TITLE : PHARMACOKINETICS IN MOTHERS AND NEONATES OF FENTANYL, ALFENTANIL AND SUFENTANIL ADMINISTERED BY EPIDURAL CONTINUOUS INFUSION DURING LABOR.

AUTHORS : M. Palot, M.D., H. Visseaux, M.D., J.C. Levron*, Ph. D., J.P. Le Moing*, Ph. D., J. Rendoing, M.D.

AFFILIATION : Dept. Anesth. Rean., Centre Hospitalier Universitaire. 51100 REIMS - FRANCE.
* JANSSEN Research Foundation. 93000 AUBERVILLIERS - FRANCE.

Epidural opiates are widely used during epidural analgesia for labor and delivery. We know that they cross the placenta. The aim of this study was to determine plasma kinetics of fentanyl, alfentanil and sufentanil in mothers and neonates, when administered by continuous epidural infusion for labor.

After approval by our Hospital Ethics Committee, thirty ASA I patients, with normal singleton pregnancy, were randomized in three groups and epidural blockade established as follows : Group I 0.25%bupivacaïne(B) 10ml and fentanyl(F) 50µg then continuous epidural infusion(CEI) 10ml/hour of B 0.125% + F 2 µg.ml-1. Group II 0.25%B 10ml and alfentanil(A) 10µg.kg-1 then CEI 10 ml/hour B 0.125% + A 5µg.ml-1. Group III 0.25%B 10ml and sufentanil (S) 20µg, then CEI 10ml/hour B 0.125% + S 0.2µg.ml-1. Maternal venous blood samples were taken at 10-20-30 then every 30 minutes until delivery and 3 hours after delivery. Samples were taken from umbilical artery and vein, gastric fluid and in the neonate 3 hours after delivery. Analgesia was evaluated by verbal pain score and neonates were assessed by Apgar score and Amiel-Tison neurological and adaptative capacity score (NACS). Plasma fentanyl, alfentanil and sufentanil were measured by RIA. The minimum level of detection was 0.05 ng.ml-1 for fentanyl and sufentanil and 1 ng.ml-1 for alfentanil.

We present here results from the first ten patients. Analgesia was similar for all patients, we did not observe any clinical respiratory depression in mothers. Apgar scores and NACS are similar for all neonates. In mothers, maximum plasma concentration of opiates was observed ten minutes after bolus injection and we observed, with fentanyl only, a late secondary peak between 120 and 180 min. Placental transfer of fentanyl was greater than placental transfer of alfentanil, UV/MV ratio is threefold higher with fentanyl than with alfentanil (Table I). We found significant levels of fentanyl and alfentanil in gastric fluid. We failed to detect any measurable concentration of sufentanil in maternal and neonatal plasma and gastric fluid at delivery and 3 hours later.

These results, if confirmed by the entire study, suggest that sufentanil and alfentanil are probably safer for mothers and neonates than fentanyl.

Table I

	nb	Fentanyl		Alfentanil		Sufentanil	
MV (ng.ml-1)	1	0.42		5.2		ND*	
	2	0.28		4.4		ND*	
	3	0.26		ND*		ND*	
	4	0.12					
UV (ng.ml-1)	1	0.32		1.5		ND*	
	2	0.26		1.0		ND*	
	3	0.16		ND*		ND*	
	4	ND*					
UA (ng.ml-1)	1	0.37		1.9		ND*	
	2	0.45		NS		ND*	
	3	0.14		ND*		ND*	
	4	ND*					
UV/MV UA/UV	1	0.76	1.16	0.29	1.25	-	
	2	0.93	1.73	0.23	NS	-	
	3	0.61	0.87	-		-	
GF (ng.ml-1)	1	0.74		3.6		ND*	
	2	0.53		8.8		ND*	
	3	1.59		ND*		ND*	
	4	NS					
3 hours MV BV (ng.ml-1)	1	0.36	0.54	NS	ND*	ND*	ND*
	2	0.22	NS	ND*	ND*	ND*	ND*
	3	0.11	ND*	ND*	ND*	ND*	ND*

MV=Maternal vein; UV=umbilical vein; UA=umbilical artery; BV=baby vein; ND*=<0.05 ng.ml-1; NS=no sample
GF = gastric fluid