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Authors: Hynek Herman, Petr Velebil, Iva Urbankova, Petr Krepelka, Michal Emingr, Lucie Hympanova, Ladislav Krofta, Jiri Hanacek

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The amenorrhea as a protective factor for healing of hysterotomy — a retrospective analysis one year postpartum

Short title: Amenorrhea improves hysterotomy healing

Hynek Herman, Petr Velebil, Iva Urbankova, Petr Krepelka, Michal Emingr, , Lucie Hympanova, Ladislav Krofta, Jiri Hanacek

Institute for the Care of Mother and Child, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

Corresponding author:

Jiri Hanacek

Institute for the Care of Mother and Child, 3rd Faculty of Medicine, Charles University, Podolské náb. 157, 14000 Praha 4, Czech Republic

e-mail: jiri.hanacek@upmd.eu

ABSTRACT

Objectives: The good healing of the hysterotomy after cesarean section is important for subsequent pregnancies. However, the factors which improve this healing have not been completely described, yet. In this study, we focused on factors which may affect healing of hysterotomy within one year after delivery, such as menstruation, breastfeeding, and the use of the contraception.

Material and methods: Following delivery, total of 540 women were invited for three consecutive visits at six weeks, six months, and 12 months postpartum. The presence of menstruation, frequency of breastfeeding and contraception use were recorded. The scar was evaluated by vaginal ultrasound as already described. The impact of menstruation, breastfeeding, and contraception method on presence of niche was evaluated.

Results: The presence of menstruation increased odds to have niche by 45% (CI 1.046–2.018, $p = 0.026$). Secondly, our results demonstrated a statistically significant protective effect of breastfeeding on the incidence of niche with OR 0.703 (CI 0.517–0.955, $p = 0.024$). Breastfeeding decreases odds to have niche by 30%. Also, the use of gestagen contraception

lowered the odds by 40% and intrauterine device (IUD) or combine oral contraceptive (COC) by 46.5%. The other possibly intervening factors were statistically controlled.

Conclusions: Amenorrhea, breast-feeding and progesterone-contraceptive decreases the risk of uterine niche within one year follow up.

Key words: cesarean section; uterus; contraception; niche; breastfeeding

INTRODUCTION

Over the last few decades percentage of Caesarean section (CS) deliveries has dramatically increased worldwide [1, 2]. The increasing trend is most probably related to the demographic changes taking place in the society (aging population of pregnant women, declining number of children, legal consequences of delivery complications etc.). The increasing CS rate has stimulated an interest in the related short- and long-term morbidity of CS scars and niche. The most common long-term consequence of the CS niche may cause intermenstrual spotting (34–64%), dysmenorrhea (53.1%), chronic pelvic pain (36.9%), dyspareunia (18.3%) and infertility (4–19%) [3–6]. The scar defect may also cause serious complications in the subsequent pregnancy, i.e., uterine dehiscence (0.6–3.8%), uterine rupture (0.2–3.8%), or pregnancy in the scar, and placenta accreta spectrum. Postpartum evaluation of the CS scar is usually performed by a transvaginal ultrasound, or by contrast-enhanced sonohysterography which offers even better visibility of niche. Another option is hysteroscopy or hysterosalpingography. The prevalence of niche is between 24 and 80.9% using the transvaginal sonography [7–11] and 56–84% [4, 8, 12] when using sonohysterography.

Interestingly, not all women have a niche after a caesarean section. Thus, there must be risk and protective factors for niche development. The risk factors can be: 1) obstetrical and partially un-avoidable such as acute caesarean section, vaginal dilatation before CS, duration of labor, oxytocin use, preeclampsia; 2) surgical and mostly avoidable, i.e., uterine incision location, one or two layer hysterotomy suture, ex-/inclusion of the endometrium in the suture, un-/locked suture, peritoneum closure, formation of adhesions in the hysterotomy area, etc. 3) lastly, there are patient-related risk factors such as individual pre-disposition to healing process, BMI, smoking [13].

The impacts of amenorrhea, breastfeeding and contraception have not been, to our knowledge, investigated yet. Therefore, hereby, we present retrospective analysis of the

available data on impact of amenorrhea (breastfeeding, contraception) on healing of hysterotomy.

MATERIAL AND METHODS

Within this study we retrospectively analysed available secondary data obtained from large prospective study, carried out 2011–2014 in the tertiary perinatal center [7]. The study was approved by the institutional ethics committee (ethics committee number 3/2010).

Included were healthy primiparous women with a singleton pregnancy delivered at or beyond 37 weeks, who underwent CS and signed informed consent. Patient characteristics, which were recorded and have a relation to our study are in Table 1. The follow up was set on 6 weeks, 6 months and one year postpartum.

We recorded presence of menstruation or amenorrhea, defined as the absence of menses [14]. Additionally, we noted breastfeeding frequency (> 4 times a day, < 4 times a day, or not breastfeeding) and contraception type (none, combined oral contraceptive (COC), gestagen, or intrauterine device (IUD)). The presence of niche was evaluated by transvaginal ultrasound as already described [7, 15]. Within this study niches were categorized as A/niche present or B/ not present. As niche we recognized any defect (missing part) of the myometrium, including defects without contact with endometrial cavity. The special niche characteristics (i.e., niche length) were not in the scope of this study.

Statistics were carried out in SPSS software version 13.0 (IBM Corp., Armonk, NY, USA). The homogeneity was tested with Fisher's exact test. The p value < 0.05 was considered significant. To test the development of categorized variables (including dichotomous variables) over time and dependence on amenorrhea (breastfeeding, contraception), we used the generalized linear mixed model with logit link function, binomial distribution, and first-order autoregressive covariance structure. The dependent variable was the presence of niche diagnosed at visits. Hence the reference category is absence of the niche the estimated Odds Ratios are related to presence of the niche.

RESULTS

Population characteristics

A total of 540 women and were included in the study. During the follow up 477 women attended at 6 weeks, 391 women at 6 months and 324 women at one year postpartum. Their demographic and other characteristics are in Table 1. We observed statistically more frequent menstruation in women with higher BMI (p = 0.002). Due to low count of women using

COC, IUD those data were pooled to group called other contraception. The group of women using gestagen contraception had lower mean age compared to groups with other or no contraception (30 vs 32 vs 32 years; $p = 0.002$). There were no other significant differences in demographic and other characteristics, between groups related to 1) menstruation 2) breastfeeding frequency and 3) type of contraception (Tab. 1).

The breastfeeding as causative factor for amenorrhea

We observed that with the decrease in breastfeeding the presence of menstruation gradually increased from 10.6% at six weeks to 88.7% in one year after the CS (Fig. 1A). Frequency of breastfeeding more than 4 times per day decreased from 85.3% at 6 weeks to 59.7% at 6 months and further to 15.3% at 1 year follow up. While only 9.9% of women did not breastfeed at all at 6 weeks, more than half did not breastfeed at 1 year (Tab. 2). The relation of breastfeeding and menstruation is described in Table 3. Breastfeeding and menstruation effect were statistically insignificant in models containing both effects together. This fact is in concordance with the assumption that the direct effect on scar presence has presence of menstruation. The effect of breastfeeding is indirect and is mediated by menstruation.

Contraception use one year postpartum

When evaluating the use of contraception, we have found that the most frequent was gestagen hormonal contraception in all three post-partum periods (9.3 % at 6 weeks, 18.2% at 6 months, and 13.7% at 1 year) (Tab. 2).

Impact of menstruation on presence of cesarean niche

Based on statistical models menstruation increases the risk of cesarean niche by 45% (Tab. 4). Breastfeeding indirectly decreases the risk of niche by 30%. The use of gestagen contraception lowers the risk of niche by 40% and IUD or COC by 46.5%.

DISCUSSION

This study confirmed our hypothesis that amenorrhea might decrease the risk of niche. Breastfeeding and contraception, the most usual causative factors of amenorrhea, also showed an indirect positive impact on CS-scar healing.

Our hypothesis comes out of the general wound healing process. Even though under physiologic conditions, non-injured endometrium completely restores the lost structure each

month [16], the situation may change after the external injury [17]. In example, the extensive amount of fluid may impair wound healing [18]. Either blood or exudate can either flow or create a collection, both having a possible impact on healing. The mechanical effect could be pressure or washing out cells or chemokines. The presence or absence of chemokines may impact tissue healing and remodeling. All these factors can change the healing process and lead to prolonged inflammation and weaker scar tissue. The remodeling process is known to take up to one-year post-injury [19]. That is why we think amenorrhea after puerperium still could have an impact. Prolonged or excessive pressure at the wound site may compress the capillary network and disrupt the blood supply resulting in delayed healing. We hypothesize, but we have no data to confirm, that menstruation may increase intrauterine pressure and, therefore, may put pressure on the healing scar. We would like to further investigate this. In the case of a vulnerable wound, these collapses and creates a niche. Also, regular menstruation can be a repetitive trauma and can lengthen the healing process or stop it completely [20]. It has long been recognized that the collection of free blood, liquefied fat, and cellular debris are both physical and chemical deterrents to wound healing.

We acknowledge several limitations of our study. Firstly, we set the study hypothesis after completing the primary project [7]. Therefore, the available data are limited and obtained retrospectively. However, we think that our finding is clinically very relevant and needs further investigation. For further study, we suggest enrolling more women using different types of contraception. We are aware that healing widely differs concerning wound location. Therefore, we encourage the investigation of the healing processes of the uterine myometrium and endometrium complex. We are aware that puerperium is a period of lochia discharge; in this period, we can in future investigate if some stage of lochiometra may have impact on the healing process.

This study also has several strengths. By the statistical model, we confirmed that the primary impact is caused by amenorrhea, and breastfeeding and contraception are indirect. Moreover, we statistically controlled for possible confounders (age, BMI, type of CS, and suture type (single, double layer — not reported)).

With an increased CS and knowledge of the risk of uterine rupture, we should pay attention to the healing of hysterotomy as any other body wound. We should try to find factors that increase the risk (find correlates with risk factors for general wound healing, i.e., diabetes mellitus or protective factors (i.e., good nutrition and rest). We can postpone menstruation using various methods of contraception or by lactation amenorrhea. Therefore, breastfeeding support among women after CS may positively impact the child's health as

well as maternal health. We consider this an essential additional argument for early initiation and duration of breastfeeding after cesarean birth. We can assume that the absence of menstruation, regardless of the cause, provides a better condition for un-disturbed healing. Considering the potential risks and health problems related to improperly healed scars, the finding that delayed menstruation lowers the risk of niches is essential and may have significant public health consequences.

CONCLUSIONS

Our main finding is that women delivered by caesarean section who did not menstruate within the one-year period had lower risk of uterine niches. Breastfeeding had a positive effect mediated by absence of menstruation.

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Authorship confirmation/contribution statement

Author 1 (HH): Investigation, writing — original draft; formal analysis. Author 2 (PV): Conceptualization, review and editing; Author 3 (IU): writing – original draft; formal analysis; Author 4 (PK): Conceptualization, review and editing, methodology (lead); Author 5 (ME): Conceptualization (supporting), Funding acquisition, Resources, review and editing; Author 6 (LH): Project administration, Writing – original draft (supporting); Author 7(LK): Supervision, Author 8 (JH) : Conceptualization, investigation, writing – original draft and editing

Conflict of interests

None for all authors.

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Table 1. Demographic and other characteristics at 6 weeks postpartum related to A/menstruation B/breastfeeding C/contraception

A/ Parameter	Menstruation		P-value
	Yes (n = 51)	No (n = 417)	
Age (years)	30 (28–34)	31 (29–34)	0.121 ^a
BMI (kg/m ²)	23.4 (21.4–26.8)	22.2 (20.3–24.4)	0.002 ^a
Gestational week	40 (39–41)	40 (39–41)	0.906 ^a
Type of caesarean section			
<i>Acute by delivery</i>	20 (10.4)	172 (89.6)	0.967 ^b
<i>Acute in preanancy</i>	1 (6.3)	15 (93.8)	
<i>Planned by delivery</i>	24 (11.9)	178 (88.1)	
<i>Planned in preanancy</i>	6 (10.3)	52 (89.7)	
B/ Parameter	Breastfeeding		P-value
	More than 4 in day (n = 404)	None or less than 4 in day (n = 60)	
Age (years)	31 (29–34)	31 (28–34.5)	0.701 ^a
BMI (kg/m ²)	22.3 (20.4–24.7)	22.2 (20.1–25.1)	0.884 ^a
Gestational week	40 (39–41)	40 (39.5–41)	0.993 ^a
Type of caesarean section			
<i>Acute by delivery</i>	169 (86.2)	27 (13.8)	0.074 ^b
<i>Acute in preanancy</i>	12 (75)	4 (25)	
<i>Planned by delivery</i>	178 (88.1)	24 (11.9)	
<i>Planned in preanancy</i>	45 (76.3)	14 (23.7)	

C/ Parameter	Contraception			P-value
	Gestagen (n = 60)	IUD or COC (n = 21)	None (n = 207)	
Age (years)	30 (28–32.5)	32 (28.5–35)	32 (30–34)	0.002 ^a
BMI (kg/m ²)	22.8 (20.7–24.4)	21.2 (19.7–	22.3 (20.2– 24.8)	0.143 ^a
Gestational week	40 (40–41)	41 (39.5–41)	40 (39–41)	0.775 ^a
Type of caesarean section				
<i>Acute by delivery</i>	32 (19.6)	6 (3.7)	125 (76.7)	0.100 ^b
<i>Acute in pregnancy</i>	5 (33.3)	0 (0)	10 (66.7)	
<i>Planned by delivery</i>	28 (16.9)	9 (5.4)	129 (77.7)	
<i>Planned in</i>	4 (8.3)	6 (12.5)	38 (79.2)	

^aWilcoxon-Mann-Whitney test

^bFisher's Exact Test

Characteristics are presented as median and interquartile range. Categorical variables are presented as total number (percentage in group)

BMI — body mass index

Table 2. Breastfeeding, menstruation and a use of contraception during follow up

	6 weeks. n = 477	6 months. n = 391	1 year. n = 324
Menstruation	51 (10.6%)	221 (55.9%)	287 (88.7%)
Breastfeeding			
> 4 times a day	407 (85.3%)	233 (59.7%)	50 (15.3%)
< 4 times a day	23 (4.7%)	51 (12.9%)	99 (30.5%)
none	47 (9.9%)	107 (27.3%)	175 (54.2%)
Contraception			
Gestagen	44 (9.3%)	71 (18.2%)	44 (13.7%)
IUD	7 (1.5%)	12 (3.0%)	9 (2.7%)
COC	9 (1.9%)	9 (2.3%)	10 (3.3%)
none	417 (87.4%)	299 (76.5%)	261 (80.3%)

COC — combined oral contraceptive; IUD — intrauterine device

Table 3. Relation of menstruation and breastfeeding at 6 weeks. Variables are presented as total number (percentage in group)

Menstruation

Parameter	Yes (n = 52)	No (n = 424)	P-value
Breastfeeding			
More than 4 in day	28 (6.9)	379 (93.1)	< 0.001 ^a
None or Less than 4 in day	24 (34.8)	45 (65.2)	

^aFisher's Exact Test

Table 4. Effect of menstruation, contraception and breastfeeding on presence of defect.

Estimated Odds Ratios (Subjects = 481)

Parameter	Value	OR ^b	P	95% CI for OR	
				Lower	Upper
Menstruation	Yes	1.453	0.026	1.046	2.018
	No ^a	1.000			
Contraception	Gestagen	0.607	0.031	0.386	0.954
	IUD or COC	0.535	0.073	0.270	1.059
	None ^a	1.000			
Breastfeeding	Yes	0.703	0.024	0.517	0.955
	No ^a	1.000			

^aReference category

^bReference category of dependent variable Scar Defect is No.

Only subjects with non-interrupted sequence of values are included in the model

CI — confidence interval; COC — combined oral contraceptive; IUD — intrauterine device

OR — odd ratio

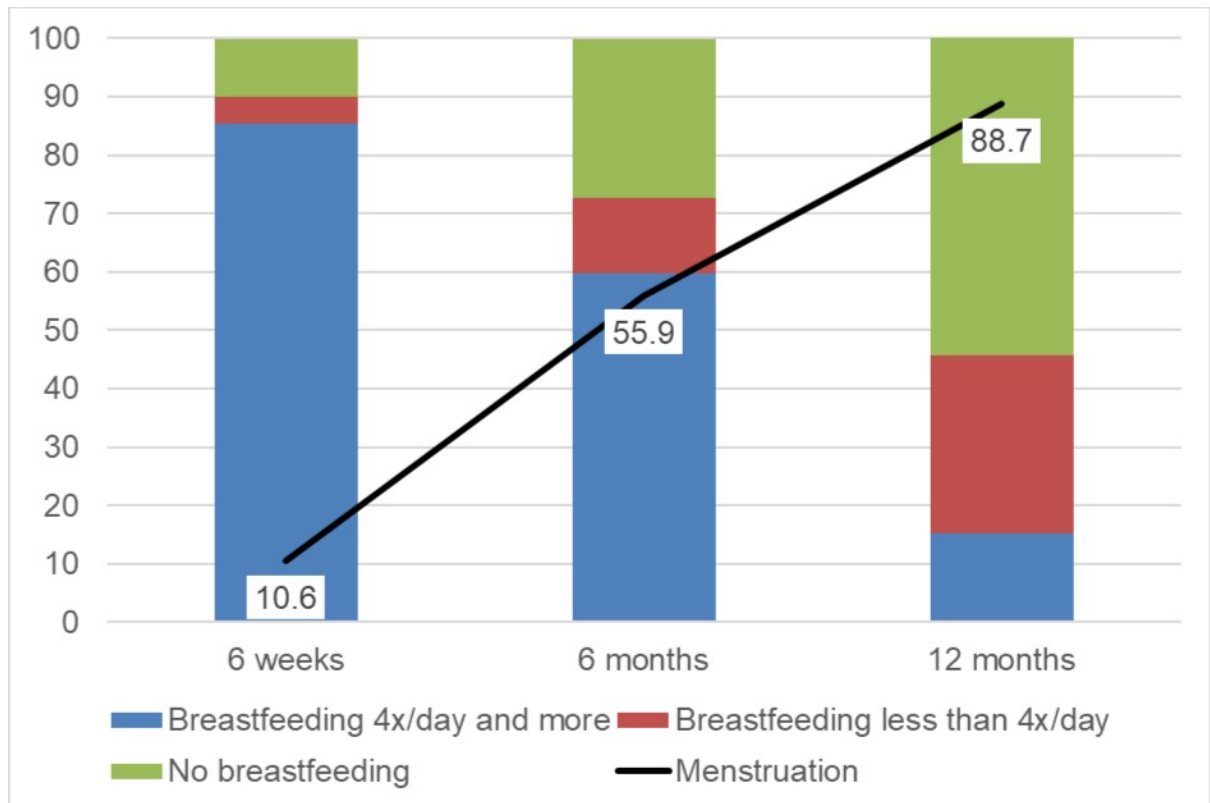


Figure 1. Frequency of breastfeeding and menstruation during follow up