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TITLE: PHARMACOKINETIC PROFILES UNDER MORPHINE, METHADONE, FENTANYL AND SUFENTANIL EPIDURAL PATIENT-CONTROLLED ANALGESIA (ePCA)

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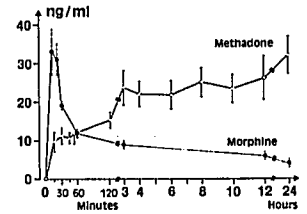
The aim of the study was to evaluate opiate concentrations (OC) under morphine (Mo), methadone (Meth), fentanyl (F) and sufentanil (S) ePCA for postoperative pain.

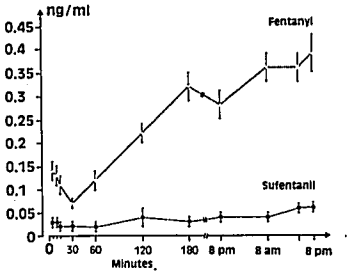
With institutional approval and informed written consent 82 patients scheduled for abdominal operations received ePCA (dose regimens see Table 1) when complaining of severe postoperative pain (scale 0 - 10). The infusion was reduced by 50 % if possible at predetermined times. Blood samples were taken at various intervals to determine serum Mo,F and S by RIA (sensitivities (Sen,ng/ml) 0.1 (Mo), 0.01 (F), 0.01 (S) and plasma Meth by gas-chromatography (Sen 0.5 ng/ml). For statistics ANOVA, measurements ANOVA and paired t-test were used.

Table 1

	Mo	Meth	F	S
No of patients	36	16	15	15
µg loading dose	2000	2000	60	15
infusion (µ/hr)	200	460	20	5
µg on-demand	625	200-1000	12.5	3.1

Pain was well controlled in all patients. Within 15 min mean maximum OC (± SEM) of 33 ± 6 (Mo), 10 ± 2 (Meth), 0.14 ± 0.02 (F) and 0.03 ± 0.01 (S) ng/ml were achieved in all groups. Serum Mo dereased steadily thereafter ($p < 0.001$). In contrast, plateaus of around 10 (Meth), 0.11 (F) and 0.025 (S) ng/ ml were reached with Meth, F and S and maintained at least over 60 min followed by an OC increase ($p < 0.001$, Meth; $p < 0.05$, F).





The OC range causing systemic analgesia (MEC; 9 - 23 ng/ml,Mo (1);22 - 89 ng/ml,Meth (1); 0.2 - 1.2 ng/ml,F (2); 0.06 - 0.13 ng/ml,S (own research) was reached for a short time soon after the beginning of Mo ePCA. In contrast, MEC values were reached and maintained only several hours after the beginning of Meth, F and S ePCA. This indicates that the epidural space serves as a reservoir for lipophilic opiates and confirms the spinal site of epidural opiate action.

References

1 ANESTHESIOLOGY 61:19-26,1984

2 Anesth Analg 67:329-337,1988

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TITLE : EPIDURAL VERSUS INTRAVENOUS ALFENTANIL BY PCA IN POSTOPERATIVE PATIENTS

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Patient-controlled analgesia (PCA) is an effective technique in relieving postoperative pain. This technique is described mainly by intravenous (IV) route. Recent papers have reported the efficacy of PCA with opioids by the epidural (EP) route. The purpose of this study was to compare analgesia and side effects between IV and EP alfentanil PCA..

After informed consent and institutional approval, 26 patients ASA I or II scheduled for digestive, urologic, vascular or orthopedic surgery were studied during 18 h after surgery. They were randomly assigned to receive EP or IV alfentanil with the PCA when the postoperative pain was present. The EP catheter was inserted preoperatively close to the metameric level of surgical pain (thoracic in 5 patients, lumbar in 8). Pain was assessed using a visual analog scale(VAS : 0-10). Oxygen saturation was continuously monitored and recorded in a computer to analyse number and duration of desaturation (< 85 % for more than 1 minute). Cumulative dose of alfentanil was noted in each group. 0.25 mg (1 ml) alfentanil bolus were injected on demand with a 5 min lockout period for the IV group and a 10 min lockout for the EP group. In each group the dose could not excess 6 mg for 4 hours. The Student's t-test for unpaired data and chi-square with the Yates correction were used for statistical analysis. Values are given as the mean ± S.D.

Onset of analgesia and VAS scores were comparable in the 2 groups (fig. 1). The cumulative alfentanil dose was significantly higher ($p < 0.05$) in the IV group from the first hour to the end of study (fig. 2). More patients in the EP group have oxygen desaturation (10 in EP vs 4 in IV group, $p < 0,05$). But there was no statistical difference between groups for number (17 in IV vs 27 in EP group) and duration of desaturation (3,5 ± 6,4 min in IV vs 5,3 ± 5,4 min in EP group). The lowest desaturation was 70 % in each group. These data show that quality of analgesia is not different between IV and EP alfentanil when using PCA. However the amount of opioid administered was reduced in the EP group. This is in agreement with a direct spinal effect of epidural opiate. The incidence of hypoxemia appears to be lower in this study with alfentanil epidurally administered than in previous ones using EP morphine (1,2). This difference may reflect either the titration by PCA or the limited cephalad spread of a lipophilic opiate such as alfentanil.

References: 1- Anesthesiology 70 : 948-953 ,1989

2- Br J Anaesth 64 :267-275 ,1990

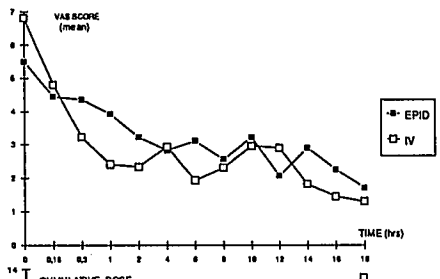

Fig1: Mean values of VAS scores in the 2 groups.

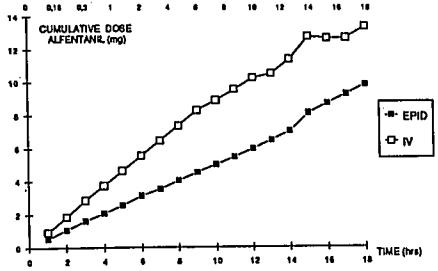

Fig2: Mean values on the cumulative alfentanil dose