Painless childbirth? Epidural and spinal techniques in obstetric anesthesia

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Chapter 2

Uterine contraction frequency after initiation of labour epidural analgesia using electrohysterography monitoring: a prospective pilot study

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ABSTRACT

Background

The introduction of electrohysterography into clinical practice provides new opportunities to study the impact of labour epidural analgesia on uterine contractility because electrohysterography has a greater sensitivity in detecting uterine contractions than external tocodynamometry. We determined the uterine contraction frequency before and after initiation of labour epidural analgesia using an electrohysterography-derived tocogram.

Methods

This prospective study included 23 pregnant women between 36-42 weeks' gestation with a singleton cephalic presentation who requested epidural analgesia in active labour. The primary study outcome was the difference in mean uterine contraction frequency 60 minutes before and 120 minutes after epidural analgesia initiation. The secondary aim was to measure changes in mean contraction frequency over time, using the mean uterine contraction frequency per 10 minutes, derived from 30-minute averages.

Results

In the 120 minutes after epidural analgesia initiation, the average contraction frequency decreased significantly (-0.37 contractions/10 minutes [95% CI -0.64 to -0.11]; P = 0.007) compared to the 60 minutes before epidural analgesia initiation. The largest decrease occurred 60-90 minutes after epidural analgesia initiation (-0.47 contractions/10 minutes [95% CI -0.89 to -0.05]; P = 0.029).

Conclusion

During active labour, electrohysterography identified a statistically significant, although clinically small, reduction in uterine contraction frequency after epidural analgesia initiation. This pilot study demonstrates the potential value of electrohysterography monitoring for obstetric anaesthesia research and might renew interest in the still poorly understood interaction between labour epidural analgesia and uterine activity.

INTRODUCTION

Neuraxial labour analgesia is considered the gold standard for pain relief during labour. It provides optimal analgesia with minimal side effects and results in higher maternal comfort and satisfaction compared to other techniques.[1] The effects of labour epidural analgesia (LEA) on uterine activity and contraction frequency are difficult to determine, and therefore are poorly understood.

Surrogate markers of uterine contractility are often used. In the past, increased rates of operative vaginal delivery were reported with LEA use, as well as more frequent use of oxytocin augmentation, and prolonged duration of first and second stage of labour. The use of contemporary solutions of low-concentration local anaesthetics and opioids has mitigated most of these effects, but an increased incidence of oxytocin augmentation persists, although a causal relationship has never been determined.[1]

When measuring uterine activity immediately after LEA initiation, reports of decreased, unchanged, and enhanced uterine activity have been described.[2-4] These conflicting observations may be explained by the wide variety of clinical settings and epidural medication administered as well as different methods used to evaluate uterine activity. These methods include manual palpation, external tocodynamometry, and intrauterine pressure catheter (IUPC).[2]

In current obstetric practice, external tocodynamometry is most commonly used—a non-invasive and easy-to-apply uterine monitoring method. However, the quality is affected by maternal body mass index and maternal and fetal movements, with a poor intra- and interobserver agreement.[5-6] The IUPC provides a more precise measurement of uterine activity, but it is an invasive technique associated with potentially serious complications such as uterine or placental perforation.[7] Since IUPC use does not significantly improve perinatal outcomes, routine use is not recommended.[8]

Electrohysterography has recently become clinically available as a noninvasive monitoring technique; it is more accurate and reliable compared to external tocodynamometry. [9] Electrohysterography measures the electrical myometrial activity, and the resulting parameters can be converted into immediately interpretable waveforms, comparable to intrauterine pressure curves.[5,9-12] It has been shown to have a higher sensitivity for detecting uterine contractions than external tocodynamometry.[2,9,13]

The use of electrohysterography provides an opportunity to improve our understanding of the relationship between epidural analgesia initiation and uterine activity.[14] The primary aim of this pilot study was to use a real-time electrohysterography-derived tocogram to identify potential differences in the mean contraction frequency 60 minutes prior to and 120 minutes following LEA initiation. We hypothesized that no significant change in uterine contraction

frequency would be measurable. Our secondary aim was to measure potential changes in mean contraction frequency over time during the study observation period.

METHODS

This pilot study was part of a prospective observational study on the implementation of non-invasive electrophysiological monitoring during labour in a tertiary care teaching hospital in the Netherlands, which was performed from March 2021 to July 2021.[14] Institutional ethical approval and oral and written informed consent were obtained from healthy pregnant women between 36 and 42 weeks' gestation, with a singleton cephalic fetus with no fetal cardiac arrhythmias and with an indication for continuous intrapartum monitoring. Exclusion criteria were contraindication for the use of the electrohysterography-monitoring device (presence of external or implanted electro-neurostimulators, pacemakers, maternal abdominal dermatologic disease, water-birthing), contraindication for the use of a fetal scalp electrode (maternal infectious disease, inheritable clotting disorder), and the presence of fetal cardiac arrhythmias, or language barriers. Of the 50 patients in active labour who were included in the original study, 36 women received LEA on patient request; 23 were included in this pilot study, as electrohysterography recording was incomplete in 13 cases (Supplementary Material Figure S1).

In the 30 minutes before LEA initiation, intravenous normal saline 500 mL was administered. Maternal heart rate, blood pressure, and oxygen saturation were monitored, as per institutional practice. The blood pressure measurement obtained immediately before the start of the epidural procedure served as the baseline blood pressure. The most recent cervical dilation measured within the 2 hours of initiating analgesia was recorded. The electrophysiological cardiotocogram (CTG) registration continued without interruption during and after epidural analgesia initiation. With the woman in a sitting position, an epidural catheter was sited between L1 and L5. An epidural test dose of bupivacaine 0.25% 3 mL with 1:200,000 adrenaline was administered, followed within a few minutes by an additional 5-7 mL of the same solution. A continuous infusion of ropivacaine 0.1% with sufentanil 0.5 mcg/mL at 8-10 mL/hour was initiated to maintain analgesia.

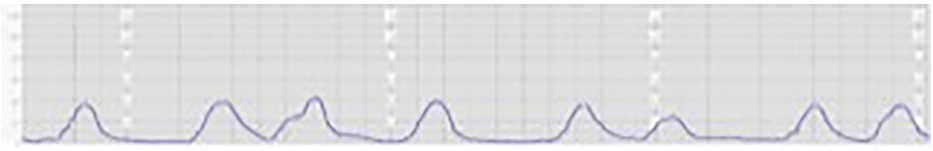
Uterine contraction frequencies were extracted from the electrohysterography-derived tocogram, generated by the Nemo® Fetal Monitoring System (NFMS) (Nemo Healthcare B.V., Veldhoven, The Netherlands). The NFMS consists of a base, a link, and a self-adhesive patch incorporating six electrodes (Fig. 1) that measures electrical activity on the abdominal surface.

Fig. 1. The NFMS (Nemo® Fetal Monitoring System, Nemo Healthcare B.V., Veldhoven, The Netherlands) consists of a base, a link and a self-adhesive patch incorporating six electrodes.

Extraneous electrical activity from sources such as abdominal musculature and the maternal and fetal cardiac myometrium is suppressed by incorporated band-pass filters between 0.3 and 0.8 Hz.[9,11] The remaining bioelectrical activity measured by the NFMS reflects the uterine-generated and propagated action potentials, which underlie uterine muscle contractions.[11] Electrohysterography data are processed in real-time by the NFMS and converted into a measure of uterine activity, which correlates with intrauterine pressures based on a mathematical model.[11] After processing and converting all NFMS data, a real-time CTG waveform is generated for clinical decision-making (Fig. 2).[11,14]

For this study, a locally developed tool for uterine activity annotation was used to analyse the electrohysterography-derived tocograms. One researcher annotated the onset and offset of each uterine contraction and manually eliminated all artefacts from the electrohysterography recordings. Artifacts were visually recognized by specific waveforms.[9] Another investigator was consulted in case of doubt regarding the onset and offset of uterine contractions and this second investigator randomly checked approximately one third of all recordings to confirm accurate contraction detection.[11,13] Both investigators were blinded to fetal heart rate tracings and clinical information during the annotation of the recordings, except for the timing of LEA initiation.

Fig. 2. Example of an electrohysterography recording, as processed real-time by the NFMS.



The mean contraction frequency was defined as the contraction frequency per 10 minutes, derived from 30-minute averages, according to the International Federation of Gynecology and Obstetrics (FIGO) recommendations.[15] The 30-minute windows used for this analysis were nonoverlapping. The mean contraction frequency was extracted from the 60 minutes before and until 120 minutes following LEA initiation, divided into 30-minute phases; phase 0 between 60 and 30 minutes before LEA initiation, phase 1 between 30 minutes before and LEA initiation, phase 2 starting at LEA initiation (test dose) until 30 minutes following LEA initiation, phase 3 between 30 and 60 minutes, phase 4 between 60 and 90 minutes and phase 5 between 90 and 120 minutes following LEA initiation, respectively. All patient-related obstetric and anaesthetic data were obtained from the electronic patient data management system.

All continuous variables were reported as median with interquartile range (25% and 75% quantiles), while counts and percentages were used for binary and categorical variables. The outcome variable (average contraction frequency per 10 minutes) was modelled using a linear mixed model to account for the repeated measurements. For the primary analysis, a dichotomous variable (before vs. after epidural initiation) was included in the model to estimate the difference between the average contraction frequency in the 60 minutes before LEA initiation (phases 0 and 1) and the average contraction frequency in the 120 minutes following LEA initiation (phase 2 to 5).

The linear mixed model included variables that might have a confounding effect on the outcome measure (average contraction frequency per 10 minutes): oxytocin infusion rate at the start of each 30-minute phase, cervical dilation before initiation of epidural analgesia, labour initiation (spontaneous/induced), and maternal hypotension defined as >20% reduction of systolic blood pressure from baseline with epidural analgesia initiation (yes/no). The choice of the (Toeplitz) correlation structure for the residuals was performed based on AICC (Akaike information criterion, corrected for small sample sizes), BIC (Bayesian information criterion), and visual inspection of the residuals. In case of discordant conclusions from the AICC and BIC, the indication from the AICC was followed unless the choice visibly led to a violation of the assumptions on the residuals. To evaluate the longitudinal trend in time in the average contraction frequency, we fitted the same model as for the primary analysis but replaced the dichotomous variable with the phase number as a categorical variable to avoid making an a priori assumption on the shape of the trend. The phase directly preceding epidural analgesia initiation was defined as the reference (phase 1). Statistical analyses were performed using SAS Software 9.4, PROC MIXED. A P value of <0.05 (two-tailed) was considered statistically significant.

Table 1. Baseline characteristics of the study population.

	Value (n = 23)
Age (years)	32.0 [29.0, 34.0]
Body Mass Index (kg/m^2)	24.7 [22.8, 32.5]
Gestational age (weeks + days)	39 + 0 [38 + 0, 40 + 3]
Nulliparous, n	13 (56.5%)
Induction of labour, n	18 (78.3%)
Cervical dilation before labour epidural analgesia initiation (cm)	4.0 [3.0, 5.0]
Oxytocin use during study period, n	18 (78.3%)
Mode of delivery	
Spontaneous vaginal delivery, n	17 (73.9%)
Assisted vaginal delivery, n	1 (4.6%)
Caesarean delivery, n	5 (21.7%)

Data presented as median with interquartile range [IQR] or number of patients (%).

RESULTS

The summary statistics of baseline characteristics of all included cases (N = 23) are presented in Table 1. After LEA initiation, eight cases of maternal hypotension (defined as a >20% reduction of systolic blood pressure) occurred; one patient received an extra bolus of IV fluid as treatment. No patient received a tocolytic agent during the study period. During the 120 minutes following LEA initiation, the average contraction frequency was lower compared to the 60 minutes before LEA initiation (-0.37 contractions/10 minutes [95% CI -0.64 to -0.11]; P = 0.007) (Table 2). The estimated effect of possible confounders (i.e. oxytocin infusion rate at the beginning of each phase, maternal hypotension, labour induction, and cervical dilation) was not statistically significant, but these variables were kept in the model as a correction because they were expected to affect uterine activity from a clinical standpoint. The calculated mean contraction frequencies per 10 minutes in the 30-minute phases are presented in Figure 3.

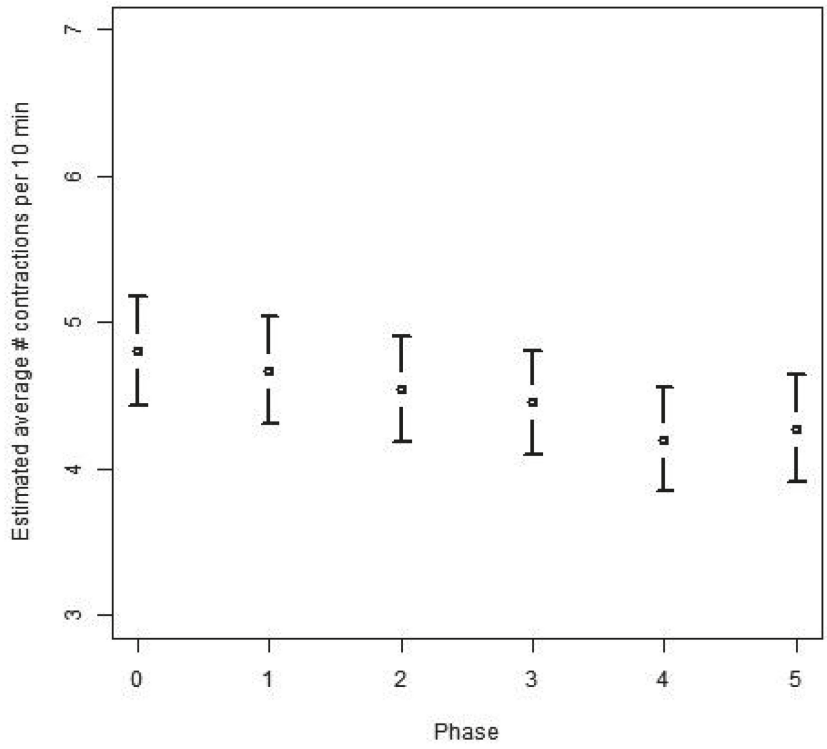
Table 2. Estimates of the fixed effects coefficients.

Effect	Estimate	Standard Error	Pr > |t|	Lower	Upper
Intercept	4.32	0.45	<0.01	3.38	5.25
Start LEA*	-0.37	0.13	0.007	-0.64	-0.11
Oxytocin	27.66	17.86	0.13	-8.06	63.38
SBP drop >20%**	-0.39	0.22	0.09	-0.85	0.07
Induction***	-0.33	0.25	0.21	-0.86	0.2
Dilation	0.16	0.09	0.11	-0.04	0.35

Model with contraction frequency per 10 minutes as outcome, and dichotomous time variable (before/after LEA initiation) as covariate of interest. Oxytocin dosage (U.min^-1^), dilation (cm) and two dichotomous variables: systolic blood pressure drop (>20% decrease from baseline) and start of labour by induction, are included in the model as covariates.
Abbreviations: LEA, labour epidural analgesia; SBP, systolic blood pressure.
** Pre-LEA is reference.*
*** No SBP hypotension is reference.*
**** Spontaneous labour is reference.*

When comparing the uterine contraction frequency in each phase, a statistically significant decreased mean contraction frequency per 10 minutes was found in phase 4 (60-90 minutes following epidural analgesia initiation) compared to the reference phase (phase 1, 30-0 minutes prior to epidural analgesia initiation) (-0.47 contractions/10 minutes [95% CI -0.89 to -0.05]; P = 0.029) (Supplementary Material Table S1).

Fig. 3. Estimated mean contraction frequency per 10 minutes per 30-minute phase.



Phases are plotted on the horizontal axis, phases 0–5 (phase 0: from 60 to 30 minutes before LEA initiation; phase 1: from 30 to 0 minutes before LEA initiation; phase 2: from 0 to 30 minutes after LEA initiation; phase 3: from 30 to 60 minutes after LEA initiation; phase 4: from 60 to 90 minutes after LEA initiation; phase 5: from 90 to 120 minutes after LEA initiation). The estimated mean number of contractions per 10 minutes (95% confidence intervals) are plotted on the vertical axis. The phases before labour epidural analgesia initiation are presented in grey with circle markers, while the phases after initiation are presented in black with triangle markers.

DISCUSSION

This prospective pilot study using electrohysterography to compare the mean uterine contraction frequency before and after LEA initiation identified a reduction in uterine activity in the 2 hours following initiation compared to the hour prior. The decrease was most pronounced 60 to 90 minutes following initiation. However, the average decrease of 0.37 contractions per 10 minutes might be considered clinically negligible as the contraction frequency remained within the normal range per FIGO guidelines.[15] Nevertheless, we found a decreased uterine activity, which may contribute to the persisting association between neuraxial labour analgesia and oxytocin augmentation.[1,16]

To our knowledge, this is the first study using real-time electrohysterography to examine uterine contraction frequency after initiation of LEA in a clinical context. Our study analysed uterine activity up to 2 hours after LEA initiation, a longer evaluation period than in most studies. As each patient acted as their control by comparing contraction frequencies pre- and post-LEA initiation, we did not include comorbidities or parity in our analyses. Variables that might have given insight into LEA effectiveness were also not assessed, such as pain scores or prior analgesics. We used expert-based uterine contraction annotation of the electrohysterography recordings. Intra- and inter-observer disagreements have been demonstrated in electrohysterography derived tocograms.[17] By blinding the researcher to fetal heart rate tracings and clinical information during the annotation, and by assistance of a second researcher for confirmation, we aimed to minimize any discrepancies, although awareness of the time of LEA initiation could have contributed to confounding.[17]

Causality between neuraxial labour analgesia and uterine activity changes has never been convincingly determined and performing well-designed trials to evaluate various analgesic modalities and drugs in labouring patients is challenging.[18] Recording uterine activity alterations provides an additional challenge which results in the use of surrogate outcomes, such as labour duration, mode of delivery, use of oxytocin augmentation, or the occurrence of fetal heart rate abnormalities. Only a handful of recent studies examined the effect of neuraxial labour analgesia techniques on uterine contraction parameters, with conflicting results; increased, decreased and unchanged uterine activity have each been reported.[19-20,2-4]

There are two retrospective studies reporting increased uterine activity following neuraxial labour analgesia, which contradict our findings.[3,19] Heuser et al. identified LEA as a risk factor for tachysystole (defined as >5 contractions in 10 minutes), with a relative risk of 1.55 (95% CI 1.37 to 1.74).[3,21] The second study, in patients at risk for uteroplacental insufficiency, observed a statistically significant increase in fetal heart rate abnormalities after either LEA or combined spinal-epidural analgesia (CSE) initiation.[19] Fetal heart rate abnormalities served as a surrogate for either increased uterine activity and/or maternal hypotension, although there was no increase in the rate of systolic blood pressure <100 mmHg. LEA and CSE analgesia were both associated with statistically significant increased rates of uterine hypertonus, defined as a uterine contraction lasting longer than 2 minutes, while LEA initiation was also associated with increased rates of tachysystole.[19]

Our findings align with three studies reporting decreased or unchanged uterine activity following epidural analgesia initiation.[2,4,20] One prospective study compared the effects of LEA and CSE analgesia on the first stage of labour, using external tocodynamometry to monitor uterine activity, assessed as augmented, reduced, or unchanged, without further specification.[4] There was no difference in first-stage labour duration; however, a statistically significant uterine activity reduction was reported in women following initiation of LEA compared with CSE analgesia.[4] One retrospective study using an IUPC found no significant

changes in contraction frequency during the first 60 minutes following LEA initiation, which does not contradict our findings since the statistically significant reduction of uterine contraction frequency found in our study occurred 60 to 90 minutes following LEA initiation. [2] One case-control study used electrohysterography and external tocodynamometry simultaneously to compare uterine activity in women with and without patient-controlled epidural analgesia (PCEA).[20] They only analysed bursts of electrical activity occurring during contractions, which were verified by external tocodynamometry. All electrohysterography parameters, as well as the tocodynamometry-determined contraction frequency, were significantly lower after the initiation of PCEA compared with the control group. The largest reductions occurred 30 minutes after PCEA initiation, earlier than in our study, as we found the largest decrease in uterine contraction frequency to occur 60 to 90 minutes after LEA initiation. We believe these conflicting results not only show the wide variety of neuraxial labour analgesia approaches, the range of clinical circumstances, and the different measurement techniques and study designs, but they also demonstrate the lack of proper understanding of the underlying (patho)physiology.

There are several possible explanations for the direct or indirect effect of neuraxial labour analgesia on uterine activity. Local anaesthetics and opioids display direct depressant effects on the myometrium in vitro, however only in much higher concentrations than detected in plasma during neuraxial labour analgesia in vivo.[22-23] Intravenous fluid boluses, local anaesthetics with adrenaline and opioids may change uterine action potentials or intracellular calcium concentrations and thus indirectly affect uterine activity.[24-25] Rapid administration of an intravenous fluid administration (e.g. 1 L) may temporarily reduce uterine contractility, possibly through decreasing vasopressin and oxytocin release from the posterior pituitary gland.[26-30] However, the late uterine activity changes found in our study suggest that the pre-procedure fluid bolus was unlikely the cause of the decreased uterine activity. Epidural adrenaline may elicit a systemic beta-adrenergic tocolytic effect, which has been associated with a prolonged first stage of labour and increased oxytocin augmentation.[31-32] In our study, epidural adrenaline was only used once with the initial epidural dose, while we observed the largest reduction of uterine activity 60 to 90 minutes following LEA initiation. Thus, epidural adrenaline is an unlikely cause for the observed effect, especially given other studies that describe changes in uterine activity without epidural adrenaline administration. [4,20] Epidural opioids can reduce plasma concentrations of endogenous oxytocin during labour.[33-34] There was no opioid given with LEA initiation, but sufentanil was administered for LEA maintenance in the epidural infusion. This could explain the reduced contraction frequency we observed later compared with other studies. The late decrease in uterine activity could also be attributable to the different local anaesthetics used for initiation (bupivacaine) and maintenance (ropivacaine) of analgesia, as different inhibitory effects on uterine activity may exist.[35]

The use of electrohysterography in clinical practice may provide, apart from more reliable CTG monitoring, a tool to study labour physiology and the impact of clinical interventions

such as LEA.[2,36] By using electrohysterography, other parameters can also be examined in addition to the uterine contraction frequency such as entropy or conduction velocity. These parameters may offer more insight into the causal mechanism of the effects found in this study.

This small observational pilot study was conducted in a single hospital, with each patient serving as their control (i.e. before versus after initiation of LEA). While LEA procedures were consistent, the inability to blind participants and researchers to the time of intervention might introduce bias. Unknown confounding factors could be present, and the limited observation period may exclude long-term effects. More studies are needed to validate our observation.

In conclusion, using electrohysterography to assess uterine contractility, we observed a statistically significant reduction of 0.37 contractions per 10 minutes after LEA initiation, with the largest reduction occurring 60 to 90 minutes after initiation of LEA. It is not clear whether this decrease is clinically significant, but it demonstrates that electrohysterography can be used to identify changes in uterine contractility. Further examination of the underlying relevant electrophysiology and exploration of electrohysterography applications in clinical anaesthesia and obstetric research are needed to improve peripartum safety and increase our knowledge of how uterine contractility is affected by common interventions and medications during labour.

SUPPLEMENTARY DATA

Fig. S1. STROBE diagram of patient recruitment and data analysis

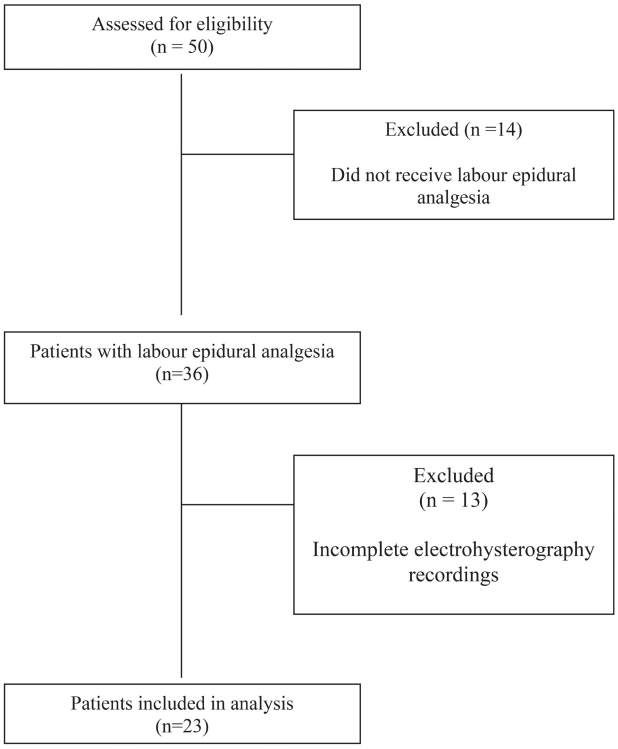


Table S1. Estimates of the fixed effects coefficients.

Effect		Estimate	Standard Error	Pr >|t|	Lower	Upper
Intercept		4.28	0.5	<.01	3.34	5.22
Phase*	0	0.13	0.20	0.51	-0.27	0.53
	2	-0.13	0.22	0.56	-0.56	0.3
	3	-0.22	0.18	0.21	-0.57	0.13
	4	-0.47	0.21	0.03	-0.89	-0.05
	5	-0.40	0.21	0.06	-0.81	-0.01
Oxytocin		25.1	17.74	0.16	-10.48	60.5
SBP drop >20%**		-0.38	0.22	0.10	-0.84	0.08
Induction***		-0.33	0.25	0.20	-0.86	0.19
Dilation		0.15	0.09	0.11	-0.04	0.35

Model with contraction frequency per 10 minutes as outcome and phase as categorical time variable as covariate of interest. Oxytocin dosage (U.min^{-1}), dilation (cm) and two dichotomous variables: systolic blood pressure drop (>20% decrease from baseline) and start of labour by induction, are included in the model as covariates.

Phase 0 from 60 to 30 minutes before LEA initiation, phase 1 from 30 to 0 minutes before LEA initiation, phase 2 from 0 to 30 minutes after LEA initiation, phase 3 from 30 to 60 minutes after LEA initiation, phase 4 from 60 to 90 minutes after LEA initiation, phase 5 from 90 to 120 minutes after LEA initiation.

Abbreviations: LEA, labour epidural analgesia; SBP, systolic blood pressure.

**Phase 1, from 30 minutes to 0 minutes before LEA initiation is the reference.*

***No SBP hypotension is the reference.*

****Spontaneous labour is the reference.*

REFERENCES

1. Anim-Somuah M, Smyth RMD, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev. 2018; 2018(5). https://doi.org/10.1002/14651858.CD000331.pub4.
2. Benfield R, Song H, Salstrom J, Edge M, Brigham D, Newton ER. Intrauterine contraction parameters at baseline and following epidural and combined spinal-epidural analgesia: A repeated measures comparison. Midwifery. 2021;95:102943. https://doi.org/10.1016/j.midw.2021.102943.
3. Heuser CC, Knight S, Esplin MS, et al. Tachysystole in term labor: Incidence, risk factors, outcomes, and effect on fetal heart tracings. Am J Obstet Gynecol. 2013;209(1):32.e1-32.e6. https://doi.org/10.1016/j.ajog.2013.04.004.
4. Poma S, Scudeller L, Verga C, et al. Effects of combined spinal-epidural analgesia on first stage of labor: a cohort study. J Matern Fetal Neonatal Med. 2019;32(21):3615-3621. doi:10.1080/14767058.2018.1467892.
5. Euliano TY, Nguyen MT, Darmanjian S, et al. Monitoring uterine activity during labor: A comparison of 3 methods. Am J Obstet Gynecol. 2013;208(1):66.e1-66.e6. https://doi.org/10.1016/j.ajog.2012.10.873.
6. Hruban L, Spilka J, Chudáček V, et al. Agreement on intrapartum cardiotocogram recordings between expert obstetricians. J Eval Clin Pract. 2015;21(4):694-702. https://doi.org/10.1111/jep.12368.
7. Wilmink FA, Wilms FF, Heydanus R, Mol BWJ, Papatsonis DNM. Fetal complications after placement of an intrauterine pressure catheter: A report of two cases and review of the literature. J Matern Fetal Neonatal Med. 2008;21(12):880-883. https://doi.org/10.1080/14767050802220508.
8. Bakker JJH, Verhoeven CJM, Janssen PF, et al. Outcomes after internal versus external tocodynamometry for monitoring labor. N Engl J Med. 2010;362(4):306-313. https://doi.org/10.1097/OGX.0b013e3181e59d45.
9. Vlemminx MWC, Thijssen KMJ, Bajlekov GI, Dieleman JP, Van Der Hout-Van Der Jagt MB, Oei SG. Electrohysterography for uterine monitoring during term labour compared to external tocodynamometry and intra-uterine pressure catheter. Eur J Obstet Gynecol Reprod Biol. 2017;215:197-205. https://doi.org/10.1016/j.ejogrb.2017.05.027.
10. Frenken MWE, Thijssen KMJ, Vlemminx MWC, van den Heuvel ER, Westerhuis MEMH, Oei SG. Clinical evaluation of electrohysterography as method of monitoring uterine contractions during labor: A propensity score matched study. Eur J Obstet Gynecol Reprod Biol. 2021;259:178-184. https://doi.org/10.1016/j.ejogrb.2021.02.029.
11. Rabotti C, Mischi M, van Laar JOEH, Oei GS, Bergmans JWM. Estimation of internal uterine pressure by joint amplitude and frequency analysis of electrohysterographic signals. Physiol Meas. 2008;29(7):829-841. https://doi.org/10.1088/0967-3334/29/7/011.
12. Rooijakkers MJ, Rabotti C, Oei SG, Aarts RM, Mischi M. Low-complexity intrauterine pressure estimation using the Teager energy operator on electrohysterographic recordings. Physiol Meas. 2014;35(7):1215-1228. https://doi.org/10.1088/0967-3334/35/7/1215.

13. Vlemminx MWC, Rabotti C, van der Hout-van der Jagt MB, Oei S. Clinical Use of Electrohysterography During Term Labor: A Systematic Review on Diagnostic Value, Advantages, and Limitations. Obstet Gynecol Surv. 2018;73(5):303-324. https://doi.org/10.1097/00019616-200203000-00015.
14. Frenken MWE, Van Der Woude DAA, Vullings R, Oei SG, Van Laar JOEH. Implementation of the combined use of non-invasive fetal electrocardiography and electrohysterography during labor: A prospective clinical study. Acta Obstet Gynecol Scand. 2023;102(6):687-695. https://doi.org/10.1111/aogs.14571.
15. Ayres-de-Campos D, Arulkumaran S. FIGO consensus guidelines on intrapartum fetal monitoring: Physiology of fetal oxygenation and the main goals of intrapartum fetal monitoring. Int J Gynecol Obstet. 2015;131(1):5-8. https://doi.org/10.1016/j.ijgo.2015.06.018.
16. Rousseau A, Burguet A. Oxytocin administration during spontaneous labor: Guidelines for clinical practice. Chapter 5: Maternal risk and adverse effects of using oxytocin augmentation during spontaneous labor. J Gynecol Obstet Hum Reprod. 2017;46(6):509-521. doi:10.1016/j.jogoh.2017.04.009.
17. Thijssen KMJ, Tissink JGLJ, Dieleman JP, et al. Qualitative assessment of interpretability and observer agreement of three uterine monitoring techniques. Eur J Obstet Gynecol Reprod Biol. 2020;255:142-146. https://doi.org/10.1016/j.ejogrb.2020.10.008.
18. Wong CA. Epidural and Spinal Analgesia: Anesthesia for Labor and Vaginal Delivery. In: Chestnut's Obstetric Anesthesia. Sixth Edition. Elsevier Inc.; 2019:474-539. doi:10.1016/B978-0-323-56688-9.00023-5.
19. Maetzold E, Lambers DS, Devaiah CG, et al. The effect of combined spinal epidural versus epidural analgesia on fetal heart rate in laboring patients at risk for uteroplacental insufficiency. J Matern Fetal Neonatal Med. 2022;35(1):46-51. https://doi.org/10.1080/14767058.2020.1711724.
20. Ye Y, Song X, Liu L, et al. Effects of Patient-Controlled Epidural Analgesia on Uterine Electromyography during Spontaneous Onset of Labor in Term Nulliparous Women. Reprod Sci. 2015;22(11):1350-1357. https://doi.org/10.1177/1933719115578926.
21. Macones GA, Hankins GDV, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring - Update on definitions, interpretation, and research guidelines. Obstet Gynecol. 2008;112(3):661-666. https://doi.org/10.1097/AOG.0b013e3181841395.
22. Fanning RA, Campion DP, Collins CB, et al. A comparison of the inhibitory effects of bupivacaine and levobupivacaine on isolated human pregnant myometrium contractility. Anesth Analg. 2008;107(4):1303-1307. https://doi.org/10.1213/ane.0b013e3181804245.
23. Yoo KY, Lee JU, Kim HS, Jeong SW. The effects of opioids on isolated human pregnant uterine muscles. Anesth Analg. 2001;92(4):1006-1009. https://doi.org/10.1097/00000539-200104000-00037.
24. Nakao K, Inoue Y, Okabe K, Kawarabayashi T, Kitamura K. Oxytocin enhances action potentials in pregnant human myometrium - A study with microelectrodes. Am J Obstet Gynecol. 1997;177(1):222-228. https://doi.org/10.1016/S0002-9378(97)70465-4.
25. Wray S, Arrowsmith S. Uterine Excitability and Ion Channels and Their Changes with Gestation and Hormonal Environment. Annu Rev Physiol. 2021;83:331-357. https://doi.org/10.1146/annurev-physiol-032420-035509.

26. Cheek TG, Samuels P, Miller F, Tobin M, Gutsche BB. Normal saline i.v. fluid load decreases uterine activity in active labour. Br J Anaesth. 1996;77(5):632-635. https://doi.org/10.1093/bja/77.5.632.
27. Zamora JE, Rosaeg OP, Lindsay MP, Lou CM. Haemodynamic consequences and uterine contractions following 0.5 or 1.0 litre crystalloid infusion before obstetric epidural analgesia. Can J Anaesth. 1996;43(4):347-352. https://doi.org/10.1007/BF03011712.
28. Bieniarz J, Burd L, Motew M, et al. Inhibition of uterine contractility in labor. Am J Obstet Gynecol. 1971;111(7):874-885. https://doi.org/10.1016/0002-9378(71)90942-2.
29. Arrowsmith S. Oxytocin and vasopressin signalling and myometrial contraction. Curr Opin Physiol. 2020;13:62-70. https://doi.org/10.1016/j.cophys.2019.10.006.
30. Benfield R, Feng D, Salstrom J, Brigham D, Newton ER. Uterine Contraction Parameters Before and During the Pre-Epidural Fluid Bolus: A Pilot Study. Biol Res Nurs. 2019;21(5):547-555. https://doi.org/10.1177/1099800419858667.
31. Gunther RE, Bauman J. Obstetrical caudal anesthesia: I. A randomized study comparing 1 per cent mepivacaine with 1 per cent lidocaine plus epinephrine. Anesthesiology. 1969;31(1):5-19. https://doi.org/10.1097/00000542-196907000-00003.
32. Jouppila R. Maternal and fetal effects of epidural analgesia during labour. Zentralbl Gynakol. 1985;107(9):521-531.
33. Rahm VAN, Hallgren A, Högberg H, Hurtig I, Odlind V. Plasma oxytocin levels in women during labor with or without epidural analgesia: A prospective study. Acta Obstet Gynecol Scand. 2002;81(11):1033-1039. https://doi.org/10.1034/j.1600-0412.2002.811107.x.
34. Scull TJ, Hemmings GT, Carli F, Weeks SK, Mazza L, Zingg HH. Epidural analgesia in early labour blocks the stress response but uterine contractions remain unchanged. Can J Anaesth. 1998;45(7):626-630. https://doi.org/10.1007/BF03012090.
35. Qian X, Wang Q, Ou X, Li P, Zhao B, Liu H. Effects of Ropivacaine in Patient-Controlled Epidural Analgesia on Uterine Electromyographic Activities during Labor. Biomed Res Int. 2018;2018:7162865. https://doi.org/10.1155/2018/7162865.
36. Vlemminx MWC, Thijssen KMJ, Bajlekov GI, Dieleman JP, Van Der Hout-Van Der Jagt MB, Oei SG. Could electrohysterography be the solution for external uterine monitoring in obese women? J Perinatol. 2018;38(5):580-586. https://doi.org/10.1038/s41372-018-0065-3.