

Influence of Different Methods of Intrapartum Analgesia on the Progress of Labour and on Perinatal Outcome

Einfluss verschiedener intrapartaler Analgesiemethoden auf den Geburtsverlauf und das perinatale Outcome



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ABSTRACT

Background Various methods of intrapartum analgesia are available these days. Pethidine, meptazinol and epidural analgesia are among the most commonly used techniques. A relatively new one is patient-controlled intravenous analgesia with remifentanyl, although the experiences published so far in Germany are limited. Our goal was to study the influence of these analgesic techniques (opioids vs. patient-controlled intravenous analgesia with remifentanyl vs. epidural analgesia) on the second stage of labour and on perinatal outcome.

Material and Methods We conducted a retrospective study with 254 parturients. The women were divided into 4 groups based on the analgesic technique and matched for parity, maternal age and gestational age (opioids n = 64, patient-controlled intravenous analgesia with remifentanyl n = 60, epidural analgesia n = 64, controls without the medicinal products mentioned n = 66). Maternal, fetal and neonatal data were analysed.

Results The expulsive stage was prolonged among both primiparas and multiparas with patient-controlled intravenous analgesia with remifentanyl (79 [74] vs. 44 [55] min, p = 0.016, and 28 [68] vs. 10 [11] min, p < 0.001, respectively) and epidural analgesia (90 [92] vs. 44 [55] min, p = 0.004, and 22.5 [73] vs. 10 [11] min, p = 0.003, respectively) compared with the controls. The length of the pushing stage was similar among primiparas in all groups but prolonged compared with the controls in multiparas with patient-controlled intravenous analgesia with remifentanyl (15 [17] vs. 5 [7] min, p = 0.001) and epidural analgesia (10 [15] vs. 5 [7] min, p = 0.006). The Apgar, umbilical arterial pH and base excess values were similar between the groups, as were the rates of acidosis and neonatal intensive care unit admission.

Conclusion Parturients with patient-controlled intravenous analgesia with remifentanyl and epidural analgesia showed a prolonged expulsive stage compared with the opioid group and controls. The short-term neonatal outcome was not influenced by the three methods examined.

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ZUSAMMENFASSUNG

Hintergrund Heutzutage stehen verschiedene intrapartale Analgesiemethoden zur Verfügung. Pethidin, Meptazinol und Periduralanalgesie zählen zu den am häufigsten angewendeten Verfahren. Ein relativ Neues ist die patientengesteuerte intravenöse Analgesie mit Remifentanyl, wobei die bisherigen publizierten Erfahrungen in Deutschland limitiert sind. Unser Ziel war es, den Einfluss dieser Analgesieverfahren (Opioide vs. patientengesteuerte intravenöse Analgesie mit Remifentanyl vs. Periduralanalgesie) auf die 2. Phase der Geburt sowie auf das perinatale Outcome zu untersuchen.

Material und Methoden Wir führten eine retrospektive Studie mit 254 Gebärenden durch. Die Frauen wurden abhängig vom analgetischen Verfahren in 4 Gruppen eingeteilt und nach Parität, maternalem Alter und Schwangerschaftsalter „gematched“ (Opioide $n = 64$, patientengesteuerte intravenöse Analgesie mit Remifentanyl $n = 60$, Periduralanalgesie $n = 64$, Kontrollen ohne die genannten Medikamente $n = 66$). Maternale, fetale und neonatale Daten wurden analysiert.

Ergebnisse Die Austreibungsperiode war sowohl bei Primiparae als auch bei Multiparae mit patientengesteuerter intravenöser Analgesie mit Remifentanyl (79 [74] vs. 44 [55] min, $p = 0,016$ bzw. 28 [68] vs. 10 [11] min, $p < 0,001$) sowie Periduralanalgesie (90 [92] vs. 44 [55] min, $p = 0,004$ bzw. 22,5 [73] vs. 10 [11] min, $p = 0,003$) im Vergleich zu den Kontrollen verlängert. Die Dauer der Pressphase war bei Primiparae in allen Gruppen ähnlich, aber bei Multiparae mit patientengesteuerter intravenöser Analgesie mit Remifentanyl (15 [17] vs. 5 [7] min, $p = 0,001$) sowie Periduralanalgesie (10 [15] vs. 5 [7] min, $p = 0,006$) verlängert verglichen mit den Kontrollen. Die Apgar-, Nabelschnurarterien-pH- und Base-Exzess-Werte sowie die Azidose- und Aufnahmezeit auf die Neugeborenenintensivstation waren ähnlich zwischen den Gruppen.

Schlussfolgerung Gebärende mit patientengesteuerter intravenöser Analgesie mit Remifentanyl und Periduralanalgesie zeigten im Gegensatz zur Opioidgruppe und Kontrollen eine verlängerte Austreibungsperiode. Das kurzfristige neonatale Outcome wurde durch die 3 untersuchten Methoden nicht beeinflusst.

Introduction

For the labouring woman, birth is one of the most beautiful but also most painful experiences of her life. Pain perception is individual, however. Cultural, social and religious factors can play a role in this regard. The fear of pain can have a decisive influence on the birth experience. The stress resulting from pain also triggers hyperventilation, catecholamine release and increased blood pressure [1]. This can lead to diminished contractions and a decrease in uterine blood flow with the resulting effect on the progress of labour and on the fetal oxygen supply. Although these deleterious effects are tolerated in the vast majority of births, without causing serious complications, they should be taken into account in the case of high-risk patients in particular.

Pain relief in labour is one of the most important advances in modern obstetrics and is increasingly accepted by parturients. Various methods of intrapartum analgesia are available these days [2]. Parenterally administered opioids and epidural analgesia (EDA) are among the most commonly used techniques [3]. The latter is currently considered the gold standard for pain relief in labour. The use of patient-controlled intravenous analgesia (i.v. PCA) with remifentanyl in obstetrics is relatively new in Germany [4]. Despite the clear benefit of pain reduction, management measures should not interfere with the normal birth process. The literature has become increasingly focused on the maternal and fetal effects of intrapartum analgesia [5–7], although little is known still about the use of i.v. PCA with remifentanyl in a German population [8].

Our goal was to study the influence of various methods of intrapartum analgesia (opioids vs. i.v. PCA with remifentanyl vs. EDA) on the second stage of labour and on perinatal outcome.

Material and Methods

We conducted a retrospective study in pregnant women who gave birth in the Department of Gynaecology of the Rechts der Isar Hospital of the Technical University of Munich between January 2013 and December 2014. The study protocol was approved by the Ethics Committee.

Inclusion and exclusion criteria

The inclusion criteria were: maternal age between 17 and 45 years, singleton pregnancy between 37 + 0 and 42 + 0 gestational weeks (GW) with digitally stored intrapartum CTG available, head-first fetal presentation and spontaneous vaginal delivery. The following were defined as exclusion criteria: lack of CTG traces from 30 minutes (min) before and after the analgesic intervention and 60 min before delivery, and fetal malformation.

The population was divided into 4 groups based on the intrapartum analgesic technique: Parturients without analgesia or with paracetamol or butylscopolamine bromide (control group), with intravenous opioid injection (pethidine or meptazinol), with i.v. PCA with remifentanyl or with epidural analgesia (EDA). No labouring women who subsequently received i.v. PCA/EDA were included in the opioid group. Some of the parturients included in the i.v. PCA/EDA group received i.v. opioids beforehand.

Analgesia protocol

The analgesic interventions were administered as follows: Paracetamol 1 gram (g) intravenously (i.v.) as a short infusion, butylscopolamine bromide 20 milligrams (mg) i.v., pethidine 100 mg or meptazinol 100 mg in 250 ml NaCl 0.9% at 300 ml/h. For the i.v. PCA, 1 mg remifentanyl was dissolved in 50 ml NaCl 0.9%. Boluses of 20 micrograms (μg) with a lockout interval of 4 min were administered by the women at the onset of uterine contractions. For the EDA, a test dose of 3 ml bupivacaine 0.125% was injected

initially through an epidural catheter. This was followed by epidural administration of 8–10 mg ropivacaine 0.2% with 6–7.5 µg sufentanil. This dose could be accessed repeatedly by the patient every 60–90 min. If the patient did not actively request a dose, 6 mg ropivacaine 0.2% with 4.5 µg sufentanil was administered automatically via the pump after 60–90 min as the “programmed intermittent epidural bolus”.

The decision regarding the type of analgesia was taken jointly by the treating team (physician/midwife) and the labouring women. In general, analgesia without opioids was used at a cervical dilation of ≤ 3 cm. Subsequently, we offered the labouring women opioids, if necessary followed by EDA or primary EDA. If EDA was not desired, not possible or contraindicated, i.v. PCA was offered. Both i.v. PCA and EDA were continued until delivery.

Analysed data

The following maternal, fetal and neonatal data were collected and analysed: Age, body mass index (BMI), gravidity, parity, gestational age, tobacco use, pre-existing conditions (the following pre-existing conditions were present in our population: autoimmune diseases [antiphospholipid antibody syndrome, autoimmune hepatitis, idiopathic thrombocytopenic purpura], cardiovascular diseases [essential hypertension, arrhythmia], thyroid diseases [hypothyroidism], metabolic disorders [diabetes mellitus, obesity], psychiatric disorders [depression], neurological disorders [epilepsy, multiple sclerosis, stroke], lung diseases [bronchial asthma]), existing medication, start of analgesia (date, time, cervical dilation), need for induction (indications for induction in our population were: late term pregnancy $\geq 41 + 1$ GW, premature rupture of membranes ≥ 12 hours, oligohydramnios, poorly controlled diabetes mellitus/gestational diabetes, preeclampsia, cholestasis of pregnancy), need for oxytocin augmentation of labour (usually initiated in cases of protracted labour with a cervical dilation of < 1 cm/2 h because of secondary uterine inertia or in the presence of weakening contractions), CTG assessment, length of the expulsive stage, length of the pushing stage, birth (date, time), birth weight, Apgar after 1 and 5 min, umbilical arterial pH and base excess. The gestational age was determined according to the measurement of the crown-rump length in the first trimester. The CTG trace was rated by the obstetrician as normal, suspect or pathological based on FIGO criteria [9]. The expulsive stage was defined as the time from full cervical dilation to complete delivery of the baby.

Statistical analysis

Because the i.v. PCA population was the smallest, this group was processed first. This group was also limiting for the group sizes. All 4 groups were matched for parity, maternal age and gestational age. The labouring women who were identical in terms of parity were matched first, followed by those who were most similar in terms of maternal age and gestational age. In the case of several candidates in the larger groups, the parturients were selected at random. The normal distribution of the data was tested with the Shapiro-Wilk test. Because all the continuous variables were not normally distributed, the Mann-Whitney U test was used. Pearson's χ^2 test/Fisher's exact test was used for categorical variables. All tests were performed as two-sided tests. In addition, the influ-

ence of variables such as tobacco use, BMI, pre-existing conditions, medication, induction of labour, augmentation of labour, maternal age, gestational week and parity on the length of the expulsive stage was tested using regression analysis. In order to adjust between the methods of analgesia for multiple comparisons with the control group/for the comparisons of cervical dilation at “start of analgesia” and of the time between “start of analgesia and delivery”, a p-value of < 0.017 was considered as statistically significant (Bonferroni correction). Data analysis was conducted using the SPSS (Statistical Package for the Social Sciences) 24.0 software package (SPSS Inc., Chicago, IL, USA).

Results

Over the study period mentioned, 126 parturients received i.v. PCA with remifentanyl. Of these, 66 were excluded (27 lack of CTG, 13 fetal malformations, 26 surgical deliveries), which resulted in a total of 254 labouring women being able to be included according to the matching criteria: 64 with opioids, 60 with i.v. PCA, 64 with EDA and 66 controls. Risk factors were identified in 80% ($n = 204$) of the parturients. The median maternal age was 32 (17–43) years and the median gestational age was 39.6 (37–42) weeks. The proportion of primiparas was 61% ($n = 155$).

Characteristics of the parturients

The characteristics of the patient population, grouped according to analgesic technique, are shown in the ► **Table 1**. There was no difference between the groups in terms of age, BMI, tobacco use, pre-existing conditions, existing medication, gestational diabetes, parity and gestational age, with maternal age, parity and gestational diabetes being the matching criteria.

Only 9% ($n = 6$) of the labouring women in the control group received a single administration of analgesia with butylscopolamine bromide ($n = 4$) or paracetamol ($n = 2$). In the opioid group, the parturients received one (97%, $n = 62$) or two (3%, $n = 2$) administrations. In addition, 62% ($n = 37$) of the women in the i.v. PCA group and 31% ($n = 20$) in the EDA group received an opioid administration beforehand.

Obstetric course

With regard to the intrapartum and obstetric variables, the 3 analgesia groups showed a higher proportion of inductions of labour compared with the control group (opioids, $p = 0.032$; i.v. PCA, $p = 0.056$; EDA, $p = 0.004$) (► **Table 2**). Late term pregnancy $\geq 41 + 1$ GW and premature rupture of membranes ≥ 12 h represented the most frequent indications for induction (controls 100% [$n = 7$], opioids 75% [$n = 12$], i.v. PCA 79% [$n = 11$], EDA 75% [$n = 15$]). All 3 groups with analgesia received oxytocin augmentation of labour more frequently than the controls (opioids, $p = 0.049$; i.v. PCA, $p < 0.001$; EDA, $p < 0.001$). The proportion of CTG abnormalities was similar between the groups. The EDA group showed the longest and the i.v. PCA group the shortest time between the start of analgesia and delivery, with i.v. PCA being administered at the latest point of the dilation phase (► **Table 2**). 88% ($n = 53$) of the labouring women received i.v. PCA at cervical dilation of ≥ 8 cm, while the other 12% ($n = 7$) received it at cervical dilation of 5–7 cm.

► **Table 1** Characteristics of the overall population.

	Controls n = 66	Opioids n = 64	i. v. PCA n = 60	EDA n = 64
Maternal age (years)	33 (6)	32 (6)	32 (6)	33 (10)
BMI (kg/m ²)	21.2 (3.2)	21.7 (4.7)	21.8 (3.5)	21.8 (4)
Tobacco use	1 (2)	1 (2)	1 (2)	0
Pre-existing conditions	21 (32)	17 (27)	21 (35)	24 (38)
Gestational diabetes	5 (8)	4 (6)	5 (8)	7 (11)
Existing medication	12 (18)	7 (11)	13 (22)	12 (19)
Primiparas	35 (53)	40 (63)	38 (63)	42 (66)
Gestational age (weeks)	39.9 (1.9)	39.6 (1.6)	39.7 (1.7)	39.5 (1.8)

The data are listed as a median (interquartile range) or as n (%). Mann-Whitney U test, χ^2 test. i. v. PCA = patient-controlled intravenous analgesia; EDA = epidural analgesia

► **Table 2** Obstetric course.

	Controls n = 66	Opioids n = 64	i. v. PCA n = 60	EDA n = 64
Induction of labour	7 (11)	16 (25)*	14 (23)	20 (31)*†
Augmentation of labour	18 (27)	28 (44)*	39 (65)*†	45 (70)*†
Suspect/pathological CTG	2 (3)	7 (11)	7 (12)	6 (9)
Cervical dilation with analgesia (cm)		4 (4)	9 (2)§†	6 (4)
Time from analgesia to delivery (min)		109 (137)	96.5 (126)	228.5 (248)§†

The data are listed as a median (interquartile range) or as n (%). Mann-Whitney U test, χ^2 test. * p < 0.05 compared with controls, § p < 0.05 compared with other methods of analgesia, † p < 0.017 (Bonferroni adjusted). i. v. PCA = patient-controlled intravenous analgesia; EDA = epidural analgesia

The course of the second stage of labour was analysed (► **Table 3**). In the overall population, both the expulsive stage and the pushing stage were prolonged in the i. v. PCA group (p < 0.001 and p = 0.002 respectively) and in the EDA group (p < 0.001 and p = 0.003 respectively). This significant difference remained even when possible influencing variables such as tobacco use, BMI, pre-existing conditions, medication, induction of labour and augmentation of labour were taken into account in the regression analysis (i. v. PCA vs. control: p < 0.001; EDA vs. control: p = 0.013). A subanalysis according to parity showed a prolonged expulsive stage both among primiparas and among multiparas in the i. v. PCA group (p = 0.016 and p < 0.001 respectively) and in the EDA group (p = 0.004 and p = 0.003 respectively). The length of the pushing stage was similar among primiparas in all groups but prolonged among multiparas in the i. v. PCA group (p = 0.001) and in the EDA group (p = 0.006).

Neonatal outcome

With regard to neonatal outcome, no difference was found between the groups in terms of weight, Apgar values after 1 and 5 min, umbilical arterial pH and base excess values. There was also no difference with regard to moderate/severe acidosis rate. All 4 groups had a similar neonatal intensive care unit admission rate, although the tendency was slightly higher in the i. v. PCA group

(► **Table 4**). The indications for neonatal admission were: controls (hyperbilirubinaemia as a result of ABO isoimmunization), opioids (birth weight < 3rd centile), i. v. PCA (birth weight < 10th centile, birth weight 12th centile with moderate acidosis [umbilical arterial pH 7.12], birth weight 96th centile with poorly controlled gestational diabetes, 2 cases of chorioamnionitis), EDA (hyperbilirubinaemia as a result of ABO isoimmunization).

Discussion

This study compares the influence of the most commonly used intrapartum analgesic techniques (EDA, opioids, i. v. PCA) on the second stage of labour in a German population. Our data show that parturients with EDA have a prolonged expulsive stage. This is consistent with a systematic review of 38 studies (n = 9658) which showed a prolongation of the expulsive stage with the intrapartum use of EDA, and with the data of Cheng et al., which identified a prolonged expulsive stage in primiparas and multiparas with EDA (n = 21 090) [10, 11]. The reason for the prolonged expulsive stage with the use of EDA is still not entirely clear. In the last two decades, the motor block associated with EDA has been decreased through a combination of local anaesthetics in low concentrations with opioids as adjuvants [8]. However, administration of analgesia in the vicinity of the spinal cord might

► **Table 3** Course of the second stage of labour.

	Controls	Opioids	i. v. PCA	EDA
Overall population	n = 66	n = 64	n = 60	n = 64
Expulsive stage (min)	23 (43)	33 (48)	66 (89)*†	77 (103)*†
Pushing stage (min)	14 (20)	15 (16)	20 (15)*†	20 (25)*†
Primiparas	n = 35	n = 40	n = 38	n = 42
Expulsive stage (min)	44 (55)	44.5 (51)	79 (74)*†	90 (92)*†
Pushing stage (min)	25 (15)	20 (20)	20 (11)	25 (24)
Multiparas	n = 31	n = 24	n = 22	n = 22
Expulsive stage (min)	10 (11)	10 (25)	28 (68)*†	22.5 (73)*†
Pushing stage (min)	5 (7)	8 (10)	15 (17)*†	10 (15)*†

The data are listed as a median (interquartile range). Mann-Whitney U test. * p < 0.05 compared with controls, † p < 0.017 (Bonferroni adjusted). i. v. PCA = patient-controlled intravenous analgesia; EDA = epidural analgesia

► **Table 4** Neonatal outcome.

	Controls n = 66	Opioids n = 64	i. v. PCA n = 60	EDA n = 64
Weight (g)	3450 (448)	3390 (588)	3375 (590)	3295 (524)
Apgar 1 min	9 (0)	9 (1)	9 (1)	9 (1)
Apgar 5 min	10 (0)	10 (1)	10 (1)	10 (1)
Apgar 1 min < 7	1 (2)	2 (3)	2 (3)	1 (2)
Apgar 5 min < 7	0	0	0	0
Umbilical arterial pH	7.28 (0.13)	7.28 (0.12)	7.27 (0.11)	7.25 (0.09)
Umbilical arterial pH < 7.15	3 (5)	4 (6)	4 (7)	4 (6)
Umbilical arterial pH < 7.10	1 (2)	1 (2)	1 (2)	1 (2)
Base excess	- 5.2 (4.4)	- 5.2 (4.8)	- 5.7 (3.8)	- 5.1 (3.8)
Base deficit ≥ 12 mmol/l	1 (2)	1 (2)	1 (2)	4 (6)
Neonatal intensive care unit	1 (2)	1 (2)	5 (8)	1 (2)

The data are listed as a median (interquartile range) or as n (%). Mann-Whitney U test, χ^2 test. i. v. PCA = patient-controlled intravenous analgesia; EDA = epidural analgesia

also interfere to a degree with uterine motor activity. The release of oxytocin as a result of the distension of the birth canal might also be reduced as a result of EDA [12, 13]. The resulting reduced uterine contractility is reflected in the need for augmentation of labour with medicinal oxytocin. Although all 3 analgesic technique groups in our population received augmentation of labour, it was used most frequently in the EDA group (70% of cases).

Earlier studies reported a significantly increased rate of operative vaginal delivery in parturients with EDA [10, 14]. One of the possible causes of this was a prolonged expulsive stage. The classical definitions of the length of the stages of labour are based on studies by Friedmann et al. in the 1950s [15–17]. There have since been considerable changes in the parturient population and obstetrics. Decisions regarding operative (vaginal) deliveries in individual cases should not therefore be based solely on the length of the stages of labour, in order to avoid unnecessary interventions [11].

Because of the pharmacological properties of remifentanyl with its ultra-short half-life, i. v. PCA is an effective pain relief option during labour, particularly if EDA is contraindicated/not desired [7, 18, 19]. Although the risk of severe adverse effects is low, close monitoring of vital parameters and/or midwife and anaesthetist support is necessary. Because we are reporting on the experience in the first 2 years after the introduction of i. v. PCA in our department, this early stage might explain the use of i. v. PCA at an advanced stage of dilation. In fact, 88% of the labouring women received i. v. PCA at a cervical dilation of ≥ 8 cm. In the i. v. PCA group, the expulsive stage was prolonged in the overall population as was the pushing stage among multiparas. There is hardly any information regarding this in the literature to date. Ismail et al. also found a significantly prolonged expulsive stage in primiparas receiving i. v. PCA with remifentanyl and with EDA compared with combined spinal and epidural analgesia [20]. Freeman et al., on the other hand, showed a shorter expulsive

stage in primiparas receiving i.v. PCA with remifentanyl compared with EDA [21]. In the latter study, however, the i.v. PCA was discontinued in the expulsive stage in order to reduce the collateral neonatal effects. In our population, although transfer to the neonatal intensive care unit was four times more frequent in the i.v. PCA group, this was not statistically significant. This might rather be a consequence of obstetric complications such as chorioamnionitis which occurred only in this group by chance.

The intrapartum use of intravenous opioids without subsequent additional i.v. PCA or EDA did not give rise to any change in the length of the expulsive/pushing stage in our study. It is possible that the motor nerve fibres are slightly inhibited by long-acting opioids. Nevertheless, opioids are combined with other analgesic techniques relatively frequently during labour because of their low analgesic activity and/or their side effect profile [22]. In our population, approx. $\frac{2}{3}$ of the i.v. PCA and approx. $\frac{1}{3}$ of the EDA group had been treated previously with opioids.

The possible consequences of intrapartum analgesia, such as a prolonged expulsive stage and increased need for oxytocin, could cause fetal stress [23]. In this study, the short-term neonatal outcome, that was assessed on the basis of the Apgar score after 1 and 5 min and on the umbilical arterial pH and base excess, was nevertheless similar to that for all analgesic techniques. This has also been described in the literature [11, 18, 20]. The median umbilical arterial pH in the EDA group is slightly reduced, however, although it is still within the lower normal range. Because the fetal response to stress in utero is largely dependent on the acid-base balance, a reduction in the pH even within the normal range might limit the fetal haemodynamic, metabolic and endocrine response to acute hypoxaemia [24].

Non-pharmacological methods of reducing fear, stress and pain during labour might be an alternative in particular for those parturients who do not want pain medication [25–27]. These should be investigated in more depth as a primary/concomitant intervention in order to enable women to have a better labour experience. Methods such as acupuncture, massages or music interventions were not recorded in our population.

This study has some strengths and weaknesses. The inclusion of a control group and the homogeneity of the groups mean that a number of interfering factors that can influence the main results are ruled out. The retrospective study design is one limitation of our study. The size of the groups was also considerably limited by the number of women in the i.v. PCA group, which resulted in a small total population being analysed overall. It is possible that, where the birth process is likely to be complicated and in the presence of abnormal position/presentation, doctors will tend to recommend the current gold standard (EDA) for the labouring woman, so the fact that EDA is indicated might be responsible for a prolonged expulsive stage rather than the EDA itself. It is not possible to test this hypothesis with the data recorded by us, however. We also analysed data from parturients in a university clinic with a high proportion of high-risk pregnancies, which might limit the potential to generalize the study results to a broader population.

In summary, we can conclude that, in our population with the statistical model used, the use of i.v. PCA with remifentanyl and EDA was associated with a prolonged expulsive stage, unlike

opioids and the controls. The need for oxytocin was increased in all three medication groups. The short-term neonatal outcome was not influenced in a clinically relevant manner by the analgesic techniques.

Conflict of Interest

The authors declare that they have no conflict of interest.

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