Labor neuraxial analgesia and breastfeeding: An updated systematic review

Philip Heesen[1*], Stephen H. Halpern[2], Yaakov Beilin[3], Paola A. Mauri[4], Leonid A. Eidelman[5], Michael Heesen[6] and Sharon Orbach-Zinger[5]

[1]University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland. heesenphilip99@gmail.com
[2]Department of Anesthesia, University of Toronto and Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
[3]Department of Anesthesiology, Perioperative and Pain Medicine, and Obstetrics, Gynecology and Reproductive Sciences, Icahn School of Medicine at Mount Sinai, New York, USA
[4]School of Midwifery, Department of Clinical Sciences and Community Health, Università degli Studi di Milano
[4]Department of mother child and newborn health, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
[5]Department of Anesthesia, Rabin Medical Center, Beilinson Hospital, Petach Tikvah, Israel
[6]Department of Anesthesia, Kantonsspital Baden, Baden, Switzerland

Correspondence to: Philip Heesen, heesenphilip99@gmail.com; Faculty of Medicine, University of Zurich, Winterthurerstrasse 190, 8057 Zurich, Switzerland
[6]Department of Anesthesia, Kantonsspital Baden, Baden, Switzerland

Abstract

Background: Breast milk is the ideal nutrient for the newborn. There have been numerous studies performed to determine the effect of neuraxial labour analgesia on breastfeeding success, but the results are not consistent.

Methods: We performed a systematic review by searching Medline, EPub, embase.com (Embase plus Medline), Cochrane Central, Web of Science, Google scholar for studies that compared neuraxial analgesia to other forms or no labour analgesia. Where possible, the results were combined using random effects meta-analytic techniques. The outcomes were percentage of women who were able to breastfeed immediately postpartum, women who were breastfeeding within the first three days after delivery and women who were breastfeeding at 2 to 12 weeks postpartum. Where possible, nulliparous parturients were analysed separately. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. If the p-value was below 0.05, the effect was considered statistically significant.

Results: We included 16 studies with 20,805 mother-baby dyads. In low risk of bias studies, neuraxial analgesia had a negative effect on breastfeeding immediately postpartum, OR 0.91 (95% CI; 0.88 - 0.95, I^2=1%, p=0.39). We also found a decreased incidencein short term breastfeeding in the neuraxial group, OR 0.63 (95% CI, 0.47 - 0.85, I^2=71%, p=0.0002). There was no significant difference in the incidence of continued breast feeding between groups, OR 0.94 (95% CI, 0.86 - 1.03, I^2= 81%, p<0.0001).
There was no statistically significant difference in the incidence of breastfeeding success at any time point when nulliparous parturients were considered separately. Short-term analysis resulted in OR 0.62 (95% CI, 0.31 - 1.22, I^2=78%, p=0.001) and continued breastfeeding analysis resulted in OR 0.86 (95% CI, 0.51 - 1.46, I^2=77%, p=0.002).

Conculsion: When looking at a mixed-parity population we found a significant reduction of breastfeeding in the neuraxial analgesia group of 9% immediately postpartum and of 37% in the short-term. Intrapartum labour analgesia does not seem to play an important role in long term breastfeeding success. Confounding factors that influence choice of analgesia, such as parity and social factors may also influence the choice to breastfeed. Education programs and accessible breastfeeding support are likely more important than intrapartum labour analgesia in determining long term breastfeeding success.

Introduction

The World Health Organization advises initiating breastfeeding within the first hour of birth and continuing for at least six months.1 Breast milk is considered the ideal food for the newborn, containing both nutrients

and antibodies, thus protecting infants from diarrhea and pneumonia, the two main causes of child mortality worldwide.1 Infants that are breastfed have a lower chance of developing sudden infant death syndrome, respiratory infections, asthma, type I and II diabetes and leukemia.2 Adults that were breastfed as infants have been shown to be less obese and have higher IQ scores.3

For the mother, breastfeeding has many advantages. Early breastfeeding leads to increased uterine contraction and decreased postpartum hemorrhage.4 Breastfeeding has been shown to accelerate the return to the mother's pregestational weight and is associated with a decreased risk of developing postpartum depression.5 Long term beneficial effects of breastfeeding for the mother are decreased chances of developing type II diabetes and both ovarian and breast cancer.2

Neuraxial analgesia (NA) is the analgesia of choice for women in labor. In the United States, 73% of all deliveries are done using NA.6 However, some studies have shown that NA leads to a lower incidence of breastfeeding postpartum.7,8 In a large prospective observational study, women who received NA had a reduced likelihood of breastfeeding when compared with their counterparts who had not received NA.9 In contrast, in two other studies there was no effect of NA on breastfeeding success at 6-8 weeks.12,13

30 In order to resolve this discrepancy, we set out to gather all available evidence by performing a systematic literature search of studies that looked at the effect of NA versus non-NA or no analgesia on breastfeeding.

Breastfeeding was defined as a binary variable (breastfeeding success yes/no) where any breastfeeding was considered breastfeeding success. We looked at three time stages: immediate (≤ 3 hours), early (>3 and ≤72 hours) and continued breastfeeding (2 to 12 weeks). The retrieved data were analysed and we then conducted a meta-analysis with sensitivity analysis as well as a subgroup analysis only including nulliparous women.

Methods

Our study conforms with the Preferred Reporting Items for Systematic and Meta-Analyses (PRISMA) statement.12 We conducted a systematic literature search in the following databases: Medline, EPub, embase.com (Embase plus Medline), Cochrane Central, Web of Science, Google scholar (until 27.09.2019). Details of the search strategy are given in the online supplement [ref]. Figure 1 shows a flow chart of the literature search.

The articles found were then entered into endnote X9 (Clarivate Analytics, Jersey) which was further used for de-duplication. The bibliography of the retrieved articles was also hand searched to identify additional references. Language restrictions were English, French, German, Hebrew. In addition, we contacted authors

of retrieved manuscripts for additional data.

The PICO format was used to develop our search strategy: P: women intending to undergo vaginal delivery and that had the intervention (I) of NA (either epidural analgesia (EA) or a combined spinal-epidural analgesia (CSE)). Our comparison (C) group included parturients having either non-neuraxial analgesia (neither CSE nor EA) or no analgesia at all. The primary outcome (O) was defined as any breastfeeding success at three different time stages: immediate (≤ 3 hours), short term (>3 and ≤72 hours) and continued breastfeeding (2 to 12 weeks) and as a dichotomous variable (yes or no breastfeeding). Breastfeeding success was measured as a binary variable (yes/no) at each of the three time points postpartum. For immediate breastfeeding in analysed manuscripts breastfeeding was assessed either via initiation of breastfeeding (yes/no) or using the Infant Breastfeeding Assessment Tool (IBFAT) with a score ≥ 10 as an indication of breastfeeding.10 The IBFAT tool allows for a maximum score of 12, with three points in each of the four categories that evaluate sucking-, feeding and rooting- patterns as well as the time it took from placing the baby on the mother's breast to latch and suck.

Short term breastfeeding in the manuscripts included were assessed by one of three methods according to outcome measurements of individual authors: The first method was presence of breastfeeding (yes/no). The second method that used was via the LATCH score with a LATCH score of ≥7 out of 10 and 2/2 on the latch component was considered breastfeeding.11 The third method used was via the LATCH score only looking at the L, A and C-components with a score of 6/6 considered breastfeeding.

The LATCH score assesses individual breastfeeding sessions and looks at the following components: L: latching, A: amount of audible swallows, T: mother's nipple type, C: mother's level of comfort, H: amount of help the mother needs to hold her infant to the breast.

For continued breastfeeding, breastfeeding was only assessed via a binary variable (yes/no).

The reporting quality of all of the observational studies considered eligible was assessed using the ROBINS-I

tool.15
Two researchers (SOZ, PH) independently screened the articles retrieved from the literature search for eligibility and three researchers (SOZ, PH, SH) independently performed the quality assessment and extraction of data and then compared. Disagreement was determined by consensus or by assessment by a third investigator (SH, MH). These reviewers did not judge their own studies, but a third reviewer was involved (SH and PH for SOZ).
The retrieved data were then entered into a RevMan file (Review Manager Version 5.3. Copenhagen: The Nordic Cochrane Centre, 2014). We calculated the odds ratio (OR) and the 95% confidence interval (95% CI) using the random-effects model. The I2 value assessed heterogeneity. P-values < 0.05 were considered as indicator of statistical significance.
After performing a meta-analysis on the above mentioned PICO, we conducted a subgroup analysis only including nulliparous women. We performed this analysis for short-term and continued breastfeeding. Not enough data for looking at immediate breastfeeding in the nulliparous-only group or for performing a second subgroup analysis only including multiparous women were available.
We performed a sensitivity analysis excluding the studies considered to have a critical risk of bias according to the ROBINS-I tool.15

Results

We have included 16 studies with 20,805 participants that fit our inclusion criteria. Fourteen studies were observational studies, one study was a secondary analysis of a randomized controlled trial and one study was a case-control study.16,17 Study details are presented in Table 1, the risk of bias assessment of each study is presented in Table 2. We found one study with a critical risk of bias, ten studies with a serious risk of bias, four studies with a moderate risk of bias, and one study with a low risk of bias.
Since only Mahomed et al gave numbers of adjusted odds ratios, we did not perform calculations that combined adjusted (for the articles that reported adjusted ORs) and unadjusted odds ratios.
57 Immediate breastfeeding
We analysed five studies looking at a total of 4,392 patients.14,18-21 Of these studies, in terms of risk of bias
one was rated low16, three were rated serious 18,19,21, and one was critical.20 Four articles 16,18-20 defined
breastfeeding as a binary variable (yes/no). One article used the IBFAT score ≥ 10 as an indication ofbreastfeeding.21 In the NA group three studies 18,19,21 used epidural analgesia only. One study used either a CSE or EA16 and in one study there were no details given20. Four studies 18,19,20,21 used fentanyl in their
neuraxial solution and in one study some parturients received fentanyl and others did not 16, and in one study there were no details given.20 In the control groups, in one study no analgesia was administered 18, in
one study women received either 50% nitrous oxide (Entonox ®) or no analgesia 21, in one study women received either meperidine, 50% nitrous oxide (Entonox ®), transcutaneous electrical nerve stimulation or no analgesia. 16 Two studies gave no details. 19,20
Three studies assessed immediate breastfeeding at 2 hours 16,18,19, one study at 3 hours 20 and one study
only stated that the measurement was conducted postpartum. 21
Our meta-analysis including all studies showed no difference between NA and non-NA, OR 0.94 (95% CI; 0.89 - 1.00; I2=44%, p=0.13). After performing a sensitivity analysis by removing a study with a critical risk of
13 bias [19], we found a significantly lower incidence of breastfeeding in the NA group, OR 0.91 (95% CI; 0.88 -
14 0.95, I2=1%, p=0.39).

Short-term breastfeeding

A total of 12 studies were analysed with 12,721 parturients. 8,9,12,16,17,20,22-27 Of these studies, one was found
to have a low risk of bias16, three were found to have a moderate risk of bias 8,9,22, seven were found to have a serious risk of bias 12,17,22-24,26,27, and one was rated critical.20
Ten studies used a binary variable (yes/no) to examine breastfeeding.8,12,16,17,20,22,25-27 One study

used the L,
A and C component of the LATCH score with a composite score of 6/6 considered positive for breastfeeding.24 One study considered 7/10 on the LATCH score with 2/2 on the latch component as breastfeeding.23
Ten studies 8,17,20,22,25-27 used EA only and two studies used either CSE or EA for NA.8,16 Two studies administered fentanyl in their neuraxial solution9,26, two studies administered sufentanil8,12, in one study some patients received fentanyl and others did not16, the other studies gave no details about the opioids given 17,20,22-25,27. Eight studies used no analgesia as control group.8,9,17,20,22,24,25,27 One study used either
meperidine, 50% nitrous oxide (Entonox ®), transcutaneous electrical nerve stimulation or no analgesia16; one study 26used either subcutaneous morphine or no analgesia, and in two studies there were no details 34 given.12,23
One study assessed breastfeeding at 8 to 12 hours postpartum 24, one study at 24 hours postpartum 22, one
study at 24 to 48 hours postpartum 16, two studies at 48 to 72 hours postpartum 23,27, three studies at hospital discharge (days not given) 8,17,26, one study at 24 hours postpartum 20, and three studies at three
39 days postpartum.9,12,25
In short-term breastfeeding, we found a significantly lower incidence of breastfeeding in the NA group, OR 0.64 (95% CI, 0.48 - 0.85, I2=68%, p=0.0004). After removing the study that had a critical risk of bias [20], there was still a lower incidence of breastfeeding in the NA group, OR 0.63 (95% CI, 0.47 - 0.85, I2=71%, p=0.0002).

Continued breastfeeding
We looked at nine studies with 3692 participants.7,9,12,20-22,24-26
Three studies were rated as moderate risk of bias 7,9,22, five studies 12,21,23,25 as serious and one study as
critical.20 All studies measured breastfeeding as a binary variable (yes/no).
In eight studies neuraxial analgesia was done with EA only.9,10,22-22,24-26 In one study neuraxial analgesia was
done with CSE.7 In five studies neuraxial solution contained fentanyl.7,9,21,24,26 In two studies sufentanil was
used for neuraxial solution.12,22 In two studies, no details about NA solution were given.20,25 Five studies used no analgesia as control group.9,12,20,22,24 One study used nitrous oxide (Entonox ®) or no analgesia as
control.21 One study used morphine or no analgesia as control group.26 One study used meperidine, nitrous
oxide (Entonox ®) or no analgesia as control.7 One study gave no details.25 One study assessed breastfeeding at 20 days postpartum 22, four studies at four weeks postpartum 20,21,24,25, three studies 89,12,26
at six weeks postpartum and one study at two months postpartum.7In long-term breastfeeding, we found no significant effect of neuraxial analgesia on breastfeeding, OR 0.97 (95% CI, 0.90 - 1.05, I2=84%, p<0.00001). After conducting a sensitivity analysis, there was still no significant effect, OR 0.94 (95% CI, 0.86 - 1.03, I2= 81%, p<0.0001).

Subgroup analysis: nulliparous
We performed a subgroup analysis only including nulliparous women.
When looking at short-term breastfeeding, we included five studies with 2464 parturients.9,12,16,22,26 Three studies defined nulliparity as an inclusion criterium12,16,26, two studies divided their sample into nulliparous and multiparous women.9,22 None of the studies included were rated to have a critical risk of bias.
This analysis resulted in no significant effect of NA on short-term breastfeeding, OR 0.62 (95% CI, 0.31 -
17 1.22, I2=78%, p=0.001).
For our analysis of long-term breastfeeding, we found five studies with 1803 participants.7,9,12,22,26 In three
studies7,12,26 nulliparity was an inclusion criterium and two studies divided their sample into a nulliparous

and multiparous group.9,22 None of the studies included had a critical risk of bias.
In our subgroup analysis, we found no significant effect of NA on breastfeeding, OR 0.86 (95% CI, 0.51 - 1.46, I2=77%, p=0.002).

Discussion

This is the first meta-analysis that assesses the effect of NA on breastfeeding outcomes at different time points postpartum and in different populations.
In the mixed-parity populations, looking only at high quality studies, we found a negative association between NA and breastfeeding immediately postpartum and in the short-term, but not for continued breastfeeding. The likelihood for breastfeeding was reduced by 9 % in the lower risk of bias studies of the immediate postpartum period and by 37% in the short term period when including only high quality studies. In the nulliparous population, there was no difference found between breastfeeding outcomes at any time points.
There are many possible reasons for the reduced breastfeeding rates in the mixed-parity population. Often, NA is used for very exhausting and difficult labours after which parturients may be very tired and thus choose to delay onset of breastfeeding.28 Women who needed NA may have received more exogenous oxytocin and may have had a higher rate of instrumental delivery.9 Both these factors have been shown to decrease rates of breastfeeding.9 Women who chose to deliver without neuraxial analgesia may have been more eager to breastfeed earlier on.
49 Previous authors have suggested that epidural fentanyl may have a role in decreased breastfeeding success.29 We had hypothesized that the effect of NA fentanyl has an effect on immediate and short-term breastfeeding, but will fade over time. However, the fact that breastfeeding rates in nulliparous women were not different disputes this finding and confirms the result by Lee et al that epidural fentanyl is not a factor in breastfeeding success.30
In an earlier study researchers found an effect of early breastfeeding initiation on continued breastfeeding. It was found that immediate breastfeeding initiation leads to longer duration of breastfeeding.31 Another study did not find this effect.32 In our analysis we did not find an effect of immediate breastfeeding onset on continued breastfeeding.
The strengths of our meta-analysis are the large number of studies, the different time-points analysed, the meticulous examination of risk of bias, the conduction of a sensitivity analysis and a subgroup analysis.
The limitations include possibility of having missed an article in our literature searches when the term breastfeeding was not mentioned in the title or abstract of a study. However, because we used multiple search engines and hand-searched the references, we believe that we have corrected this. The second limitation is the heterogeneity in the quality of the studies. Breastfeeding success is determined by many influences including pre-pregnancy, intrapartum and postpartum factors. Many studies have not controlled for important confounders including previous breastfeeding experience 19,20,23, immediate skin to skin placement 7,12,24 or lactation-friendly hospitals 8,16,21 or maternity-leave after labour.17,26,27 Furthermore, there is no consistency in breastfeeding education and support available in all hospitals.33,34 We were unable to do a subgroup-analysis of multiparous-only women because there were not enough
13 data available.
In conclusion, including only studies of high quality, our analysis showed that NA led to a 9% lower incidence of breastfeeding immediately after birth and to a 37% lower incidence up to three days postpartum in the mixed-parity group, but had no effect on continued breastfeeding. Neuraxial analgesia was not associated with a decreased rate of either short-term or continued breastfeeding in the nulliparous-only group.
We believe that intrapartum labour analgesia does not play a great role in continued breastfeeding success, but rather that good breastfeeding education programs and accessible breastfeeding support determine the success of continued breastfeeding.
Moreover, we believe that neuraxial analgesia for labor should not be avoided out of fear of a strong impact on continued breastfeeding success.

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Competing interests

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References

1. World Health Organization (WHO). 10 facts on breastfeeding, 2017. https://www.who.int/features/factfiles/breastfeeding/en (accessed on 02/15/2020)
2. Ip S, Chung M, Raman G, Trikalinos TA, Lau J. A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries. Breastfeeding Med 2009;4:17-30.
3. Isaacs EB, Fischl BR, Quinn BT, Chong WK, Gaian DG, Lucas A. Impact of breast milk on IQ, brain size and white matter development. Pediatr Res 2011;67:357-62.
4. Del Ciampo LA, Del Ciampo IRL. Breastfeeding and the benefits of lactation for women's health. Rev Bras Ginecol Obstet 2018;40:354-9.
5. Reifsnider E, Flowers J, Todd M, Babendure JB, Moramarco M. The Relationship Between Breastfeeding, Postpartum Depression, and Postpartum Weight in Mexican American Women. J Obstet Gynecol Neonatal Nurs 2016;45:760-71.
6. Butwick AJ, Bentley J, Wong CA. United States State-Level Variation in the Use of Neuraxial Analgesia During Labor for Pregnant Women. JAMA Netw Open 2018;1:e186567.
7. Henderson JJ, Dickinson JE, Evans SF, McDonald SJ, Paech MJ. Impact of intrapartum epidural analgesia on breast-feeding duration. Aust N Z J Obstet Gynaecol 2003;43:372-7.
8. Wetzl RG, Delfino E, Peano L et al. A priori choice of neuraxial labour analgesia and breastfeeding initiation success: a community-based cohort study in an Italian baby-friendly hospital. BMJ Open 2019;
9. Orbach-Zinger S, Landau R, Davis A et al. The effect of labor epidural analgesia on breastfeeding outcomes: a prospective observational cohort study in a mixed-parity cohort. Anesth Analg 2019;129:784-91.
10. Matthews MK. Developing an instrument to assess infant breastfeeding behaviour in the early neonatal period. Midwifery 1988;4:154-65.
11. Jensen D, Wallace S, Kelsay P. LATCH: a breastfeeding charting system and documentation tool. J Obstet Gynecol Neonatal Nurs 1994;23:27-32.
12. Ding T, Wang D, Qu Y, Chen Q, Zhu S. Epidural labor analgesia is associated with a decreased risk of postpartum depression: a prospective cohort study. Anesth Analg 2014;119:383-92.
13. Halpern SH, Levine T, Wilson DB, MacDonell J, Katsiris SE, Leighton BL. Effect of labor analgesia on breastfeeding success. Birth 1999;26:83-8.
14. BMJ (OPEN ACCESS) Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. BMJ 2009; 339:b2535,doi 10.1136/bmj.b2535.
15. Robbins: Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non- randomised studies of interventions. BMJ 2016;355:i4919.
16. Wilson MJ, MacArthur C, Cooper GM, Bick D, Moore PAS, Shennan A. Epidural analgesia and breastfeeding: a randomised controlled trial of epidural techniques with and without fentanyl and a non-epidural comparison group. Anaethesia 2010;65:145-53.
17. Armani M, Gaggiano C, Dallaglio S, Romanini E, Sospiri C, Magnani C: Are there any strategies to improve neonatal outcomes associated with epidural analgesia in labor?. Acta BioMedica 2013;84:117- 18. Gizzo S, Gangi SD, Saccardi C et al. Epidural analgesia during labor: impact on delivery outcome, neonatal well-being, and early breastfeeding. Breastfeeding Med 2012;7:262-8.
19. Herrera-Gomez A, Garcia-Martinez O, Ramos-Torrecillas J, De Luna-Bertos E, Ruiz C, Ocana-Peinado FM. Retrospective study of the association between epidural analgesia during labour and complications for the newborn. Midwifery 2015;31:613-6.
20. Mahmoodi F, Noroozi M, Adineh Mehr L, Beigi M. Breastfeeding and its outcome in women receiving epidural analgesia for childbirth. Iran J Nurs Midwifery Res 2019;24:355-9.
21. Reid SJ, Ly D. Does ultra-low dose epidural analgesia influence early breastfeeding?. Anesthesiology 2001;94,No1A.
22. Mauri PA, Guerrini Contini NN, Giliberti S, Barretta F, Consonni D, Negri M, Di Benedetto I. Intrapartum epidural analgesia and onset of lactation: a prospective study in an Italian birth centre. Matern Child Health J 2015;19:511-8.
23. Baumgarder DJ, Muehl P, Fischer M, Pribbenow B. Effect of labor epidural anesthesia on breast-feeding of healthy full-term newborns delivered vaginally. J Am Board Fam Med 2003;16:7-13.
24. Chang ZM, Heaman MI. Epidural analgesia during labor and delivery: effects on the initiation and continuation of effective breastfeeding. J Hum Lact 2005;21:305-14.
25. Dozier AM, Howard CR, Brownell EA et al. Labor epidural anesthesia, obstetric factors and breastfeeding cessation. Matern Child Health J 2013;17:689-98.
26. Mahomed K, Wild K, Brown C, Green A. Does fentanyl epidural analgesia affect breastfeeding: a prospective cohort study. Aust N Z J Obstet Gynaecol 2019;59:819-24.
27. Zuppa AA, Alighieri G, Riccardi R, Cavani M, Iafisco A, Cota F, Romagnoli C. Epidural analgesia, neonatal care and breastfeeding. Ital J Pediatr 2014;40:82.

28. Shmueli A, Salman L, Orbach-Zinger S, Aviram A, Hiersch L, Chen R, Gabbay-Benziv R. The impact of epidural analgesia on the duration of the second stage of labor. Birth 2018;45:377-84.
29. Beilin Y, Bodian CA, Weiser J et al. Effect of labor epidural analgesia with and without fentanyl on infant breast-feeding. Anesthesiology 2005;103:1211-7.
30. Lee AI, McCarthy RJ, Toledo P, Jones MJ, White N, Wong CA. Epidural labor analgesia-fentanyl dose and breastfeeding success: randomized clinical trial. Anesthesiology 2017;127:614-24.
31. DiGirolamo AM, Grummer-Strawn LM, Fein S. Maternity care practices: implications for breastfeeding. Birth 2001,28:94-100.
32. Renfrew MJ, Lang S, Woolridge MW. Early versus delayed initiation of breastfeeding. Cochrane database of systematic reviews 2000: CD000043.
33. Merten S, Dratva J, Ackermann-Liebrich U. Do baby-friendly hospitals influence breastfeeding duration on a national level?. Pediatrics 2005;116:702-8.
34. Kronborg H, Vaeth M. The influence of psychosocial factors on the duration of breastfeeding. Scand J Public Health 2004;32:210-6.

Table 1- Study details

Table 1
Study data. Results are presented as Odds Ratio (OR) and 95% Confidence intervals.

Study/Year/ Country	Type of Study	Outcome	Participants	Neuraxial	Control Group	Inclusion	Exclusion	Results
Armani/2013/ Italy [18]	Retrospective case-control	Breastfeeding at discharge (yes/no)	1963 (287 Neuraxial 1676 Control)	EA Levobupivacaine or ropivacaine	No analgesia (No details)	n.d.	CS, multiple pregnancies, < 34 weeks of gestation	OR 1.09 (0.46; 2.60)
Baumgarder/ 2002/USA [24]	Prospective observational	Two successful breastfeeding by 24 h (i.e. LATCH ≥7/10 + latch 2/2)	231 (115 Neuraxial 116 Control)	EA (No details)	Non-EA (No details)	healthy full term neonate, delivered vaginally, mothers aged 16 to 41 with no complication	n.d.	OR 0.53 (0.29; 0.99)
Chang/2005/ Canada [15]	Prospective cohort	Breastfeeding at 8 to 12 h (IAC score of the LATCH = 6) and at 4 weeks (yes/no)	115 (52 Neuraxial 63 Control)	EA Bupivacaine or Ropivacaine Fentanyl (n = 112) Epinephrine (n = 16)	No analgesic medication (No details)	> 18 years, uncomplicated pregnancy + labor + vaginal delivery, healthy term and breastfeeding infant	n.d.	At 8–12 h: OR 0.65 (0.31; 1.36) At 4 weeks: OR 1.48 (0.54; 4.08)
Ding/2014/China [10]	Prospective cohort	Breastfeeding at 3 days and at 6 weeks (yes/no)	214 (107 Neuraxial 107 Control)	EA or CSE Ropivacaine Sufentanil	No analgesic medication (No details)	consecutive nulliparas with term singleton cephalic pregnancy who were admitted to the delivery room and preparing to deliver vaginally during daytime working hours	history of psychiatric disease, obesity, EA contraindications	At 3 days: OR 1.18 (0.38; 3.63) At 6 weeks: OR 2.39 (1.36; 4.19)
Dozier/2013/ USA [31]	Observational study with one prospective and one retrospective part	Breastfeeding cessation at 3 days and at 4 weeks	727 (437 Neuraxial 290 Control)	EA (No details)	Non-EA (No details)	English speaking, ≥18 years old, singleton term, low risk pregnancy, vaginal delivery	n.d.	At 3 days: OR 0.24 (0.10; 0.57) At 4 weeks: OR 0.59 (0.44; 0.80) aOR 1.26 (1.10; 1.44)
Gizzo/2012/Italy [32]	Prospective observational	Correct sucking within the first 2 h postpartum (yes/no)	128 (64 Neuraxial 64 Control)	EA: Ropivacaine Fentanyl	No analgesic medication (No details)	primipara, 38–42 weeks of gestation, spontaneous or induced labor, neonatal birth weight 2500 to 4300 g, Apgar 1 > 7, Apgar 5 > 8	n.d.	OR 0.50 (0.17; 1.44)
Henderson/2003/ Australia [7]	Prospective observational	Breastfeeding at 2 months (yes/no)	663 (364 Neuraxial 299 Control)	CSE Bupivacaine Fentanyl	Non-CSE meperidine, nitrous oxide (Entonox®) or no analgesia	nullipara, singleton fetus, planned vaginal	< 37 weeks, contraindication to NA, refusal to participate	OR 0.63 (0.46; 0.88)
Herrera-Gomez/ 2015/Spain [22]	Retrospective cohort	Breastfeeding onset within first 2 h (yes/no)	2399 (551 Neuraxial 1848 Control)	EA: Ropivacaine or bupivacaine Fentanyl	Non-EA (No details)	> 37 weeks of gestation	induced labor, elective CS, pregnancy risk-factor (preexisting medical diseases or pregnancy/labor complication)	OR 0.46 (0.35; 0.60) aOR 0.76 (0.64; 0.93)
Mahmoodi/2019/ Iran [23]	Prospective cohort	Breastfeeding success at 3 h, at 24 h and at 4 weeks (yes/no)	383 (142 Neuraxial 241 Control); 4 weeks: 235 (86 Neuraxial 149 Control)	EA (No details)	Non-EA (No details)	vaginal birth, Iranian national, no infant abnormality	n.d.	At 3 h: OR 0.75 (0.32; 1.76) at 24 h: OR 0.78 (0.17; 3.55) at 4 weeks: OR 0.86 (0.14; 5.27)

(*continued on next page*)

Study/Year/ Country	Type of Study	Outcome	Participants	Neuraxial	Control Group	Inclusion	Exclusion	Results
Mahomed/2019/ Australia [20]	Prospective cohort	Breastfeeding at discharge and at 6 weeks (yes/no)	304 (107 Neuraxial 197 Control)	EA Fentanyl	Non-EA subcutaneous morphine or no analgesia	nullipara, intent to breastfeed, ≥ 37 weeks of gestation, understanding of English language	n.d.	At discharge: OR 0.44 (0.27; 0.71) at 6 weeks: OR 1.45 (0.87; 2.40) aOR 0.75 (0.41; 1.38)
Mauri/2014/Italy [19]	Prospective observational	Breastfeeding at 24 h and at 20 days (yes/no)	366 (209 Neuraxial 157 Control)	EA Ropivacaine or Levobupivacaine Sufentanil	Non pharmacologic or non-EA (No details)	healthy neonate, vaginal, 38 to 41 weeks of gestation, intention to breastfeed	< 18 years old, BMI < 18 or > 25, PPH with blood loss > 500 mL	At 24 h: OR 0.36 (0.13; 0.98) At 20 days: OR 0.72 (0.26; 1.98)
Orbach-Zinger/ 2018/Israel [9]	Prospective observational cohort	Breastfeeding at 3 days and at 6 weeks (yes/no)	1204 (806 Neuraxial 398 Control)	EA Bupivacaine Fentanyl	Non pharmacologic (No details)	singleton vaginal delivery ≥ 37 weeks	< 18 years, contraindication for EA, no knowledge of Hebrew, baby in NICU, no intention to breastfeed	At 3 days: OR 0.45 (0.27; 0.76) at 6 weeks: OR 0.57 (0.41; 0.78)
Wetzl/2019/Italy [8]	Community-based cohort study	Breastfeeding at discharge (yes/no)	3183 (637 Neuraxial 2546 Control)	CSE or EA Ropivacaine Sufentanil	Non-EA (No details)	vaginal delivery, singleton cephalic newborn, intention to breastfeed	dead fetus, unmarried women	OR 0.65 (0.55; 0.78)
Wilson/2010/ England [17]	Randomized controlled trial	Breastfeeding initiation up to 2 h and at 24–48 h (yes/no)	1392 (1041 Neuraxial 351 Control)	CSE or EA: Fentanyl (only some of the parturients)	meperidine, 50% nitrous oxide (Entonox ®), transcutaneous electrical nerve stimulation or no analgesia	nullipara	contraindication to NA	At 3 h: OR 1.02 (0.80; 1.30) at 24–48 h: OR 1.17 (0.91; 1.50)
Zuppa/2014/ Italy [25]	Cohort retrospective	Breastfeeding at 48–72 h/discharge (yes/ no)	2840 (1223 Neuraxial 1617 Control)	EA Ropivacaine Sufentanil	No analgesic medication (No details)	≥ 37 weeks, vaginal and uncomplicated delivery	Apgar 1/5 < 7, high risk pregnancy	OR 1.14 (0.40; 3.20)

EA- Epidural analgesia, CSE- Combined Spinal and Epidural analgesia, CS- Cesarean section, NA- Neuraxial analgesia, NICU- Neonatal Intensive Care Unit, PPH- Postpartum hemorrhage, BMI- Body Mass Index. n.d.- not determined, OR- odds ratio, aOR- adjusted odds ratio.

Table 2
Risk of Bias assessment.

Article	Baumgarder [24]	Mahomed [20]	Zuppa [25]	Wetzl [8]
- Bias due to confounding	Moderate	Low/Moderate	Moderate/Serious	Low
- Bias in selection of participants into the study	Moderate	Moderate	Moderate/Serious	Low
- Bias in classification of interventions	Serious	Low/Moderate	Moderate	Low/Moderate
- Bias due to deviations from intended interventions	Low/Moderate	Moderate	Moderate	Low/Moderate
- Bias due to missing data	Moderate	Moderate	Moderate	Low
- Bias in measurement of outcomes	Moderate/Serious	Serious/Critical	Moderate	Low/Moderate
- Bias in selection of the reported result	Moderate/Serious	Moderate	Moderate	Low
Overall	Serious	Serious	Serious	Moderate

Article	Ding [10]	Mahmoodi [23]	Dozier [31]	Herrare Gomez [22]	Chang [15]
- Bias due to confounding	Critical	Critical	Moderate/Serious	Serious	Moderate
- Bias in selection of participants into the study	Serious/Critical	Critical	Serious	Serious	Moderate
- Bias in classification of interventions	Moderate	Critical	Moderate/Serious	Serious	Serious
- Bias due to deviations from intended interventions	Moderate	Critical	Moderate	Serious	Low/Moderate
- Bias due to missing data	Critical	Critical	Serious	Moderate	Moderate
- Bias in measurement of outcomes	Critical	Critical	Moderate/Serious	Serious	Serious
- Bias in selection of the reported result	Moderate	Critical	Low/Moderate	Low/Moderate	Low/Moderate
Overall	Critical	Critical	Serious	Serious	Serious

Article	Henderson [7]	Orbach-Zinger [9]	Mauri [19]	Armani [18]
- Bias due to confounding	Moderate	Low	Low/Moderate	Serious
- Bias in selection of participants into the study	Moderate	Moderate	Moderate	Serious
- Bias in classification of interventions	Moderate	Low	Moderate	Moderate/Serious
- Bias due to deviations from intended interventions	Low	Low	Moderate	Moderate
- Bias due to missing data	Low	Low/Moderate	Serious	Moderate
- Bias in measurement of outcomes	Moderate	Low	NI	Serious
- Bias in selection of the reported result	Low	Low/Moderate	Low	Serious
Overall	Moderate	Moderate	Moderate	Serious

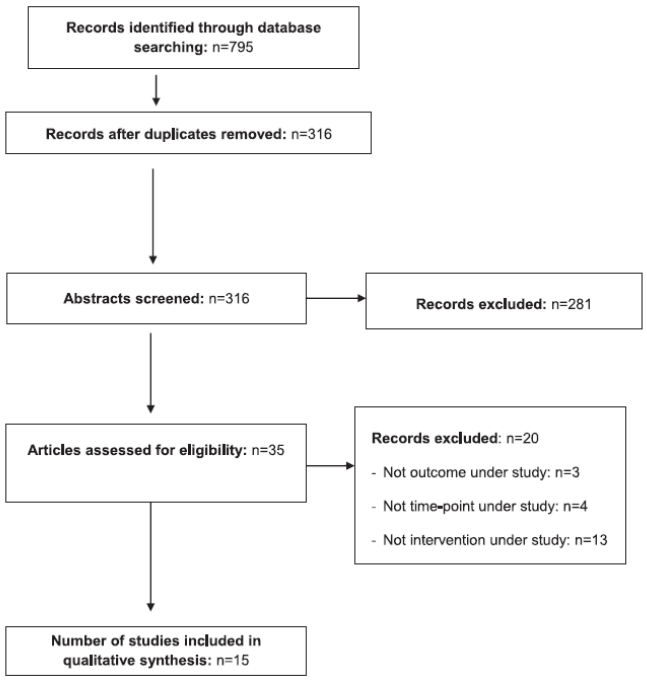
Article	Gizzo [32]	Wilson [17]
- Bias due to confounding	Serious	Low
- Bias in selection of participants into the study	Serious	Low
- Bias in classification of interventions	Moderate	Low
- Bias due to deviations from intended interventions	Moderate/serious	Low
- Bias due to missing data	Moderate	Low
- Bias in measurement of outcomes	Serious	Low
- Bias in selection of the reported result	Serious	Low
Overall	Serious	Low

Table 3
Results listed in a chronological order. Results are presented as Odds ratios (OR) and 95% Confidence Intervals.

Time-period	No significant difference between groups	Significantly lower rate of breastfeeding in the NA group	Significantly higher rate of breastfeeding in the NA group
2 h	2 OR 0.50 (0.17; 1.44) [32] OR 1.02 (0.80; 1.30) [17]	1 OR 0.46 (0.35; 0.60) [22] aOR 0.76 (0.64; 0.93) [22]	
3 h	1 OR 0.75 (0.32; 1.76) [23]		
8 to 12 h	1 OR 0.65 (0.31; 1.36) [15]		
24 h	2 OR 0.78 (0.17; 3.55) [23] OR 1.17 (0.91; 1.50) [17]	2 OR 0.36 (0.13; 0.98) [19] OR 0.53 (0.29; 0.99) [24]	
Discharge	2 OR 1.09 (0.46; 2.60) [18] OR 1.14 (0.40; 3.20) [25]	2 OR 0.65 (0.55; 0.78) [8] OR 0.44 (0.27; 0.71) [20]	
3 days	1 OR 1.18 (0.38; 3.63) [10]	2 OR 0.45 (0.27; 0.76) [9] OR 0.24 (0.10; 0.57) [31]	
1 week	1 OR 0.78 (0.17; 3.55) [23]		
20 days	1 OR 0.72 (0.26; 1.98) [19]		
4 weeks	2 OR 1.48 (0.54; 4.08) [15] OR 0.86 (0.14; 5.27) [23]	1 OR 0.59 (0.44; 0.80) [31] aOR 1.26 (1.10; 1.44) [31]	
6 weeks	1 OR 1.45 (0.87; 2.40) [20] aOR 0.75 (0.41; 1.38) [20]	1 OR 0.57 (0.41; 0.78) [9]	1 OR 2.39 (1.36; 4.19) [10]
8 weeks		1 OR 0.63 (0.46; 0.88) [7]	

aOR- adjusted Odds ratio.

Fig. 1. Flow chart of the literature search.



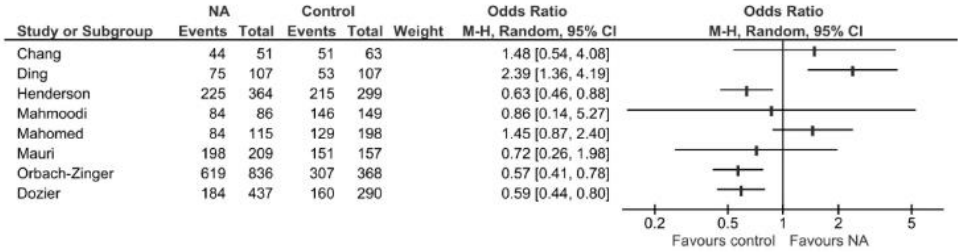


Fig. 2. Forest plot presenting Odds ratios and 95% Confidence Intervals (95% CI) of studies assessing breastfeeding success at 2 to 8 weeks postpartum.