Fall 8-10-2019

Guideline-Based Approach for the Precautious Use of Oxytocin in Labor Augmentation and Emergency Cesarean Section Rates

Kelley O'Connell
Pacific University

Guideline-Based Approach for the Precautious Use of Oxytocin in Labor Augmentation and Emergency Cesarean Section Rates

Abstract

Background: Exogenous oxytocin was approved by the FDA in 1962 and has been administered to help induce labor, advance a prolonged labor, assist with placental delivery, and manage postpartum bleeding. However, the use of this synthetic oxytocin is commonly both inconsistent and incautious in timing and dosing, with outcomes of uterine tachysystole (hyperstimulation), subsequent fetal oxygen desaturation and alterations in fetal heart rate patterns, all potentially leading to emergency cesarean sections (CS). Since such associations have been established, would the implementation of a guideline-based approach on the precautious use of synthetic oxytocin in labor augmentation reduce emergency CS rates?

Methods: An exhaustive literature search was performed using MEDLINE-PubMed, CINAHL, Proquest, and Web of Science databases. Key terms searched include oxytocin, intervention, fetal distress, reduc*, obstetric labor complications, education, guidelines as topic, protocol, and checklist. Articles that included a guideline approach to using oxytocin in labor augmentation and reported on emergency CS rates were included. Exclusion criteria included guidelines based on the third stage of labor. The remaining articles and their references were screened for eligibility, were critically appraised, and the quality of their evidence was assessed with the GRADE working group approach.

Results: Four studies met the inclusion and exclusion criteria and were eligible to be included in this systematic review. All were observational studies, 2 prospective and 2 retrospective. One study reported a significant reduction in the frequency of oxytocin use and a significant increase in overall emergency CS, but also a significant increase in oxytocin used in labors without dystocia. A second study found a significant reduction in the frequency of oxytocin use, emergency CS overall, and emergency CS indicated for fetal distress with a non-significant decrease in CS due labor dystocia. A third study reported a statistically significant reduction in the maximum oxytocin dose, with a non-significant decrease in CS rate post-checklist. The fourth study found a statistically significant reduction in the frequency of oxytocin use, a non-significant decrease in CS rate, a statistically significant increase in CS due to labor dystocia with a statistically significant reduction in those due to fetal distress. All studies were assessed as very low quality of evidence based on GRADE.

Conclusion: The studies collectively demonstrate that a guideline-based approach on the precautious use of synthetic oxytocin during labor management leads to a reduced frequency of its use and/or a decrease in the maximum dose. However, the impact on emergency CS rates became a moving target as each study used different guidelines. This reveals the necessity of a standardized approach that includes a universal definition of labor dystocia and a protocol that guides when to start, continue, or stop oxytocin. This could be accomplished by a future study that assessed a dose response curve to evaluate if a low or high dose oxytocin regimen, in combination with a universal guideline with provided markers for when to initiate and stop synthetic oxytocin, would correlate to a decline in emergent CS rates.

Keywords: oxytocin, intervention, fetal distress, reduc*, obstetric labor complications, education, guidelines as topic, protocol, and checklist.

Degree Type

Capstone Project

Degree Name

Master of Science in Physician Assistant Studies

Guideline-Based Approach for the Precautious Use of Oxytocin in Labor Augmentation and Emergency Cesarean Section Rates

Kelley O'Connell

A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

Hillsboro, OR

For the Masters of Science Degree, 08/10/2019

Faculty Advisor: Professor Allison McLellan

Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS

Biography

Kelley O'Connell is a native of Colorado and in the Global Health Track at Pacific University's Physician Assistant (PA) Program. She was part of the first cohort of PA students to complete a clinical rotation in Banepa, Nepal in January 2019. As a PA, she hopes to focus on preventative medicine and continue to provide care to both local and global communities alike.

Kelley majored in Integrative Physiology at the University of Colorado, Boulder, and graduated as a member of Phi Beta Kappa Association. She was actively involved in the CU Chapter of the Timmy Global Health Foundation, which included participating in their medical service trip and supporting the creation of a sustainable and accessible healthcare system in the underserved communities surrounding Quito, Ecuador.

Abstract

Background: Exogenous oxytocin was approved by the FDA in 1962 and has been administered to help induce labor, advance a prolonged labor, assist with placental delivery, and manage postpartum bleeding. However, the use of this synthetic oxytocin is commonly both inconsistent and incautious in timing and dosing, with outcomes of uterine tachysystole (hyperstimulation), subsequent fetal oxygen desaturation and alterations in fetal heart rate patterns, all potentially leading to emergency cesarean sections (CS). Since such associations have been established, would the implementation of a guideline-based approach on the precautious use of synthetic oxytocin in labor augmentation reduce emergency CS rates?

Methods: An exhaustive literature search was performed using MEDLINE-PubMed, CINAHL, Proquest, and Web of Science databases. Key terms searched include oxytocin, intervention, fetal distress, reduc*, obstetric labor complications, education, guidelines as topic, protocol, and checklist. Articles that included a guideline approach to using oxytocin in labor augmentation and reported on emergency CS rates were included. Exclusion criteria included guidelines based on the third stage of labor. The remaining articles and their references were screened for eligibility, were critically appraised, and the quality of their evidence was assessed with the GRADE working group approach.

Results: Four studies met the inclusion and exclusion criteria and were eligible to be included in this systematic review. All were observational studies, 2 prospective and 2 retrospective. One study reported a significant reduction in the frequency of oxytocin use and a significant increase in overall emergency CS, but also a significant increase in oxytocin used in labors without dystocia. A second study found a significant reduction in the frequency of oxytocin use, emergency CS overall, and emergency CS indicated for fetal distress with a non-significant decrease in CS due labor dystocia. A third study reported a statistically significant reduction in the maximum oxytocin dose, with a non-significant decrease in CS rate post-checklist. The fourth study found a statistically significant reduction in the frequency of oxytocin use, a non-significant decrease in CS rate, a statistically significant increase in CS due to labor dystocia with a statistically significant reduction in those due to fetal distress. All studies were assessed as very low quality of evidence based on GRADE.

Conclusion: The studies collectively demonstrate that a guideline-based approach on the precautious use of synthetic oxytocin during labor management leads to a reduced frequency of its use and/or a decrease in the maximum dose. However, the impact on emergency CS rates became a moving target as each study used different guidelines. This reveals the necessity of a standardized approach that includes a universal definition of labor dystocia and a protocol that guides when to start, continue, or stop oxytocin. This could be accomplished by a future study that assessed a dose response curve to evaluate if a low or high dose oxytocin regimen, in combination with a universal guideline with provided markers for when to initiate and stop synthetic oxytocin, would correlate to a decline in emergent CS rates.

Keywords: oxytocin, intervention, fetal distress, reduc*, obstetric labor complications, education, guidelines as topic, protocol, and checklist.

Acknowledgements

To my parents: Thank you for your unwavering support. For being my sounding boards, my moral compasses, my motivators, and my friends.

Table of Contents

List of Tables

List of Abbreviations

PA	Physician Assistant
CS	Cesarean Section(s)
WHO	World Health Organization

Guideline-Based Approach for the Precautious Use of Oxytocin in Labor Augmentation and Emergency Cesarean Section Rates

BACKGROUND

Oxytocin is an endogenous hormone that is produced by the hypothalamus and stored in the pituitary gland. It is naturally released from the posterior lobe of the pituitary gland during spontaneous labor and stimulates uterine smooth muscle contractions. Synthetic oxytocin is an exogenous form of oxytocin that increases the rate and amplitude of labor contractions, and, like any contraction, also momentarily obstructs blood flow to the uterus. This exogenous source of oxytocin is frequently used to augment labor, as it was approved by the FDA in 1962 to precipitate physiologically analogous contractions.[1] Specifically, it is indicated to induce labor, advance a prolonged labor (labor dystocia), assist with the delivery of the placenta (third stage of labor), and manage postpartum bleeding.[2]

The many indications of synthetic oxytocin leaves room for subjective interpretation and currently there is no clear consensus on when to initiate oxytocin nor how much to administer in both the induction of labor and augmentation of a spontaneous labor. This review will focus on those 2 areas of labor, the induction of labor and the augmentation of the first or second stages of labor. Even with this emphasis, there are still low-dose and high-dose regimens that vary in the initial dose as well as in titration schedules, and, when given, synthetic oxytocin is usually "dosed to effect" meaning until a particular uterine contraction pattern is reached.[2] Not surprisingly, inconsistent and unnecessary use of synthetic oxytocin is common.[3] This is concerning, as oxytocin administration has been associated with uterine tachysystole (hyperstimulation)[2,4] and subsequent fetal oxygen desaturation and alterations in fetal heart rate patterns[5] which potentially leads to emergency cesarean sections (CS).[6]

Hyperstimulation and tachysystole of the uterus reduces the time between the end of a contraction and the start of another, also known as relaxation time. One study[7] evaluated umbilical artery pH in relation to contraction characteristics during the first stage of labor, and found that umbilical artery acidosis was significantly associated with contractions that were longer in duration, increased in amplitude, frequency, and pressure, and subsequently a shorter relaxation time. The concern lies here.

Furthermore, due to synthetic oxytocin's potential to cause "significant patient harm" when used inappropriately,[2,4] it is now considered a "high alert medication" by the Institute for Safe Medication Practices.[8] They also require both maternal and fetal monitoring while the synthetic oxytocin is being administered.[1,9] Since such associations have been established, would the implementation of a guideline-based approach on the precautious use of synthetic oxytocin in labor augmentation reduce emergency CS rates?

METHODS

An initial search of medical literature was performed using MEDLINE-PubMed, CINAHL, Proquest, and Web of Science. Key terms searched include "oxytocin," "intervention," "fetal distress," and "reduc*." An additional search was then conducted using the PubMed search engine with the keywords "obstetric labor complications," "education," "guidelines as topic," "protocol," and "checklist." References were screened for eligibility. Articles that included a guideline approach to using synthetic oxytocin in labor augmentation and reported on emergency CS rates were included. Exclusion criteria included guidelines based on the third stage of labor or post-partum hemorrhage, and articles not published in English language. The quality of evidence was assessed with the GRADE working group approach.[10]

RESULTS

The initial search yielded 55 studies and the supplementary search yielded 90 articles for a total of 145 articles. Duplicates were removed, the remaining articles were reviewed for eligibility criteria, and 3 articles remained. The 3 article's bibliographies were then screened for eligibility criteria, leading to a total of 4 observational studies.[9,11,13,14]

Gaudernack et al

This prospective observational intervention study[9] implemented both a guideline and an educational program on the mindful use of oxytocin during labor in at-term, first time mothers at a Norwegian University Hospital. They collected patient data from electronic records pre-guideline, from October 2012 to May 2013, and then again post-guideline, from April 2014 to April 2015. The authors noted that the post-guideline data period was purposefully extended as "effect of quality improvement interventions is known to diminish with time."[9] The authors specifically focused on this population due to a recent report[3] showing an increase and imprudent use of oxytocin, specifically in primiparous women. Their guidelines recommended that oxytocin only be used in the setting of labor dystocia, and the authors hypothesized that this intervention would lead to an overall reduction in oxytocin administration and, when given, would exclusively be to women with the diagnosis of labor dystocia.[9]

The hospital used the Proactive Labor Support definition of dystocia pre-intervention, which specified that labor began at 1cm cervical dilation with effacement and painful, regular contractions, and that dystocia occurred when dilation progressed less than 1cm/hr. Post-intervention, dystocia was diagnosed when there was 2 hours of labor without progress. However, the new guidelines did not change the definition of the start of labor and did not modify oxytocin augmentation during the second stage of

labor. The study also incorporated an educational component, where the midwives participated in a course that reviewed the new guidelines and the positives and negatives of oxytocin therapy. A "project leader" then gave a lecture to both the midwives and doctors.[9]

The study included primiparous women with spontaneous labor onset and whose patient data included dystocia information. They excluded women with induced labors. The pre-intervention cohort included 431 women and the post-intervention cohort included 664 women. Post-intervention, there was a significant increase in overall emergency CS (6.7% vs. 10.2%; $p<0.05$) but with no significant change in dystocia or asphyxia as indications for CS. As hypothesized, they reported a significant reduction in frequency of oxytocin used (63.3% vs. 54.1%; $p<0.001$) and in woman diagnosed with dystocia (68.9% vs. 52.9%; $p<0.001$). Interestingly, oxytocin was administered in significantly more labors without dystocia (8.4% vs. 18.9%; $p<0.001$), falling under the category of oxytocin given without indication, the very concept that they were trying to improve.[9]

The authors argued that the increase in CS rates was most likely due to other variables and explored the idea that their definitions on the start of labor and dystocia may have been too strict and prevented labor to progress at a slower rate without augmentation.[9]

Rossen et al

This prospective observational study[11] implemented a guideline on the "judicious" use of oxytocin in labor augmentation at the Stavanger University Hospital in Norway. The study included 10 overall groups but listed 4 specific: nulliparous, single, cephalic presentation, $\geq$37 weeks in spontaneous labor (group 1), nulliparous, single, cephalic presentation, $\geq$37 weeks induced before labor (group 2a), multiparous (excluding previous CS), single, cephalic presentation, $\geq$37 weeks in spontaneous labor (group 3),

multiparous (excluding previous CS), single, cephalic presentation, ≥37 weeks induced before labor (group 4a). The study collected data from an electronic birth journal from January 2009 to December 2013, with the implementation of the guideline occurring in January 2010.[11]

Their guideline restricted the use of oxytocin to patients with the diagnosis of labor dystocia in both nulliparous and multiparous women, during the first stage of labor of spontaneous onset (groups 1 and 3), or before the start of the active phase in the setting of induced labors and/or after dystocia in the first stage of labor after induction (groups 2a and 4a). Oxytocin was administered until contractions reached a rate of 3-5 every 10 minutes. Pre-guideline, the beginning of labor was defined by regular and painful contractions and the active phase of labor definition used was by The World Health Organization (WHO) of cervical dilation of 4cm with cervical effacement. There was no definition to diagnose dystocia and instead oxytocin was used subjectively by individual physicians and midwives. Post-guideline, the 2014 WHO definition of dystocia[12] was employed, which delineated a prolonged labor as 4 hours without cervical dilation progress once the active phase of labor is reached. However, their guideline did not alter oxytocin use in the second or third stages of labor.[11]

The pre-guideline cohort included 3926 patients and the post-guideline cohort included 16 301 patients for a total of 20 227. Group 1 comprised 28.6%, group 2a was 8.9%, group 3 was 37.2%, and group 4a was 9.2%. Post-guideline, they found a significant decrease in both emergency CS overall (6.9% vs. 5.3%; $p<0.05$) and overall emergency CS indicated for fetal distress (3.2% vs. 2.0%; $p<0.01$). In subgroup analysis, statistical significance was reached for emergency CS due to fetal distress in groups 1 and 2a only. Interestingly, the frequency of prolonged labor leading to emergency CS did not change significantly (2.2% vs. 1.7%; $p=0.75$). As hypothesized, there was a significant reduction in the frequency of oxytocin use in labor augmentations across all groups (all $p<0.01$).[11]

The authors concluded that the observed reduction in oxytocin administration correlated to the reduction of overall emergency CS rates and cases of fetal distress leading to emergency CS.[11]

Clark et al

This retrospective observational study[13] applied a detailed checklist-based protocol on the use of oxytocin in labor augmentation of women with at term, vertex position, and singleton pregnancies without a history of CS across the Hospital Corporation of America health care system. The Hospital Corporation of America system includes physicians, pharmacists, nurses, and consultants in 125 obstetrics and gynecology departments across 20 states. The study initially reviewed 100 charts specifically from St. Mark's Hospital in Salt Lake City, Utah both before and after the implementation of the checklist-based protocol on March 1, 2005. After this, data was analyzed and the checklist-based protocol was then employed across the Hospital Corporation of America system.[13]

The protocol included 2 checklists, including a pre-oxytocin checklist and an "in use" oxytocin checklist. The pre-oxytocin checklist was required to be completed before the start of oxytocin therapy and included specifications such as "pelvis is documented by physician to be clinically adequate," "status of the cervix is assessed," "presentation is assessed," "indication for induction," and "fetal assessment completed," among others. When oxytocin had already been started, a subsequent checklist was to be completed every 30 minutes. If the checklist could not be completed, oxytocin was recommended to be either decreased or stopped. This second checklist focused on fetal assessment regarding the number of accelerations and decelerations, as well as a uterine contraction review on the rate, duration, palpation, and pressure. The authors note that their protocol was "purposefully far more conservative than would be required by current standards of care" but felt it was necessary since oxytocin is "the drug most

commonly implicated in avoidable medication related adverse outcomes."[13] This being said, the protocol focused overall on fetal and uterine contraction response but allowed both low and high dose regimens.[13]

The piloted study at St. Mark's Hospital found no change in the rate of CS and a significant decrease in the maximum dose of oxytocin in the checklist managed group. When the study was then employed across the system, the first year data on 220 000 deliveries found a decrease in CS rates (23.6% vs. 21.0%), a change from previously reported annual increases (1-4%) in CS rates in years prior. Intriguingly, such stringent guidelines might be forecasted to increase the rate of CS, not a system wide decrease as this study observed. The authors argued that this is most likely related to the overall reduction in maximum oxytocin dose post-checklist (17% decrease; $p<0.003$) leading to less uterine hyperstimulation, as this adverse event is dose-related.[13]

This study implemented a stringent protocol for the use of oxytocin but permitted medical providers to administer oxytocin across the range of acceptable dosing regimens without judgement. This allowed for the guideline-based approach to be assessed on its own, as a foundation to reaching the goal of using oxytocin in a conservative, evidenced based manner.

Rohn et al

This retrospective observational study[14] implemented a low-dose, checklist-based oxytocin protocol in an urban tertiary care center. The study collected data from delivering women with singleton pregnancies using electronic medical records. They included data from 4370 deliveries 15 months prior to the implementation of the protocol in July 2009, then allowed for a 9-month wash-out period after the initiation of the guideline, and then included data from 4347 deliveries for the 15 months following. The total study period was between January 1, 2008 and March 31, 2011. Notably, women who delivered between April 1, 2009 and December 31, 2009 were not included

in the study to allow for both a transition period and to minimize seasonal or monthly confounding variables.[14]

The protocol included 1 dosing regimen with a specified maximum dose rate, for 2 checklists. The first checklist was to be completed before oxytocin could be used for labor induction or labor augmentation, and included the same specifications as Clark et al[13] such as "pelvis is documented by physician to be clinically adequate," "status of the cervix is assessed," "presentation is assessed," "indication for induction," and "fetal assessment completed." Similarly, the second checklist was completed every 30 minutes after to determine if oxytocin could be continued and focused on a fetal assessment regarding the number of accelerations and decelerations, as well as a uterine contraction review on the rate, duration, palpation, and pressure. Dissimilar to Clark et al,[13] the second checklist also specified the dosing rate of oxytocin titration.[14]

The study found a non-significant decrease in overall emergency CS rates (662 women vs. 641 women; p=0.6) as well as emergency CS rates in deliveries augmented with oxytocin post-checklist (484 women vs. 463 women; p=0.28). They also reported an overall statistically significant increase in emergency CS due to labor dystocia (40.9% vs. 50.6%; p<0.001) and in women who received oxytocin (44.8% vs. 57.5%; p<0.001), but a statistically significant decrease in overall emergency CS due to fetal distress (38.7% vs. 32.5%; p=0.02) and in women who received oxytocin (42.0% vs. 27.4%; p<0.001) post-checklist. There were no significant changes observed for women who did not receive oxytocin for rates of emergency CS for dystocia nor fetal distress. Additionally, they found both a significant reduction in the frequency of oxytocin use (61.2% vs. 55.3%; p<0.001) and in the maximum dose administered (11 mU/min vs. 10 mU/min; p<0.001) post-checklist.[14]

This study was distinctive in that it used a similar protocol already assessed by a previous study.[13] However, it altered 2 variables concurrently by adding a low dose

regimen to a new checklist-based protocol, and then drew conclusions on individual obstetric outcomes.

DISCUSSION

Collectively, these 4 studies[9,11,13,14] demonstrate that a guideline-based approach regarding the precautious use of synthetic oxytocin during labor management leads to a reduced frequency of its use and/or a decrease in the maximum dose. However, the impact on emergency CS rates became a moving target. This is unsurprising when one considers the variability in each study's justification of when and how to implement oxytocin. Gauderneck et al[9] and Rossen et al[11] both used "labor dystocia" as the basis for initiating oxytocin, but then they used 2 different definitions of labor dystocia. Gauderneck et al[9] diagnosed labor dystocia when there was 2 hours of labor observed without progress, while Rossen et al[11] diagnosed labor dystocia when there was 4 hours of labor without cervical dilation progress once the women was in the active phase of labor. Furthermore, the Clark et al[13] and Rohn et al[14] studies did not base their protocols off of labor dystocia and instead used various measures on both maternal and fetal status. The 2 studies[13,14] used near-identical checklist protocols, which went a step further than Gauderneck et al[9] and Rossen et al[11] by including not only a guide for when to initiate oxytocin, but also used a checklist for the continuation of oxytocin augmentation. However, Rohn et al[14] differs from all 3 other studies in that they also implemented a new low-dose regimen in conjunction with the new guideline-based protocol.

Due to the focus of this review, a noteworthy study[15] considers the outcome of CS to be overly broad and the CS rate to be "arbitrary" and no longer a concern due to the safety of the surgery today. Unfortunately, this tolerance of the rate of CS does not fully consider the safety of CS globally. The World Health Organization (WHO)[12]

considers the high, increasing CS rate worldwide a substantial issue and recently released a new guideline[16] on the reduction of unnecessary CS. Alongside this, the WHO places a high priority on the safety of labor and delivery and on a woman's "autonomy"[12] during that process. A woman's autonomy during her labor is stifled when maternal and fetal monitoring is required during synthetic oxytocin therapy[1,9] and it is removed completely when surgery becomes the emergent, life-saving option. Since there is a high frequency of labors currently augmented with oxytocin in developed countries, the research and outcomes considered, which eventually lead to the protocols executed, impact high-income countries and low-income countries alike.[12] As synthetic oxytocin becomes more accessible, these low-income developing countries that operate in low resource settings will be looking to both local and global protocols for how to safely and effectively induce and augment labor. Partly in response to the WHO guideline, The Lancet also recently released a 3 paper series[17-19] on the optimization of CS globally. The series addressed the inequalities surrounding the use of CS,[17] evaluated the short and long term health effects of CS in mothers and their children,[18] and discussed approaches for the reduction of unnecessary CS.[19] A CS is a surgical procedure involving not just 1 but 2 individuals and therefore should require forethought. Overall, the outcome of the rate of CS is far from "arbitrary."

The 4 reviewed studies[9,11,13,14] agree that the current approach to oxytocin use is too variable, lacks an evidence based regimen, leads to inappropriate use, and also to unwanted obstetric and fetal outcomes. Yet their guidelines vary so much that, when considered together, the confounding variables cannot fully be teased out from synthetic oxytocin's effect on emergency CS rates.

In addition, the studies[9,11,13,14] are all observational cohort studies and so the conclusions made are indirect correlations since they assume that the reduction in oxytocin use and/or a reduction in the maximum dosage is related to the change in emergency CS rates observed. Gaudernack et al[9] assumes that the reduction in labors

augmented with oxytocin post-guideline correlates to the increased emergency CS rate. However, they provide insufficient explanation for supplementary findings. They reported a decrease in woman diagnosed with dystocia, but then a significant increase in labors augmented with oxytocin in patients without labor dystocia diagnosed, and also reported no significant changes in the number of emergency CS due to dystocia or asphyxia. The study's departing thought of their observed increase in emergency CS rates was most likely due to other variables is not explicit enough for an outcome such as emergency CS. The strength of this study is that they did specifically include an educational program as part of their protocol.

Rossen et al[11] also assumes that the reduction in labors augmented with oxytocin post-guideline correlates to the reduced emergency CS rate. One strength is that they included 20 227 labors and did subgroup analysis of their outcomes using combinations of nulliparous and multiparous women experiencing induction of labor and/or active labor augmentation with oxytocin.

Clark et al[13] makes the assumption that a checklist-based approach to starting, continuing, and/or stopping oxytocin correlated with decreased emergency CS. Notably, the study permitted the current range of low and high dose oxytocin regimens as long as the checklists could be completed. Precision is low for the results from the initial segment of the study where they piloted the checklist protocol in 1 hospital and only reviewed 200 charts in total. However, the true strength of this study is that they then extended the checklist-based protocol across an entire health system, reaching 125 departments in 20 states and reviewing charts on 220 000 deliveries.

Lastly, Rohn et al[14] used a near identical checklist-based approach as the one assessed in Clark et al[13] but with an additional requirement of a low-dose oxytocin regimen. However appealing, they created a confounding variable without having a high-dose oxytocin regimen to compare outcomes to. The study[14] also made the assumption that the checklist approach to starting, continuing, and/or stopping oxytocin with a low-

dose regimen correlated with the non-significant decrease in emergency CS rates. Additionally, it did not exclude women with a prior CS history, which is not only a separate topic up for debate but significantly separates their study population from the other 3 studies[9,11,13] that specified a history of prior CS as exclusion criteria. Unfortunately, the authors did not address this point directly nor speak to the potential adverse outcomes.

The very low quality of evidence of these studies as assessed by the GRADE working group[10] makes the process of delivering a definite conclusion difficult. Better studies might include a dose response curve assessment, comparing a low-dose vs. a high-dose regimen, with a universal protocol that provides markers for when to initiate, continue, or stop oxytocin therapy. The protocol aspect allows for shift workers, including nurses, midwives, and medical providers, all with a range of experience, to understand and pick up where the last medical professional left off without any confusion. This might relieve any pressure felt to "hurry along" a naturally progressing labor for the benefit of a work schedule.[13] Additionally, a low-dose vs. high-dose oxytocin regimen comparison will assess the current notion of administering oxytocin in the manner of a titration to effect.[2] This method would also address the effect of the dose on uterine tachysystole (hyperstimulation),[2,4] subsequent fetal oxygen desaturation, and alterations in fetal heart rate patterns[5] potentially leading to emergency CS.[6]

Understandably, there are great risks involved when we consider meddling with outcomes of maternal and fetal health. This is precisely why guidelines based on safety and evidence are more than appropriate.

CONCLUSION

Current use of synthetic oxytocin during labor augmentation is unstructured and irregular in both the range of dosing and its indications, often times leading to unnecessary administration.[3] Excessive use has been implicated as a means for an expedited birth for both the provider and the patient.[15] However innocent the intent, synthetic oxytocin is very commonly cited in preventable, medication associated negative side effects.[13,15] Errors such as these can lead to patient harm and be a professional liability to the healthcare provider and the institution.[4] Best medical practice is prioritizing patient safety and applying evidence based care, therefore a standardized approach regarding labor augmentation with oxytocin, including a universal definition of labor dystocia and guidelines for when to initiate, stop, or continue oxytocin therapy is essential.

REFERENCES

1. Oxytocin. ClinicalKey. Elsevier. Available at: https://www-clinicalkey.com.proxy.lib.pacificu.edu:2443/#!/content/drug_monograph/6-s2.0-458. Accessed July 27, 2018.

2. Ehsanipoor RM, Satin AJ. Normal and Abnormal Labor Progression. In: Post T, ed. *UpToDate*. Waltham, MA: UpToDate; 2018. https://www-uptodate-com.proxy.lib.pacificu.edu:2443/contents/normal-and-abnormal-labor-progression?search=Normal%20and%20Abnormal%20Labor%20Progression&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1 . Accessed July 27, 2018.

3. Selin L, Almström E, Wallin G, Berg M. Use and abuse of oxytocin for augmentation of labor. *Acta Obstetricia et Gynecologica Scandinavica*. 88(12):1352-1357. doi:10.3109/00016340903358812.

4. Simpson KR, Knox GE. Oxytocin as a high-alert medication: implications for perinatal patient safety. *MCN, The American Journal of Maternal/Child Nursing*. 2009;34(1):8-15. doi:10.1097/01.NMC.0000343859.62828.ee.

5. Simpson, KR, James, DC (2008). Effects of oxytocin-induced uterine hyperstimulation on fetal oxygen status and fetal heart rate patterns during labor. American Journal of Obstetrics and Gynecology, 199, 34.e1-5.

6. Hidalgo-Lopezosa P, Hidalgo-Maestre M, Rodríguez-Borrego MA. Labor stimulation with oxytocin: effects on obstetrical and neonatal outcomes. *Rev Lat Am Enfermagem*. 2016;24. doi:10.1590/1518-8345.0765.2744.

7. Bakker PCAM, Kurver PHJ, Kuik DJ, Van Geijn HP. Elevated uterine activity increases the risk of fetal acidosis at birth. *American Journal of Obstetrics and Gynecology*. 2007;196(4):313.e1-313.e6. doi:10.1016/j.ajog.2006.11.035

8. High-Alert Medications in Acute Care Settings. Institute For Safe Medication Practices. https://www.ismp.org/recommendations/high-alert-medications-acute-list. Accessed March 19, 2019.

9. Gaudernack LC, Frøslie KF, Michelsen TM, Voldner N, Lukasse M. De-medicalization of birth by reducing the use of oxytocin for augmentation among first-time mothers - a prospective intervention study. *BMC Pregnancy Childbirth*. 2018;18(1):76. doi:10.1186/s12884-018-1706-4.

10. GRADE Working Group. Grading of recommendations assessment, development and evaluation. http://www.gradeworkinggroup.org/. Accessed March 19, 2019.

11. Rossen J, Østborg TB, Lindtjørn E, Schulz J, Eggebø TM. Judicious use of oxytocin augmentation for the management of prolonged labor. *Acta Obstet Gynecol Scand*. 2016;95(3):355-361. doi:10.1111/aogs.12821.

12. World Health Organization, ed. *WHO Recommendations for Augmentation of Labour*. Geneva, Switzerland: World Health Organization; 2014.

13. Clark S, Belfort M, Saade G, et al. Implementation of a conservative checklist-based protocol for oxytocin administration: maternal and newborn outcomes. *American Journal of Obstetrics & Gynecology*. 2007;197(5):480.e1-480.e5. doi:10.1016/j.ajog.2007.08.026.

14. Rohn A, Bastek J, Sammel M, Wang E, Srinivas S. Unintended Clinical Consequences of the Implementation of a Checklist-Based, Low-Dose Oxytocin Protocol. *American Journal of Perinatology*. 2014;32(04):371-378. doi:10.1055/s-0034-1387932.

15. Oxytocin: new perspectives on an old drug- ClinicalKey. https://www-clinicalkey-com.proxy.lib.pacificu.edu:2443/#!/content/journal/1-s2.0-S0002937808006200 Accessed July 27, 2018.

16. WHO | WHO recommendations: non-clinical interventions to reduce unnecessary caesarean sections. WHO. http://www.who.int/reproductivehealth/publications/non-clinical-interventions-to-reduce-cs/en/. Accessed October 14, 2018.

17. Boerma T, Ronsmans C, Melesse DY, et al. Global epidemiology of use of and disparities in caesarean sections. *The Lancet*. 2018;392(10155):1341-1348. doi:10.1016/S0140-6736(18)31928-7.

18. Sandall J, Tribe RM, Avery L, et al. Short-term and long-term effects of caesarean section on the health of women and children. *The Lancet*. 2018;392(10155):1349-1357. doi:10.1016/S0140-6736(18)31930-5.

19. Betrán AP, Temmerman M, Kingdon C, et al. Interventions to reduce unnecessary caesarean sections in healthy women and babies. *The Lancet*. 2018;392(10155):1358-1368. doi:10.1016/S0140-6736(18)31927-5.

TABLES

Table 1: Quality Assessment of Reviewed Articles

Study	Design	Downgrade Criteria					Upgrade Criteria	Quality
		Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		
Gaudernack et al[9]	Cohort	Not Serious	Serious[a]	Serious[b]	Not Serious	Unlikely	None	Very low
Rossen et al[11]	Cohort	Not Serious	Serious[a]	Not Serious	Not Serious	Unlikely	None	Very low
Clark et al[13]	Cohort	Not Serious	Serious[a,c]	Not Serious	Not Serious[d]	Unlikely	None	Very low
Rohn et al[14]	Cohort	Serious[e]	Serious[a]	Not Serious	Not Serious	Unlikely	None	Very low

[a] Made an indirect correlation between oxytocin use and emergency CS rates.
[b]Lacked sufficient explanation for their findings, which include a significant increase in oxytocin augmentation in patients without dystocia and an increase in emergency CS, but with no change in the rate of dystocia as an indication for emergency CS post-guideline.
[c]The study permitted the range of low and high dose oxytocin regimen accepted by ACOG.
[d]Only 100 charts were reviewed each for the pre- and post- guideline groups, but then the protocol was employed across an entire health care system.
[e]Inadequate control of variables led to confounding: a new low-dose oxytocin regimen and a new checklist-based protocol. Also, the study did not exclude women with a history of CS which created a significant population difference from the other studies.