompart. and elimin. clearance
$V_{C,D}$: central and total distrib. volume

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