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European Journal of Obstetrics and Gynecology 271 (2022) 1–6

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Full length article

The association between uterine contraction frequency and fetal scalp pH in women with suspicious or pathological fetal heart rate tracings: A retrospective study

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ARTICLE INFO

Keywords:
Uterine activity
Uterine contractions
Tachysystole
Fetal hypoxia
Fetal acidosis
Fetal scalp pH

ABSTRACT

Objective: Current guidelines provide little supporting literature for the definition of uterine tachysystole during labour and no distinction is made for optimal contraction frequency depending on the clinical situation. We hypothesize that fetal hypoxia is frequently caused by uterine tachysystole and that high uterine contraction frequencies are especially harmful when fetal heart rate (FHR) abnormalities are present. We studied the association between contraction frequency and fetal scalp pH values in women with an indication for fetal blood sampling (FBS) based on FHR abnormalities.

Study design: A retrospective study including 762 women was performed in a tertiary teaching hospital in the Netherlands from January 2015 until January 2020. Women with a singleton pregnancy with a gestational age $\geq 34^{+0}$ weeks were included when FBS was performed because of suspicious or pathological FHR tracings. Exclusion criteria were maternal age < 18 years, failed fetal scalp pH values, lack of thirty minute registration by tocodynamometry prior to FBS, poor quality of uterine monitoring, intrauterine resuscitation in the thirty minutes prior to FBS, maternal body mass index ≥ 30 kg/m^2 and neonatal birth weight < 10th percentile.
Uterine contractions in the thirty minutes prior to FBS were manually annotated by a researcher who was blinded to FBS values, FHR and other obstetrical data. Linear and logistic analysis were used to explore the association between uterine contraction frequency and FBS results.

Results: Low fetal scalp pH values were significantly associated with contraction frequency prior to FBS. Fetuses of women with four to five contractions per ten minutes prior to FBS were 2.4 times more likely to have hypoxia as compared to fetuses of women with two to three contractions per ten minutes (aOR 2.4, 95% CI 1.1–5.4). With increasing contraction frequency, the risk of fetal hypoxia further increased.

Conclusions: Contraction frequency above four per ten minutes prior to FBS is significantly associated with fetal hypoxia in women with FHR abnormalities. We suggest to aim for a maximum contraction frequency of four per ten minutes in these women.

Introduction

Cardiotocography is the most established method for continuous monitoring of fetal wellbeing. Cardiotocography simultaneously records the fetal heart rate (FHR) and uterine activity (UA) over time, generating a cardiotocogram. Most of the emphasis of cardiotocography has centred on FHR monitoring, although UA monitoring is essential as well. Too little UA can lead to a prolonged course of labour while too much UA can lead to fetal oxygenation problems [1–4]. During uterine contraction, the supply of oxygenated blood to the placenta, and ultimately the fetus, is temporarily constricted [5,6]. A fetus can withstand a certain degree of diminished oxygenation. However, if contractions are too strong, last too long, occur too frequently, or there is too little rest in between, this can lead to a dangerous level of oxygen deprivation [3–5,7].

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https://doi.org/10.1016/j.ejogrb.2022.01.023
Received 18 September 2021; Received in revised form 22 January 2022; Accepted 27 January 2022
Available online 1 February 2022

Fetal oxygen saturation ($FSpO_2$) decreases during contractions, with recovery to its baseline level after an average of one to two minutes [6,7]. When contraction intervals are too short, $FSpO_2$ levels decrease incrementally with each contraction [8]. Therefore, UA may have a major impact on the course of labour as well as the fetal condition.

According to International Federation of Gynecology and Obstetrics (FIGO) and American College of Obstetricians and Gynecologists (ACOG) guidelines, five or less contractions in ten minutes, averaged over thirty minutes, is considered a normal contraction frequency, while it is considered uterine tachysystole if this frequency exceeds five [9,10]. The same guidelines recommend to consider treatment of tachysystole in case of FHR abnormalities [9,10]. However, current guidelines provide little supporting literature for their recommendations. Besides, no distinction is made in recommendations for contraction frequency depending on the clinical situation (e.g. women with an induction of labour, a trial of labour after a previous caesarean delivery, women with natural UA or women whose labour is augmented with oxytocin) or depending on the classification of the FHR tracing (i.e. normal, suspicious, or pathological).

We hypothesize that fetal hypoxia is frequently caused by uterine tachysystole and that high uterine contraction frequencies are especially harmful when FHR abnormalities are present. We therefore determined the association between uterine contraction frequency and fetal scalp pH values in women with an indication for fetal blood sampling (FBS) based on a suspicious or pathological FHR tracing.

Methods

This retrospective case-control study was performed in a tertiary teaching hospital in the Netherlands from January 2015 until January 2020.

All singleton pregnancies with a gestational age $\geq 34^{+0}$ weeks were included when FBS was performed during labour because of suspicious or pathological FHR tracings [10]. Exclusion criteria were maternal age $<$ 18 years, failed fetal scalp pH values, uterine monitoring for less than thirty minutes prior to FBS, uterine monitoring using other monitoring methods than external tocodynamometry (TOCO), poor quality of uterine monitoring as assessed by the researcher (defined as registrations with no recognizable UA pattern [11]), and intrauterine resuscitation in the thirty minutes prior to FBS (i.e. ephedrine, fluid challenge, maternal oxygen therapy, uterorelaxantia or discontinuation of oxytocin infusion). Women with a maternal body mass index (BMI) ≥ 30 kg/m^2 or unknown BMI were also excluded since the sensitivity of uterine contraction detection using TOCO is adversely affected by BMI [12,13]. Moreover, when the neonatal birth weight was $<$ 10th percentile, women were excluded as this may predispose the fetus to decompensation in labour [14]. Women pregnant with fetuses with expected congenital heart anomalies were only excluded when fetal cardiac surgery was indicated directly after labour.

Fetal blood sampling

FBS was indicated when the cardiotocogram was classified as either suspicious or pathological for at least one hour based on the modified FIGO-classification of intrapartum fetal monitoring [10,15]. Two samples were obtained at every FBS moment to increase successful sampling [16–18]. Droplets were collected in heparinised tubes which were immediately closed thereafter to prevent gas exchange between blood and air. FBS were analysed in a point-of-care blood gas analyser (ABL90 Flex Plus, Radiometer, Copenhagen, Denmark), assuring quickly available results for obstetric caregivers. According to the National Institute for Health and Care Excellence (NICE) guidelines, fetal scalp pH levels of $\geq$ 7.25 were considered normal, pH levels between 7.20 and 7.25 were considered borderline, and pH levels of $\leq$ 7.20 were considered abnormal [19]. Fetal hypoxia was defined as fetal scalp pH $\leq$ 7.20.

Uterine monitoring

Uterine contractions were monitored with TOCO, which measures contractions indirectly based on abdominal wall distension [12,20]. Tocogram registrations of the thirty minutes prior to FBS were extracted from electronic patient files and subsequently analysed in a programme for manual annotation of contractions (UAannotator, MatLab R2020a, MatWorks, Natick, Massachusetts, USA). All tocograms were annotated by a single researcher (M.F.) blinded to FHR, FBS results, and all other obstetric outcomes. The researcher was trained in analysing uterine contractions from a cardiotocogram. After annotation of contractions, the tool automatically calculated the total number of contractions. A previous study showed a moderate inter-observer agreement (mean weighted kappa 0.63) and a substantial intra-observer agreement (mean weighted kappa 0.77) of the uterine contraction count based on TOCO [21]. According to FIGO and ACOG guidelines, normal contraction frequency is defined as five or less contractions in ten minutes, averaged over thirty minutes, whereas more than five contractions in ten minutes, averaged over thirty minutes, is defined as uterine tachysystole [9,10].

Study outcomes

We examined the association between the mean number of uterine contractions in ten minutes, averaged over thirty minutes, and fetal scalp pH taken at the end of the 30-minute period. We also examined maternal and neonatal outcomes for women with and without fetal hypoxia (i.e. mode of delivery, episiotomy rate, 5-minute Apgar score $<$ 7, neonatal metabolic acidosis and admission to the neonatal intensive care unit (NICU)).

Data collection

In case of repeated FBS within one delivery, the last FBS was used for analysis as annotation of uterine contractions becomes easier with progression of labour due to more pronounced contractions [22]. When multiple fetal scalp pH values were available from one sampling moment, the lowest pH value was chosen since it is the most reliable value [23].

Arterial and venous umbilical cord pH levels had to differ by at least 0.02, otherwise, both pH levels were considered to be venous umbilical cord pH [24,25]. Metabolic acidosis was defined as umbilical artery pH $<$ 7.05 and base deficit (BD) $>$ 12.0 mmol/l or, when only the umbilical vein pH was available, as pH $<$ 7.10 and BD $>$ 12.0 mmol/l [26].

Statistical analyses

We used linear regression analyses to model the association between the mean contraction frequency and FBS results. We analysed the FBS results in a dichotomous manner, based on the presence or absence of fetal hypoxia (fetal hypoxia was defined as fetal scalp pH $\leq$ 7.20). To further explore the association between uterine contraction frequency and FBS results, we performed logistic regression analysis with FBS pH $\leq$ 7.20 as the dependent variable. The mean contraction frequency was categorised into 1.00–2.00, 2.01–3.00, 3.01–4.00, 4.01–5.00, 5.01–6.00 and 6.01–7.00 per ten minutes. The category with the lowest percentage of fetal hypoxia served as the reference category (2.01–3.00 contractions per 10 min) so as to estimate the relative risk increase of fetal hypoxia per contraction category. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Multivariate logistic regression was performed to adjust for confounders. Confounders were variables that were associated with the outcome at a p-value of $<$ 0.05 and changed the OR for contraction frequency by$>$5%. The variables nulliparous women (yes/no), stage of labour (first/second), oxytocin at time of FBS (yes/no), induction of labour (yes/no) and BMI met this definition and were included in the final model.

Descriptive statistics were used to describe demographic

characteristics and outcomes. Differences between groups were tested with independent samples T-Tests for normally distributed numerical data and Pearson Chi-Square Test or Fisher's Exact Test for categorical data. Two sided p-values of <0.05 were considered statistically significant. All analyses were conducted in SPSS software version 27 (IBM Corp., Armonk, NY, USA).

Ethical considerations

The Board of the Medical Ethics Committee of Máxima MC confirmed on the 20th of January 2020 that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this study (METC-number N20.006). Individual patient consent was not considered necessary.

Results

The total study population consisted of 762 women (Fig. 1). A total of 105 (14%) women had uterine tachysystole prior to FBS. Fetal hypoxia was present in 138 (18%) fetuses. Baseline characteristics are presented in Table 1. Uterine tachysystole was significantly associated with fetal hypoxia during labour ($p < 0.001$) (Table 1). The mean contraction frequency per ten minutes, averaged over the thirty minutes prior to FBS, was 4.4 ± 1.1 for women pregnant with a fetus with hypoxia and 4.0 ± 1.0 for women pregnant with a fetus without hypoxia ($p < 0.001$).

A poor linear correlation was seen between the continuous variables fetal scalp pH and mean contraction frequency prior to FBS: $r = -0.212$ ($p < 0.001$), indicating that fetal scalp pH values decrease with an increasing contraction frequency (Fig. 2).

Prevalence of fetal hypoxia according to uterine contraction categories showed a J-shaped curve (Fig. 3); fetal hypoxia occurred in 13% (95% CI: 9.7%-16.3%) of fetuses if the mother had a maximum frequency of four contractions per ten minutes, 20% (95% CI: 15.8%-25.5%) if the mother had four to five contractions per ten minutes and 33% (95% CI: 18.9%-73.3%) if the mother had more than five contractions per ten minutes.

Multivariate logistic regression analysis showed that increasing uterine contraction frequency prior to FBS was associated with fetal hypoxia (Table 2). The lowest risk of fetal hypoxia was observed in women having 1–4 contractions per ten minutes and the highest risk was observed with > 6 contractions per ten minutes. Fetuses of women with four to five contractions per ten minutes prior to FBS were 2.4 times more likely to have hypoxia as compared to fetuses of women with two to three contractions per ten minutes prior to FBS (aOR 2.4, 95% CI: 1.1–5.4). With increasing contraction frequency, the risk of fetal hypoxia further increased.

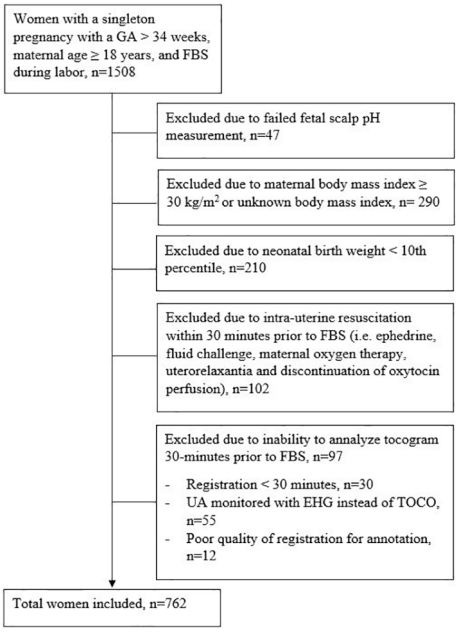

Fig. 1. Patient inclusion flowchart.

Table 1
Demographic characteristics of women with and without hypoxia of their fetus during labour.

	Fetal scalp pH > 7.20 (n = 624)	Fetal scalp pH ≤ 7.20 (n = 138)	P-value
Maternal age (years)	31.25 ± 4.28	31.34 ± 4.21	0.812[a]
Body Mass Index (kg/m^2)	22.91 ± 2.85	23.39 ± 2.80	0.075[a]
Nulliparous women	468 (75.0)	121 (87.7)	**0.001**[b]
Previous caesarean delivery	52 (8.3)	6 (4.3)	0.110[b]
Induction of labour	225 (36.1)	58 (42.0)	0.189[b]
Meconium stained amniotic fluid	178 (28.5)	44 (31.9)	0.452[b]
Intrapartum fever (>38.0 °C)	132 (21.2)	28 (20.3)	0.822[b]
FBS during second stage of labour	297 (47.6)	100 (72.5)	**0.000**[b]
Oxytocin at time of FBS	371 (59.5)	88 (63.8)	0.132[b]
Uterine tachysystole (>5 contractions per 10 min, averaged over 30 min)	70 (11.2)	35 (25.4)	**0.000**[b]
Uterine contraction frequency per 10 min, averaged over 30 min	3.96 ± 0.99	4.44 ± 1.07	**0.000**[a]

All data presented as n (%) or mean ± SD.
a. Independent samples T-test.
b. Pearson X^2.

Table 3 shows significantly more short-term adverse maternal and neonatal outcomes in women with fetal hypoxia during labour compared to women without fetal hypoxia. Two of the neonates admitted to the NICU were diagnosed with congenital heart diseases (one neonate with a ventricular septal defect and bicuspid aortic valve, and one neonate with total anomalous pulmonary venous return).

Discussion

Main findings

This study aimed to determine the association between uterine contraction frequency and fetal scalp pH values in women with FHR abnormalities during labour. Our findings indicated that low fetal scalp pH values were significantly associated with uterine contraction frequency prior to FBS in a non-linear way and that uterine tachysystole prior to FBS was significantly associated with fetal hypoxia, as was a uterine contraction frequency of more than four per ten minutes. Moreover, significantly more adverse maternal and neonatal outcomes were seen in women with abnormal FBS results (fetal scalp pH ≤ 7.20) during labour.

Strengths and limitations

One of the strengths of our study is the relatively large sample size and the unbiased assessment of the contraction frequency. The researcher was blinded to FHR, FBS results and other obstetric data during contraction annotation. Moreover, the assessment of contraction frequency occurred in a visually comparable tocogram to the one used in clinical practice (i.e. digital assessment, and equal scales and colors). Another strength is the exclusion of women that gave birth to a neonate with a birth weight < 10th percentile to prevent selection bias, as these fetuses may be predisposed to hypoxia during labour [14].

Multiple UA characteristics are important to estimate the risk of fetal oxygen deprivation, such as relaxation time, baseline tone, contraction amplitude and contraction duration. However, TOCO is only able to detect the uterine contraction frequency, which could be considered a study limitation [20]. Therefore, we would ideally use other uterine

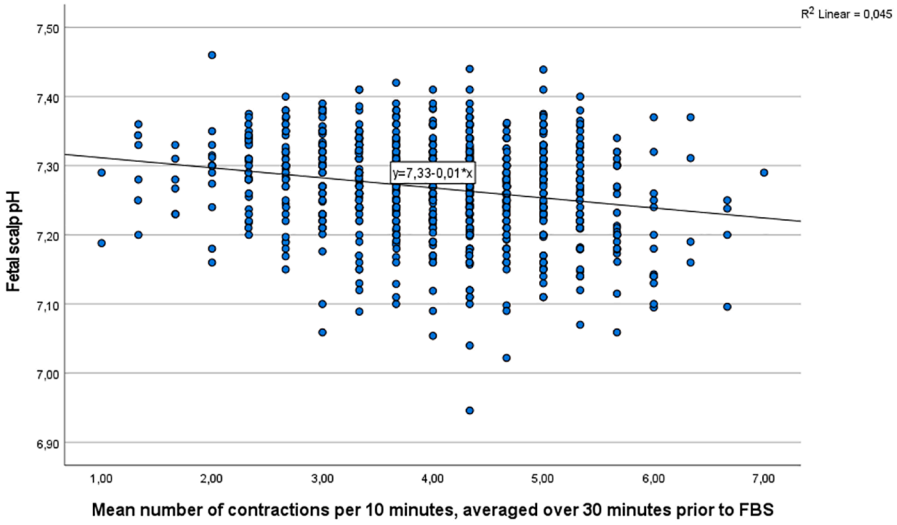

Fig. 2. Scatterplot to correlate numerical outcomes of FBS results and mean contractions frequencies prior to FBS.

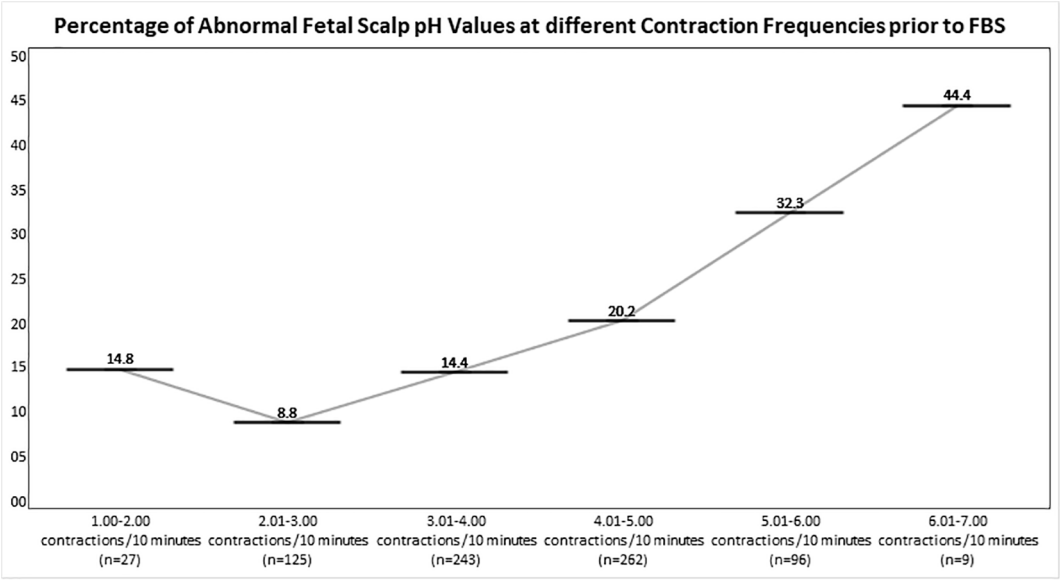

Fig. 3. Prevalence of fetal hypoxia at different uterine contraction frequencies prior to FBS.

Table 2
Association between uterine contraction frequency and fetal hypoxia, presented as odds ratio (OR) and adjusted odds ratio (OR_{adj}) with 95%-confidence interval (95% CI).

Uterine contraction frequency per 10 min, averaged over 30 min	N	OR (95% CI)	OR_{adj} (95% CI)*
Categorical			
1.00–2.00	27	1.8 (0.5–6.2)	1.8 (0.4–7.7)
2.01–3.00**	125	1 (reference)	1 (reference)
3.01–4.00	243	1.7 (0.9–3.6)	1.8 (0.8–4.2)
4.01–5.00	262	**2.6 (1.3–5.2)**	**2.4 (1.1–5.4)**
5.01–6.00	96	**4.9 (2.3–10.5)**	**4.2 (1.7–10.1)**
6.01–7.00	9	**8.3 (1.9–35.5)**	**10.2 (2.0–50.9)**

*Adjusted for nulliparous women (yes/no), FBS during second stage of labour (yes/no), oxytocin at time of FBS (yes/no), induction of labour (yes/no) and BMI.
**Reference category.

Table 3
Perinatal outcomes of women with and without hypoxia (i.e. fetal scalp pH ≤ 7.20 or > 7.20) of their fetus during labour.

Perinatal outcomes	Fetal scalp pH > 7.20 (n = 624)	Fetal scalp pH ≤ 7.20 (n = 138)	P-value
Mode of delivery			**0.000[a]**
Spontaneous	394 (63.1)	26 (18.8)	
Assisted vaginal delivery	147 (23.6)	80 (58.0)	
Secondary caesarean delivery	83 (13.3)	32 (23.2)	
Episiotomy	355 (56.9)	95 (68.8)	**0.010[a]**
5-minute Apgar score < 7	20 (3.2)	14 (10.1)	**0.000[a]**
Neonatal metabolic acidosis	5 (0.8)	6 (4.3)	**0.007[b]**
NICU admission	15 (2.4)	14 (10.1)	**0.000[a]**

All data presented as n (%) or mean ± SD.
a. Pearson X^2.
b. Fisher's exact test.

monitoring techniques such as the intra-uterine pressure catheter or electrohysterography [12]. Moreover, TOCO mostly reports a lower contraction frequency as compared to the intra-uterine pressure catheter, which is considered the gold standard [12]. Nevertheless, TOCO is the most commonly used method for uterine monitoring and our data is therefore well applicable to the majority of labouring women [20].

Interpretation

This study reveals that a contraction frequency prior to FBS of more than four per ten minutes is significantly associated with fetal hypoxia in women with FHR abnormalities. Therefore, the maximum contraction frequency may need to be adjusted downwards to avoid fetal hypoxia in these women.

As expected, in women with abnormal FBS results (fetal scalp pH $\leq$ 7.20) during labour, significantly more operative interventions and short-term adverse neonatal outcomes were seen. Lowering the maximum contraction frequency to avoid fetal hypoxia may therefore also result in less adverse neonatal outcomes as well as operative interventions. However, we did not directly study the association between contraction frequency and neonatal outcomes as the study design is not ideal for answering that research question. We analysed the tocograms from women with suspicious or pathological FHR tracings in the 30-minutes prior to FBS and excluded women with intra-uterine resuscitation. We chose not to analyse the tocograms in the 30-minutes directly prior to childbirth as neonatal umbilical cord pH values may be influenced by the interventions performed by the obstetric caregiver (e.g. mode of delivery and related time-interval between UA recording and birth).

Few studies have already suggested changing the definition of uterine tachysystole to five or more contractions per ten minutes, instead of more than five [4,27]. Simpson et al. described that fetal oxygen saturation decreased with increasing contraction frequency (<5 versus $\geq$ 5 versus $\geq$ 6 contractions per ten minutes) [4]. Our study is of additional value since we explore the association between contraction frequency and fetal hypoxia in women who all had FHR abnormalities, whereas the study of Simpson et al. was conducted in 56 healthy nulliparous women with induction of labour using oxytocin. Our study was thus focused on a very specific group of women (i.e. women with suspicious or pathological FHR tracings during labour) and also with a larger sample size.

A few other studies compared UA during labour to neonatal outcomes [27–29], whereas our study focused on fetal scalp pH values assessed at the end of the analysed UA-registration instead of neonatal outcomes to prevent bias from the elapsed time between the tocograms analysed and the outcome of interest. Moreover, as mentioned before, the 30-minute period prior to FBS was chosen instead of the 30-minute period prior to childbirth to prevent bias from medical interventions.

Previous studies described an association between oxytocin perfusion and uterine tachysystole [30,31]. In our cohort, we excluded all women in whom oxytocin was discontinued prior to FBS as discontinuation of oxytocin perfusion was considered as intra-uterine resuscitation. Intra-uterine resuscitation affects fetal oxygenation, and in case of interventions using uterorelaxantia or discontinuation of uterotonica (i.e. oxytocin), it also affects the analysed UA prior to FBS. We therefore excluded these women. A total of 35.4% (n = 252) of the included women had no oxytocin perfusion at the time of FBS, indicating that a considerable amount of women had FHR abnormalities in the presence of naturally occurring uterine contractions. It would be interesting to perform a subgroup analysis for women without oxytocin perfusion at the time of FBS. Nevertheless, we did not perform this analysis as we believed our study population was too small for an adequate analysis, especially since we divided the population according to different contraction frequencies.

Interestingly, oxytocin perfusion was continued in 57 women despite the presence of uterine tachysystole (i.e. iatrogenic uterine tachysystole). Possibly, oxytocin perfusion was continued as obstetric caregivers thought this would expedite the delivery (37 women (65%) were already in the second stage of labour when FBS was performed). Another explanation is that obstetric caregivers did not recognize uterine tachysystole [32], potentially causing iatrogenic complications (i.e. an increased risk of fetal hypoxia). Increased alertness to uterine tachysystole in women with FHR abnormalities can ensure timely intra-uterine resuscitation which may in turn permit continuation of labour and reduce operative interventions as well as adverse neonatal outcomes [33].

Future studies should focus on the optimal contraction frequency for women pregnant with small for gestational age fetuses, women with a BMI $\geq$ 30 kg/m^2, and women with and without oxytocin perfusion during labour.

Conclusion

Low fetal scalp pH values are significantly associated with high uterine contraction frequency prior to FBS. In women with suspicious or pathological FHR tracings, uterine tachysystole (more than five contractions per ten minutes) prior to FBS is significantly associated with fetal hypoxia, as is a uterine contraction frequency of more than four per ten minutes. Therefore, we suggest to aim for a maximum contraction frequency of four per ten minutes in women with FHR abnormalities.

Details of Ethics approval

The Board of the Medical Ethics Committee of Máxima MC confirmed on the 20th of January 2020 that the rules laid down in the Medical Research Involving Human Subjects Act do not apply to this study (METC-number N20.006).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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