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Review

Breastfeeding Outcomes After Oxytocin Use During Childbirth: An Integrative Review

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Elise N. Erickson, CNM, MS, Cathy L. Emeis, CNM, PhD

Introduction: Despite widespread use of exogenous synthetic oxytocin during the birth process, few studies have examined the effect of this drug on breastfeeding. Based on neuroscience research, endogenous oxytocin may be altered or manipulated by exogenous administration or by blocking normal function of the hormone or receptor. Women commonly cite insufficient milk production as their reason for early supplementation, jeopardizing breastfeeding goals. Researchers need to consider the role of birth-related medications and interventions on the production of milk. This article examines the literature on the role of exogenous oxytocin on breastfeeding in humans.

Methods: Using the method described by Whittemore and Knafl, this integrative review of literature included broad search criteria within the PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane, and Scopus databases. Studies published in English associating a breastfeeding outcome in relation to oxytocin use during the birth process were included. Twenty-six studies from 1978 to 2015 met the criteria.

Results: Studies were analyzed according to the purpose of the research, measures and methods used, results, and confounding variables. The 26 studies reported 34 measures of breastfeeding. Outcomes included initiation and duration of breastfeeding, infant behavior, and physiologic markers of lactation. Timing of administration of oxytocin varied. Some studies reported on low-risk birth, while others included higher-risk experiences. Fifty percent of the results (17 of 34 measures) demonstrated an association between exogenous oxytocin and less optimal breastfeeding outcomes, while 8 of 34 measures (23%) reported no association. The remaining 9 measures (26%) had mixed findings. Breastfeeding intentions, parity, birth setting, obstetric risk, and indications for oxytocin use were inconsistently controlled among the studies.

Discussion: Research on breastfeeding and lactation following exogenous oxytocin exposure is limited by few studies and heterogeneous methods. Despite the limitations, researchers and clinicians may benefit from awareness of this body of literature. Continued investigation is recommended given the prevalence of oxytocin use in clinical practice.
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INTRODUCTION

While increasing numbers of women are breastfeeding their newborns at birth, the ability to maintain breastfeeding may be affected by factors contributing to maternal milk production. This is reflected by the Centers for Disease Control and Prevention (CDC) 2016 Breastfeeding Report Card, which shows that while 81.1% of women initiate breastfeeding after birth, only 44.4% of women are still exclusively breastfeeding at 3 months, falling to 22.3% of infants by the 6-month target.[1] Common reasons for early cessation of exclusive or any breastfeeding is the perception of insufficient milk supply[2,3] and the early introduction of formula.[4,5] Therefore, factors that may influence physiologic milk production are compelling targets for translational research.

Understanding possible causes of suboptimal breastfeeding may have implications for improving maternal and infant health. Infants receiving formula or solid foods before 6 months of age are at increased risk for acute and chronic illnesses, as well as sudden infant death syndrome.[6] The number of infant deaths potentially preventable by meeting breastfeeding goals are estimated upwards of 700 annually.[7,8] Furthermore, a growing body of literature is examining the long-term effect of breastfeeding on maternal health. Women who have no breastfeeding history have poorer indices of cardiovascular health in later life.[9] Another study used a simulation model to estimate the impact of suboptimal breastfeeding on many maternal health outcomes, reporting a potential annual excess mortality of 3340 deaths and more than $14 billion in costs in the United States due to premature death.[7]

Milk production and successful breastfeeding require oxytocin-driven neuroendocrine pathways that are primed by pregnancy and the process of childbirth.[10] Endogenous oxytocin function is essential for onset of lactation and milk ejection in mammals.[11] Manipulation of oxytocin in experimental animal models can lead to deficits in lactation, maternal behavior, and abnormal behavioral development of offspring.[12,13] Oxytocin is commonly administered in modern maternity care for labor augmentation, induction of labor,[14] and to minimize or treat uterine bleeding in the third stage of labor.[15] There is evidence that exogenous oxytocin can pass through the placenta and into fetal circulation.[16] Therefore, depending on the timing of administration, this synthetic hormone and neurotransmitter could affect neonates as well as women.

The significance of these questions relate to the extensive use of oxytocin in practice. Estimates of induction of labor, typically involving exogenous oxytocin, range from 23% to 29% of births[17,18] but may be in the range of 31% to 42% in

Address correspondence to Elise N. Erickson, CNM, MS, Oregon Health & Science University, School of Nursing, 3455 SE US Veterans Hospital Rd, Portland, OR 97239-2941. E-mail: ericksel@ohsu.edu

Quick Points

- Oxytocin administration during childbirth is widespread; few studies have investigated the effects of this on breastfeeding, and most of these have not directly studied the relationship.
- The effect of exogenous oxytocin on breastfeeding has been measured through infant breastfeeding behavior, physiologic lactation, maternal initiation, and duration or exclusivity of breastfeeding.
- While oxytocin administration has an important role in modern maternity care, potential effects on lactation should be explored more, as the research on breastfeeding outcomes is incomplete.

some settings, based on US data.[19,20] Among women who start labor spontaneously, augmentation of labor with oxytocin due to slow progress is also frequent,[20] though exact national rates are not published. Epidural analgesia is also associated with induced and augmented labor, with more than 75% of women using epidural analgesia undergoing induction or augmentation, according to 2008 CDC data.[21] During cesarean birth, accounting for 32.7% of births,[18] oxytocin is administered after extracting the placenta to slow bleeding.[15] Finally, to help minimize bleeding, the World Health Organization (WHO) promotes prophylactic administration of oxytocin as the standard of care following vaginal birth.[15] It is also a mainstay treatment for postpartum hemorrhage.

Despite widespread use of oxytocin and the importance of the physiology of oxytocin for successful lactation, clinical studies have rarely explored long-term effects on women and infants, such as breastfeeding outcomes.[22,23] The purpose of this integrative review is to understand 1) what breastfeeding outcomes (maternal or infant) have been reported following any clinical oxytocin administration and 2) any patterns in the published results to better inform future research.

METHODS

An integrative approach described by Whittemore and Knafl informed the procedure for this review, as a preliminary literature search revealed significant heterogeneity in methods and outcomes among relevant studies.[24] We were unable to identify articles synthesizing the body of literature regarding oxytocin administration in humans and breastfeeding outcomes. The complexity of this question is owed to both the various indications and timing of oxytocin use during the birth process and the multifactorial nature of breastfeeding and lactation research outcomes. In an effort to capture all possible oxytocin administration during the birth process, our review included intrapartum oxytocin and/or third-stage labor administration. Breastfeeding outcomes were defined as any maternal and infant breastfeeding-related measure.

Literature Search

Due to the exploratory nature of this investigation, the approach included broad search terms and no limits on publication date. We performed a Boolean search (as shown in Table 1) of PubMed Medical Subject Heading (MeSH) terms including: 1) "oxytocin," "labor (induced)," "labor (obstetric)," "labor stage (third)," or "epidural analgesia"; and 2) "breastfeeding," "feeding behavior," "lactation," or "lactation (disorder)," yielding 1847 results after limiting to human studies. A duplicate search in the Cumulative Index to Nursing and Allied Health Literature (CINAHL) yielded 268 citations ("infant behavior" substituted for "feeding behavior"). A total of 2115 abstracts (including duplicates) were scanned for inclusion by 1) data-based studies published in English and 2) noting oxytocin administration and a breastfeeding outcome (maternal or infant). If a potential match did not mention oxytocin administration in the abstract, the full text was reviewed in detail. Induction of labor studies not evaluating oxytocin specifically were excluded, as well as studies assessing infant bottle feeding. The resulting group consisted of 26 studies published between 1978 and 2015.

Data Evaluation

Significant heterogeneity in the study objectives, design, and outcomes complicated the evaluation of this body of literature. The majority of the studies were descriptive or secondary analysis reports (either prospective or retrospective); however, one randomized controlled trial, 2 quasi-experimental studies, and 2 case-control studies also made up the sample.

While studies in this review considered oxytocin exposure during birth with at least one breastfeeding measure, most did not set out to study this relationship. Many noted the association between oxytocin and breastfeeding as a subanalysis of the primary aim or as a covariate or control for another objective. We identified 3 groups of research objectives within the sample studies. Only 9 studies examined the effect of oxytocin use on breastfeeding. Four studies examined factors (general health and obstetric) associated with delayed lactogenesis and poor breastfeeding generally. In these reports, use of oxytocin was among many variables considered. The largest group of studies, however, sought to understand broad outcomes of specific obstetric interventions: epidural analgesia ($n = 4$), medication use ($n = 3$), active management of third-stage labor (AMTSL) ($n = 1$), or as part of an induction of labor ($n = 5$). These studies included a breastfeeding measure among other outcomes.

Time point of oxytocin administration varied among the studies, illustrated in Figure 1. The majority considered intrapartum oxytocin administration only. Four of these assessed the postpartum dose of oxytocin as well.[25–28] Another 3 studies mention that oxytocin was routinely given postpartum but was not included in the analysis in terms of exposure.[29–31] Three other studies addressed the third-stage issue generally by reporting "increased need for postpartum uterotonics"

Table 1. Search Strategy for Oxytocin Use During Birth and Breastfeeding

Database	Search Terms (MeSH and Keyword)	Results	Unique Studies Included
PubMed	Oxytocin, labor (induced), labor (obstetric), labor stage (third), epidural analgesia AND breastfeeding, feeding behavior, lactation, lactation disorder	598	14
	Lactogenesis (keyword)	131	3
	Labor (induced) AND oxytocin	1118	4
CINAHL	Oxytocin, labor (induced), obstetric care, labor stage (third), epidural analgesia AND breastfeeding, infant behavior, lactation, lactation disorder		89
	Lactogenesis	54	1
	Labor (induced) AND oxytocin	125	0
Cochrane	Induced labor AND breastfeeding	13	0
	Active management (third stage) labor	1	1
Scopus			1
Hand check of reference lists			1
Total			26

Abbreviation: CINAHL, Cumulative Index to Nursing and Allied Health Literature.

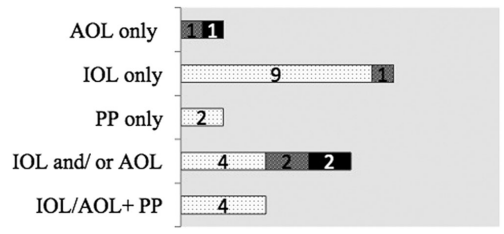

Figure 1. Number of Studies by Time Point of Oxytocin Exposure and Type of Breastfeeding Measures Reported

Maternal Measures of Breastfeeding (Initiation or Duration of Breastfeeding, Physiology of Lactation).

Infant Measures of Breastfeeding (Infant Feeding Behavior).

Both Maternal and Infant Measures.

Abbreviations: AOL, augmentation of labor; IOL, induction of labor; PP, postpartum prophylaxis.

(ie, oxytocin and other medications),[32–34] or commenting on the relationship of postpartum hemorrhage and breastfeeding outcomes.[35]

Breastfeeding outcomes included maternal behaviors like initiation, duration of breastfeeding, measures of physiologic milk production (eg, hormones, lactogenesis), and infant breastfeeding behavior. A total of 34 measures in the 26 studies were examined in relationship to oxytocin use as illustrated in Figure 2. Some studies reported more than one outcome in the findings. Due to the variety of study objectives, methods, and outcomes used in the sample, rigor of the studies was not evaluated by a standardized rubric or score. Instead, we addressed quality of the studies by assessing and synthesizing themes that may introduce bias or limit generalizability.

RESULTS

Breastfeeding Outcomes

No primary study outcome associated oxytocin use with a more favorable breastfeeding outcome. Data were arranged into 3 categories: 1) use of oxytocin (intrapartum and/or postpartum) and a less optimal breastfeeding outcome, 2) no association, or 3) having mixed findings. Results were labeled mixed if they were the subanalyses of the primary aim of the study or significance was seen in certain subgroups of the sample (ie, primiparas). Of the 34 measures reported in the studies, 50% found oxytocin use was associated with a less optimal breastfeeding outcome (n = 17). Mixed or qualified support of less optimal outcomes was reported by 26% (n = 9), and 23% showed no differences in breastfeeding outcomes with oxytocin use or not (n = 8). Table 2 lists the measures, statistical data, and information about the study design and limitations.

Initiation of Breastfeeding

Eleven studies examined associations between breastfeeding initiation and oxytocin administration; 7 studies reported on initiation only.[28,32,33,36–39] Initiation of breastfeeding was defined by various time points ranging from 10 minutes after birth through 7 days postpartum. An additional 4 studies reported duration measures as well as initiation measures of breastfeeding.[30,40–42]

Four of these 11 studies were generated from large data sets and controlled for multiple covariates in their analyses.[28,32,33,36] Two noted delay in initiation of breastfeeding following induction of labor and elective induction of labor in Latin American countries.[32,33] Another reported lower breastfeeding rates at hospital discharge following AMTSL in

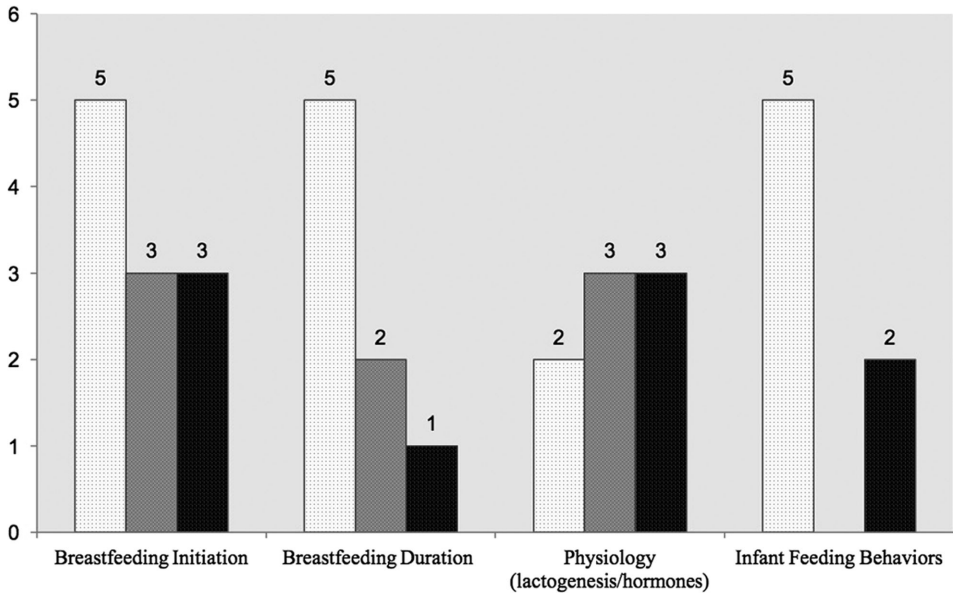

Figure 2. Number of Measures by Direction of Findings Reporting Relationship Between Oxytocin Use and Breastfeeding Outcomes

Measures Showing Less Optimal Breastfeeding Outcome With Oxytocin Use.

Measures Reporting Mixed Findings: Less Optimal Outcome With Oxytocin Use in Subgroup Analysis.

Measures Reporting No Association Between Oxytocin and Breastfeeding.

the United Kingdom.[28] In this study, after controlling for multiple intrapartum factors and examining a subgroup of women with low-risk, physiologic labors, AMTSL was still associated with an approximate 7% reduction in breastfeeding at 2 days postpartum.

However, the study by Prendiville,[39] the only randomized controlled trial in the sample, did not find an association between AMTSL and breastfeeding at hospital discharge. This study is limited by a lack of fidelity to the randomization; only 403 of 849 participants allocated to physiologic management had it performed. In addition, the physiologic group was also more likely to put the newborn to breast 10 minutes after birth per midwives' recommendation.

Brown and Jordan[42] also did not find that AMTSL affected rates of breastfeeding initiation in a self-report study of breastfeeding and administration of postpartum oxytocin.[42] However, they did report a reduction in duration of breastfeeding at both 2 and 6 weeks postpartum among participants who had AMTSL. The most often reported reasons for cessation were pain, difficulty, and embarrassment compared to women who had physiologic management. This study did not control for prenatal intentions to breastfeed.

Altogether, the definition of initiation of breastfeeding was variable but appeared to reflect the first several postpartum days. Five papers associated delayed initiation of breastfeeding with induction or augmentation of labor compared to spontaneous labor or no augmentation (postpartum use not reported)[30,32,33,37] or postpartum administration of oxytocin compared to expectant management.[28] Mixed findings were reported in 3 studies.[36,40,41]

Duration of Breastfeeding

Eight studies examined duration of breastfeeding. This was defined as the time of breastfeeding cessation,[25] report of exclusive breastfeeding at 3 months after birth,[30,31] at 6 weeks postpartum,[42,43] or breastfeeding at 8 weeks.[26,40,41] Shorter duration or exclusivity of breastfeeding was associated with intrapartum oxytocin use by 4 studies compared to spontaneous labor[25,26,30,31] and with postpartum use in the study by Brown and Jordan.[42] Two reports had mixed findings on duration of breastfeeding.[40,43] One paper reported no difference.[41]

The total dosage of oxytocin was examined in terms of duration of breastfeeding by 2 authors. Both Gu et al[26] and Olza-Fernandez[31] noted that higher levels of exposure to oxytocin during the birth process were associated with reduced exclusive breastfeeding at 2 and 3 months postpartum, respectively. Additionally, the participants in the study by Dozier et al[25] most likely to cease breastfeeding by one month postpartum were those with both epidural analgesia and oxytocin exposure during labor (HR, 1.34; 95% confidence interval [CI], 1.00-1.79).[25] Women with epidural analgesia in this study were more likely to have oxytocin administered during labor (58.8% vs 38.3%, $P < .01$). Breastfeeding was not analyzed by total dosage specifically in this study, but this may imply that women with epidural analgesia had more need for oxytocin administration, possibly representing higher total dosage.

Physiology of Lactation

Eight studies examined breastfeeding as a measure of physiologic milk production. Six of these examined lactogenesis

Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Gu et al,[26] 2015 Canada	**Oxytocin Time Point** Intrapartum and postpartum **Design** Prospective longitudinal Baby-Friendly setting[a] Mixed parity sample	Self-report: Exclusivity of breastfeeding at 2 months Plasma oxytocin levels at 2 months	N = 386 92% of women received oxytocin **Duration** Exclusively breastfeeding mothers at 2 months postpartum had received significantly less oxytocin during labor (33 units) when compared to formula (44 units) or mixed feeding mothers (43 units) (after controlling for education level) ($P < .0001$) **Physiology of Lactation** Circulating oxytocin at 2 months postpartum was positively correlated to dosage given during birth (Pearson, 0.16, $P < .01$)	Did not specify the rates of analgesia, mode of birth, indication for oxytocin use, or neonatal problems Breastfeeding intention not reported Did not control for parity or other neonatal or obstetric issues in breastfeeding outcomes
Brimdyr et al,[49] 2015 United States	**Oxytocin Time Point** Intrapartum **Design** Prospective Comparative Baby-Friendly setting Mixed parity sample	Widström's 9 instinctive stages of neonatal behavior	N = 63 84% of women having oxytocin with or without epidural analgesia **Infant Behavior** Infants born after exposure to oxytocin were less likely to suck in the first hour after birth ($P = .03$). Dose dependent response. Groups examined with use of epidural analgesia, which also exhibited a main effect by dosage and was frequently interrelated with oxytocin use	Breastfeeding intention not reported Duration of oxytocin exposure not analyzed in relation to infant behavior Duration of labor overall not controlled
Marín-Gabriel et al,[29] 2015 Spain	**Oxytocin Time Point** Intrapartum **Design** Prospective cohort Baby-Friendly setting Mixed parity sample Breastfeeding intentions reported (inclusion criteria)	Primitive neonatal reflexes related to feeding on days 1-2 postnatal	N = 98 53 women received oxytocin, 45 women did not **Infant Behavior** Fewer reflexes noted in newborns exposed to oxytocin infusion compared to nonexposed, (β, −12.7; 95% CI, −25 to −0.5) Adjusted for parity, labor difficulty, epidural analgesia use	Nulliparas and epidural analgesia were more common in the oxytocin group, though this was controlled in the analysis Dose of oxytocin not reported

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Mauri et al,[47] 2015 Italy	**Oxytocin Time Point** Intrapartum **Design** Prospective longitudinal descriptive Mixed parity sample	Self-report: timing and intensity of lactogenesis-related breast symptoms	N = 366 62.8% of women received oxytocin **Physiology of Lactation** No association between oxytocin infusion alone and onset of lactation symptoms (HR, 1.06; 95% CI, 0.77-1.45) Epidural analgesia related to oxytocin infusion ($P <$ .001) and suboptimal breastfeeding at 20 days ($P =$ .02)	Baby-Friendly not reported Skin-to-skin not reported[b] Rooming-in not protocol Breastfeeding intention not reported Intrapartum oxytocin protocol lower than other studies: 5 units/500 mL Oxytocin dose not recorded/reported
Brown & Jordan,[42] 2014 United Kingdom	**Oxytocin Time Point** Postpartum **Design** Retrospective descriptive Mixed parity	Self-report: feeding method at birth, duration of breastfeeding	N = 288 84.1% of sample reported postpartum oxytocin administration **Initiation** No differences between active and physiologic third stage on breastfeeding after birth (OR, 0.57; 95% CI, 0.23-1.42) **Duration** AMTSL associated with reduced levels of breastfeeding at 2 weeks (OR, 0.35; 95% CI, 0.18-0.71) and 6 weeks (OR, 0.38; 95% CI,0.19-0.78), but not at birth 90.2% of the formula-feeding group at 2 weeks received AMTSL compared to 76.3% of the breastfeeding group Relationship held when women with epidural analgesia and gestational age >41 weeks were removed from analysis (to control for possible intrapartum exposure)	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Self-report of labor procedures subject to recall bias Could not control for all intrapartum synthetic oxytocin use

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
García-Fortea et al,[30] 2014 Spain	**Oxytocin Time Point** Intrapartum **Design** Retrospective descriptive cohort (randomly selected) Parity not reported	Self-report breastfeeding status and duration of breastfeeding	N = 316 59.8% women received oxytocin **Initiation** Synthetic oxytocin was associated with fewer reports of breastfeeding (63.5% of exposed group vs 92.1% nonexposed) (RR, 1.45; 95% CI, 1.288-1.635) **Duration** For duration (n = 237), use of synthetic oxytocin (120/237) associated with average of 33 fewer days of breastfeeding.	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Parity not reported Medical record used for clinical variables; self-report (5 years prior): breastfeeding status (study does not report which time point this report represents) and duration of breastfeeding (reported in days) Duration not specified as exclusive or partial breastfeeding Large proportion of sample was twin gestation (30.7%)
Bell, White-Traut, & Rankin,[48] 2013 United States	**Oxytocin Time Point** Intrapartum **Design** Prospective descriptive Mixed parity	Prefeeding behaviors Neonatal Behavioral Assessment Scale 45 minutes after birth	N = 47 76.5% of women received oxytocin **Infant Behavior** Newborn behaviors in the exposed group were more likely to show low levels of feeding behavior compared to unexposed who had more high-level prefeeding behavior (OR, 11.5; 95% CI, 1.8-73.3) Adjusted for labor length and epidural analgesia use	Newborns went to a warmer following birth per hospital routine, skin-to-skin not routine Breastfeeding intention not reported
Vogel, Souza, & Gülmezoglu,[36] 2013 16 Africa/Asian Countries	**Oxytocin Time Point** Intrapartum **Design** Retrospective descriptive	WHO Global Survey Initiation of breastfeeding <24 h – 7 days	N = 192,538 11,700 (6%) induction with oxytocin **Initiation** Increased odds of not breastfeeding in first 24 hours in Asian sample (OR, 2.17; 95% CI, 1.27-3.73); also associated with increased risk of low Apgar, birth weight, and ICU admission	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Oxytocin effect not examined with controls for obstetric complications (per aim of study)

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Olza Fernández et al,[31] 2012 Spain	**Oxytocin Time Point** Intrapartum **Design** Prospective longitudinal descriptive Mixed parity Skin-to-skin noted (not Baby-Friendly)	Duration exclusivity at 3 months Primitive neonatal reflexes on second day of life	N = 20 100% received oxytocin for induction or augmentation 100% had epidural analgesia; 30% forceps rate **Infant Behavior** Negative association between rate of newborn sucking reflex after birth and dosage of oxytocin administered ($P = .03$). **Duration** Women exclusively breastfeeding at 3 months were exposed to significantly less oxytocin during birth ($P = .04$).	Breastfeeding intention not reported Small sample, pilot study All women had epidural analgesia, effect of epidural analgesia could not be controlled statistically
Dozier et al,[25] 2012 United States	**Oxytocin Time Point** Intrapartum and postpartum **Design** Prospective cohort Baby-Friendly in part of sample (controlled for in analysis) Breastfeeding goals and confidence reported	Secondary analysis of self-report and medical record data: duration at 2 months postpartum	N = 727 50% of women received intravenous oxytocin 14.8% had intramuscular oxytocin. **Duration** Combination of epidural analgesia and intrapartum oxytocin had increased early cessation (HR, 1.34; 95% CI, 1.00-1.79); absence of epidural analgesia and oxytocin were most protective of ongoing breastfeeding Women giving birth in a Baby-Friendly hospital who had oxytocin IV were less likely to have early breastfeeding cessation (HR, 0.67; 95% CI, 0.53-0.86) Women giving birth in non-Baby-Friendly hospitals who had oxytocin IV were more likely to have early breastfeeding cessation (HR, 1.50; 95% CI, 1.25-1.80)	Postpartum dose not included in oxytocin exposure for analyses Indication for oxytocin use was not specified

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Guerra et al,[33] 2011 8 Latin American countries	**Oxytocin Time Point** Intrapartum **Design** Retrospective descriptive (secondary analysis)	WHO Global Survey: Initiation of breastfeeding <24 h – 7 days	N = 37,597 Subset of elective induction of labor compared to low-risk spontaneous labor 4.4% oxytocin exposure for elective induction of labor **Initiation** Increased risk of delayed initiation (compared to first hour after birth) of breastfeeding adjusting for parity, mode of birth, etc. (RR, 1.59; 95% CI, 1.24-2.05).	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Oxytocin effect not examined with controls for obstetric complications (per aim of study)
Nommsen-Rivers et al,[35] 2010 United States	**Oxytocin Time Point** Intrapartum **Design** Prospective longitudinal descriptive Primiparous Breastfeeding intention: inclusion criteria	Onset of lactogenesis—maternal report	N = 431 56.6% of women received oxytocin for induction or augmentation Overall delayed lactogenesis rate 44.3% **Physiology of Lactation** Delayed lactogenesis not associated with oxytocin exposure Shorter labor predicted less delayed lactogenesis but only for non-oxytocin group	Baby-Friendly not reported Duration of labor reported but not duration of oxytocin exposure—only if it were part of the labor Indications for labor induction or augmentation not reported
Matias et al,[45] 2009 Peru	**Oxytocin Time Point** Intrapartum **Design** Prospective longitudinal descriptive Baby-Friendly Primiparous	Onset of lactogenesis-maternal report Researcher observation of breastfeeding behavior with Infant Breastfeeding Assessment scale; infant weight loss	N = 156 2.3% induction of labor rate 15% augmentation of labor with oxytocin rate **Physiology of Lactation** Of the augmented group, 30.4%, reported delayed onset of lactogenesis compared to 15% of the nonaugmented group ($P = .1$); not associated with excess weight loss or suboptimal breastfeeding behavior	Breastfeeding intention not reported Breastfeeding outcomes of women with labor induction not reported in table Low number of women with oxytocin exposure for labor augmentation (n = 25)

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Guerra et al,[32] 2009 8 Latin American countries	**Oxytocin Time Point** Intrapartum **Design** Retrospective descriptive	WHO Global Survey: Initiation of breastfeeding <24 h – 7 days	N = 97,095 87% of inductions used oxytocin (11,077 total inductions) **Initiation** Induction associated with delayed initiation of breastfeeding until after the first day (RR, 1.31; 95% CI, 1.22-1.43) adjusted for multiple risk factors	*See Guerra[33]
Jordan et al,[28] 2009 United Kingdom	**Oxytocin Time Point** Intrapartum and postpartum **Design** Prospective data collection, secondary analysis Mixed parity	Medical record: Initiation of breastfeeding by 48 hours	N = 48,366 79% of women received uterotonic medication (oxytocin and/or ergometrine) in the third stage of labor 10% were induced with oxytocin **Initiation** Third-stage labor uterotonic associated with reduced breastfeeding at 48 hours postpartum in all women ($P < .001$) and primiparous subset ($P < .001$) for IM or IV oxytocin and ergometrine; this controlled for other medications in labor, social class, parity, age, and deprivation rank	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Classification of women breastfeeding at 48 hours included women partially breastfeeding and excluded women who were expressing milk Outcome variable of breastfeeding at 48 hours unclear if referring to entire 48 hours or just the last feeding at that time (ie, discharge feeding diagnosis).
Jonas et al[27] 2009 Sweden	**Oxytocin Time Point** Intrapartum and postpartum **Design** Prospective descriptive comparative Skin-to-skin reported, number of feeds during first 2 days not different between groups Breastfeeding intention reported	Oxytocin and prolactin levels during breastfeeding on second day postpartum	N = 63 **Physiology of Lactation** Prolactin levels peaked earlier (10 minutes) ($P = .01$) and were higher in the oxytocin intrapartum groups ($P = .006$) for up to 60 minutes ($P = .001$) Negative correlation between amount of oxytocin during labor and median level of oxytocin in blood on second postpartum day ($r_s = -.495$, $P = .02$)	No clinical measures of breastfeeding outcomes were linked to the hormone data to correlate clinical significance

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Kong & Bajorek,[46] 2008 Australia	**Oxytocin Time Point** Intrapartum **Design** Prospective descriptive Breastfeeding intention was reported	Onset of lactogenesis—maternal report	N = 75 6.7% of the sample received oxytocin for induction of labor; postpartum use not reported **Physiology of Lactation** Average (SD) time to onset of lactogenesis was 77.0 (34.7) hours for induction of labor with oxytocin (n = 5), compared to 68.1 (22.8) hours for spontaneous labor (n = 28) ($P = .66$).	Baby-Friendly not reported Skin-to-skin not reported Sample receiving oxytocin small, underpowered for this comparison
Wiklund et al,[37] 2007 Sweden	**Oxytocin Time Point** Intrapartum **Design** Comparative retrospective: matched control Mixed parity (analysis did control for parity, length of labor in regression analyses)	Initiation after birth, formula supplementation	N = 702 54% of the women received oxytocin during labor **Initiation** Oxytocin administration associated with delayed initiation >4 hours of breastfeeding (OR, 3.28; 95% CI, .1.57-6.84) and giving artificial milk supplement (OR, 2.15; 95% CI, 1.28-3.61).	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported

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Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Dewey et al,[34] 2003 United States	**Oxytocin Time Point** Intrapartum (postpartum?) **Design** Prospective longitudinal descriptive Breastfeeding intention: inclusion criteria	Self-report onset lactogenesis Infant behavioral observation Infant Breastfeeding Assessment Tool	N = 280 31% of the women received oxytocin for labor augmentation; no data on induction of labor **Physiology of Lactation** 32% of augmented group had delayed onset lactogenesis compared to 18% of nonaugmented group ($P < .05$) 64% of the sample received "postpartum hemorrhage medications," which may have included oxytocin, and 26% of this group had delayed onset of lactogenesis compared to 16% ($P < .1$) Multiple regression analysis was not significant for oxytocin **Infant Behavior** No differences in suboptimal infant breastfeeding behavior scores or weight loss of infant	Baby-Friendly not reported Skin-to-skin not reported Duration/dosage of oxytocin augmentation not reported; comparison of lactogenesis outcomes from augmentation include women who had scheduled cesarean births (n = 11), which may affect the results
Radzyminski,[50] 2003 United States	**Oxytocin Time Point** Intrapartum **Design** Prospective comparative Multiparous only	Preterm Infant Breastfeeding Behavior, Neurologic and Adaptive Capacity Score	N = 56 dyads Unknown percentage of sample receiving oxytocin **Infant Behavior** 6 infants scored below the mean for breastfeeding behavior; these had a higher incidence of labor induction	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention: not reported Data outcomes on breastfeeding behavior incomplete: percent not reported, no descriptive statistics

(*Continued*)

Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Chapman & Perez-Escamilla,[44] 1999 United States	**Oxytocin Time Point** Intrapartum **Design** Longitudinal prospective descriptive Mixed parity	Self-report onset lactogenesis	N = 192 **Physiology of Lactation** Induction with oxytocin was not associated with delayed onset of lactogenesis in chi-square test	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Number of women induced with oxytocin not reported; cannot make comparison to those not exposed
Rajan,[43] 1994 United Kingdom	**Oxytocin Time Point** Intrapartum **Design** Descriptive retrospective, secondary analysis	Self-report breastfeeding at 6 weeks	N = 1064 18% of the sample reported oxytocin for induction of labor **Duration** Chi-square analysis showed relationship between oxytocin use and shorter duration of second stage (<1 hr) was associated with reduced exclusive breastfeeding compared to women who had a longer second stage or were not receiving oxytocin ($P = .04$)	Baby-Friendly not reported Skin-to-skin not reported Breastfeeding intention not reported Statistical analysis not robust; no regression analysis; multiple chi-square tests cannot control for confounding variables
Out, Vierhout, & Wallenburg,[41] 1988 Netherlands	**Oxytocin Time Point** Intrapartum **Design** Prospective quasi-experimental with control group Mixed parity Intention to breastfeed recorded at 36 weeks of pregnancy	Nursing staff report "any serious attempt" and self-report 3-4 days postpartum and at 6 months	N = 185 26% of the sample received oxytocin for induction and 16% for augmentation **Initiation & Duration** More women decided not to breastfeed in the elective induction of labor group than the others; rates of breastfeeding beyond initiation did not differ over the reported 1 and 2 month postpartum time points	Skin-to-skin not reported Statistical analysis not robust Did not control for confounding factors: duration of labor or parity

(*Continued*)

Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Prendiville et al,[39] 1988 United Kingdom	**Oxytocin Time Point** Postpartum **Design** Randomized trial	Medical records: breastfeeding at discharge	N = 1695 74% of sample received active management **Initiation** No difference between groups in breastfeeding at discharge (OR, 0.96; 95% CI, .77-1.19)	Skin-to-skin: not specifically reported; women in control group encouraged to put baby to breast in first 10 minutes after birth more than AMTSL group (225/849 vs 63/846) Breastfeeding intention not recorded Lack of fidelity to treatment group: only 403/849 in physiologic management had this performed compared to 840/846 in the treatment group Breastfeeding outcome not examined by parity, oxytocin intrapartum exposure
Yudkin et al,[38] 1979 United Kingdom	**Oxytocin Time Point** Intrapartum **Design** Retrospective case control Breastfeeding intention: recorded at first prenatal visit Mixed parity	Breastfeeding at discharge	N = 400 185/200 induction group received oxytocin 18 of the spontaneous group had oxytocin augmentation **Initiation** Of the women intending to breastfeed during antenatal care, 86% of the spontaneous group were breastfeeding at "discharge" compared to 82% of induction group	Skin-to-skin not reported Inconsistent outcome variable; discharge outcome was "when records stop," which include some follow-up postpartum care

(*Continued*)

Table 2. Studies Reporting an Association Between Synthetic Oxytocin Use and a Breastfeeding Outcome

Author, Year, Location	Design	Measures	Results	Limitations
Ounsted et al[40] 1978 United Kingdom	**Oxytocin Time Point** Intrapartum **Design** Prospective longitudinal quasi-experimental with 3 induction methods and control group Primiparous only Breastfeeding intention recorded	Breastfeeding self-report at birth and 4 days later and at 2 months postpartum	N = 184 26% of women received oxytocin for induction of labor Intention to breastfeed ranged from 66% to 71% of each comparison group **Initiation** Fewer women changed to bottle feeding in spontaneous labor group compared to all induction methods **Duration** Oxytocin group alone were breastfeeding 37.1% at 2 months compared to 68% of the spontaneous group (NS $P < .1$)	Skin-to-skin not recorded Statistical methods limited analysis of oxytocin group alone due to high number of cells in the chi-square analysis; did not control for multiple confounding variables like length of labor or neonatal issues

Abbreviations: AMTSL, active management of third-stage labor; HR, hazard ratio; IM, intramuscular; IV, intravenous; NS, nonsignificant; OR, odds ratio; RR, relative risk; SD, standard deviation; WHO, World Health Organization.
[a] Baby-Friendly Initiative certification noted in study for research site.
[b] Skin-to-skin: the practice of mothers holding their infants skin-to-skin after birth.

onset, consistently defined by maternal report of breast fullness by 72 hours postpartum.[34,35,44–47] Three studies reported no association between lactogenesis and synthetic oxytocin use during labor.[44,46,47] Three papers reported mixed findings.[34,35,45] None of these studies' primary aim was to examine the role of synthetic oxytocin on lactogenesis; thus, these findings were the result of subanalyses or covariate data. All of these studies were prospectively conducted and sampled mixed populations regarding modes of birth (eg, vaginal, cesarean, instrument assisted) and use of analgesia. None reported information on postpartum oxytocin exposure.

Augmentation of labor with exogenous oxytocin (compared with no oxytocin) was associated with delayed lactogenesis in a bivariate analysis by Dewey et al[34] ($P < .05$) but not in regression analysis. Matias et al[45] found a marginal association with labor augmentation in bivariate analysis as well ($P < .10$), but adjusted analyses found only low Apgar score predicted delayed lactogenesis. Nommsen-Rivers et al[35] found no difference in delayed lactogenesis with oxytocin administration for induction or augmentation compared to women who had none. Postpartum oxytocin use was not considered by these studies, except as implied by Dewey et al, noting that women receiving "postpartum hemorrhage medications" were more likely to have delayed lactogenesis (26% compared to 16%, $P < .10$).

The final 2 maternal studies examined physiologic response by measuring hormone levels in maternal plasma in relation to oxytocin use. Jonas et al[27] examined physiologic response to exogenous oxytocin during birth via blood samples collected during a breastfeeding session 2 days postpartum. Maternal oxytocin and prolactin levels were measured; however, this was not reported in relationship to any clinical marker of lactation (ie, lactogenesis). They further demonstrated an inverse relationship ($r = -.495$, $P = .02$) between the total dosage administered during labor and level of oxytocin found in women's blood at 48 hours during breastfeeding ($n = 61$). Prolactin levels in women who received third-stage prophylaxis with oxytocin ($n = 13$) were lower compared to the 20 women who received no oxytocin.

Gu et al[26] measured exclusivity of breastfeeding as well the level of plasma oxytocin in maternal blood at 2 months postpartum. The authors found higher levels of oxytocin in women exposed to higher collective dosages of oxytocin (intrapartum and postpartum), which were also linked to higher likelihood of formula or nonexclusive breastfeeding at 2 months.

Infant Behavior

In relationship to oxytocin administration, authors examined prefeeding behaviors,[48] Primitive Neonatal Reflexes,[29,31] the Widström 9 stages of instinctive newborn behavior after birth,[49] suboptimal infant breastfeeding behavior as measured by the Infant Breastfeeding Assessment Tool,[34,35,45] and finally, the Premature Infant Breastfeeding Behavior Scale.[50]

Four infant studies reported a significant negative relationship between oxytocin used for induction or augmentation of labor and infant behaviors or feeding-related reflexes in healthy newborns. Three of these found that higher dosages of oxytocin predicted lower infant behaviors,[31,48,49] while one did not.[29] Radzyminski[50] reported that term infants undergoing oxytocin-induced labor scored below the mean for breastfeeding behavior on the Premature Infant Breastfeeding Behavior Scale; however, no statistics were provided. In contrast, oxytocin exposure did not associate with differences between groups on the Infant Breastfeeding Assessment Tool when assessed during the first week.[34,45]

Questions about the generalizability of the infant-focused studies arise from the variation in the measurement of neonatal behavior. The Primitive Neonatal Reflex tool has not been widely used in clinical breastfeeding assessment,[29] but these innate reflexes (eg, hand to mouth, finger flexion and extension, gazing, head turning, bobbing, sucking, swallowing) relate to behaviors necessary to locate the maternal breast, latch, and suckle unassisted. The study by Bell et al[48] recorded "prefeeding" behaviors, which are a subset of reflexes more associated with feeding (eg, hand to mouth, rooting, sucking on hand). Brimdyr et al[49] video-recorded the first hour of skin-to-skin contact following birth and reported the Widström stages, which lead to unassisted suckling at the breast by the newborn when placed skin-to-skin with the mother during this period. Conversely, the Infant Breastfeeding Assessment Tool is a validated measure that assesses an infant's breastfeeding mechanics.[34] This measure evaluates 4 behaviors—readiness, rooting, latching, and sucking—on a 12-point scale; these measures were used for infants beyond the immediate birth period. While it may imply neurobehavioral organization, it is also influenced by positioning and maternal efforts to assist her infant, as the infants are not assessed for unassisted latching as during Widström stages.

Overall, the body of literature reports breastfeeding outcomes from birth through several months postpartum including mothers' and infants' experiences. Notably, only 3 studies[31,34,45] measured both maternal and infant factors. While the results do demonstrate various statistical associations, generalizability of these findings may be affected by the aim of the study or limitations of study setting, sample, and control of confounding variables.

Setting

The majority of studies originated in Western Europe and Australia ($n = 15$) and the United States and Canada ($n = 8$). A minority of studies were in the developing world ($n = 4$). Three of these utilized large international data sets from the WHO Global Survey,[32,33,36] 2 of which, conducted by Guerra et al[32-33], addressed 2 different questions within Latin America (induction of labor and elective induction of labor).

Five studies described "baby-friendly" or early skin-to-skin practices following birth.[25,27,29,31,49] In the report by Bell et al,[48] neonates went to a warmer after birth, per hospital routine. This study utilized an open crib for observation of prefeeding behavior at 40 minutes of life, in contrast to the other 3 early infant behavior studies that reported observations while the neonate remained in physical contact with the mother. Despite these differences, the infant behavior studies

did report similar diminished feeding-related behavior associated with oxytocin use.

Setting of the studies is important as likelihood of use of exogenous oxytocin during birth, and the promotion of early breastfeeding best practices, would affect outcomes related to this study question. Studies observing low rates of induction or augmentation of labor,[32,33,36,43,45,46] using lower volumes of oxytocin for induction of labor (ie, 5 units/500 mL),[47] or those that do not report the percentage of the sample exposed[44,50] would be more difficult to compare to populations with higher rates. Newborns that had no or interrupted skin-to-skin time following birth may also have a different breastfeeding course than others. Standardizing these study elements would be important for interpreting the findings.

Sample

Parity

Many studies in this review did not control for parity, and 2 did not report parity.[30,43] Parity predicted not only breastfeeding differences[34,37,44,47] but also risk of oxytocin exposure.[29] Dewey et al[34] noted that use of oxytocin was greater for primiparous women than multiparous (38% vs 23%), though the variable was not included in the regression model of delayed lactogenesis with interactions of parity. Interestingly, of the studies that found no association between exogenous oxytocin and suboptimal breastfeeding, all used a sample of women of mixed parity. However, 2 studies reported a significant effect of oxytocin on decreased expression of primitive neonatal reflexes[29] and breastfeeding initiation[28] even after controlling for parity.

Intention to Breastfeed

Three studies linking oxytocin administration to poor breastfeeding outcomes did not report intentions to breastfeed among their samples, only initiation and duration.[26,30,42] This factor introduces study bias, as women with strong intentions to breastfeed may persist if difficulties arise. Of the 4 studies that reported risks for delayed lactogenesis, only 2 recorded maternal intentions to breastfeed, which were inclusion criteria.[34,35] A minority of studies examining interventions during birth on breastfeeding reported maternal intention to breastfeed[38,40,41,46,47] or breastfeeding confidence[25]; as such, the risk of bias in the findings for breastfeeding attrition should be considered with this limitation in mind.

Obstetric Risk Level

Twelve studies focused on a lower-risk sample (eg, vaginal birth, healthy newborns) versus higher risk (eg, cesarean birth, preterm birth, neonatal intensive care unit [NICU] admission). Seven of the 12 low-risk studies' samples examined the role of synthetic oxytocin on breastfeeding as a primary aim, highlighting the outcomes of healthy, lower-risk women and neonates born vaginally in relation to oxytocin exposure specifically. For example, the 4 infant behavioral studies examining feeding reflexes included healthy neonates (normal Apgar score and no NICU admission) born vaginally; all studies controlled for epidural analgesia use, which was not significantly related to the neonatal behaviors except for the study by Brimdyr et al.[49] While using a lower-risk sample reduces the risk of confounding variables contributing to the breastfeeding outcomes, it limits generalizability to women with more complex courses of care and surgical birth. However, differences noted among lower-risk women in breastfeeding strengthen the possible association of exogenous oxytocin and suboptimal breastfeeding.

In contrast, the studies examining delayed lactogenesis, those using the Infant Breastfeeding Assessment Tool, and outcomes of obstetric interventions included varied levels of obstetric risks for breastfeeding problems. The effect of this single intervention of oxytocin is therefore difficult to discern from the rest. Only 3 studies in these categories focused on low-risk vaginal birth.[25,37,47] Several other studies in these groups reported low rates of oxytocin use[34,45,46] or did not report the proportion of sample exposed,[44] which limit the interpretation of the findings.

Indications for Synthetic Oxytocin Use

Despite studies in this review stating that healthy or lower-risk women participated, authors did not routinely report the indications for the use of oxytocin. Various labor-related factors may drive the use of oxytocin, such as use of epidural analgesia or length of labor. Eight studies examined labor duration in relation to breastfeeding outcomes. Four of the 8 associated longer labor with less optimal breastfeeding.[34,35,37,50] Notably, 3 of these studies grouped primiparous and multiparous women together for this analysis, and multiparous women are more likely to have shorter labors as well as less difficulty breastfeeding.

Epidural analgesia and oxytocin use are often correlated.[21] This finding may be due to the potential for epidural analgesia to lower endogenous oxytocin levels in maternal circulation, which may slow second-stage labor[51,52] or lead to other factors (eg, fetal malposition) that may contribute to augmentation.[51,53] Oxytocin-induced or augmented labor may be perceived as more painful, thereby women opt for neuroaxial analgesia.[54,55] However, some research has not considered the specific role of oxytocin when studying the effect of epidural analgesia on lactation.[56]

Exogenous oxytocin may be useful in reducing risks associated with prolonged labor. Breastfeeding problems may also be associated with longer labors, but researchers should try to tease apart the role of oxytocin from labor duration. For example, Nommsen-Rivers et al[35] reported an association between length of labor and prevalence of delayed lactation; women with spontaneous labors less than 14 hours in duration had significantly less delayed lactogenesis, 35.7% compared to 57% of women with labors longer than 14 hours. In contrast, women with oxytocin who labored less than 14 hours had 47.1% delayed lactogenesis compared to 40.1% of those who labored greater than 14 hours. However, the authors did not report the dose of oxytocin nor proportion of labor exposed to oxytocin which limits the analysis. Finally, Matias et al,[45] looking only at primiparas, did not find a relationship between long labor and delayed lactation.

Second-stage labor was also examined by 6 studies.[34,35,37,43,44,46] Three reported less delayed lactation in women who pushed for less than 60 minutes compared to longer second stage[34,44,46]; however, they included multiparous women in their analysis. Data by Rajan[43] contrasted with other study findings; administration of oxytocin was associated with higher bottle-feeding at 6 weeks postbirth but only when second stage was less than one hour compared with greater than one hour when receiving oxytocin.

The primiparas in the Jonas study that evaluated levels of endogenous oxytocin and prolactin[27] had augmentation of labor due to slow or stalled labor. Therefore, the differences seen in blood levels of oxytocin may be attributable to other physiologic differences in the women who required oxytocin administration. However, in this small sample, third-stage administration was prophylactic, and changes in prolactin following oxytocin administration in this group could be more directly linked to the drug itself. It is unknown if women requiring induction or augmentation of labor are innately different physiologically, which may also impact breastfeeding.

DISCUSSION

The purpose of this review was to conduct a thorough exploratory search for research on synthetic oxytocin and breastfeeding outcomes. No 2 studies were similar enough to provide results at the level of meta-analysis. Given the variations in study design, we cannot conclude that oxytocin use during the birth process contributes to altered breastfeeding outcomes. However, because many of the studies did show associations between exogenous oxytocin and less optimal breastfeeding outcomes, especially in lower-risk samples, this question deserves more research before ruling out the possibility of an effect.

Exposure to Synthetic Oxytocin

Augmentation of labor tends to occur when labor is already prolonged. Oftentimes synthetic oxytocin can be infused for many hours or days during a lengthy induction process. The availability of the oxytocin receptor in uterine tissue may be a function of duration and/or the level of oxytocin in circulation.[57,58] Whether oxytocin receptors located in breast tissue respond similarly to those in uterine tissue has not been researched directly. However, use of oxytocin in this review was often reported as a binary outcome rather than a continuous outcome of dosage or duration. Study participants with minimal augmentation would have been grouped together with those having significantly longer exposure. Furthermore, study designs that do not adequately sample women exposed to oxytocin have more limited generalizability or power to detect a difference between groups. Consideration of the duration and dosage of oxytocin rather than a binary outcome may be more relevant to this line of research.

Measurement of Breastfeeding

As illustrated by this review, the measure of breastfeeding varies greatly. The only outcome reported with consistency was the maternal report of timing of lactogenesis. This measure has been found to be linked to the increased likelihood of continued breastfeeding.[59] Maternal report of breast fullness is considered reliable and valid.[60] However, significant variation in the initiation and duration outcomes were a function of the design, feasibility of the studies as well as the origin of the data (ie, medical records). The binary nature of the breastfeeding variable in many of the studies also cannot consider the women who are partially breastfeeding and supplementing formula or donor milk. Several studies measured breastfeeding duration via maternal report, one occurring 5 years after birth, leaving room for recall bias.[30] While some research has noted that early exclusive breastfeeding may predict longer-term outcomes,[4] many of these studies did not include any longitudinal data.

Infant behavioral studies in this review, particularly those examining the primitive and feeding reflex behaviors of healthy newborns, did share similarities in design and findings. As explained by the authors, the underpinnings of these designs rest on the potential for oxytocin to cross the placenta and act within the brain of the newborn either indirectly through feedback mechanisms (afferent vagus nerve) or directly by possibly crossing the blood-brain barrier itself or as an effect of increased lactate levels,[49] all of which are hypothesized to alter the behaviors based on animal research models.[61,62]

Limitations

This review has clear limitations due to high variability within the reviewed studies' designs. It is also not exhaustive; many elements of statistical analysis and synthesis of other outcomes (eg, role of cesarean birth or postpartum hemorrhage) were outside the scope.

Research Implications

Broadly, this review highlights the paucity of literature on this topic, despite the known physiology of oxytocin and lactation, frequent use of the hormone in childbirth, and growing emphasis on improving breastfeeding. Addressing this gap is possible through 2 main lines of common maternal-infant research. First, many studies published on lactation outcomes do not address the role of oxytocin use during labor and birth or control for its use.[56,63] Second, studies of labor induction or AMTSL are commonly done to compare intervention protocols, yet they rarely report lactation outcomes. These studies often utilize larger sample sizes, more rigorous randomized designs, and can control for more factors like parity or duration of labor, which would be helpful in addressing this question.

Several specific recommendations stem from this review. First, future lactation research regarding oxytocin should consider neonatal behaviors as well as maternal function. Differences in newborn behavior may manifest as maternal report of decreased milk supply or duration of exclusive breastfeeding. Second, setting and selection bias should be considered, including breastfeeding intentions of the participants and birth practices. Third, measurement of oxytocin used in labor should be more comprehensive, including indicated or elective administration, combined

intrapartum and postpartum dosages, and those following cesarean birth. Fourth, better reporting on epidural analgesia use and timing of oxytocin administration, including the order and duration of events, would help address the temporal role of the 2 often concurrent interventions on subsequent outcomes. Finally, cumulative pharmacokinetic effects should be considered (dosage and duration). As research on oxytocin outside of childbirth has shown a dosage response in terms of behavioral and biological effects,[61,64] dosage-related (rather than binary) data would be more informative when characterizing exposure to oxytocin.

Clinical Implications

Use of synthetic oxytocin has an important place in modern midwifery and obstetric care, as its use can reduce morbidity or mortality in the setting of prenatal complications or dystocia or during postpartum hemorrhage. We have reviewed and organized this body of literature to inform clinicians about existing research. We recommend counseling clients that there is no proven effect of this medication on lactation or breastfeeding outcomes while noting that research is incomplete. While the existing research does not provide a clear answer of the effects of oxytocin, care providers may want to be observant for breastfeeding challenges among women and newborns who received oxytocin. Including oxytocin exposure as part of a risk assessment for suboptimal breastfeeding may allow for early intervention.

CONCLUSION

This article is the first known review of literature reporting synthetic oxytocin administered during childbirth on breastfeeding outcomes. We used a comprehensive and integrative approach including data from studies examining other research questions. This strength, combined with inclusion of multiple breastfeeding outcomes (maternal and infant), adds needed complexity to the discussion of routine birth interventions and our knowledge about any lasting consequences.

Since oxytocin was first used clinically in the early 1900s,[65] research has inadequately addressed the possibility of an impact on the human breastfeeding relationship. As lactation is an oxytocin-dependent process, the role of oxytocin administered during birth is worth considering when examining suboptimal breastfeeding outcomes. Women's perceptions of inadequate milk supply are a leading cause of supplementation or discontinuation of breastfeeding. These perceptions deserve validation by clinicians and researchers by examining the issue through a holistic lens that includes physiologic foundations to this problem.

AUTHORS

Elise N. Erickson, CNM, MS, is a PhD student and adjunct clinical instructor at Oregon Health & Science University.

Cathy L. Emeis, CNM, PhD, is an Assistant Professor and the program director of the Nurse-Midwifery Education Program and the Clinical Department Chair of Nurse-Midwifery at Oregon Health & Science University.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

REFERENCES

1. Centers for Disease Control and Prevention. *Breastfeeding Report Card, 2016*. 2016:1-8.
2. Kent JC, Gardner H, Geddes DT. Breastmilk production in the first 4 weeks after birth of term infants. *Nutrients*. 2016;8(12):756.
3. Stuebe AM, Horton BJ, Chetwynd E, Watkins S, Grewen K, Meltzer-Brody S. Prevalence and risk factors for early, undesired weaning attributed to lactation dysfunction. *J Womens Health (Larchmt)*. 2014;23(5):404-412.
4. Chantry CJ, Dewey KG, Peerson JM, Wagner EA, Nommsen-Rivers LA. In-hospital formula use increases early breastfeeding cessation among first-time mothers intending to exclusively breastfeed. *J Pediatr*. 2014;164(6):1339-1345.e5.
5. Semenic S, Loiselle C, Gottlieb L. Predictors of the duration of exclusive breastfeeding among first-time mothers. *Res Nurs Health*. 2008;31(5):428-441.
6. Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics*. 2012;129(3):e827-e841.
7. Bartick MC, Schwarz EB, Green BD, et al. Suboptimal breastfeeding in the United States: Maternal and pediatric health outcomes and costs. *Maternal & Child Nutrition*. September 2016.
8. Bartick M, Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010;125(5):e1048-e1056.
9. Schwarz EB, McClure CK, Tepper PG, et al. Lactation and maternal measures of subclinical cardiovascular disease. *Obstet Gynecol*. 2010;115(1):41-48.
10. Uvnäs-Moberg K, Prime D. Oxytocin effects in mothers and infants during breastfeeding. *Infant*. 2013;9(6):201-206.
11. Crowley WR. Neuroendocrine regulation of lactation and milk production. *Compr Physiol*. 2015;5(1):255-291.
12. Hammock EAD. Developmental perspectives on oxytocin and vasopressin. *Neuropsychopharmacology*. 2015;40(1):24-42.
13. Nephew B, Murgatroyd C. The role of maternal care in shaping CNS function. *Neuropeptides*. 2013;47(6):371-378.
14. Martin JA, Hamilton BE, Ventura SJ, et al. Births: final data for 2009. *Natl Vital Stat Rep*. 2011;60(1):1-70.
15. World Health Organization. *WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage*. Geneva, Switzerland: World Health Organization; 2012:1-48.
16. Kenkel WM, Yee JR, Carter CS. Is oxytocin a maternal-foetal signalling molecule at birth? Implications for development. *J Neuroendocrinol*. 2014;26(10):739-749.
17. Dublin S, Johnson KE, Walker RL, et al. Trends in elective labor induction for six United States health plans, 2001-2007. *J Womens Health (Larchmt)*. 2014;23(11):904-911.
18. Osterman MJ. National Vital Statistics Reports. *January* 2015; 64(1):1-68.
19. Laughon SK, Zhang J, Grewal J, Sundaram R, Beaver J, Reddy UM. Induction of labor in a contemporary obstetric cohort. *Am J Obstet Gynecol*. 2012;206(6):486.e1-486.e9.
20. Freeman RK, Nageotte M. A protocol for use of oxytocin. *Am J Obstet Gynecol*. 2007;197(5):445-446.
21. Osterman MJ, Martin JA. National Vital Statistics Reports. March 2011;59(5):1-14.
22. Carter C. Developmental consequences of oxytocin. *Physiol Behav*. 2003;79(3):383-397.
23. Odent MR. Synthetic oxytocin and breastfeeding: Reasons for testing an hypothesis. *Med Hypotheses*. 2013;81(5):889-891.

24.Whittemore R, Knafl K. The integrative review: updated methodology. *J Adv Nurs*. 2005;52(5):546-553.
25.Dozier AM, Howard CR, Brownell EA, et al. Labor epidural anesthesia, obstetric factors and breastfeeding cessation. *Matern Child Health J*. 2012;17(4):689-698.
26.Gu V, Feeley N, Gold I, et al. Intrapartum synthetic oxytocin and its effects on maternal well-being at 2 months postpartum. *Birth*. 2016;43(1):28-35.
27.Jonas W, Johansson LM, Nissen E, Ejdeback M, Ransjö-Arvidson AB, Uvnas-Moberg K. Effects of intrapartum oxytocin administration and epidural analgesia on the concentration of plasma oxytocin and prolactin, in response to suckling during the second day postpartum. *Breastfeed Med*. 2009;4(2):71-82.
28.Jordan S, Emery S, Watkins A, Evans JD, Storey M, Morgan G. Associations of drugs routinely given in labour with breastfeeding at 48 hours: analysis of the Cardiff Births Survey. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2009;116(12):1622-1632.
29.Marín-Gabriel MA, Olza-Fernández I, Malalana-Martínez AM, et al. Intrapartum synthetic oxytocin reduce the expression of primitive reflexes associated with breastfeeding. *Breastfeed Med*. March 2015:10(4):150318121046004.
30.García-Fortea P, González-Mesa E, Blasco M, Cazorla O, Delgado-Ríos M, González-Valenzuela MJ. Oxytocin administered during labor and breast-feeding: a retrospective cohort study. *J Matern Fetal Neonatal Med*. 2014;27(15):1598-1603.
31.Olza-Fernández I, Marín Gabriel M, Malalana Martínez A, Fernández-Cañadas Morillo A, López-Sánchez F, Costarelli V. Newborn feeding behaviour depressed by intrapartum oxytocin: a pilot study. *Acta Paediatrica*. 2012;101(7):749-754.
32.Guerra GV, Cecatti JG, Souza JP, et al. Factors and outcomes associated with the induction of labour in Latin America. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2009;116(13):1762-1772.
33.Guerra GV, Cecatti JG, Souza JP, et al. Elective induction versus spontaneous labour in Latin America. *Bull World Health Organ*. 2011;89(9):657-665.
34.Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics*. 2003;112(3 Pt 1):607-619.
35.Nommsen-Rivers LA, Chantry CJ, Peerson JM, Cohen RJ, Dewey KG. Delayed onset of lactogenesis among first-time mothers is related to maternal obesity and factors associated with ineffective breastfeeding. *Am J Clin Nutr*. 2010;92(3):574-584.
36.Vogel JP, Souza JP, Gülmezoglu AM. Patterns and outcomes of induction of labour in Africa and Asia: a secondary analysis of the WHO Global Survey on Maternal and Neonatal Health. Bhutta ZA, ed. *PLoS ONE*. 2013;8(6):e65612-11.
37.Wiklund I, Norman M, Uvnas-Moberg K, Ransjo-Arvidson A, Andolf E. Epidural analgesia: breast-feeding success and related factors. *Midwifery*. 2007;25(2):e31-e38.
38.Yudkin P, Frumar AM, Anderson AB, Turnbull AC. A retrospective study of induction of labour. *Br J Obstet Gynaecol*. 1979;86(4):257-265.
39.Prendiville WJ, Harding JE, Elbourne DR, Stirrat GM. The Bristol third stage trial: active versus physiological management of third stage of labour. *BMJ*. 1988;297(6659):1295-1300.
40.Ounsted MK, Hendrick AM, Mutch LM, Calder AA, Good FJ. Induction of labour by different methods in primiparous women I. Some perinatal and postnatal problems. *Early Hum Dev*. 1978;2(3):227-239.
41.Out JJ, Vierhout ME, Wallenburg HCS. Breast-feeding following spontaneous and induced labour. *Eur J Obstet Gynecol Reprod Biol*. 1988;29(4):275-279.
42.Brown A, Jordan S. Active management of the third stage of labor may reduce breastfeeding duration due to pain and physical complications. *Breastfeed Med*. 2014;9(10):494-502.
43.Rajan L. The impact of obstetric procedures and analgesia/anaesthesia during labour and delivery on breast feeding. *Midwifery*. 1994;10(2):87-103.
44.Chapman DJ, Perez-Escamilla R. Identification of risk factors for delayed onset of lactation. *J Am Diet Assoc*. 1999;99(4):450-454.
45.Matias SL, Nommsen-Rivers LA, Creed-Kanashiro H, Dewey KG. Risk factors for early lactation problems among Peruvian primiparous mothers. *Matern Child Nutr*. 2009;6(2):1-14.
46.Kong MS, Bajorek B. Medications in pregnancy: impact on time to lactogenesis after parturition. *J Pharm Pract Res*. 2008;38(3):205-208.
47.Mauri PA, Contini NNG, Giliberti S, et al. Intrapartum epidural analgesia and onset of lactation: a prospective study in an Italian birth centre. *Matern Child Health J*. 2015;19(3):511-518.
48.Bell AF, White-Traut R, Rankin K. Fetal exposure to synthetic oxytocin and the relationship with prefeeding cues within one hour postbirth. *Early Hum Dev*. 2013;89(3):137-143.
49.Brimdyr K, Cadwell K, Widström A-M, et al. The association between common labor drugs and suckling when skin-to-skin during the first hour after birth. *Birth*. 2015;42(4):319-328.
50.Radzyminski S. The effect of ultra low dose epidural analgesia on newborn breastfeeding behaviors. *J Obstet Gynecol Neonatal Nurs*. 2003;32(3):322-331.
51.Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. Anim-Somuah M, ed. *Cochrane Database Syst Rev*. 2011;(12):CD000331.
52.Worstell T, Ahsan AD, Cahill AG, Caughey AB. Length of the second stage of labor. *Obstet Gynecol*. 2014;123:84S.
53.Rahm V, Hallgren A, Hogberg H, Hurtig I, Odlind V. Plasma oxytocin levels in women during labor with or without epidural analgesia: a prospective study. *Acta Obstet Gynecol Scand*. 2002;81(11):1033-1039.
54.Glantz JC. Elective induction vs. spontaneous labor associations and outcomes. *J Reprod Med*. 2005;50(4):235-240.
55.Henderson J, Redshaw M. Women's experience of induction of labor: a mixed methods study. *Acta Obstet Gynecol Scand*. 2013;92(10):1159-1167.
56.Lind JN, Perrine CG, Li R. Relationship between use of labor pain medications and delayed onset of lactation. *J Hum Lact*. 2014;30(2):167-173.
57.Phaneuf S, Rodriguez Linares B, TambyRaja R, Mackenzie I, Lopez Bernal A. Loss of myometrial oxytocin receptors during oxytocin-induced and oxytocin-augmented labour. *J Reprod Fertil*. 2000;120(1):91-97.
58.Balki M, Erik-Soussi M, Kingdom J, Carvalho JCA. Oxytocin pretreatment attenuates oxytocin-induced contractions in human myometrium in vitro. *Anesthesiology*. 2013;119(3):552-561.
59.Brownell E, Howard CR, Lawrence RA, Dozier AM. Delayed onset lactogenesis II predicts the cessation of any or exclusive breastfeeding. *J Pediatr*. 2012;161(4):608-614.
60.Chapman DJ, Perez-Escamilla R. Maternal perception of the onset of lactation is a valid, public health indicator of lactogenesis stage II. *J Nutr*. 2000;130(12):2972-2980.
61.Bales K, van Westerhuyzen J, Lewis-Reese A, Grotte N, Lanter J, Carter C. Oxytocin has dose-dependent developmental effects on pairbonding and alloparental care in female prairie voles. *Horm Behav*. 2007;52(2):274-279.
62.Hashemi F, Tekes K, Laufer R, Szegi P, Tothfalusi L, Csaba G. Effect of a single neonatal oxytocin treatment (hormonal imprinting) on the biogenic amine level of the adult rat brain: could oxytocin-induced labor cause pervasive developmental diseases? *Reprod Sci*. 2013;20(10):1255-1263.
63.Bai DL, Wu KM, Tarrant M. Association between intrapartum interventions and breastfeeding duration. *J Midwifery Womens Health*. 2013;58(1):25-32.

64. Freeman SM, Samineni S, Allen PC, et al. Plasma and CSF oxytocin levels after intranasal and intravenous oxytocin in awake macaques. *Psychoneuroendocrinology*. 2016;66:185-194.
65. Holmes JM. The use of continuous intravenous oxytocin in obstetrics. *Lancet*. 1954;267(6850):1191-1193.

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