A Review of the Existing Evidence-based Protocols/guidelines on Oxytocin Dosing during Elective Cesarean Section to Prevent Post-partum Hemorrhage- A Creation of a Class A Pharmacology Continuing Educational Module for Certified Registered Nurse Anesthetist

Khadijah Lyons, BSN, RN and Eunice Martinez, BSN, RN

Department of Nurse Anesthesia, AdventHealth University

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Project Chair: Steve Fowler, DNAP, CRNA

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Abstract

Oxytocin is an endogenous hormone, and Pitocin is its synthetic analog often administered in the parturient patient to induce labor and further dilate the cervix. Per the American College of Obstetricians and Gynecologists (ACOG) and American Society of Anesthesiologists (ASA), there are standard dosage and administration guidelines to ensure safe delivery and decrease postpartum hemorrhage (PPH) (2020). Anesthesia providers must understand these administration guidelines to ensure more favorable health outcomes in the laboring woman. Globally, PPH is the leading cause of maternal mortality. A literature review suggests Pitocin via intravenous administration during active labor can significantly reduce postpartum hemorrhage, thus leading to more favorable health outcomes in the parturient patient (Salati et al., 2019).

Education is a method of affecting change. A 60-minute evidenced-based Class A pharmacology continuing education (CE) module on the appropriate use of Pitocin to prevent PPH during elective cesarean section was developed for Certified Registered Nurse Anesthetists (CRNAs) and Student Registered Nurse Anesthetists (SRNAs). The goal of the module is to discuss the role of oxytocin in the parturient patient, to provide evidence-based recommendations for intravenous Pitocin dosing during elective cesarean section to prevent PPH, and to understand the physiological changes associated with increased levels of oxytocin.

Keywords: Postpartum Hemorrhage, Cesarean section, Oxytocin, Dosage, educational module

Table of Contents

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Introduction

Pitocin is routinely administered after cesarean and vaginal delivery to initiate and maintain adequate urine contractility to reduce blood loss and prevent postpartum hemorrhage (PPH) (Bhattacharya et al., 2013; Kim et al., 2011; Yaliwa et al., 2020). Knowledge of standard dosage and administration guidelines for oxytocin is essential for the anesthetist to provide safe, high-quality patient care. Inappropriate oxytocin administration during cesarean section may result in fetal distress, maternal hemodynamic instability, and poorer maternal health outcomes (Kim et al., 2011; Seagraves et al., 2020; Stephens et al., 2012).

Although various studies have been conducted on the ideal intravenous oxytocin dose to prevent PPH during elective cesarean section, there is a lack of consensus on the safest dose. Therefore, we propose a quality improvement project with a Class A pharmacology CE module to provide CRNAs with evidence-based recommendations on intravenous oxytocin use during elective cesarean section to prevent PPH.

Significance & Background of Clinical Problem

ACOG defines PPH as loss of at least 1,000 ml of blood or blood loss coinciding with indications of hypovolemia within 24 hours after delivery (2020). According to the National Institute for Children's Health Quality (NICHQ), PPH is one of the leading causes of maternal morbidity and mortality in the United States (US) (2020). An estimated 3% of deliveries resulted in PPH (NICHQ, 2020), with an increased incidence after cesarian delivery (Butwick et al.,

2018). In 2018, the Center for Disease Control and Prevention (CDC) reported more than 31% of all deliveries in the US were via cesarian section, which is double the ideal 10-15% established by the World Health Organization (WHO) (Betran et al., 2016). With the increasing prevalence of PPH in cesarian sections, ACOG recommends that all hospitals implement systematic processes to help coordinate the response and management of postpartum hemorrhage

Oxytocin is the preferred drug used to prevent PPH due to its effectiveness and lower side effect profile (ACOG, 2020). It is an endogenous hormone that induces labor, stimulates contractions, and reduces postpartum hemorrhage (PPH) (Kim et al., 2011; Seagraves et al., 2020; Stephens et al., 2012; Yaliwa et al., 2020). High doses of oxytocin lead to numerous adverse effects, including tachycardia, hypotension, uterine hypertonicity, uterine tetanic contraction, and rupture (Kim et al., 2011; Seagraves et al., 2020; Stephens et al., 2012). Therefore, it is imperative to identify optimal oxytocin dosing to prevent PPH and maintain favorable health outcomes in the parturient patient.

In the United States, CRNAs provide most of the anesthetic services in the Armed Forces and throughout the country's rural areas (American Association of Nurse Anesthetists [AANA], 2020). Thus, it is critical to understand the dosing, mechanism of action, pharmacodynamics, and pharmacokinetics of each drug administered in the perioperative and intraoperative period (AANA, 2019). The absence of consensus on the safest and most effective IV oxytocin dose to prevent PPH during elective cesarian section requires an ongoing review of evidence-based recommendations to maintain competency among CRNAs.

PICOT Search Format Questions

Two questions, posed in PICO format, guided the systematic review of literature. The first addresses the clinical problem: In women who deliver via cesarean section (P), what is the optimum dose of oxytocin(I) for the treatment of post-partum hemorrhage due to uterine atony(O)?

The second question addresses the clinical innovation: At AdventHealth University (P), what is the feasibility of a SRNA developed educational module on the existing evidence-based protocols and guidelines of oxytocin dosing in preventing post-partum hemorrhage during elective cesarean section (I) submitted to the American Association of Nurse Anesthetist (AANA) for a 1 Class A pharmacology CE credit approval (O) by March 2023 (T)?

Search Strategy/Results

The search strategy included the following databases and professional practice organizations as well as reference lists: the ACOG, American Society of Anesthesiologist (ASA), National Board of Certification and Recertification for Nurse Anesthetists (NBCRNA), AANA, CDC, WHO, NICHQ, PubMed, Google Scholar, and National Guidelines Clearinghouse. A total of 672 articles were initially retrieved, and 22 studies met inclusion criteria. Articles not focusing on healthcare and studies not conducted within the last 10 years were omitted. Key Search Terms and MESH combinations included*: Oxytocin* AND *Pitocin* AND *caesarean section* AND *postpartum hemorrhage*, AND *female* AND *Prevention* AND *obstetric*, AND *labor and delivery* AND *pregnancy*, AND *anesthesia* AND *intravenous* AND *treatment outcome,* AND *intravenous bolus*. MESH terms included: Pitocin, oxytocin, pregnancy, postpartum hemorrhage, cesarean section, vaginal delivery. The search limits were English language, research article, and human subjects.

GRADE Criteria

The literature was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria. Initially, the supporting evidence yielded a high GRADE level, as the literature was primarily derived from systematic reviews, randomized control trials, and meta-analyses. Due to methodological flaws, imprecision, and publication bias, the literature was rated down-1. Methodological flaws included a lack of blinding and convenience sampling. Problems associated with imprecision consisted of small sample sizes and wide confidence intervals. Potential publication bias existed as medical personnel and authors formed part of the committee conducting the study. Research supports the idea of using various oxytocin dosing regimens to prevent PPH. Since the quality of evidence is moderate, inclusion of oxytocin dose regimens within clinical practice is highly recommended.

Literature Review and Synthesis of Evidence

Among the various uterotonic agents utilized to treat and prevent PPH, oxytocin is the preferred drug. (Reale et al., 2020). It is used to avoid unwanted physiological effects such as anterior pituitary ischemia, coagulopathy, cardiovascular collapse, and postpartum depression associated with PPH (Kim et al., 2011; Ngwenya, 2016). After delivery, oxytocin is typically administered by IV infusion to initiate and maintain uterine contractility to reduce blood loss. Unfortunately, an ideal IV dose of oxytocin to prevent PPH has not been identified. However, various regimens for oxytocin use have been proposed, which has led to varying practices among anesthesia providers (Devikarani et al., 2010). This study will discuss the role of oxytocin in the parturient patient, evidence-based recommendations for oxytocin dosing during elective cesarean section to prevent PPH, and highlight the physiological changes associated with increased levels of oxytocin.

Route of Administration

Oxytocin for prophylactic PPH can be administered intramuscularly (IM) or intravenously (IV). IM administration of oxytocin is associated with fewer hemodynamic effects; however, research revealed that IV administration more effectively prevents and manages PPH (Adnan et al., 2017; Charles et al., 2019). According to a 2019 study performed by Charles et al., when compared to IM injection, mean blood loss was 5.9% less in the IV infusion arm and 11.1% less in the IV bolus arm. Also, risk of postpartum blood loss ≥500 ml in the IV infusion arm was significantly less compared to IM injection (0.8% vs. 1.5%). Thus, research supports IV oxytocin administration as the more favorable route in the treatment of PPH.

Dosing

Intravenous infusion has been the accepted oxytocin administration route; however, several IV bolus regimens have been proposed. According to Sartain et al. (2008) and Murphy et al. (2008), an IV bolus of 2 and 3 units(U) is as safe and more effective than an IV bolus of 5 and 7 units of oxytocin in PPH management (2018). Additionally, an IV bolus of ≤ 1U can attain effective uterine contractions with the minimum effective dose of 0.35U (Devikarani et al., 2010). While IV boluses of as much as 10 U of oxytocin have been used, higher IV boluses and infusion rates are associated with myometrial cellular receptor desensitization (Evensen et al., 2017; Hidalgo-Lopezosa et al., 2016; Kim et al., 2011). It is also known that rapid infusion of large oxytocin dosing can lead to water intoxication, pulmonary edema, increased heart rate, nausea, vomiting, and decreased mean arterial pressure (Charles et al., 2019; Stephens et al., 2012). Thus, increased safety with lower oxytocin dosing regimens.

Despite the numerous studies advocating for IV bolus, the overwhelming majority indicate that rapid intravenous oxytocin administration results in harmful hemodynamic effects

after cesarean delivery (WHO,2020). Therefore, slow intravenous infusion is safer in these patients. Commonly, IV infusion dosing regimens for oxytocin range between 10-40IU diluted into 500ml or 1000ml of crystalloid (Charles et al., 2019; Stephens et al., 2012; WHO, 2020). However, Ahmadi found that using 80 units compared to a dose of 30 units of oxytocin reduces uterus atony and the need for an additional uterotonic drug (2018). Still, WHO recommends 10 IU of oxytocin diluted and administered slowly to prevent PPH (2020). When comparing dosing regimens to determine the optimal dose of intravenous oxytocin for cesarean delivery, Stephen et al. discovered that blood loss was not significantly less with higher amounts of oxytocin (2012). Thus, lower oxytocin infusion rates are efficacious in PPH prevention and help avoid the increased incidence of nausea, hypotension, and elevated heart rate associated with higher Oxytocin doses (Charles et al., 2019; Stephens et al., 2012; WHO, 2020).

Although there is extensive research on oxytocin administration, there is a lack of consensus on the optimal dosage to prevent and manage PPH in cesarean section (Seagraves et al., 2020). However, WHO recommends 10 IU of oxytocin for PPH prevention for all births (2020). Additionally, the efficacy of higher intravenous oxytocin dosing has not been proven to reduce total blood loss compared to lower intravenous dosing (Tita et al., 2012).

Applicability to Practice

Due to the constant evolution of medical research, healthcare professionals must maintain required CE credits. CE may improve medical knowledge, standard practice currency, and patient outcomes (Reigner et al., 2019). The implementation of an evidence-based educational module to increase the CRNAs' knowledge base and understanding of Pitocin may lead to a decreased incidence of PPH in the parturient patient undergoing elective cesarean section, ultimately leading to decreased morbidity and mortality.

Current Pitocin standards and guidelines do not clearly state a specific dosage; however, research does reveal that an IV bolus of 0.35 to 3 U Pitocin, followed by an infusion does decrease PPH during cesarean section. Due to lack of a common consensus on current practice and precise dosing, the proposed CE module will aim to provide evidence-based recommendations to the nurse anesthetist with the hopes of decreasing the incidence of PPH and reducing Pitocin related complications.

Project Aims

This project aims to create a 60-minute evidence-based Class A pharmacology CE module for CRNAs on the appropriate use of oxytocin to prevent PPH during elective cesarean section. The objectives of the CE module are to:

1. Discuss PPH and its effects on mortality and morbidity in the parturient patient.
2. Discuss evidence-based practice considerations for oxytocin dosing during elective cesarean section to prevent PPH.
3. Discuss physiological changes associated with increased levels of oxytocin.

The proposed module was submitted to the AANA for approval in Fall of 2022.

Methods

This project was defined as a *quality improvement (QI)* and *quality assurance* (QA) project. The setting was an online interface that included a 60-minute evidenced-based Class A pharmacology CE module for CRNAs on the appropriate use of oxytocin to prevent PPH during elective cesarean section. The module includes a brief course description, course objectives, an in-depth lesson, and a post-test with a minimum passing score of 80% to assess competency with the presented material. The post-assessment was created as part of the CE module, but data will not be collected on test results, as there will be no human subjects in this study.

Access and Recruitment Method

The completed module meets the AANA's necessary guidelines and regulations to be given as an annual credit to CRNAs who hold membership with the AANA. Due to the nature of this project the need for access and recruitment is not applicable. CE module formation was performed independently.

Planning and Procedures/Limitations

The keys stakeholders were identified by their expertise in obstetrics patient care and research. Each key stakeholder played an important role in guiding the project to implementation. Resources utilized for this project included the investigator's personal computer and Internet access. No grants were received, and no budget was needed due to the nature of the scholarly project.

Interviews of key stakeholders were conducted with the focus of maintaining integrity for the project. Before the implementation of the scenario, a preliminary educational module was developed in the spring of 2022, and a pilot study was conducted in the summer of 2022. The pilot study aimed to present the educational module to experienced anesthesia providers (i.e. CRNAs, professors) to eliminate any discrepancies in the presentation and estimate the appropriate time needed for the module. Once the presentation was finalized, it was taken through the appropriate channels to be submitted to the AANA for class A CE credit.

A significant potential barrier to this scholarly project was obtaining recent validated research on oxytocin usage and preventing PPH during the cesarian section. To aid in providing evidence-based recommendations, the research was graded with the GRADE matrix scale, and studies from the last 10 years were used.

Anticipated Limitations

This study has several limiting factors. The first limitation was heterogeneous literature. Additionally, the gathered information does not encompass all clinical situations as practitioners may alter oxytocin dose based on the case complexity. Some studies used estimated blood loss rather than measured blood loss to diagnose PPH. Also, low resource settings may have different formulations and dosage schedules for oxytocin administration. Regardless of these limitations, there are ranges of intravenous oxytocin that are deemed safe for the parturient patient.

Timeline

The topic proposal and partner submission were completed on February 21, 2021. Research and formation of matrix tables began on April 15, 2021 and were submitted for approval on June 4, 2021. The PICOT question was synthesized on June 10, 2021. PICOT revisions were made on August 12, 2021 through January 15,2022. Data collection and determination of project mentor and key players spanned from June to July of 2021. CE module data collection extened from July 2021 to December 2021. The formation of the CE module itself and voice narration began in January 2022 and was completed in June 2022. Editorial revisions were made, and the CE module was submitted to Dr.Borrero in July 2022. Application to the AANA was completed in January 2023. CE module was approved by the AANA on March 14, 2023.

Results

The development of the educational module followed the AANA criteria for Class A CE pharmacological credit and was submitted for approval on January 6, 2023. The response time from the AANA was approximately eight weeks. Feedback from the AANA was immediately considered and implemented into the educational module. Application was approved on March

14, 2023. Approval for CE credit established the feasibility of an SRNA-developed educational module.

Conclusion

There is a lack of consensus on the optimal intravenous Pitocin dosing during cesarian section to prevent PPH. An extensive literature review led to the preparation of an educational module with evidence-based recommendations for safe oxytocin usage during cesarian sections. The educational module consists of up-to-date, evidence-based recommendations for oxytocin administration and a post-test to assess effectiveness. This educational module aims to facilitate lifelong learning in anesthesia providers in hopes of maintaining and improving patient safety.

Dissemination Plan

This educational module aims to provide anesthesia providers, including SRNAs, and CRNAs, with up-to-date evidence-based recommendations for oxytocin administration during elective cesarian section. The research included in this module will be disseminated via the AANA. Application to the AANA was completed in January 2023. Upon approval from the AANA, providers that complete the module will be eligible to receive 1 Class A pharmacology CE credit, thus facilitating lifelong learning requirements for the CRNA.

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