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Title: SUFENTANIL: MATERNAL AND NEONATAL PLASMA LEVELS AFTER EPIDURAL ADMINISTRATION DURING LABOR AND DELIVERY

Authors: O. Kick, M.D., J.D. Vertommen, M.D., H. Van Aken, M.D., Ph.D., J. Gryseels, M.D.
Affiliation: Anesth. Dept., University Hospitals, Katholieke Universiteit Leuven, Herestraat 49 B-3000 Leuven, Belgium.

The addition of sufentanil in incremental doses of 10 μg up to a total maximum of 30 μg to 0.125% bupivacaine with epinephrine (1:800,000) has beneficial effects on the quality of analgesia during labor and on the incidence of instrumental deliveries without depressing the neurobehavioral status of the newborn.(1) In the present study the plasma levels of sufentanil in both mother and neonate were determined after epidural administration of bupivacaine 0.125% with epinephrine (1:800,000) and sufentanil in a dose up to 30 μg.

With institutional approval and informed consent, fifteen pregnant women (ASA physical status 1 or 2) who requested epidural analgesia for labor were studied. After insertion of an epidural catheter at either the L2-L3 or L3-L4 interspace, analgesia was induced and maintained by intermittent injections of 10 ml 0.125% bupivacaine with epinephrine (1:800,000). Each injection also contained 10 μg sufentanil. If more than three injections were required, the same solution of bupivacaine was used but without sufentanil. Immediately after delivery maternal venous and umbilical arterial and venous blood samples were drawn and assayed for sufentanil levels. The sufentanil levels were determined by radioimmuno (RIA) assay. In this way the lowest detectable concentration of sufentanil was 0.01 ng/ml in the maternal and 0.02 ng/ml in the neonatal plasma.

Nine patients received only one dose with 10 μg sufentanil. The time interval between injection and delivery ranged from 15 to 100 min. Maternal plasma levels ranged from 0.011 to 0.016 ng/ml. Four patients received two injections with 10 μg sufentanil each. The time interval between the last injection and delivery (Δ time) ranged from 55 to 170 min. Maternal plasma levels ranged from 0.012 to 0.015 ng/ml. Only two patients needed three injections and received a total dose of 30 μg sufentanil. In these two patients the time interval between the last injection and delivery was 55 and 197 min. Maternal sufentanil concentrations were 0.015 and 0.011 ng/ml respectively. There was no sufentanil detectable (ND) in the neonatal plasma in all the fifteen cases.

Patient No.	Sufentanil Dose(μg)	Δ time (min)	Sufentanil plasma level (μg/ml) mother
1	10	15	0.012
2	10	45	ND
3	10	75	0.022
4	10	62	0.014
5	10	74	ND
6	10	55	0.016
7	10	56	ND
8	10	49	0.011
9	10	100	0.011
10	20	55	ND
11	20	170	0.015
12	20	140	0.015
13	20	143	0.012
14	30	55	0.015
15	30	197	0.011

The neonatal plasma levels of sufentanil in the present study are in agreement with the clinical observations where there was no depression of the neurobehaviorial status of the newborn from adding epidural sufentanil in a dose up to 30 μg to 0.125% bupivacaine during labor and delivery.

References: 1. Anesthesiology 1991, 74 (in press)

A838

TITLE: PROGESTERONE MEDIATED POTENTIATION OF SPINAL OPIATES

AUTHORS: H. Carp, Ph.D., M.D., A. Jayaram, M.D.
AFFILIATION: Dept. of Anesthesia, Oregon Health Sciences Univ., Portland, Oregon 97201

Introduction: Pregnancy is associated with an increased sensitivity to general and local anesthetic agents. Increases in progesterone and endogenous opiates have been implicated. In fact, Datta et al[1] found that experimental treatment with progesterone decreases the MAC of halothane in rabbits. Furthermore, in vitro studies show that metabolites of progesterone inhibit nerve-cell excitability by potentiating GABA-mediated increases in chloride-ion conductance.[2] Therefore, we tested the ability of intrathecally administered progesterone to produce analgesia and to potentiate the analgesic effects of spinal opiates in rats.

Methods: Female Sprague-Dawley rats were implanted with chronically indwelling 28 gauge spinal catheters and used for all studies. The ability of progesterone to potentiate the analgesic effects of intrathecal sufentanil was measured by first determining a subanalgesic dose of intrathecal sufentanil for each animal in the absence of progesterone treatment. Next, this same dose of intrathecal sufentanil was administered following acute treatment with intrathecal progesterone (or its metabolites) and analgesia reassayed to detect potentiation. Analgesia was measured using the tail-flick technique. In all experiments, progesterone and its metabolites were dissolved in 10 μl of 9% cyclodextran prior to intrathecal injection. Cyclodextran had no effect on the tail-flick assay or the analgesic effect of intrathecal sufentanil. Bicuculline (50 p mole) was administered intrathecally and picrotoxin (1 mg/kg) was administered intraperitoneally.

Results: Pilot studies showed that up to 50 μg of intrathecal progesterone had no analgesic effect using the tail-flick assay (n=15). Therefore, we tested the ability of progesterone to potentiate the analgesic effects of a subanalgesic dose of sufentanil. Animals first pretreated with 10 μg, 20 μg or 40 μg of intrathecal progesterone (n=5, for each dose) and then given a subanalgesic dose of sufentanil now displayed near maximal analgesia. In contrast, animals not pretreated with progesterone showed no analgesia (n=15). No behavioral or motor effects were noted following progesterone treatment. CSF progesterone levels were within physiologic range. Furthermore, 40 μg of progesterone administered intramuscularly did not potentiate sufentanil analgesia. Interestingly, 1 μg, 5 μg or 10 μg of a major progesterone metabolite, 5α-Pregnane-3α-OL-20-one, (n=5, for each dose), also potentiated sufentanil analgesia when administered intrathecally. Finally, two drugs that block GABA-mediated increases in chloride ion conductance, picrotoxin and bicuculline, each blocked progesterone mediated potentiation of sufentanil analgesia.

Discussion: These results demonstrate that intrathecal progesterone potentiates the analgesic effects of neuraxial opiates. Increased progesterone levels during pregnancy may potentiate the analgesic effect of endogenous opiates and may help to explain the decreased analgesic requirements in these patients.

References
1. Anesth Analg 68:46-70, 1989.
2. Science 232:1004-1007, 1986.