Obstetric Anesthesia Update: Preeclampsia & Uterotonic Management

Review & Update
An Anesthesiologist's perspective
& what Nursing need to know

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Disclosures

- No Financial disclosures
- Fellowship research on Uterotonics previously presented at:
  - Society of Obstetric Anesthesia and Perinatology (SOAP) 2017 Bellevue
  - Canadian Anesthesia Society Annual Meeting (CAS) 2017 Niagra Falls
  - Accepted for publication

Objectives

Objectives are to discuss updated practices in:

- Preeclampsia
  - Discuss terminology
  - Revisit pathophysiology
  - Cases
  - Clinical pearls

- Uterotonic management
  - Uterine Atony
  - Elective vs. Labour arrest
  - Drug choice - Oxytocics, 2nd Line Uterotonics, Tranexamic Acid
  - Guidelines

Preeclampsia

“Being a mother is learning about strengths you didn't know you had... and dealing with fears you didn't know existed.”

- Linda Wooten

Hypertensive Disorders of Pregnancy (e.g. Preeclampsia)

- Hypertensive disorders of pregnancy (HDP) remain the leading cause of maternal and perinatal morbidity & mortality worldwide
- Incidence of preeclampsia has increased by 25% in last 2 decades (US)
- 2-8% of pregnancies are affected

Clinical Features

Signs & Symptoms

- High Blood Pressure (Hypertension)
- Proteinuria
- Swelling (Edema)#
- Headache
- Nausea or Vomiting
- Abdominal (stomach area) and/or Shoulder Pain
- Lower back pain
- Sudden Weight Gain
- Changes in Vision
- Hyperreflexia/Clonus
- Shortness of breath, anxiety
- NO Symptoms

Risk factors

Table 1
Preeclampsia Risk Factors

Maternal Considerations

Inherent

- Age < 20 or 35–40 years
- Nulliparity
- Black race
- Prior or family history of PE or cardiovascular disease
- Woman born small for gestational age

Medical conditions

- Obesity
- Chronic hypertension
- Chronic renal disease
- Diabetes mellitus (insulin resistance, type 1, and gestational)
- Antiphospholipid antibody syndrome
- Connective tissue diseases
- Thrombophilia
- Stress

Pregnancy specific

- Multiple gestation
- Oocyte donation
- Urinary tract infection
- Congenital conditions affecting the fetus
  - Hydatidiform mole
  - Hydrops fetalis
  - Structural anomalies

Paternal Considerations

Limited sperm exposure

- Barrier contraception
- First-time father
- Donor insemination

Partner who fathered a preeclamptic pregnancy in another woman

Adapted from reference 2 and Dekker G, Sibai B. Primary, secondary, and tertiary prevention of preeclampsia. Lancet 2001;357:209–15.

Terminology

- Eclampsia
- Preeclampsia
- Toxemia
- Pregnancy-induced hypertension
- Gestational hypertension +/- proteinuria

Terminology

- In women with *gestational hypertension*, *preeclampsia* should be defined as *new-onset proteinuria*, *one or more adverse conditions*, *or one or more severe complications*. (II-2B)

Classification of Hytertensive Disorders of Pregnancy (US)

- Preeclampsia-eclampsia -> after 20 weeks GA
- Chronic Hypertension (of any cause) -> predating pregnancy
- Chronic Hypertension + Preeclampsia (super-imposed)
- Gestational Hypertension -> after 20 weeks GA

Classification of Hytertensive Disorders of Pregnancy (CAN)

Disorder	Comments
Pre-existing (chronic) hypertension	This is defined as hypertension that develops either pre-pregnancy or at < 20+0 weeks' gestation
With comorbid condition(s)	Comorbid conditions (e.g., pre-gestational type I or II diabetes mellitus or kidney disease) warrant tighter BP control outside of pregnancy because of their association with heightened cardiovascular risk.
With evidence of preeclampsia	This is also known as superimposed preeclampsia, and is defined by the development of one or more of the following at ≥ 20 weeks: • resistant hypertension, *or* • new or worsening proteinuria, *or* • one or more adverse conditions,* *or* • one or more severe complications.* Severe preeclampsia is defined as preeclampsia with one or more severe complications.
Gestational hypertension	This is defined as hypertension that develops for the first time at ≥ 20+0 weeks' gestation.
With comorbid condition(s)	Comorbid conditions (e.g., pre-gestational type I or II diabetes mellitus or kidney disease) warrant tighter BP control outside of pregnancy because of their association with heightened cardiovascular risk.
With evidence of preeclampsia	Evidence of preeclampsia may appear only many weeks after the onset of gestational hypertension. Preeclampsia is defined as gestational hypertension with one or more of the following: • new proteinuria, *or* • one or more adverse conditions,* *or* • one or more severe complications.* Severe preeclampsia is defined as preeclampsia with one or more severe complications.
Preeclampsia	Preeclampsia may arise de novo. It is defined as gestational hypertension with one or more of the following: • new proteinuria, *or* • one or more adverse conditions,* *or* • one or more severe complications.* Severe preeclampsia is defined as preeclampsia with one or more severe complications.
Other hypertensive effects†	
Transient hypertensive effect	Elevated BP may be due to environmental stimuli, e.g., the pain of labour.
White-coat hypertensive effect	This is defined as BP that is elevated in the office (sBP ≥ 140 mmHg or dBP ≥ 90 mmHg), but consistently normal outside of the office (< 135/85 mmHg) by ABPM or HBPM
Masked hypertensive effect	This is defined as BP that is consistently normal in the office (sBP < 140 mmHg or dBP < 90 mmHg), but elevated outside of the office (≥ 135/85 mmHg) by ABPM or repeated HBPM.

The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Hypertension in Pregnancy

Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy

Executive Summary

The American College of Obstetricians and Gynecologists (the College) convened a task force of experts in the management of hypertension in pregnancy to review available data and publish able. Chronic hypertension is associated with fetal morbidity in the form of growth restriction and maternal morbidity manifested as severely increased blood pressure (BP). However, maternal and fetal morbidity increase dramatically

SOGC CLINICAL PRACTICE GUIDELINE

No. 307, May 2014 (Replaces No. 206, March 2008)

Diagnosis, Evaluation, and Management of the Hypertensive Disorders of Pregnancy: Executive Summary

The guideline summarized here has been prepared by the Canadian Hypertensive Disorders of Pregnancy Working Group, reviewed and approved by the Hypertension Guideline Committee, reviewed by the Maternal Fetal

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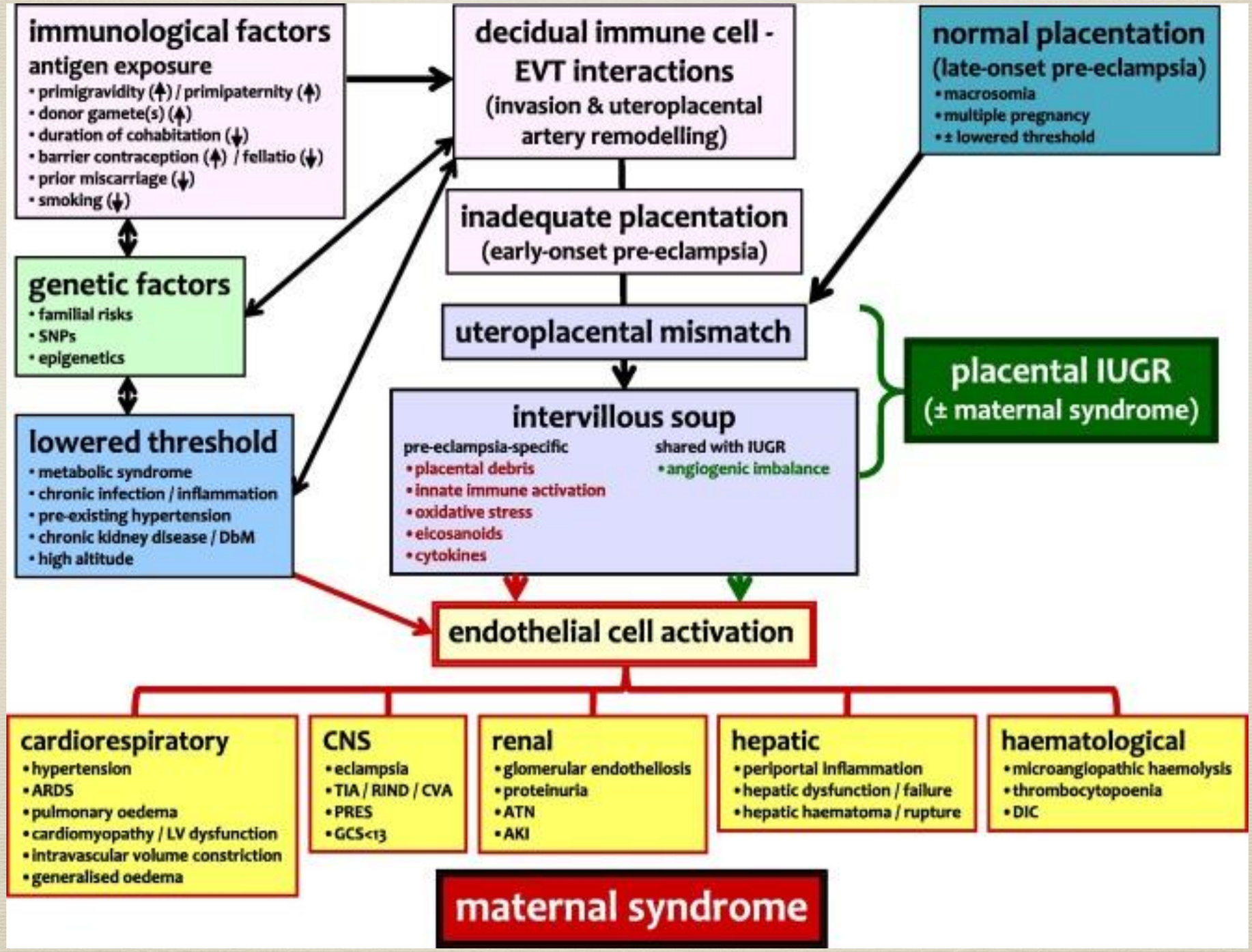
Recommendations for Magnesium Treatment

	Preeclampsia without severe features	Severe Preeclampsia	Eclampsia
ACOG	**	X	X
NICE		X	X
SOGC	X*	X	X
CMQCC	X*	X	X
WHO	X	X	X

***ACOG Executive Summary, 2013: for preeclampsia without severe features, it is suggested that magnesium sulfate not be administered universally for the prevention of eclampsia.*

Pathophysiology



CASES

Case 1

- 30yr old G1P0
- 28 weeks GA
- BP 160/102 P 88 RR 26 T 37 SpO2 93%
- IUGR
- Blurred vision, RUQ pain, hyperreflexic w/2 beats clonus

Case 1

- UA 500, AST 200, ALT 155, Alb 23, Hgb 101, Plts 77
- Concerned?

- Deliver!

Case 2

- 30 yr old G1P0
- 37 weeks GA
- Hx chronic HTN
- BP 160/90 P 88 RR 22 T 37 SpO2 97%
- Labour pain, H/A

Case 2

- UA 220, AST 22, ALT 33, Alb 33, Hgb 101, Plts 177
- Concerned?
- Treat HDP/BP and monitor (labs and patient)

Clinical Pearls

A Devastating Disease…

- Hypertensive disorders of pregnancy (HDP) remain the leading cause of maternal and perinatal morbidity & mortality worldwide

- Incidence of preeclampsia has increased by 25% in last 2 decades (US)

- 2-8% of pregnancies are affected

- Early diagnosis and control of blood pressure is paramount

Nursing Considerations

- Advocate for your patient(s)
- Make sure blood pressure in pregnancy is controlled
- Clinical suspicion of preeclampsia
- Blood work, anesthesia, plan for delivery, constant assessment...

Anesthesia Considerations

- Keep MgSO4 infusing
- Thrombocytopenia:
  - ASA/ACOG ->
    - ✓ if platelet count > 75 × 10^9/L
    - Unclear if platelet count 50 to 75 × 10^9/L
    - X if platelet count < 50 × 10^9/L
  - CAS/SOGC ->
- Anesthesiology Consult for preeclamptic patients
- Early epidural recommended

Uterotonic Management

Society for Obstetric Anesthesia and Perinatology

Section Editor: Cynthia A. Wong

Patterns of Second-Line Uterotonic Use in a Large Sample of Hospitalizations for Childbirth in the United States: 2007–2011

Brian T. Bateman, MD, MSc,*† Lawrence C. Tsen, MD,‡ Jun Liu, MD, MS,*
Alexander J. Butwick, MBBS, FRCA, MS,§ and Krista F. Huybrechts, MS, PhD*

BACKGROUND: The incidence of postpartum hemorrhage due to uterine atony has increased significantly in the United States during the past decade. For patients with refractory uterine atony after oxytocin administration, second-line uterotonics including methylergonovine maleate, carboprost, and misoprostol are recommended. In this study, we describe hospital-level patterns of second-line uterotonic use in a large, nationwide sample of admissions for childbirth in the United States.
METHODS: The Premier Research Database was used to define a cohort of 2,180,916 patients hospitalized for delivery at 1 of 367 hospitals from 2007 to 2011. Mixed-effects logistic regression models were used to estimate the hospital-specific frequency of second-line uterotonic use adjusting for measured patient-level and hospital-level characteristics that might be risk factors for uterine atony.
RESULTS: The median hospital-level frequency of second-line uterotonic use was 7.1% (interquartile range 5.2–% to 10.8%). In the fully adjusted model, the mean (SE) predicted probability of second-line uterotonic use was 7.02% (0.26%), with 95% of the hospitals having a predicted (SE) probability between 1.69% (0.12%) and 24.96% (1.28%).
CONCLUSIONS: We observed wide interhospital variation in the use of second-line uterotonics that was not explained by patient-level or hospital-level characteristics. Studies aimed at defining the optimal pharmacologic strategies for the management of uterine atony are needed, particularly in light of the increasing incidence of atonic postpartum hemorrhage in the United States and other developed countries. (Anesth Analg 2014;119:1344–9)

Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality.[1–4] In the developed world, the incidence of PPH overall, and that of severe cases resulting in transfusion and hysterectomy, have increased significantly over the past decade.[1,5–8] These increases appear to be directly linked

For prophylaxis against uterine atony, oxytocin is routinely used during the third stage of labor.[9,10] If the uterus fails to adequately contract in response to oxytocin administration, second-line uterotonics including methylergonovine maleate, carboprost, and misoprostol are recommended.[9] Although commonly used, these drugs have important side effects and

International Journal of Obstetric Anesthesia (2018) xxx, xxx–xxx

https://doi.org/10.1016/j.ijoa.2018.09.002

ORIGINAL ARTICLE

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Uterotonic drugs usage in Canada: a snapshot of the practice in obstetric units of university-affiliated hospitals

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Background

- Severe postpartum hemorrhage (PPH) related to uterine atony is on the rise**

- Firstline uterotonics - oxytocics
- Second-line uterotonics- Hemabate/Carboprost, Methyl-ergonovine/Ergot, Misoprostal
- There is a lack of consensus in US and Canada on how these are used***

The Society of Obstetricians and Gynecologists of Canada (SOGC) recommends carbetocin as the uterotonic of choice to prevent PPH at elective cesarean delivery (CD) (1-B recommendation)

Methods

- ***REB*** approval and implied consent through survey completion
- ***Study design:*** Prospective observational study in the form of a targeted, online, email survey

- ***Population:*** Chiefs or directors of Obstetrics/Gynecology and Directors of Obstetric Anesthesia (or Chief Anesthesiologists in lieu) at university-affiliated obstetric hospitals across Canada

- ***Methods:***
  - An invitation letter explaining the study was sent via email to the practitioners followed by a link to the survey.
  - Survey was integrated into the on-line program 'Survey Monkey'
  - Two reminder emails were sent at 1 week intervals from the initial send out on December 10, 2016.
  - Data obtained from the survey was integrated into excel format.

- ***Data collection:*** Participant/facility details, use of oxytocin vs. carbetocin in both vaginal (VD) and CD at 'low' and 'high' risk for PPH, use of second line uterotonics and tranexamic acid.

Results

- 34/109 respondes (31.2%) (21 anesthesiologists;13 were obstetricians/gynecologists)
- The majority of clinicians (65%) were unaware of the rate of PPH in their institution.

- **Oxytocin vs. carbetocin**
  - Oxytocin - first line agent for VD (91%), low-risk and high-risk CD by (66% and 60%)
  - Oxytocin - IV boluses (3-10 IU) with infusions (20-40 IU/L) at rate 75-300 mL/h
  - 62% (8/13) obstetricians vs. 9% (3/21) anesthesiologists used oxytocin boluses in addition to infusion for even low risk CD (median [range] dose 5 IU [3-10] IU). Rapid boluses and larger amounts were predominantly used in high-risk CD
  - The dose of carbetocin ranged from 25-100 mcg IV for all types of delivery

- **Second-line uterotonic agent for PPH**
  - The second-line uterotonic usage was highly variable with the use of carboprost by all, and ergonovine and misoprostol each by 91% of responders.
  - Carboprost was ranked as the top choice overall, followed by ergonovine by anesthesiologists and misoprostol by obstetricians.
  - The doses of both carboprost and ergonovine were consistent with SOGC guidelines.
  - Tranexamic acid (1-2g) was used by all respondents (for PPH)

- **Choice of drugs**
  - The top ranked reasons why clinicians chose their first-line or second-line uterotonics included efficacy, obstetricians' preference and anesthesiologists' preference.
  - Convenience, SOGC guidelines, cost and habit were ranked as less common reasons for use.

Discussion

- 1st Canadian study using a survey to establish patterns of uterotonic usage in Canadian academic obstetric hospitals
- oxytocin remains the predominant first-line uterotonic
- Carbetocin was also found to be widely utilized in all types of deliveries, however, its indications and doses are not consistent with SOGC guidelines.[4]
- second-line uterotonic drugs was also highly variable and depended upon perceived efficacy and physician's preference

Oxytocin

Discussion

- Canadian centers was varied with respect to dose, route and infusion parameters
- **10 IU** intravenously were common for vaginal, elective and emergent CD
- Such doses are not recommended for routine prophylaxis for vaginal and low-risk CD
- Higher oxytocin should be used with caution, especially in the presence of neuraxial blockade or hypovolemia secondary to postpartum hemorrhage, where they can be more pronounced.[13]
- ED90 for IV bolus oxytocin has been shown to be **0.35 IU** (95% CI 0.18-0.52) at elective CD and **2.99** IU (95% CI 2.32-3.67) at CD for labor arrest.[14,15]
- ED50 of IV bolus oxytocin at elective CD **0 IU** (placebo) was as effective as any other dose.[16]
- High rate oxytocin infusion (**15 IU/h**) versus low rate (**2.5 IU/h**) at elective CD does not improve uterine tone or PPH rate and that the lower rate may minimize oxytocin side effects.[17]
- Prior exposure to oxytocin for augmentation or induction (i.e. labor arrest) require a higher infusion rate ED90 44.2 IU/h (CI 33.8-55.6) compared to non-laboring ED90 16.2 IU/h (CI 13.1-19.3).[18]

Carbetocin

Discussion

- Carbetocin was used in vaginal deliveries as well as high-risk CD, despite no such recommendations in SOGC guidelines.[4]
- Carbetocin doses ranged from **25-100 mcg**
- Product monograph for DURATOCIN™ recommends 100 mcg
- ED90 for elective CD is **14.8mcg** (95% CI 13.7-15.8) and that doses >100 mcg may be required for CD after labor arrest (ED90 **121mcg**, 95% CI 111-130) or CD at high risk of PPH.[19,20]
- Carbetocin is not currently recommended by any other national guideline other than the SOGC
- 2012 Cochrane review of randomized controlled trials (RCTs) comparing carbetocin (100mcg) vs. oxytocin (varying doses) at CD, there was no difference in the incidence of PPH, less need for second-line uterotonics with carbetocin as compared to oxytocin.[21]
- Carbetocin and oxytocin share a similar side effect profile which is dose-dependent
- Oxytocics can result in nausea, vomiting, headache, flushing, water retention, pulmonary edema, hyponatremia, seizures and coma.[14]
- Cardiac side effects include tachycardia, dysrhythmia, ST depression, chest pain, hypotension, coronary vasoconstriction, myocardial ischemia and rarely cardiac arrest/death.[14]
- Special populations such as preeclamptics and those with pre-existing cardiac disease may be at increased risk from oxytocic side effects.

Discussion

Second-line Uterotonics

- Second-line uterotonic usage for PPH management is also variable in Canadian centers.
- Carboprost, ergonovine maleate and misoprostol were based on clinician preference and experience more than evidence
- Akin to the 'institution-based factors' such as practitioner experience, preference and local hospital culture described by Bateman et al.[8]
- Doses of both carboprost and ergonovine maleate were consistent with SOGC guidelines.[4]
- Additional carbetocin used despite lack of evidence or guideline recommendations.[4,6,7]
- Obstetricians and anesthesiologists considered carboprost as their first choice (2nd-line agent)
- Obstetricians chose misoprostol over ergonovine as their second choice in the event of PPH
- Misoprostol has been shown to have significant side effects (cramping, hyperthermia, shivering, convulsions, fever) and has limited efficacy.[23,25] Ergonovine is that it can be given both intravenously and intramuscularly
- Ergonovine maleate has been associated with a reduced risk of hemorrhage-related morbidity during CD as compared to carboprost.[24]
- Dose response studies done in human myometrial samples from laboring and non-laboring women also show that ergonovine provides superior contractions as compared to carboprost and misoprostol.[26]

Discussion

Tranexamic Acid

- Tranexamic acid usage was consistent across Canadian centers
- **1-2 grams** intravenously for PPH management
- Consistent with evidence reported recently by the WOMAN trial collaborators[9]
- WOMAN trial results showed a significant reduction in mortality related to hemorrhage with no increase in thrombo-embolic events when tranexamic acid was used '**early**' in the management of PPH
- Did not prevent hysterectomy
- WOMAN trial is the inclusion of tranexamic acid (1-2g IV over 10 minutes) in the WHO treatment guidelines for primary PPH as soon as possible after onset/diagnosis

Discussion

Guidelines – Where do we go from here?

Discussion

Limitations

- Response rate of 31%, although in keeping with the average response rate for surveys in the literature, is arguably low.
- It may not be representative of the practices across all Canadian centers and lack generalizability
- Inherent survey and selection bias as respondent practices are likely to differ from those who do not respond
- Anesthesiologists were over-represented when compared to their obstetrician respondent counterparts

Conclusion

- Lack of a unified approach to first and second-line uterotonic usage
- Echoes the findings of Bateman et al. in the United States.[8]
- An evidence-based approach to uterotonic usage, as well as consensus of obstetricians and anesthesiologists is warranted in order to improve the management of PPH due to uterine atony
- Consistent, evidence-based societal guidelines can help in bringing uniformity to the clinical practice

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