Studies on induced labor
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Does measurement of intrauterine pressure have predictive value for the outcome of delivery in oxytocin augmented labour?

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**ABSTRACT**

*Background* It has long been thought that measurement of intrauterine pressure improved the outcome of labour, but recently we demonstrated that use of an intrauterine pressure catheter did not improve the outcome of labour and delivery. The exact mechanism behind this lack of effect remained elusive. To provide insight in this mechanisms, we evaluated intrauterine pressure correlated with dysfunctional labour and adverse neonatal outcome.

*Methods* We performed two secondary analyses on 503 women that had intrauterine pressure measured in the intervention arm of a previously published randomised controlled trial comparing monitoring of labour with an intrauterine pressure catheter or external monitoring. Firstly, we analysed outcomes in four strata of women with different ranges of the highest intrauterine pressure registered at any time during labour, women that never reached 100 MU, 100-199 MU, 200-299 MU and women that reached intrauterine pressures 300 MU and higher. Secondly, we assessed the uterine pressure registered at the last vaginal examination in the first stage of labour in two study groups; above and below 200 MU. Outcomes were mode of delivery and a composite neonatal outcome defined as 5-minute Apgar score below 7, an umbilical-artery pH below 7.05, or a neonatal admission longer than 48 hours.

*Results* Women in the ranges with lower intrauterine pressures were statistically significant older, had pregnancies with a longer gestational age and had longer labours with children with a higher birth weight.

We found a decreasing likelihood for a caesarean section as the intrauterine pressure during labour increased. In the group women that never reached 100 MU the LR for a caesarean section was 1.6, the group between 110 MU and 200 MU the LR was 1.3, the group between 200 MU and 300 MU the LR was 0.85, the group 300 MU and higher the LR was 0.41. Intrauterine pressure measured by intrauterine tocodynamometry was not associated with poor neonatal outcome.

*Conclusion* Intrauterine pressure is associated with mode of delivery. However, as demonstrated previously, use of internal tocodynamometry does not improve birth outcomes.
BACKGROUND

Induction or augmentation of labour with intravenous oxytocin requires accurate registration of contractions.

Optimal titration of oxytocin is thought to optimize intrauterine pressure, thus resulting in progression of labour without fetal distress. In the monitoring of contractions, two strategies can be used. First, using external monitoring, oxytocin is increased until contractions are regular at a frequency of three to four per ten minutes. Alternatively, uterine activity and intrauterine pressure is measured quantitatively with an intrauterine pressure catheter (IUPC). Uterine pressure can be expressed in Montevideo Units (MU), defined in 1958 by Caldeyro-Barcia et al. as the product of frequency and peak pressure over a 10-min period. Although there is some variation in the one to one measurements, the use of an intrauterine pressure catheter is a method that gives reliable information on uterine activity over a certain period of time. In their guideline “Dystocia and Augmentation of labor”, the American College of Obstetricians and Gynecologists (ACOG) in 2003 defined adequate uterine activity during active labour as a contraction pattern exceeding 200 MU. The choice for the cut off of 200 MU was based on a retrospective study by Hauth et al., in which 91% of the 109 women with oxytocin augmented labours who had spontaneous vaginal deliveries, achieved at least 200-224 MU. The ACOG guideline mentions the definition for arrest of labour as when firstly the latent phase is completed and secondly an intrauterine pressure is present exceeding 200 MU for two hours without cervical change. In the same guideline however, the reservation was made that there is no convincing proof that intrauterine tocodynamometry results in a reduction in caesarean section rates or better neonatal outcome when the uterine activity was measured by internal tocodynamometry. Indeed, two small randomised trials indicated no benefit from the use of an IUPC. Recently, we reported the results of a larger randomised clinical trial comparing external and internal monitoring that indicated no benefit from IUPC over external monitoring, both in terms of adverse neonatal outcome as well as in terms of the instrumental delivery rate. This was confirmed in a meta-analysis on the subject. Moreover, although use of an intra uterine pressure catheter is considered safe, numerous case reports link its use to rare but serious complications, like abruptio placentae, uterine perforation, placental vessel perforation and even maternal anaphylactic shock resulting in neonatal or near maternal deaths. Although these epidemiologic data demonstrate no benefit of intrauterine monitoring, many clinicians continue to use an intrauterine pressure catheter for monitoring contractions, either routinely in oxytocin augmented labours or on an incidental basis. Such management is justified in the belief that when intrauterine activity is ‘adequate’ as defined by an intrauterine pressure of at least 200 Montevideo Units, this will improve labour outcome. Standardisation of intrauterine pressure, however, has never been performed.
The exact mechanism behind this lack of effect remained elusive. To provide insight in this mechanisms, we evaluated intrauterine pressure correlated with dysfunctional labour and adverse neonatal outcome.

In view of this dilemma, we used data from the intervention group of our previous randomised trial, and assessed whether intrauterine pressure was predictive for mode of delivery and neonatal outcome.

METHODS

We performed two secondary analyses of a previously published multicenter randomised controlled trial. The study was conducted in six hospitals in the Netherlands between May 2004 and November 2007 (ISRCTN 13667534, NTR 285). In the trial, we included women with a singleton pregnancy with a gestational age of more than 36 weeks, a foetus in cephalic position, and an indication for either induction or augmentation of labour with intravenous oxytocin. Women with a uterine scar, positive results on serologic tests for human immunodeficiency or hepatitis B virus, or signs of an intrauterine infection or fetal distress were not eligible. Women were randomised to placement of an IUPC or to management by external measurement of contractions. In women allocated to the IUPC group, a Koala 1 sensor tipped catheter system intrauterine catheter (Clinical Innovations, Inc. Murray, Utah), was inserted at the first vaginal examination after randomisation. At subsequent vaginal examinations in which we recorded variables like dilation, effacement and engagement of the fetal head, we also noted the intrauterine pressure.

For the present analysis, we selected women in which at least one measurement of the intrauterine pressure was registered at any moment after randomisation during labour. We compared patient characteristics between groups, maternal age, parity, body mass index, birth weight, gestational age, duration of labour and number of inductions and augmentations. Duration of labour was defined as time between start oxytocin drip and birth of the child. We then explored a possible correlation between intra uterine pressure expressed as MU and mode of delivery in the different study groups.

Outcome measures were vaginal instrumental delivery rate, caesarean section rate and adverse neonatal outcome. Adverse neonatal outcome was defined as the composite of a five minute Apgar score below seven and/or an umbilical artery pH below 7.05 and/or a neonatal admission longer than 48 hours. In the analysis of the vaginal instrumental delivery rate and the caesarean section rate we separately studied both interventions indicated for fetal distress and for non-progressive labour.

Analysis

Firstly, we divided women in strata with four different ranges of the highest intrauterine pressure registered at any time during labour; women that never reached 100 MU, 200
MU, 300 MU and women that reached a intrauterine pressure of 300 MU or higher. We calculated likelihood ratios of having a caesarean section or an adverse neonatal outcome for women in different ranges of highest pressure reached at any time during labour.

For the second analysis, we divided women in two study groups according to the last MU that was registered during the first stage of labour, the MU↑ group (200 MU or higher at the last vaginal examination) and the MU↓ group (lower than 200 MU at the last vaginal examination).

Continuous variables were compared with ANOVA for normally distributed variables and the Mann-Whitney U test for non-normally distributed data. For categorical variables, we used the chi-square test. For dichotomous outcomes, we calculated relative risks and 95% confidence intervals.

Multivariable logistic regression analysis was performed, to adjust the association between the intra-uterine pressure and outcomes for possible confounding variables. We adjusted for body mass index, birth weight, duration of labour, maternal age, gestational age, augmentation or induction and parity. We reported Likelihood Ratio’s (LR) and Adjusted Odds Ratios (AOR) and their 95% Confidence Intervals (CI). We calculated two-sided p values for all outcomes. P values < 0.05 were considered to indicate statistical significance. Analyses were performed with SPSS version 19.

**RESULTS**

Between May 2004 and November 2007, a total of 1456 women participated in the parent trial, of whom 734 women were allocated to IUPC. Due to crossover between the study groups, 87 women allocated to the external pressure measurement were monitored with an intrauterine pressure catheter during labour, while 668 women in the IUPC group had intrauterine pressure measured, resulting in 755 women who had intrauterine pressure measurement.

We excluded 15 women as they delivered shortly after randomisation without any subsequent vaginal examination. Moreover, we did not analyse data of 237 women where no information on uterine pressure was available, as in the first period of the study this variable was not included in the case record form. Therefore, we could analyse data of 503 women.

1. **The highest intrauterine pressure reached at any time during labour**

Table 1A reports patient characteristics for women with different ranges of highest reached level of intrauterine pressure at any time during labour. Women in the ranges with low intrauterine pressures statistically significant older, had pregnancies with a longer gestational age and had longer duration of labour with children with a higher birth weight.
Table 1B reports the Likelihood Ratio (LR) and 95% Confidence Intervals (CI) to have a caesarean section or an adverse neonatal outcome, for women in the different categories of highest intrauterine pressure reached at any time during labour. In the category women who never reached an intrauterine pressure of 100 MU, the LR for a caesarean section was 1.6, CI 0.98 to 2.5; for an adverse neonatal outcome the LR was 0.85, CI 0.45 to 1.5. In women with an intrauterine pressure between 100 MU and 200 MU, the LR for a caesarean section was 1.3, CI 0.98 to 1.8; for an adverse neonatal outcome the LR was 0.90, CI 0.51 to 1.2. In women with an intrauterine pressure between 200 MU and 300 MU, the LR for a caesarean section was 0.85, CI 0.62 to 1.1; for an adverse neonatal outcome the LR was 1.3, CI 0.99 to 1.6.

In women with an intrauterine pressure of 300 MU and higher, the LR for a caesarean section was 0.41, CI 0.18 to 0.68; for adverse neonatal outcome the LR was 0.77; CI 0.08 to 0.24. Although these outcomes were not statistically significant different there is a clear trend for an increasing likelihood for a caesarean section as the intrauterine pressure decreases. We could not find a statistically significant difference in neonatal outcome between different categories women.
2. Uterine pressure during last vaginal examination

For the second analysis, we assessed the uterine activity that was registered during the last vaginal examination during the first stage of labour. We formed two study groups, the MU↑ group that contained women with a uterine activity of 200 MU or higher (n=200) versus the MU↓ group that contained women with a uterine activity below 200 MU (n=305). These two study groups also contain women who never reached second (bearing down) phase of labour and had a caesarean section before. There were no differences between study groups in maternal age, parity, body mass index and rates of inductions or augmentations. In the MU↑ group, women had a shorter gestational age, little more than two days, this was statistically significant (279 days versus 281 days in the MU↓ group, mean difference 2 days, 95% confidence interval 0.22 to 4.1, p value 0.03). The children in the MU↑ group were statistically significant smaller (3433 grams versus 3586 gram in the MU↓ group, mean difference 163 grams, 95% confidence interval 65.4 to 260.3, p value 0.001).

A vaginal instrumental delivery occurred in 18.5% of the women in the MU↑ group versus 12.97% of the women in the MU↓ group (Adjusted Odds Ratio 1.4, 95% confidence interval 0.80 to 2.5 p value 0.24). Vaginal instrumental delivery was indicated because of lack of progression in the MU↑ group 54.0% (20/37) women and 46.2% (18/39) women in the MU↓ group.

A caesarean section was statistically significant less frequent conducted in the MU↑ group, 12.0% of the women versus 25.1% of the women in the MU↓ group (Adjusted Odds Ratio

Table 2A Patient characteristics of the study groups uterine pressure at last vaginal examination,

<table>
<thead>
<tr>
<th></th>
<th>MU↑ N= 200 (39.8%)</th>
<th>MU↓ N=303 (63.4%)</th>
<th>Relative risk (95% CI)</th>
<th>Mean difference (Δ)(CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean maternal age, years (SD)</td>
<td>31 (6)</td>
<td>31 (5)</td>
<td>Δ0.39 (-0.56 to 1.3)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>Mean BMI, kg/m2 (SD)</td>
<td>24.8 (5.2)</td>
<td>25.9 (6.0)</td>
<td>Δ1.02 (-0.08 to 2.1)</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>BMI&gt;30, n (%)</td>
<td>55 (39.6%)</td>
<td>84 (60.4%)</td>
<td>1.01 (0.68 to 1.5)</td>
<td>0.95</td>
<td></td>
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<tr>
<td>Primiparous, n (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean gestational age, days (SD)</td>
<td>279 (11)</td>
<td>281 (11)</td>
<td>Δ2.2 (0.22 to 4.1)</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Mean birth weight, grams (SD)</td>
<td>3433 (535)</td>
<td>3586 (549)</td>
<td>Δ163 (65.4 to 260.3)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Duration of labour, minutes (SD)</td>
<td>409 (278)</td>
<td>357 (183)</td>
<td>Δ-28.4 (-75.5 to 18.8)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Augmentation, n (%)</td>
<td>56 (28.0%)</td>
<td>111 (36.3%)</td>
<td></td>
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<tr>
<td>Induction, n (%)</td>
<td>144 (72.0%)</td>
<td>192 (63.4%)</td>
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</table>

Table 2B Adjusted Odds Ratio and Confidence Interval. Composite neonatal outcome was defined as an Apgar score of less than 7 at 5 minutes, an umbilical-artery pH of less than 7.05, or neonatal admission longer than 48 hours.

<table>
<thead>
<tr>
<th></th>
<th>Adjusted odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal instrumental delivery n (%)</td>
<td>37 (18.5%)</td>
<td>39(12.9%)</td>
</tr>
<tr>
<td>Caesarean section, n (%)</td>
<td>24 (12.0%)</td>
<td>76 (25.1%)</td>
</tr>
<tr>
<td>Composite neonatal outcome, n (%)</td>
<td>39 (19.5%)</td>
<td>50(16.5%)</td>
</tr>
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</table>
0.34, 95% confidence interval 0.20 to 0.69, p value 0.002). In both groups caesarean section was mostly indicated because of lack of progression; MU↑ group 79.1% (19/24) women and 76.3% (58/76) women in the MU↓ group.

Composite neonatal outcome was not statistically significant different between groups 19.5% (39/200) women in the MU↑ group versus 16.5% (50/303) women in the MU↓ group (Adjusted Odds Ratio 1.1, 95% Confidence Interval 0.13 to 182, p value 0.85).

We found that women in ranges with low intrauterine uterine pressures were more likely to have a caesarean section. Intrauterine pressure measured by intrauterine tocodynamometry was not associated with poor neonatal outcome in any of the analyses. Reproducibility of intrauterine pressure measurements in labour was assessed by Chua et al., who performed a prospective study in which they randomly assigned 20 women to a group in which two IUPC’s were tied together before insertion in the same pocket of amniotic fluid or to a group in which two IUPC’s were inserted in two different pockets of amniotic fluid. They concluded that although intrauterine pressure measurements provided reliable information on the cumulative pressure wherever the catheter tip was sited in the uterus, there were variations in pressures recorded during individual contractions. In 1991 Arulkumaran et al found in a similar study small differences between the catheters of which they judged to be unlikely of any importance in the management of labour. We can conclude that measurement of uterine pressure by use of an IUPC during labour has acceptable reliability, however, in our current trial we could not confirm that use of an intrauterine pressure catheter as diagnostic tool resulted in more vaginal labours compared to women with external monitoring. Assessment of uterine activity measured by intrauterine tocodynamometry during labour did not result in a better neonatal outcome in our analyses.

In the study of Hauth et al, 91% of the women that had a spontaneous delivery reached at least an intrauterine pressure of 200 MU. In our study, only 47% of the women that had a spontaneous delivery reached adequate uterine activity as defined by the ACOG guideline, an intrauterine pressure higher than 200 MU.

This is a significant lower percentage of women, explanation for this difference is a guess, maybe labour management in oxytocin augmented labour changed over time and oxytocin regime is different nowadays.

In our analysis, we found that women with lower intrauterine pressures were older, had a longer gestational age, longer duration of labour and a child with higher birth weight and were more likely to have a caesarean section.

Despite use of an intrauterine pressure catheter for assessment of uterine activity the clinician failed to reach high levels of uterine pressure in these women.

In physics, one calculates pressure as the ratio of force to the area over which that force is distributed. In that respect, size does matter; so when the surface is bigger the pressure will be lower.
Moreover, in our analyses we found that although not statistically significant, women with higher pressures tend to be more likely to have a vaginal instrumental delivery (18.5% versus 12.9%). At the same time, possibly as a trade off, there was a statistically significant decreased risk for a caesarean section in these women. An explanation could be that the clinician tries to achieve higher intrauterine pressures in women with arrest of labour before conducting a caesarean section. So women with higher uterine pressures progressed enough to reach second phase of labour and offered the clinician the opportunity to terminate labour by a ventouse or a forcipal extraction instead of a caesarean section.

There are a few limitations of our study. The parent randomised controlled trial was not designed to perform these analyses, so we did not have records of continuous registrations of intrauterine pressure in the participating women and no registrations of rates of tachystole. Another limitation of our study is that we did not register timing of the caesarean section in course of labour and the intrauterine pressure present at that time. One could expect that most caesarean sections were performed because of lack of progress during the first phase of labour.

Strength of our study is that, by analysing uterine pressures in a large group of oxytocin augmented labours, we could confirm that low intrauterine pressures have predictive value for a caesarean section.

Conclusion of this study is that although level of intrauterine pressure might have a predictive value whether labour will be spontaneous, use of internal tocodynamometry does not improve birth outcomes.


