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TITLE: GASTRIC FLUID ALFENTANIL CONCENTRATIONS FOLLOWING ALFENTANIL INFUSION

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Delayed respiratory depression has occurred following alfentanil infusion.[1,2,3] Secondary peaks in serum levels following infusion may account for the respiratory effects. Similar respiratory depression has been described with fentanyl and gastric sequestering of this drug has been demonstrated.

Significant gastric trapping may also occur with alfentanil. The object of this study was to demonstrate whether gastric trapping occurs during alfentanil infusions in human subjects undergoing routine anesthesia and surgery.

Following University of British Columbia Ethics Committee approval and patient informed consent, 10 ASA 1 or 2 adult patients undergoing elective gynecological surgery were studied. All patients received 30 ml. 0.3 M sodium citrate p/o and lorazepam 1 mg s/l 30 minutes preoperatively.

Induction of anesthesia consisted of dtc (50 mcg/kg), alfentanil (50 mcg/kg), sodium thiopental (4 mg/kg) and succinylcholine (1.5 mg/kg). Following endotracheal intubation a no. 18 orogastric tube was positioned in the stomach and the contents were suctioned and discarded.

Maintenance of anesthesia was 70% N_2O/30% 0_2, alfentanil infusion 1.0 - 1.5 mcg/kg/min. and isoflurane as required. Vecuronium was used for muscle relaxation.

At the completion of the procedure the alfentanil infusion was stopped and blood samples were drawn for serum alfentanil level. The stomach contents were aspirated and analyzed for volume, pH, and alfentanil concentration.

Ten patients were studied overall; one was excluded from analysis because of a maladjustment of the infusion pump. In all patients the alfentanil concentration in gastric fluid greatly exceeded that in the serum. (see table)

This study demonstrates that gastric trapping of alfentanil occurs during continuous alfentanil infusion. Subsequent reabsorption may give rise to secondary serum peaks. We noted that the amount of drug recovered from the stomach was quite variable. Those patients with a high "intragastric dose" of alfentanil may be at risk of delayed respiratory depression.

As gastric trapping remains a possible mechanism of delayed respiratory depression, we suggest that all patients should have their stomach contents evacuated following alfentanil infusion.

R.J. Hudson MD (U. of Manitoba) performed the alfentanil assays.

References

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2. Jaffe RS et al. Anesthesiology 70:151-3, 1989.
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TABLE

Case	Alf. Dose (mcg)	Gastric Fluid Volume (ml)	pH	Alfentanil Concentrations (ng/ml) Serum	Gastric	Intragastric Dose mcg. (*)
1	8300	8	7	246	6654	53.2 (0.6)
2	11675	19	4	280	1500	28.5 (0.2)
3	9085	18	2	384	8475	152.5 (1.7)
4	11970	8	2	192	7120	57.0 (0.5)
5	8565	55	1	256	3964	218.0 (2.5)
6	11930	21	4	376	3538	74.3 (0.6)
7	9390	8	1	232	3564	28.5 (0.3)
8	11220	21	4	266	2266	47.6 (0.4)
9	13170	30	1	456	13438	403.1 (3.1)

(*) % of infused dose of alfentanil.

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PREDICTION OF PLASMA CONCENTRATIONS DURING ALFENTANIL INFUSION IN VOLUNTEERS: ACCURACY OF DIFFERENT PHARMACOKINETIC MODELS

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Introduction: The purpose of this study was to compare the accuracy of prediction of computer-assisted continuous infusion (CACI) of alfentanil given to healthy volunteers, using a list of pharmacokinetic models, studied in different clinical conditions. Material and methods: 8 healthy young male adult volunteers were given the same alfentanil CACI to maintain a stable theoretical plasma concentration of 50 ng/ml during a 4-hour period, according to a population pharmacokinetic model (1). 15 venous blood samples were drawn in each volunteer at predetermined intervals. Alfentanil serum concentrations were measured by RIA. Pharmacokinetic parameters of each volunteer were calculated and averaged to furnish the model of reference. Predicted plasma concentrations were simulated for the individual pharmacokinetic parameters, the model of reference and for 7 models retrieved from the literature and studied in volunteers (2) or in surgical patients receiving either a large bolus (1,3,4) or a short infusion (5) or a bolus followed by an infusion (6,7). The accuracy of prediction was assessed by calculating the prediction error for each of the 8 samples taken during the infusion period and by determining the mean bias and the standard deviation (STD) of each patient and model. The mean bias ± STD were considered low when the mean ± 1 STD included 0, high when the mean ± 1 STD (68% confidence limit) did not include 0 and significant when the mean ± 2 STD (95% confidence limit) did not include 0.
Results: The mean bias ± STD were low with the model of each volunteer: 1.7% ± 4.4, the model of reference: -3.1% ± 29.4, the model studied in volunteers: -9.0% ± 28.4 (2) and the models studied in healthy surgical patients receiving an infusion: 42.7% ± 43.7 (5); -5.6% ± 29.0 (6); -18.5% ± 25.8 (7). The mean bias were high and even significant with the models studied after a large bolus of alfentanil: -27.8% ± 21.9 (1); -53.7% ± 14.0 (3); -39.7% ± 18.6 (4).
Conclusion: For alfentanil CACI in volunteers, the selection of the pharmacokinetic model influences the accuracy of prediction. A pharmacokinetic model, determined after a large bolus, does not predict alfentanil CACI accurately in adult volunteers.
References:

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