European Journal of Obstetrics and Gynecology 286 (2023) 1–4

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

Use of labor analgesia in trials of labor after previous cesarean section: A nationwide register-based analysis in Finland

Matias Vaajala [a,*], Maiju Kekki [b,c], Ville M. Mattila [a,d], Ilari Kuitunen [e,f]

[a] Faculty of Medicine and Life Sciences, University of Tampere, Tampere, Finland
[b] Department of Obstetrics and Gynecology, Tampere University Hospital, Tampere, Finland
[c] Center for Child, Adolescent and Maternal Health Research, Faculty of Medicine and Health, Finland
[d] Department of Orthopaedics and Traumatology, Tampere University Hospital Tampere, Finland
[e] Department of Pediatrics, Kuopio University Hospital, Kuopio, Finland
[f] Institute of Clinical Medicine and Department of Pediatrics, University of Eastern Finland, Kuopio, Finland

ARTICLE INFO

Keywords:
Trial of labor after cesarean section
Labor analgesia
Obstetrics

ABSTRACT

Objectives: The literature concerning the overall use of labor analgesia among women with trials of labor after cesarean section (TOLAC) is lacking. The primary aim of this study is to report the rate of different labor analgesia methods among women with TOLAC. The secondary aim was to compare the use of labor analgesia between women with the first TOLAC and control group consisting of nulliparous women.

Study design.

Data from the National Medical Birth Register was used to evaluate the usage of labor analgesia in TOLACs. The use of labor analgesia in the first TOLAC is compared to the pregnancies of nulliparous women. The analgesia methods were stratified into neuraxial analgesia, pudendal, paracervical, nitrous oxide, other medical, other non-medical, and no analgesia. These are analyzed as categorized dichotomy (yes or no) variables.

Results: A total of 38 596 TOLACs as second pregnancy of the mother was found during our study period. The control group consisted of a total of 327 464 pregnancies of nulliparous women. Epidural analgesia (61.6% vs 67.1%), nitrous oxide (56.1% vs 62.0%), and non-medical analgesia (30.1% vs 35.0%) were less consumed among women with TOLAC. The rate of spinal analgesia was higher among women with TOLAC (10.1% vs 7.6%) when compared to the control group. However, when only vaginal deliveries were included, the rate of labor analgesia increased especially in the TOLAC group.

Conclusions: The main finding of this study is that women with TOLAC had a generally lower rate of labor analgesia. However, the rate of spinal analgesia was higher among women with TOLAC when compared to the control group, however. The results of this study inform midwives, obstetricians, and anesthesiologists on current practices and how to improve the analgetic treatment in TOLAC.

Introduction

Trial of labor after cesarean section (TOLAC) is an alternative to repeated cesarean sections (CSs), as multiple repeat CS are known to be risk factors for adverse events, such as uterine rupture and intra-operative complications [1]. The trend of increasing CS rates had evoked worldwide attention for both healthcare workers and the general population. Many studies have assessed the worldwide incidence of CS and it has been found to be increasing rapidly [2,3]. Despite the rapidly increasing incidence in many post-industrial societies, the rates of CS have remained low in Finland. According to the Finnish Institute for Health and Welfare (THL) [4], the overall proportion of CS during the last decades in Finland was approximately 16%.

The literature concerning the overall use of labor analgesia among women with TOLAC is lacking, as most of the studies are focusing only on the use of epidural analgesia and the maternal and fetal outcomes [5-8]. Epidural analgesia is considered generally safe [9], however, some studies report that women with epidural analgesia in TOLAC might have a higher risk for uterine rupture [8,10]. However, some studies did not find any evidence of increased risk for adverse maternal and neonatal outcomes after epidural analgesia [5-7]. In addition, it has been proposed the increased risk for uterine rupture seeing in some studies, may

* Corresponding author.
E-mail address: matias.vaajala@tuni.fi (M. Vaajala).

https://doi.org/10.1016/j.ejogrb.2023.04.023
Received 16 February 2023; Received in revised form 13 April 2023; Accepted 24 April 2023
Available online 26 April 2023

be due to underlying circumstances leading to the request for an epidural rather than epidural analgesia per se [11]. However, the use of another labor analgesia among women with TOLAC is incompletely reported in previous literature. Therefore, the primary aim of this study is to report the rate of different labor analgesia methods among women with TOLAC. The secondary aim was to compare the use of labor analgesia between women with the first TOLAC and control group consisting of nulliparous women. In addition, the rate of uterine rupture among women with an epidural in TOLAC was calculated.

Materials and methods

In this nationwide retrospective register-based cohort study, data from the National Medical Birth Register (MBR) was used to evaluate the usage of labor analgesia in TOLACs. The use of labor analgesia in the first TOLAC is compared to the pregnancies of nulliparous women. The MBR is maintained by the Finnish Institute for Health and Welfare, and more information about the register can be obtained from the official site of the Finnish Institute for Health and Welfare [4]. The study period was from January 1st, 2004 to December 31st, 2018.

The MBR contains information on pregnancies, delivery statistics, and the perinatal outcomes of all births with a birthweight of $\geq$ 500 g or a gestational age of $\geq 22^{+0}$ weeks. The MBR has high coverage and quality (the current coverage is nearly 100%) [12,13]. Using this dataset, we created two cohorts. The TOLAC cohort utilized the CS history of women, which included all women with one previous delivery, which was CS, and a second delivery being attempted vaginal delivery. The second cohort consisted of all nulliparous women having an attempted vaginal delivery. Therefore, we were able to analyze the effects of previous CS on the use of labor analgesia in cases, where the women have not delivered vaginally before. For labor analgesia analysis elective CS (n = 52 876), out-of-hospital deliveries (n = 2301), and non-singleton deliveries were excluded from the analysis. A total of 366 060 pregnancies were included in this study. Forming of the study groups is shown as a flowchart in Fig. 1.

Our main outcome was the use of labor analgesia. The analgesia methods were stratified into neuraxial analgesia (epidural, spinal, and combined), pudendal, paracervical, nitrous oxide, other medical (includes opiates), other non-medical (such as bath, aqua bubbles, and TENS) and no analgesia. These are analyzed as categorized dichotomy (yes or no) variables, as the register does not contain more precise information for example on the dosage used. The register only includes/gathers information on intrapartum analgesia used during the attempted vaginal delivery. Thus, analgesia used during CS is not included. One patient may have had none or many of these during labor. As some previous studies report that women with epidural analgesia in TOLAC might have a higher risk for uterine rupture [8,10], we also calculated the rate for uterine rupture among TOLACs with epidural analgesia. Women with uterine rupture are identified using an ICD-10-code O71.0 (Rupture of the uterus (spontaneous) before the onset of labor) and O71.1 (Rupture of the uterus during labor), which are routinely collected in the MBR. Continuous variables were reported as mean with standard deviation or as median with interquartile range based on the distribution of the data. Categorized variables were presented as absolute numbers and percentages. To compare groups, Student's *t*-test, Mann-Whitney *U* test, and Chi-squared tests were utilized. A p-value under 0.05 was considered statistically significant. In addition, as the risk for CS is higher among TOLACs, sensitivity analysis with only vaginal deliveries included was performed. We also calculated the rate for CS among women with epidural analgesia, when compared to women without epidural among women with TOLAC. The results of this study are reported according to the STROBE guidelines [14]. Statistical analysis was performed using R version 4.0.3.

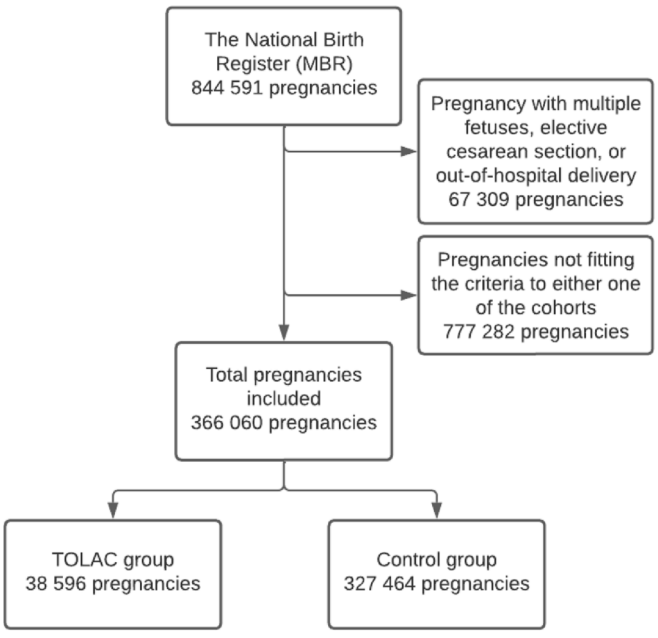

Fig. 1. Flowchart of the study groups. Trial of labor after cesarean section (TOLAC) was compared with the first pregnancy of a woman. Third or later pregnancies and second pregnancies without preceding CS were excluded from the analysis.

Ethics

The Ethical Committee of Tampere University Hospital waived the ethical committee evaluation of all retrospective studies utilizing routinely collected healthcare data and this decision is based on the law of medical research 488/1999 and the law of patient rights 785/1992. The MBR uses a pseudonymized identification number for each patient. The pseudonymization was done by the Finnish data authority Findata and the authors did not have access to the pseudonymization key. In accordance with Finnish regulations (The law of secondary use of routinely collected healthcare data 552/2019), no informed written consent was required because of the retrospective register-based study design and as the patients were not contacted. Permission for this data was granted by the Findata after the evaluation of the study protocol (Permission number: THL/1756/14.02.00/2020).

Results

A total of 38 596 TOLACs as second pregnancy of the mother was found during our study period. The control group consisted of a total of 327 464 pregnancies of nulliparous women. Women in the TOLAC group had a lower rate of smokers (11.1% vs 17.6%, $p < 0.001$) but were older than those in the control group. Women in the TOLAC group had a higher rate of diagnosed fear of childbirth (7.8% vs 1.9%, $p < 0.001$), gestational diabetes (16.4% vs 11.6%, $p < 0.001$), and urgent CS (28.2% vs 14.0%, $p < 0.001$), than women in the control group. Background information on the study groups is shown in Table 1.

Women in the TOLAC group had a lower rate of labor analgesia when compared to the control group consisting of nulliparous women. Especially, epidural analgesia (61.6% vs 67.1%, $p < 0.001$), nitrous oxide (56.1% vs 62.0%, $p < 0.001$), and non-medical analgesia (30.1% vs 35.0%, $p < 0.001$) were less consumed among women with TOLAC, when compared to the control group. The rate of spinal analgesia was higher among women with TOLAC (10.1% vs 7.6%, $p < 0.001$) when compared to the control group. Both groups had a low rate of women without labor analgesia (0.4% vs 0.2%). (Table 2).

In sensitivity analysis, where urgent CS and emergency CS were excluded, the rate of labor analgesia increased in both groups, but especially in the TOLAC group. The rate for all analgesia, except for

Table 1
Background information on patients. Trials of labor after cesarean section (TOLACs) were compared to the first pregnancy of a woman (control group) in Finland from 2004 to 2018.

	TOLAC group		Control group		
Total number of patients	38 596		327 464		
	n	%	n	%	p-value
Age (mean; sd)	31.1 (4.8)		27.8 (5.2)		< 0.001
Maternal smoking status					
smoker	4296	11.1	57 513	17.6	< 0.001
unknown	1658	4.3	7368	2.3	
Maternal BMI* (mean; sd)	25.4 (5.3)		24.0 (4.6)		< 0.001
BMI missing	407	1.1	14 653	4.5	
Diagnosed gestational diabetes	6318	16.4	38 097	11.6	< 0.001
Labor induction	10 273	26.6	75 699	23.1	< 0.001
Diagnosed fear of childbirth**	3000	7.8	6144	1.9	< 0.001
Mode of delivery					
assisted vaginal***	6059	15.7	56 666	17.3	< 0.001
urgent CS****	10 892	28.2	45 727	14.0	< 0.001
emergency CS	945	0.2	5307	0.2	< 0.001
Obstetric complications					
tear of perineum	815	2.1	5224	1.5	< 0.001
episiotomy	13 164	34.1	134 253	40.8	< 0.001

* BMI = Pre-pregnancy body mass index (Kg/m^2).
** Registered according to the International Classification of Diseases 10th revision code O99.80.
*** Includes vaginal breech delivery, vacuum, or forceps delivery.
**** CS = cesarean section.

Table 2
Use of labor analgesia in the trial of labor after cesarean section (TOLAC) and a control group consisting of first pregnancies in Finland from 2004 to 2018. Values are numbers (proportion).

	TOLAC group	Control group	
Total number of patients	38 596	327 464	
	n (%)	n (%)	p-value
Labor analgesia			
epidural	23 775 (61.6)	219 822 (67.1)	< 0.001
spinal	3889 (10.1)	25 021 (7.6)	< 0.001
combined spinal-epidural	1049 (2.7)	7797 (2.4)	< 0.001
paracervical block	4404 (11.4)	38 963 (11.9)	0.003
pudendal block	3492 (9.0)	31 807 (9.7)	< 0.001
nitrous oxide	21 669 (56.1)	202 897 (62.0)	< 0.001
other medical analgesia	7201 (18.7)	59 987 (18.3)	0.157
non-medical analgesia	11 602 (30.1)	114 653 (35.0)	< 0.001
no analgesia	146 (0.4)	746 (0.2)	< 0.001

nitrous oxide and non-medical analgesia was higher among women with TOLAC. (Table 3).

Among women with TOLAC, epidural analgesia was associated with a lower rate of uterine rupture. Among women with epidural analgesia in TOLAC, a total of 214 women had uterine rupture (0.9%). Among women without epidural analgesia in TOLAC, a total of 213 women had uterine rupture (1.4%) ($p < 0.001$). Also, among women with TOLAC, the rate for urgent CS (45.1% vs 17.7%, $p < 0.001$), and emergency CS (3.8% vs 1.6%, $p < 0.001$) was higher among women without epidural analgesia, when compared to women with epidural analgesia. (Table 4).

Table 3
Sensitivity analyses with only successful vaginal deliveries included. Use of labor analgesia in the trial of labor after cesarean section (TOLAC) and a control group consisting of first pregnancies in Finland from 2004 to 2018. Values are numbers (proportion).

	TOLAC group	Control group	
Total number of patients	26 741	276 417	
	n (%)	n (%)	p-value
Labor analgesia			
epidural	19 178 (71.7)	197 169 (71.3)	0.210
spinal	3010 (11.3)	21 474 (7.8)	< 0.001
combined spinal-epidural	924 (3.5)	7219 (2.6)	< 0.001
paracervical block	3522 (13.2)	34 836 (12.6)	0.011
pudendal block	3153 (11.8)	29 684 (10.7)	< 0.001
nitrous oxide	16 810 (62.9)	178 676 (64.6)	< 0.001
other medical analgesia	5332 (19.9)	51 239 (18.5)	< 0.001
non-medical analgesia	8970 (33.5)	101 276 (36.4)	< 0.001
no analgesia	16 (0.1)	252 (0.1)	0.118

Table 4
Women with a trial of labor after cesarean section (TOLAC) were divided into two groups based on the use of epidural analgesia. The rate for modes of delivery and uterine rupture was reported. Values are numbers (proportion).

	Women with epidural	Women without epidural	
Total number of patients	23 775	14 821	
	n (%)	n (%)	p-value
Mode of delivery			
assisted vaginal*	4630 (19.5)	1439 (9.7)	< 0.001
urgent CS**	4214 (17.7)	6678 (45.1)	< 0.001
emergency CS	376 (1.6)	569 (3.8)	< 0.001
Uterine rupture	214 (0.9)	213 (1.4)	< 0.001

* Includes vaginal breech delivery, vacuum, or forceps delivery.
** CS = cesarean section.

Discussion

The main finding of this study women with TOLAC had generally lower rates of labor analgesia. Especially epidural analgesia, nitrous oxide, and non-medical analgesia were lower among women with TOLAC. The rate of spinal analgesia was higher among women with TOLAC when compared to the control group, however. When only vaginal deliveries were included, the rate of neuraxial analgesia increased among the TOLAC group, but the overall rate of labor analgesia was similar to that in the control group. In addition, the rate of uterine rupture was not higher among women with epidural in TOLAC.

The use of labor analgesia was less frequent among women with TOLAC. However, the notably higher rate for urgent CS, leading to less time to use different methods of labor analgesia, is most likely explaining a part of the lower labor analgesia rate in the TOLAC group. In sensitivity analyses with CS excluded, the rate of labor analgesia increased markedly in the TOLAC group. In previous literature, it has been found that epidural analgesia is associated with a remarkably higher success rate of vaginal birth after cesarean section [6]. Our results might support this finding, as labor analgesia increased markedly in vaginal deliveries. However, there are also contradictory results about the safety of epidural analgesia among women with TOLAC [5,6,7,8,10]. Some studies report that women with epidural analgesia in TOLAC have a higher risk for uterine rupture [8,10]. However, the effect of these findings of previous literature on the rate of labor analgesia is most likely low. In addition, our study did not find any higher rate of uterine rupture among women with epidural analgesia in TOLAC. Epidural analgesia is generally considered safe and also women with previous CS

are encouraged to use pain relief during labor. The use of labor analgesia might partly be explained by some of the background characteristics of the women in the study groups. There are recently published studies, that have found increased use of labor analgesia in certain study groups. E.g., higher BMI, gestational diabetes, and fear of childbirth, which are found to be more common in the TOLAC group, are known to be associated with increased use of labor analgesia [15-17]. In addition, other confounding factors, not reliably registered in the MBR, such as duration of labor may explain the lower rate of labor analgesia.

Interestingly, the rate for spinal analgesia was higher among women with TOLAC, which is a markable finding, as the rate for other labor analgesia was lower. There is no previous literature about the use of spinal analgesia among women attempting TOLAC. However, the exact reason for this remains unknown and this topic should be further studied. It remains unknown whether the spinal analgesia was used for CS or other reasons, as the indications and timing of this are not recorded in the register. However, when only vaginal deliveries were included, the use of spinal analgesia was still higher among women with TOLAC, indicating that the use of spinal analgesia was more common generally among women with TOLAC. These results should raise awareness of the use of pain relief among women with previous CS. In addition, as the rates of CS, and therefore the rate for TOLACs are currently rapidly increasing [3], studies assessing this topic are warranted. The results of this study should be acknowledged by the clinician and anesthesiologists to improve satisfaction levels and to provide optimal treatment for mothers with TOLAC.

The main strength of the present study is the nationwide register coverage including practically all deliveries in Finland and the high validity and precision of the register [13]. The main limitation is the lack of data on attempted analgesia methods. For example, some parts of the slightly lower epidural rate and higher spinal analgesia rate in the TOLAC group could be due to unsuccessful attempts at epidural analgesia, as only successful analgesia methods are reported to the register. Another limitation is that the register does not have information on analgesic doses and therefore possible differences between the two groups remain unknown. Furthermore, the register only gathers information on intrapartum analgesia; hence, we have not analyzed postpartum analgesia. In addition, as we are using data from a nationwide register, the register does not observe regional differences in Finland. In addition, we have no information on the total duration of the delivery, the timing of the labor analgesia, or indications for CS as these are not reported to the register.

Conclusion

The main finding of this study is that women with TOLAC had a generally lower rate of labor analgesia. Especially epidural analgesia, nitrous oxide, and non-medical analgesia were lower among women with TOLAC. The rate of spinal analgesia was higher among women with TOLAC when compared to the control group, however. When only vaginal deliveries were included, the rate of labor analgesia, except for nitrous oxide and non-medical analgesia became higher in the TOLAC group. The results of this study inform midwives, obstetricians, and anesthesiologists on current practices and how to improve the analgetic treatment in TOLAC.

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.

Reference

[1] Gasim T, Al Jama FE, Rahman MS, Rahman J. Multiple repeat cesarean sections: operative difficulties, maternal complications and outcome. J Reprod Med 2013;58 (7–8):312–8.
[2] Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. *PloS One*. 2016;11(2):e0148343. doi:10.1371/journal.pone.0148343 [doi].
[3] Niino Y. The increasing cesarean rate globally and what we can do about it. Biosci Trends 2011;5(4):139–50. https://doi.org/10.5582/bst.2011.v5.4.139.
[4] Thl. Perinatal statistics - parturients, delivers and newborns - THL. Published 2018. https://thl.fi/en/web/thlfi-en/statistics-and-data/data-and-services/register-descriptions/newborns.
[5] Grisaru-Granovsky S, Bas-Lando M, Drukker L, Haouzi F, Farkash R, Samueloff A, et al. Epidural analgesia at trial of labor after cesarean (TOLAC): a significant adjunct to successful vaginal birth after cesarean (VBAC). J Perinat Med 2018;46 (3):261–9.
[6] Sun J, Yan X, Yuan A, Huang X, Xiao Y, Zou L, et al. Effect of epidural analgesia in trial of labor after cesarean on maternal and neonatal outcomes in China: a multicenter, prospective cohort study. BMC Pregnancy Childbirth 2019;19(1). https://doi.org/10.1186/s12884-019-2648-1.
[7] Aleksandrovich BK, Munevich SE, Alekseevna GT, Vladimirovna BM, Sharma K, Gupta S. Impact of labor epidural analgesia on maternal and neonatal outcomes with trial of labor in previous caesarean delivery: A prospective, controlled, longitudinal study. J Obstet Anaesth Crit Care 2020;10(2):123. https://doi.org/10.4103/joacc.JOACC_45_20.
[8] Studsgaard A, Skorstengaard M, Glavind J, Hvidman L, Uldbjerg N. Trial of labor compared to repeat cesarean section in women with no other risk factors than a prior cesarean delivery. Acta Obstet Gynecol Scand 2013;92(11):1256–63. https://doi.org/10.1111/aogs.12240.
[9] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 209: Obstetric Analgesia and Anesthesia. *Obstet Gynecol*. 2019;133(3):e208-e225. doi:10.1097/AOG.0000000000003132.
[10] Barger MK, Weiss J, Nannini A, Werler M, Heeren T, Stubblefield PG. Risk factors for uterine rupture among women who attempt a vaginal birth after a previous cesarean: a case-control study. J Reprod Med 2011;56(7–8):313–20.
[11] Thisted DLA, Mortensen LH, Krebs L. Uterine rupture without previous caesarean delivery: a population-based cohort study. Eur J Obstet Gynecol Reprod Biol 2015; 195:151–5. https://doi.org/10.1016/j.ejogrb.2015.10.013.
[12] Gissler M, Teperi J, Hemminki E, Meriläinen J. Data quality after restructuring a national medical registry. Scand J Soc Med 1995;23(1):75–80. https://doi.org/10.1177/140349489502300113 [doi].
[13] Gissler M, Shelley J. Quality of data on subsequent events in a routine Medical Birth Register. *Med Inform Internet Med*. 2002;27(1):33-38. doi: 0UB69R4X61VDGCDA [pii].
[14] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61 (4):344–9.
[15] Kuitunen I, Kekki M, Ponkilainen V, Huttunen T. Labor analgesia in obese and morbidly obese parturients: A nationwide register analysis in Finland From 2004 to 2018. Obstet Anesth Dig 2023;43(1):40. https://doi.org/10.1097/01.aoa.0000912372.35322.e1.
[16] Kuitunen I, Vähä-Tuisku S, Huttunen T. Gestational diabetes mellitus and labor analgesia: nationwide register-based analysis in Finland. *Acta Diabetol*. Published online August 2, 2022. doi:10.1007/s00592-022-01944-6.
[17] Fear of childbirth and use of labor analgesia: A nationwide register-based analysis in Finland - Vaajala - International Journal of Gynecology & Obstetrics - Wiley Online Library. Accessed April 11, 2023. https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/ijgo.14781.