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(adapted from several institutions)**

Postpartum/Intra-Operative Oxytocin Infusion Protocol

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Date: January 4th, 2021

Rationale:

Oxytocin is a neuropeptide hormone produced in the hypothalamus and released by the posterior pituitary gland. Its two main physiologic effects in the parturient are stimulation of uterine contraction and milk ejection. The American College of Obstetrician-Gynecologists (ACOG) recommends routine use of oxytocin as first-line prophylaxis against postpartum hemorrhage (PPH),¹ but does not offer a specific protocol. The Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) has recommended a protocol for oxytocin administration post-vaginal delivery² that is used by many labor and delivery institutions across the United States. Given the differences in postpartum oxytocin requirements following vaginal delivery and cesarean delivery (CD),³ the AWHONN protocol is not appropriate for intra-operative use during CD.

In 2019 an international group of obstetric anesthesiologists developed a consensus statement on the use of uterotonic agents during CD.³ The statement differentiates between oxytocin dosing for elective versus intra-partum CD due to the differing oxytocin requirements. One dose-finding study found that 74% of patients having an elective CD had adequate uterine tone after 2 minutes despite being randomized to receive no oxytocin.⁴ Three studies using biased-coin sequential allocation techniques have found the ED90 for elective, low-risk patients to be approximately 0.3 units.⁵⁻⁷ In trials using infusions instead of boluses of oxytocin, approximately 1 unit needs to be given to achieve adequate tone by 4 minutes after delivery.^{6,7}

In contrast, laboring patients require higher doses of oxytocin. A study of patients undergoing CD after arrest of labor following induction or augmentation with oxytocin found the ED90 to be 3 units, nine times higher than non-laboring patients.⁸ Up to 40% of patients in these trials that underwent intrapartum CD

required second-line uterotronics,^{7,9} and the consensus statement encourages early administration of second-line agents for these patients.³ After prolonged exposure to oxytocin, the receptors are desensitized¹⁰ and down-regulated⁷ making alternative agents necessary.

Oxytocin receptor desensitization and down-regulation following intra-partum exposure is the reason that one cannot rely solely on oxytocin for treatment of PPH.¹¹ While oxytocin has been extensively studied for prevention of PPH, there are no randomized trials assessing its efficacy in treating established PPH.¹² It is theorized that patients that have not responded normally to standard doses of prophylactic oxytocin may be unable to respond normally to oxytocin, meaning further oxytocin will not be efficacious.¹² This theory is supported by a Swedish register based cohort study that showed about one third of the variance in liability for PPH was due to maternal and fetal genetic effects.¹³ A genome-wide association study presented as an abstract at the Anesthesiology 2020 conference identified three loci associated with PPH risk.¹⁴ Models have shown that downregulation of oxytocin receptors does not affect the ability of myometrium to contract in response to second-line uterotronics.¹⁵ When second-line uterotronics are used, remember to consider if tranexamic acid is also indicated.¹⁶ The World Health Organization recommends tranexamic acid as a standard part of the treatment of PPH.¹⁷

Reducing unnecessary exposure to oxytocin will reduce the incidence of side effects. The incidence of the most visible adverse effect, nausea and vomiting, has been shown in studies of elective CDs to be dose-related.^{3,7,18} The hemodynamic effects of oxytocin are less visible, but more concerning. All of the following effects have been seen with oxytocin and occur at higher rates with larger doses, including hypotension, peripheral vasodilation, increased cardiac output from both increased heart rate and increased stroke volume, and ST segment changes.³ Other side effects from oxytocin include water retention, hyponatremia, flushing, feelings of warmth, nasal congestion, palpitations, dry mouth, metallic taste, headache, shivering and pruritis.³

Speed of oxytocin bolus is also associated with an increased incidence of side effects, including death.³ For this reason, the international consensus statement recommends administering all boluses slowly over at least 30 seconds.³

For elective CD the international consensus statement³ recommends a 1-unit bolus of oxytocin followed by an infusion of 2.5-7.5 units/hr. For intra-partum CD, a 3-unit bolus followed by an infusion of 7.5-15 units/hr is recommended. Atony should be treated with a 3-unit bolus then second-line uterotronics as needed. Taking into account all these considerations, and in the interest of standardization of protocol, the following recommendations are proposed:

Recommendations:

	Bolus Dose	Infusion Rate
Pre-Labor (Elective) CD	3 units	187mU/min (7.5 units/hr)
Intra-partum CD	3 units	187mU/min (7.5 units/hr)
Uterine Atony	3 additional units then second-line agents	250mU/min (10 units/hr)

For All Cases:

An Alaris pump with channels should remain in the labor and delivery operating room at all times. Ideally program and pause the pump prior to the start of the case to allow for timely initiation after delivery. Connect the oxytocin infusion line as close as possible to the IV insertion site. When a Y-type catheter extension set is used, connect oxytocin to one side and the LR bolus line to the other. Take extra care to never start the infusion prior to delivery. Chart the oxytocin bolus and infusion separately. Once the case is finished, take the Alaris pump from the OR with the patient to the PACU for continued infusion. Please be sure another Alaris pump is available in the OR after cleaning for the next case.

Uterine Atony:

In cases of uterine atony, follow the above protocol by administering an additional 3 units of oxytocin and increasing the infusion rate to 250mU/hr (10 units/hr). Should the tone remain poor, second-line uterotronics (methylergonovine, carboprost, misoprostol) are indicated with selection

dictated by patient medical history. Further increasing the infusion rate will not be clinically helpful due to receptor desensitization, and it will increase the incidence of side effects. If second-line uterotronics are used, consider whether tranexamic acid is also warranted.

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