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Epidural Analgesia during Routine Childbirth: A 10 Years Retrospective Analysis from the National Birth Registry Austria

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Abstract

Objectives To investigate the use and association of epidural analgesia (EA) on neonatal short-term outcome in vaginal childbirth at term of primiparous parturients. Design Retrospective cohort study. Setting Data of the National Birth Registry of Austria between 2008 and 2017. Population Primiparous women with spontaneous vaginal birth at term of singleton pregnancies in Austria. Methods Linear and logistic regression models to investigate an association of epidural analgesia on short-term neonatal outcome in propensity score adjusted cohorts. Main outcome measures: Short-term morbidity assessed by arterial cord pH and base excess. Secondary outcomes were admission to a neonatal intensive care unit, APGAR scores, and perinatal mortality. Results: Of 247 536 included deliveries, 52 153 received EA (21%). Differences in pH (7.24 vs. 7.25; 97.5% CI -0.0066 to -0.0047) and BE (-5.89 ± 3.2 mmol/l vs. 6.15 ± 3.2 mmol/l; 97.5% CI 0.32 to 0.40) with EA could be shown. APGAR score at 5 minutes below 7 was more frequent with EA (OR 1.45; 95% CI 1.29 to 1.63). Admission to a neonatological intensive care unit occurred more often with EA (4.7% vs. 3.4%) with an OR for EA of 1.2 (95% CI 1.14 to 1.26). EA was not associated with perinatal mortality (OR 1.33; 95% CI 0.79 to 2.25). Conclusions EA showed no relevant association with short-term morbidity. Higher rates of NICU admission and APGAR score after 5 minutes below 7 were observed with EA. Overall use of EA in Austria is low, and investigation of causes may be indicated.

Epidural Analgesia during Routine Childbirth: A 10 Years Retrospective Analysis from the National Birth Registry Austria

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Running title: Epidural analgesia and neonatal short-term outcome in Austria

Abstract

Objective To investigate the use and association of epidural analgesia (EA) on neonatal short-term outcome in vaginal childbirth at term of primiparous parturients.

Design Retrospective cohort study.

Setting Data of the National Birth Registry of Austria between 2008 and 2017.

Population Primiparous women with spontaneous vaginal birth at term of singleton pregnancies in Austria.

Methods Linear and logistic regression models to investigate an association of epidural analgesia on short-term neonatal outcome in propensity score adjusted cohorts.

Main outcome measures : Short-term morbidity assessed by arterial cord pH and base excess. Secondary outcomes were admission to a neonatal intensive care unit, APGAR scores, and perinatal mortality.

Results: Of 247 536 included deliveries, 52 153 received EA (21%). Differences in pH (7.24 vs. 7.25; 97.5% CI -0.0066 to -0.0047) and BE (-5.89 ± 3.2 mmol/l vs. -6.15 +- 3.2 mmol/l; 97.5% CI 0.32 to 0.40) with EA could be shown. APGAR score at 5 minutes below 7 was more frequent with EA (OR 1.45; 95% CI 1.29 to 1.63). Admission to a neonatological intensive care unit occurred more often with EA (4.7% vs. 3.4%) with an OR for EA of 1.2 (95% CI 1.14 to 1.26). EA was not associated with perinatal mortality (OR 1.33; 95% CI 0.79 to 2.25).

Conclusions EA showed no relevant association with short-term morbidity. Higher rates of NICU admission and APGAR score after 5 minutes below 7 were observed with EA. Overall use of EA in Austria is low, and investigation of causes may be indicated.

Keywords

Epidural analgesia, vaginal birth, neonatal outcome

Funding

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Tweetable abstract

No association of epidural analgesia on short-term neonatal outcome in primiparous women with vaginal birth at term.

Introduction

Epidural analgesia (EA) represents the gold standard for pain control during the first and second stage of labour.[1] There are indications that significant pain during childbirth is associated with an increased incidence of postpartum depression or posttraumatic stress. In deliveries without analgesia, mothers showed decreased cognitive function on the first day after delivery compared with women who received opioid analgesia.[2]Compared with systemic opioid analgesia, EA led to higher rates of pain relief satisfaction and less additional analgesic requirements.[3] For fathers attending an intensely painful delivery, this experience was humbling and stressful, leading to anxiety and a feeling of helplessness. The use of EA remarkedly ameliorated the situation and enabled the partners to become involved and supportive.[4]

Furthermore, EA leads to a reduction of vegetative stress responses, which can be essential in at-risk women with pre-existing cardiovascular comorbidities, obesity, or preeclampsia.[5]However, inadvertent intrathecal or intravascular placement of the epidural catheter, epidural hematoma or abscesses may lead to life threatening complications, cardiorespiratory arrest or significant neurological injuries and, though rare, must be discussed with the patient.[6]

In addition, when doses of local anesthetics are inadequately high (i.e. epidural bupivacaine >0.125% or ropivacaine >0.17%), EA may be associated with a prolonged duration of labour, and elevated rates of instrumental or assisted deliveries.[3,7]In about 20% of deliveries with EA, maternal aseptic hyperthermia occurs.[8] This epidural-related maternal fever may worsen the newborns' outcome by an increased risk for hypotension, assisted ventilation or treatment with antibiotics for suspected neonatal sepsis.[9,10]EA was associated with increased neonatal morbidity in means of APGAR score at 5 minutes <7 in a population-based register study, however information on concomitant circumstances with potential influence on outcome were limited.[11] Heart rate changes in neonates after EA are described.[12]Still, the causal association of EA and neonatal morbidity remains unclear.

The National Birth Registry of Austria reported 15.5% EA use for vaginal deliveries in 2017.[13] A recently published comprehensive national survey on obstetric anesthesia practice in Austria revealed rates <30% of EA use in 86% of the responding hospitals. As this was a subjective survey in health care providers, no conclusions on feto-maternal health care could be drawn.[14]

The objective of this study was to retrospectively analyse data from 2008-2017 of the Austrian National Birth Registry to assess quality of care and association of EA with neonatal short-term outcome in women undergoing labour and vaginal delivery at term.

Methods

Setting

Data were gathered from the National Birth Registry of Austria between 2008 and 2017 after approval (EK Nr: 1576/2018) by the ethics committee of the Medical University of Vienna, Austria (Chairperson Dr. Juergen Zezula) on 8 August 2018, and reported according to the STROBE statement.[15] The registry is operated and maintained by the Institute of Clinical Epidemiology of the Tirol Kliniken, collecting birth records of all 75 hospitals in Austria providing inpatient obstetric care, and thereby representing 99% of annual deliveries.

Study design, participants

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For this retrospective register study, primiparous parturients with spontaneous vaginal delivery at term (gestation week [?]37+0) were included and divided into two groups depending on their EA status (yes/no). Multiple pregnancies were excluded. These criteria were applied to keep the study population as homogenous as possible, because the National Birth Registry contains limited information on the medical condition of each individual. Antepartum intrauterine foetal demise (IUFD) were excluded for analysis of primary and secondary objectives. No parturients or patients were involved in the planning and design of the study. Hospitals were divided into four categories: (1) hospitals with less than 500 deliveries per year, (2) hospitals with >500 deliveries per year, (3) Perinatalcentre 2, defined as specialised centre for obstetric cases with paediatric in-house services for 24 hours, (4) Perinatalcentre 1, defined as specialised centre for complex obstetric cases with paediatric in-house services for 24 hours including a neonatological intensive care unit, a paediatric surgery department and radiology particularly trained for foetal diagnostic.

Variables

As primary objective, neonatal short-term outcome was assessed by pH and base excess (BE) in arterial umbilical cord blood from routinely performed arterial blood gas analyses depending on receiving EA or not. Secondary, differences in APGAR scores at 1, 5 and 10 minutes, APGAR score at 5 minutes <7 (AS5<7), admission to a neonatological intensive care unit (NICU) or paediatric ward and perinatal mortality up to day 7 postpartum were tested for an association with EA. Duration of labour, perineal laceration grade III and IV, instrumental delivery rates and episiotomy were compared for descriptive purposes. The following thresholds were applied for inclusion of data sets, as there appeared obviously mistyped or unrealistic values: a birth weight > 500g and <6000g, head circumference >20 cm and <45 cm, pH >6.6 and BE [?]+-35 mmol/l.

Statistical methods

Due to the observational nature of the data, propensity score methods were chosen to estimate the treatment effect of EA. Prior to any inferential analysis, 10-fold multiple imputation was performed to handle missing values. For each multiply imputed dataset, a propensity score was calculated for receiving EA. Propensity score calculation was based on factors potentially influencing the decision of obstetric caretakers whether or not to use EA, and were maternal age, weight, height, gestation week, foetal position, gender, year, hospital category, length and head circumference of the foetus. Predicted probabilities of receiving EA from these models were used as propensity scores in all further analyses. Results from the multiply imputed datasets were combined using Rubin's rules as implemented in the R package mice.[16] For every endpoint, only cases that had no missing values in this endpoint prior to imputation were used. Linear regression models were used for the continuous endpoints pH, BE and APGAR scores after 1, 5 and 10 minutes. Logistic regression models were used for admission to NICU, perinatal mortality, and AS5<7. The covariates in every model were the propensity scores and EA (yes/no).

Since two primary objectives were investigated, Bonferroni correction for multiple testing was applied with a significance level of $0.05/2 = 0.025$. Furthermore, 97.5% confidence intervals for the effect of EA were reported. Since p-values for secondary objectives served only descriptive purposes, no multiple testing corrections were applied and 95% confidence intervals were reported. As the duration and mode of delivery as well as an episiotomy may indicate cases with higher perinatal morbidity, additional multivariable regression models for all outcome variables were additionally fitted adjusting for these confounders.

Differences in perineal laceration rates of higher degree, duration of birth and instrumental delivery were reported descriptively. As a sensitivity analysis, the same analysis strategy (except for the imputation related steps) was applied to the original data, leading to relevant differences in the estimated effect sizes, i.e. the results seem to heavily depend on the analysis strategy. All analyses were performed using R (version 3.5.1; Foundation for Statistical Computing, Vienna, Austria).

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Results

Participants and descriptive data

Of 531 129 screened parturients, 247 536 met the inclusion criteria (Figure 1). The mothers showed a mean age of 28 years and a gestation week of 39+6. An overview of the demographic data of all parturients are listed in Table 1. Forty-one percent of deliveries took place in hospitals with less than 500 deliveries per year.

Outcome data

Outcome variables are listed in Table 2. An episiotomy was performed in 28.6%, with a mediolateral technique in 97.6%. In 16.9% of deliveries, an instrumental delivery was carried out, mainly by vacuum extraction (16.7%). Perineal lacerations of grade III or IV occurred in 7034 (2.8%) deliveries. Neonates were admitted to a NICU or paediatric ward in 3.7%. Perinatal mortality was 0.03%, including all fatalities that occurred intrapartum (n =9) and up to seven days postpartum (n =65). An antepartum IUFD was present in 324 (0.13%) vaginal deliveries.

Twenty-one percent (52 153) of parturients received EA. In women with EA, the median length of stay was 4 days compared to 3 days without EA. An episiotomy was more often performed with EA (33.6%) compared with no EA (27.3%; Table 1).

Main results

Arterial umbilical cord pH was significantly different between groups and the use of EA was a significant predictor for alterations in arterial umbilical cord pH in the propensity score adjusted linear regression model (7.25 +- 0.09 in no EA vs. 7.24+-0.08 in the EA group (effect size -0.0057; 97.5% CI -0.0066 to -0.0047;P <0.001)). EA was associated with a less negative BE compared to no EA use (-5.89 +- 3.2 mmol/l compared to -6.15 +- 3.23 mmol/l (effect size 0.36; 97.5% CI 0.32 to 0.40;P <0.001)). In 23.5% of deliveries, BE was missing, while pH values were absent in 3.7%. Both linear regression model results were similar when additionally adjusting for morbidity (see Table 3).

APGAR scores after 1, 5, and 10 minutes were similar between groups. An AS5<7 was more likely in neonates of mothers with EA (1.0% compared to 0.6%; OR 1.45; 95% CI 1.29 to 1.63;P <0.001). The postpartum admission rate of neonates to a NICU or paediatric ward was significantly higher in the EA group (4.7% versus 3.4%) with an estimated OR for EA of 1.39 (95% CI 1.33 to 1.46; P <0.001). EA was not significantly associated with increased perinatal mortality (OR 1.33; 95% CI 0.79 to 2.25;P =0.288).

Other analyses

Higher degree perineal lacerations occurred more frequently in women with EA (3.2% vs. 2.8%). Women with EA experienced longer duration of delivery (7 hours vs. 10 hours) and instrumental delivery was drastically more common in women with EA (13.5% vs. 29.8%) (Table 2). Rates of EA increased per year, ranging from 19% in 2008 to 24% in 2017. Hospitals categorised as Perinatalcentre 2 in the registry had the highest rates of EA in vaginal delivery (25.5%).

Discussion

Main findings

In this retrospective registry study, the association of EA with neonatal short-term outcome in Austria was assessed. The application of EA for spontaneous vaginal birth in primiparous women at term was associated with short-term outcome regarding lower pH and less negative BE in arterial umbilical cord blood. However the magnitude of these findings lack clinical importance. In neonates of parturients with EA, APGAR scores after 5 minutes <7 were observed, and admitted to a NICU more frequently. Perinatal mortality was similar in both groups.

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Strengths and Limitations

The National Birth Registry of Austria is maintained by obstetric departments, therefore collected information mainly focuses on obstetric and gynaecologic rather than on anaesthesiologic aspects. No information on cervical dilatation or timepoint of the application of EA, as well as a differentiation of duration of birth between first and second stage of labour, is recorded. Further, type of local anaesthetic, dosage and application modality (bolus, patient-controlled EA, programmed intermittent epidural bolus, dural puncture epidural) for EA is not documented, making it difficult to draft assumptions about the impact of EA technique on the altered outcome variables. It is described that epidural related maternal fever occurs frequently and was shown to be associated with worse neonatal outcome. Maternal body temperature is unfortunately not incorporated in the registry, so an association of EA and maternal fever could not be investigated in this analysis. The use of oxytocin for labour augmentation is also not available. Obstetricians may adapt their procedural decision on the presence of adequate pain relief, which could lead to higher rates of instrumental vaginal deliveries and episiotomies. This bias could not be considered in the statistical models. Outcome variables were sufficiently reported, except for BE, which was missing in 23.5%, although, missing data were equally distributed between EA (22.4%) and noEA (23.8%). All hospitals registered for obstetric services in Austria provide data to the National Birth Registry, representing 98% of annual births. The analysed data is therefore close to the basic population of primiparous women with spontaneous vaginal delivery at term, thereby avoiding a meaningful selection bias.

Interpretation

Overall EA use in vaginal birth in Austria was increasing over the last ten years, but still differ from other European countries with comparable health care systems.[11,17,18]The pH of umbilical arterial cord blood is a practical measure for evaluating foetal acidosis and is routinely measured with blood gas analysis.[19]Our findings were comparable to a single and a multicentre study, showing no relation of EA on neonatal morbidity, defined as pH<7.1, APGAR score after 5 minutes <7, neonatal resuscitation, or composite morbidity.[20,21]Anim-Somuah and colleagues could not demonstrate a significant difference in the frequency of acidosis, defined as pH<7.2 or 7.15 in a 2018 published Cochrane review comparing opioid administration or other non-epidural pain therapies and EA.[3]BE reflects metabolic acid-base abnormalities. The potentially beneficial effects of EA on BE may be explained by increased uterine blood flow after EA when hypotension is prevented, however observed effect estimates appear clinically not relevant. In a 2002 published meta-analysis of studies comparing EA with systemic analgesics, BE was less negative in the EA groups in randomised as well as observational studies.[22]

Even though AS5<7 was only present in 0.7% of neonates, it was significantly more often observed in the EA group (adjusted OR 1.18). A Swedish population-based study based on data from 1999-2008 demonstrated an adjusted OR of 1.27 for AS5<7 with EA, with quite similar rates (0.8% vs. 1.3%),[11]while in more recent trials, AS5<7 was not related to EA use.[3,20]When low concentrations of local anesthetics for EA were used in nulliparous women, AS5<7 was observed with an incidence of 0.15% and showed no significant difference to non-epidural opioid pain relief in a meta-analysis published by Liu et al. in 2004.[23]Short-term morbidity may be higher when prolonged duration of birth was present and instrumental delivery was applied, which could be the case when higher doses of local anesthetics potentially led to motor blockade. Both of these circumstances were present in the examined EA group without clear association to EA itself. This assumption is supported by a recently published survey, asking for current obstetric anaesthesia practice in Austria, in which 51% reported to use ropivacaine 0.2%, while only up to 11% using potent epidural opioid adjuncts to reduce local anaesthetic dose. Further, the survey revealed, that only 42% of respondents generally perform EA independently of cervical dilatation, making it more likely that the indication for EA was an already prolonged or unusually painful birth period.[14] So, EA may be used more extensively in already complicated and complex or induced deliveries, in request for relief of emerging pain. This in mind, our data analysis was not adjusted for cases of EA, in which parturients received EA in a very late phase of delivery, probably not affecting birth progression at all, or were even given due to complications in progress of labour.

The association of admission to NICU with EA, even after correcting for instrumental delivery, duration

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of birth and episiotomy, may support an actual effect of EA as the underlining cause of admission. These findings may be in part explained by higher rates of neonatal encephalopathy[11] or seizures[10] and possible sepsis in mother and newborn with EA when maternal fever occurred, or with respiratory depression, e.g. due to opioid adjuncts.[24] Unfortunately, NICU admission diagnoses are not documented in the registry, which makes it difficult to elucidate reasons and rationale explanations of the role of EA, especially with lack of information on the drugs applied. There was no association between overall perinatal mortality and EA in our collective, and an impact on mortality could generally be assumed to be more likely by secondary complications instead of EA itself. Hasegawa et al. stated that morbidity as assessed by pH and APGAR scores were associated with instrumental delivery, regardless of EA being used or not.[25]

The rate of instrumental delivery with vacuum or forceps was more than twofold increased in deliveries with EA (13.5% vs. 29.8%). Higher proportions of women experienced instrumental delivery with EA in a recent Cochrane review, although when studies conducted before 2005 were excluded, no difference was present anymore.[3]The authors direct this finding to modern techniques, e.g. low concentration of local anesthetics, intermittent bolus application and patient controlled analgesia. In a 2013 published meta-analyses comparing low with higher concentration of local anesthetics for EA, the use of low concentrations, i.e. ropivacaine [?]0.17% or bupivacaine [?]0.1%, was also associated with a reduction in assisted vaginal delivery. When low concentration EA was compared with nonepidural analgesia, Wang et al. could not demonstrate any difference in instrumental delivery rates or prolonged second stage of labour in a 2017 published meta-analysis.[26]Importantly, the authors stated that also low-quality studies were included, with an overall decline in quality and certainty of the conclusions drawn. If EA was directly related to the tremendously higher rate of instrumental delivery in our study population, it may be due to divergence of practice from universally accepted guidelines in modern obstetric anesthesia.[14]Also, obstetricians may attempt an instrumental vaginal delivery more liberally with successful EA in place, leading to an increased number of difficult deliveries in the EA group. Wassen et al. showed that with increasing EA rates from 7.7% to 22% over ten years in the Netherlands, no similar increase in instrumental delivery was accompanied,[27]questioning the role of EA as a risk factor. Instrumental delivery is a known risk factor for higher grade perineal lacerations,[28,29] although the differences between groups in our study were quite close (2.8 vs. 3.2%) and are comparable to the literature[30–32] even with a more than twofold higher instrumental delivery rate with EA. The effect of EA on perineal lacerations is controversially reported, depending on the collective with beneficial,[28,31,33] negative[34]or no impact.[3] In women with vaginal birth receiving low dose combined spinal-epidural analgesia for vaginal birth, no association with neuraxial analgesia could be shown.[35]

The duration of labour was also markedly prolonged in the EA group. These findings differ from recent literature, describing an acceptable prolongation of the second stage of labour[23,36]or even no effect with low concentrations.[26]Still, the data of the National Registry gives no information on distinct stages and the timepoint of EA, hindering meaningful comparisons. The low EA rates let assume, that the choice of epidural use is more likely due to underlying circumstances of labour progress than the women's choice, making it more likely that EA was used in already prolonged labour cases.

Conclusion

The results of this population-based registry study showed, that EA is only administered in 20% of nulliparous women undergoing a singleton vaginal delivery. For the primary outcomes pH and BE in umbilical cord blood, no worse short-term outcomes for neonates were associated with use of EA. The association of EA with increased NICU admission rates and Apgar scores below 7 after 5 minutes are most likely related to different indications for the use of neuraxial analgesia. Further insight into a causal relation between EA and neonatal outcome can only be gained when EA is applied independently of cervical dilatation, labour progress and underlying circumstances that led to these comparably low EA rates. A discussion on EA might enhance visibility and thereby improve the quality of care in obstetric anesthesia in Austria.

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Disclosure of interests

The authors have no conflict of interest to declare.

Contribution to authorship

FK was involved in drafting and reviewing the manuscript, as well as gathering, analysing and interpreting the data. PW contributed in data analysis, writing and reviewing the final manuscript. ELM performed the statistical analysis and gave advice and input on data interpretation including review of the manuscript. HH helped design and direct the study, as well as manuscript revision. HL provided the data and was involved in drafting and revision of the manuscript. HK designed the study and organised the initiation and collaboration of all participating authors. He gave advice on data interpretation and was involved in drafting the manuscript. SJ gave valuable input in data interpretation and reviewed the draft and final manuscript. CMO helped with concept and writing of the manuscript, and gave advice on data interpretation. KUK was responsible for the design of the protocol, data interpretation, manuscript revision, and coordination of the research team.

Details of ethics approval

All analyses and gathering of data were initiated after approval (EK Nr: 1576/2018) by the ethics committee of the Medical University of Vienna, Austria (Chairperson Dr. Juergen Zezula) on 8 August 2018.

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Table 1: Demographic and delivery characteristics

Variables	No EA n = 195 383	EA n = 52 153	Total n = 247 536
Age (years)	28.1 ± 5.2	28.5 ± 5.4	28.2 ± 5.3
BMI (kg/m^2)	22.8 ± 4.1	23.2 ± 4.3	22.9 ± 4.1
Gestation week	39.4 ± 1.1	39.6 ± 1.1	39.4 ± 1.1
Birth weight (grams)	3339 ± 412	3394 ± 412	3351 ± 412
Length of stay (days)	3 [3 to 4]	4 [3 to 4]	3 [3 to 4]
Hospital classification			
<500 deliveries per year	79 883 (40.9%)	21 688 (41.6%)	101 571 (41.0%)
>500 deliveries per year	51 800 (26.5%)	12 222 (23.4%)	64 022 (25.8%)
Perinatalcentre 1	21 823 (11.2%)	3871 (7.4%)	25 694 (10.4%)
Perinatalcentre 2	42 023 (21.5%)	14 411 (27.6%)	56 434 (22.8%)
Episiotomy	53 335 (27.3%)	17 541 (33.6%)	70 876 (28.6)

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median	1195 (0.6%)	438 (0.8%)	1633 (0.7%)
mediolateral	52 134 (26.7%)	17 100 (32.8%)	69 234 (27.9%)

Values are reported as mean ± SD, median [IQR] or absolute and relative n (%), respectively.

BMI, body mass index; EA, epidural analgesia

Table 2: Outcome variables

	No EA n = 195 383	EA n = 52 153	Total N = 247 536
pH	7.25 ± 0.09	7.24 ± 0.08	7.25 ± 0.08
BE (mmol/l)	-6.2 ± 3.3	-5.9 ± 3.2	-6.1 ± 3.2
Admission to NICU	6673 (3.4%)	2446 (4.7%)	9119 (3.7%)
Duration of delivery (h)	7 [4 to 9]	10 [7 to 13]	7 [5 to 10]
APGAR score 1 min	9 [9 to 9]	9 [9 to 9]	9 [9 to 9]
APGAR score 5 min	10 [10 to 10]	10 [10 to 10]	10 [10 to 10]
APGAR score 10 min	10 [10 to 10]	10 [10 to 10]	10 [10 to 10]
APGAR score 5 min <7	1128 (0.6%)	546 (1.0%)	1674 (0.7%)
Perineal laceration	5380 (2.8%)	1654 (3.2%)	7034 (2.8%)
Instrumental delivery	26 433 (13.5%)	15 564 (29.8%)	42 025 (16.9%)
Vacuum	26 083 (13.3%)	15 326 (29.4%)	41 411 (16.7%)
Forceps	350 (0.2%)	238 (0.5%)	588 (0.2%)
Perinatal mortality	206 (0.11%)	191 (0.36%)	397 (0.16%)
antepartum or IUFD	152 (73.8%)	171 (90.1%)	323 (81.6%)
intrapartum	7 (3.4%)	2 (1.0%)	9 (2.3%)
postpartum [?]7 days	47 (23.2%)	17 (8.9%)	64 (16.3%)

Values are reported as mean and ± SD, median [IQR] or absolute and relative n (%), respectively.

BE, base excess; NICU, neonatal intensive care unit; IUFD, intrauterine foetal demise

Table 3: Effect of epidural analgesia on foetal outcome parameters

Endpoint	Type	(A)	Effect Est	CI	P	(B)	Effect Est	Effect Est	CI
pH	Linear		-0.0057	(-0.0066 to 0.0047)+	<0.001		-0.0012	-0.0012	(-0.0022 t
BE	Linear		0.36	(0.32 to 0.4)+	<0.001		0.64	0.64	(0.59 to 0
NICU admission	OR		1.39	(1.33 to 1.46)*	<0.001		1.19	1.19	(1.13 to 1
APGAR score 1	Linear		-0.18	(-0.19to -0.17)*	<0.001		-0.1	-0.1	(-0.1 to -0
APGAR score 5	Linear		-0.09	(-0.1 to -0.09)*	<0.001		-0.05	-0.05	(-0.05 to -
APGAR score 10	Linear		-0.03	(-0.03 to -0.02)*	<0.001		-0.01	-0.01	(-0.02 to -
perinatal mortality	OR		1.33	(0.79 to 2.25)*	0.288		1.25	1.25	(0.71 to 2
AS5<7	OR		1.45	(1.29 to 1.63)*	<0.001		1.18	1.18	(1.04 to 1

Effects of EA on pH, BE, admission to NICU, APGAR scores and perinatal mortality were tested with linear or logistic regression, respectively, as

appropriate. Propensity scores were used as covariates to adjust for potential risk factors (A). Duration and mode of delivery and episiotomy were

included in all models as further confounders (B). Due to missing values in the outcome variables, the absolute number of cases for the underlying

models differed between endpoints. In the logistic regressions, a positive effect estimate is understood as a higher chance of the endpoint to

happen, when EA is applied. In linear regressions, the effect estimates are the proposed mean changes in the end-point variable with EA being used.

BE, base excess; NICU, neonatal intensive care unit; AS5<7, Apgar score after 5 minutes below 7.

+, 97.5% CI; *, 95% CI

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