Obstetrical and Pediatric Anesthesia

Patient-controlled intravenous analgesia using remifentanil in the parturient

Fabienne Roelants MD,
Emmanuelle De Franceschi MD,
Francis Veyckemans MD,
Patricia Lavand'homme MD PhD

Purpose: To show the use of the short acting opioid remifentanil for labour analgesia when epidural analgesia is considered to be contraindicated.

Clinical features: After Ethics Committee approval and informed consent, six patients (36–40 wk gestation), in whom epidural analgesia was considered contraindicated (women refusing regional analgesia, presenting with coagulation or platelet abnormalities or sepsis) benefited from patient-controlled intravenous analgesia (PCIA) with remifentanil. The Abbott Lifecare patient-controlled analgesia (PCA) pump with remifentanil 50 $\mu g \cdot ml^{-1}$ was set to deliver remifentanil continuous background infusion of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 25 µg boluses with a five minutes lockout period. The PCIA was started when the parturients experienced regular painful contractions (cervical dilatation of at least 4 cm) and stopped just before delivery (cervix fully dilated). Maternal monitoring included non-invasive blood pressure measurements, heart rate, percutaneous arterial oxyhemoglobin saturation and respiratory rate. Percutaneous fetal heart rate was continuously monitored. All patients remained alert or sleepy but easily arousable and were satisfied with their analgesia. No particular side effects have been noticed. Apgar scores were between 6 and 10.

Conclusion: Remifentanil PCIA combining low continuous background infusion and small bolus doses is an alternative when epidural analgesia in labour is contraindicated. Under careful anesthesia monitoring, the technique seems to be safe for both mother and baby, at least when delivery occurs at or near the normal term of pregnancy.

Objectif : Décrire l'utilisation de l'opioïde de courte durée, rémifentanil, pour l'analgésie pendant le travail obstétrical lorsque l'analgésie épidurale est contre-indiquée.

Éléments cliniques : Six patientes (de 36 à 40 sem de grossesse), chez qui l'analgésie épidurale était contre-indiquée (des femmes qui refusaient l'analgésie régionale, présentaient des anomalies de coagulation ou de plaquettes ou de la septicémie), ont consenti à participer à l'étude, approuvée par le Comité d'éthique, et ont bénéficié de l'analgésie intraveineuse autocontrôlée (AIAC) avec du rémifentanil. Une pompe Abbott Lifecare pour l'analgésie autocontrôlée (AAC) a été installée avec 50 µg·ml–1 de rémifentanil administrés en perfusion de fond continue de 0,05 µg·kg–1·min–1 et en bolus de 25 µg entrecoupés de périodes réfractaires de cinq minutes. Le début de l'AIAC correspondait à des contractions douloureuses régulières (dilatation cervicale d'au moins 4 cm) et la fin, avec la naissance du bébé (col complètement dilaté). Le monitorage des mères comprenait la mesure non effractive de la tension artérielle, de la fréquence cardiaque, de la saturation percutanée du sang artériel en oxyhémoglobine et de la fréquence respiratoire. La fréquence cardiaque foetale a été placée aussi sous monitorage continu. Toutes les patientes sont demeurées éveillées ou somnolentes, mais faciles à réveiller et ont été satisfaites de l'analgésie. Aucun effet secondaire particulier n'a été noté. Les indices d'Apgar se situaient entre 6 et 10.

Conclusion : Pendant le travail obstétrical, l'administration de rémifentanil en AIAC combinant une faible perfusion de fond continue et de petites doses en bolus peut remplacer une analgésie épidurale contre-indiquée. Utilisée sous monitorage attentif de l'anesthésie, la technique semble sans risque pour la mère et le bébé, du moins lorsque la naissance survient à terme ou près du terme normal de la grossesse.

From the Department of Anesthesiology, Université Catholique de Louvain Medical School, Cliniques universitaires St-Luc, Ave Hippocrate, 10-1821, 1200 Brussels, Belgium.
Address correspondence to: Dr. Fabienne Roelants, Phone: 32-2-764-18-21; Fax: 32-2-764-36-99; E-mail: fabienne.roelants@anes.ucl.ac.be
Accepted for publication October 24, 2000.

EPIDURAL analgesia is an effective and safe method of analgesia during labour. However, the technique may be contraindicated in women who refuse regional analgesia, who present with coagulation abnormalities, local infection or sepsis, and may be technically impossible or provide inadequate analgesia in parturients with previous surgery of the lumbar spine. When epidural analgesia is not available or contraindicated, labour analgesia is often poorly managed. Remifentanil is a synthetic opioid that provides rapid onset of analgesia with an ultra short duration of action. Its unique pharmacokinetic profile stems from rapid metabolism by non specific esterases in blood and tissues both in the mother and in the fetus.[1] These properties make it an ideal agent for labour analgesia. We present the cases of six women in whom epidural analgesia was considered contraindicated by our anesthesiology staff and who benefited from patient-controlled intravenous analgesia (PCIA) with remifentanil during labour. The patients enjoyed good analgesia without clinically important side-effects.

Case series

Six patients received PCIA with remifentanil for labour. Demographic data are shown in the Table I. The first was a 36-yr-old, 70 kg, nulliparous woman admitted at 36 wk gestation for preeclampsia. Laboratory investigations showed a decreasing platelet count from 180,000·mm^{-3} to 136,000·mm^{-3}, a decreasing fibrinogen concentration from 490 mg·dl^{-1} to 366 mg·dl^{-1} and the presence of fibrin degradation products (80 µg·ml^{-1}) when the obstetrician decided to induce labour and asked to provide labour analgesia. The second case, a 39-yr-old woman, 65 kg, para 1, was admitted for induction of labour at 39 wk 6/7. The day before admission, she had a temperature of 38.5°C. On the day of induction, body temperature (axillary) was 37.5°C, C-Reactive Protein was raised to 13.1 mg·dl^{-1} and the white cell count was 14,410·mm^{-3} (with 12,820·mm^{-3} neutrophils). The third case was a 29-yr-old, 112 kg, nulliparous, woman with von Willebrand disease admitted at 36 wk 6/7 gestation after spontaneous rupture of the membranes. The fourth case was a 30-yr-old, 82 kg, nulliparous woman admitted at 40 wk gestation for induction of labour. She had a C-Reactive Protein at 3.5 mg·dl^{-1}, white cells at 25,590·mm^{-3} (with 24,130·mm^{-3} neutrophils) and a body temperature of 37.8°C. The fifth case was a 25-yr-old, 80 kg, nulliparous woman, at 38 wk gestation who had such severe backache than she refused epidural analgesia. The sixth case was a 31-yr-old, 85 kg, para 3, admitted in spontaneous labour at 40 wk gestation with a temperature of >38°C, treated with paracetamol; continued to increase C-Reactive Protein (15.5 mg·dl^{-1}) and white cells count (15,290·mm^{-3}) despite antibiotic therapy.

It was considered unwise to proceed with epidural analgesia in these parturients. After the risks and benefits of the technique were explained, we proposed to use a remifentanil PCIA. The patients were aware that this was an unlicensed indication and their informed consent was obtained before initiating therapy. Remifentanil, 1 mg, was diluted in 20 ml saline (50 µg·ml^{-1}). The patient-controlled analgesia pump (Abbott Lifecare) was set to deliver, with an anti-siphon valve, a continuous infusion of 0.05 µg·kg^{-1}·min^{-1} remifentanil and to deliver boluses of 25 µg with a lockout period of five minutes. All the parturients experienced painful, regular contractions with cervical dilatation of at least 4 cm when the PCIA technique was initiated. Labour was induced by artificial rupture of the membranes (except for patient #3) and an oxytocin infusion was started. Only the sixth patient had a spontaneous labour without oxytocin. An anesthesiologist was immediately available on request at all times during the labour. Maternal monitoring included non-invasive blood pressure measure-

TABLE I Demographics data and evoked reason for contraindication to epidural labour analgesia

Patients	*Age (yr)*	*Weight (kg)*	*Gravid para*	*Cervical dilatation (cm)**	*Birth weight (g)*	*Contra-indication*
1	36	70	G2P0	4	2440	Coagulopathy
2	39	65	G2P1	4	3120	Sepsis
3	29	112	G1P0	4	2990	Coagulopathy
4	30	82	G1P0	6	3600	Sepsis
5	25	80	G1P0	4	4200	Epidural refusal
6	31	85	G4P3	5	3700	Sepsis

*Cervical dilatation when remifentanil infusion was started

ments (every five minutes), continuous heart rate and percutaneous arterial oxyhemoglobin saturation, and the respiratory rate was recorded every five minutes. The sedation assessments (alert, sleepy, asleep, not arousable) and pain assessments (on a verbal rating scale of none, mild, moderate or severe) were also recorded. Fetal heart rate was monitored continuously percutaneously. For four patients, the PCIA was discontinued when the cervix was fully dilated and they had vaginal deliveries. The obstetrician administered local anesthesia with lidocaine 2% if he performed an episiotomy. The postpartum course of both mothers and babies was excellent and the patients expressed great satisfaction with their analgesia during labour and delivery. Among the six parturients, two required Cesarean section: one for frequent heart rate decelerations (late decelerations during contractions, but such decelerations were already present before the start of remifentanil infusion) and the second after failed induction (no progress of cervical dilatation). In these two cases, Cesarean section was performed under general anesthesia.

For all six patients the analgesia provided by PCIA of remifentanil was adequate. They felt uterine contractions but reported pain as "mild" (even "no pain" in one case). Three patients described their pain as "moderate" at 9 cm cervical dilatation: the level of continuous infusion was then raised at 0.075 $\mu g \cdot kg^{-1} min^{-1}$ for five minutes prior to delivery. In five parturients, the sedation assessments mainly showed sleepy patients at the beginning of PCIA infusion but who were alert and cooperative for the delivery or when the Cesarean section was decided upon. One patient remained alert throughout labour and delivery. The average values of vital signs are shown on Table II The time from discontinuation of the remifentanil infusion and vaginal delivery or Cesarean section varied from three to 45 min (Table III). The total dose, the dose per kg of lean body mass and per hour of remifentanil received by the patient, the time from discontinuation of the remifentanil to delivery, Apgar scores and the weight of the babies are shown on Table III. Side effects like nausea, vomiting or pruritus were asked and were not noticed.

Discussion

Fentanyl PCIA has been used previously in parturients.[2–5] Studies with remifentanil demonstrate cardiovascular and side effects profiles similar to fentanyl,[1] but remifentanil offers potential advantages. It has a

TABLE II Vital signs (mean and range) : systolic blood pressure (SBP), heart rate (HR), oxygen saturation (SpO_2) and respiratory rate (RR) for each patient

Patient	*Mean SBP (range) (mmHg)*	*Mean SpO_2 (%)*	*Mean RR (range) (breath·min^{-1})*	*Mean HR (range) (beats·min^{-1})*
1	122 (110-135)	97	18 (16-20)	72 (65-83)
2	126 (111-150)	97	16 (12-20)	96 (81-108)
3	121 (82-140)	96.7	18 (16-24)	107 (95-130)*
4	111 (93-140)	98	18 (12-20)	81 (70-95)
5	139 (123-160)	97	16 (14-18)	97 (85-135)
6	120 (110-130)	96	20	103 (92-115)

*Ritodrine impregnation

TABLE III Duration and doses of remifentanil (R) infusion, number of received boluses, time from discontinuation of the remifentanil to delivery and Apgar scores for each patient

Patients	*PCIA duration (hr)*	*Total dose R (µg)*	*Dose R (µg·kg^{-1}·hr^{-1})*	*Boluses received*	*Apgar score (1,5,10 min)*	*Remifentanil discontinuation before birth (min)*
1	2	695	4.96	11	9,9,9	15
2	2.45	772	4.40	16	8,9,9	6
3*	4.45	1207	3.63	5	9,10,10	20
4*	5.45	2287	4.89	29	9,10,10	22
5	3	1192	4.9	16	6,9,10	45
6	2.28	930	4.44	6	7,9,10	3

*Cesarean section

more rapid onset of action and is rapidly hydrolysed by non-specific blood and tissue esterases to an inactive metabolite. In addition, the metabolism of remifentanil is independent of renal and hepatic function, and it does not accumulate even after prolonged administration.[1] Kan *et al*. have shown its rapid placental passage, metabolism, redistribution and the absence of pernicious consequences to the new-born at full term during Cesarean section.[1]

The efficacy of PCIA regimens is primarily dependent on the dose of the bolus. If the bolus is too small, the patient loses confidence in the technique and if it is too large, side-effects can develop.[6] For example, during childbirth, maternal sedation and fetal heart rate decelerations are possible following too large bolus doses.[6] Taking its pharmacokinetic properties into account, remifentanil seems to represent a safe analgesic alternative to the use of other systemic opioids since major side-effects, like apnea, should be short-lasting and should not necessitate harmful treatment for either the mother or the baby. To obtain effective analgesia with this ultra-short acting opioid, we combined a low rate continuous infusion of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ with boluses. The use of a continuous background infusion allowed the use 25 µg bolus doses which is lower than the 50 or 75 µg reported by others.[6] As a consequence, we did not observe undesirable profound maternal sedation or other side effects. Furthermore, the analgesic doses per pregnant kg of lean body mass and per hour seem to be very similar for all the patients. Morley-Foster *et al.*[5] used five minute lockout periods for both fentanyl and alfentanil. Thurlow *et al.*[8], using 20 µg remifentanil boluses, reported a three-minute lockout period for remifentanil without continuous background infusion. We choose a lockout of five minutes.

The degree of satisfaction reported by our patients with intravenous remifentanil analgesia contrasts with reported failures to alleviate labour pain with systemic opioids[7] but confirms other reports describing successful labour analgesia with fentanyl or remifentanil PCIA.[2–6,8] With the PCIA system, the patient benefits from a greater sense of control over her pain management, an important psychological effect which contributes to the success of this technique.[9] We did not observe side effects in babies but all neonates were 36 wk old or more.

In conclusion, PCIA with remifentanil is an attractive alternative when epidural analgesia appears to be contraindicated. With careful anesthesia monitoring, we did not observe adverse maternal or neonatal side effects in six women who received PCIA remifentanil as an alternative to epidural labour analgesia. Nevertheless, further studies are needed particularly concerning safety in case of premature birth.

References

1 *Kan RE, Hughes SC, Rosen MA, Kessin C, Preston PG, Lobo EP.* Intravenous remifentanil. Placental transfer, maternal and neonatal effects. Anesthesiology 1998; 88: 1467–74.

2 *Rosaeg OP, Kitts JB, Koren G, Byford LJ.* Maternal and fetal effects of intravenous patient-controlled fentanyl analgesia during labour in a thrombocytopenic parturient. Can J Anaesth 1992; 39: 277–81.

3 *Kleiman SJ, Wiesel S, Tessler MJ.* Patient-controlled analgesia (PCA) using fentanyl in a parturient with a platelet function abnormality. Can J Anaesth 1991; 38: 489–91.

4 *Nikkola EM, Ekblad UU, Kero PO, Alihanka JJM, Salonen MAO.* Intravenous fentanyl PCA during labour. Can J Anaesth 1997; 44: 1248–55.

5 *Morley-Foster PK, Reid DW, Vandeberghe H.* A comparison of patient-controlled analgesia fentanyl and alfentanil for labour analgesia. Can J Anesth 2000; 47: 113–9.

6 *Jones R, Pegrum A, Stacey RGW.* Patient-controlled analgesia using remifentanil in the parturient with thrombocytopaenia. Anaesthesia 1999; 54: 461–5.

7 *Olofsson CH, Ekblom A, Ekman-Ordeberg G, Granström L, Irestedt L.* Analgesic efficacy of intravenous morphine in labour pain: a reappraisal. Int J Obst Anesth 1996; 5: 176–80.

8 *Thurlow JA, Waterhouse P.* Patient-controlled analgesia in labour using remifentanil in two parturients with platelet abnormalities. Br J Anaesth 2000; 84: 411–3.

9 *Young Park W, Watkins PA.* Patient-controlled sedation during epidural anesthesia. Anesth Analg 1991; 72: 304–7.