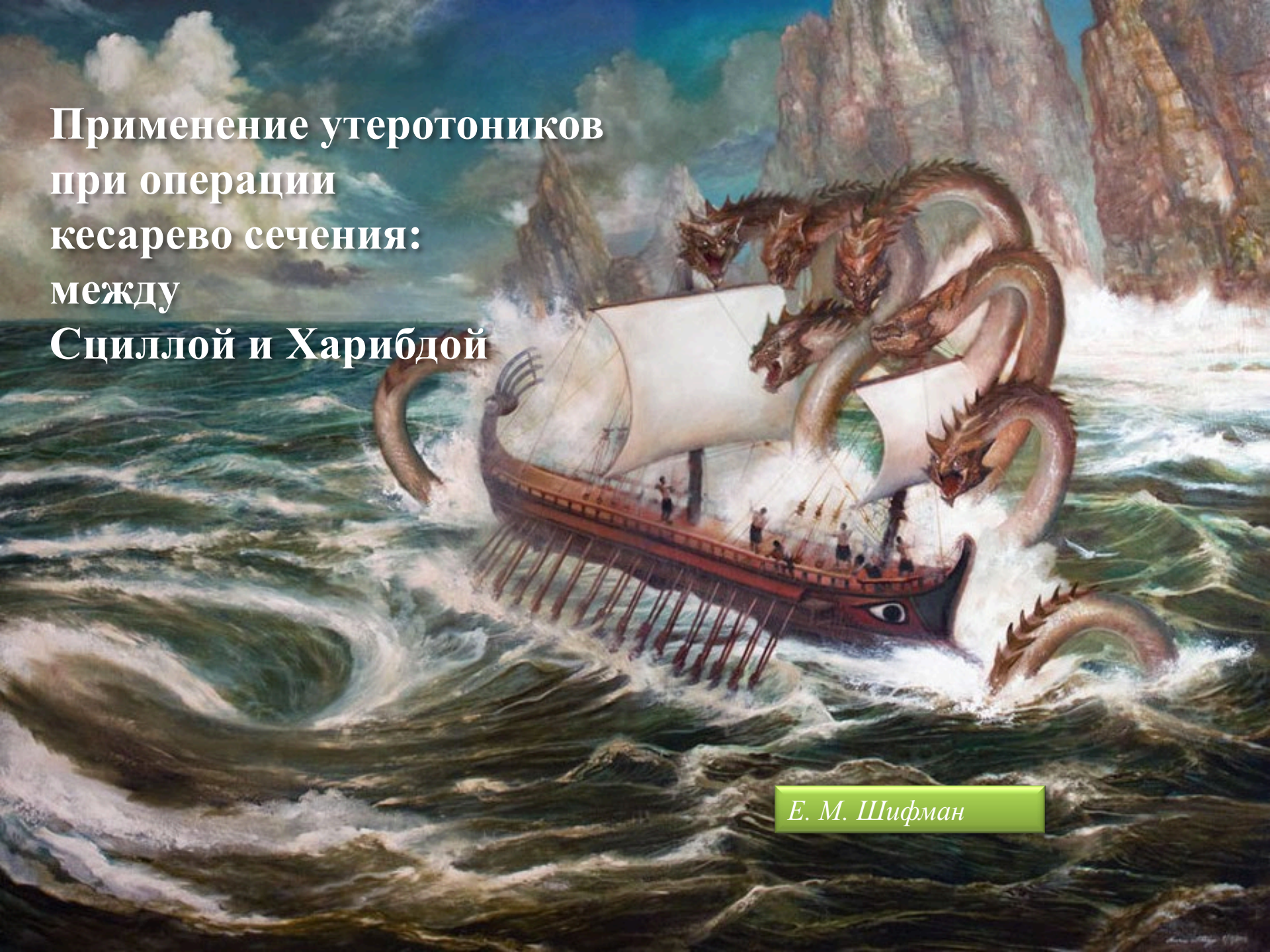
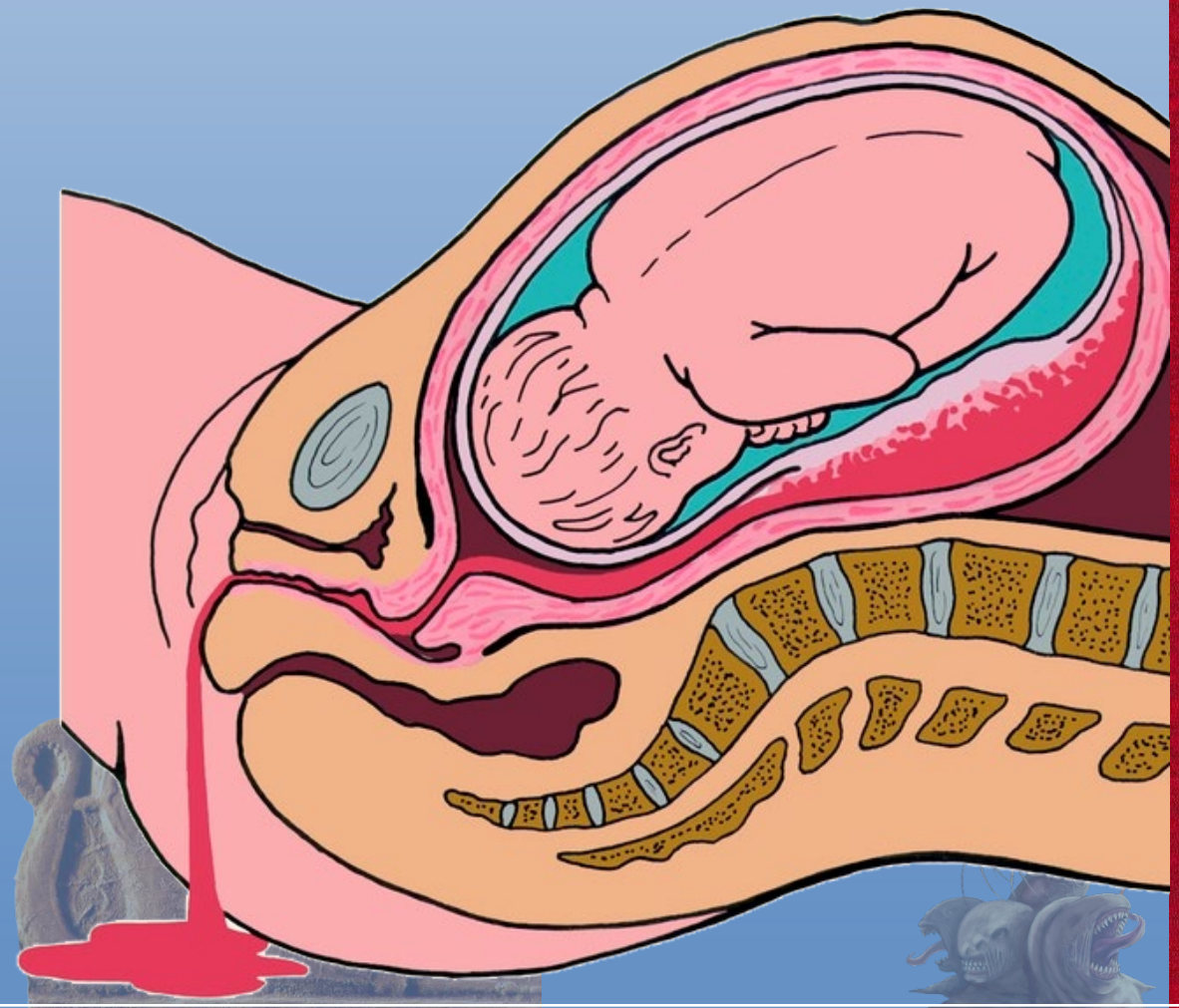
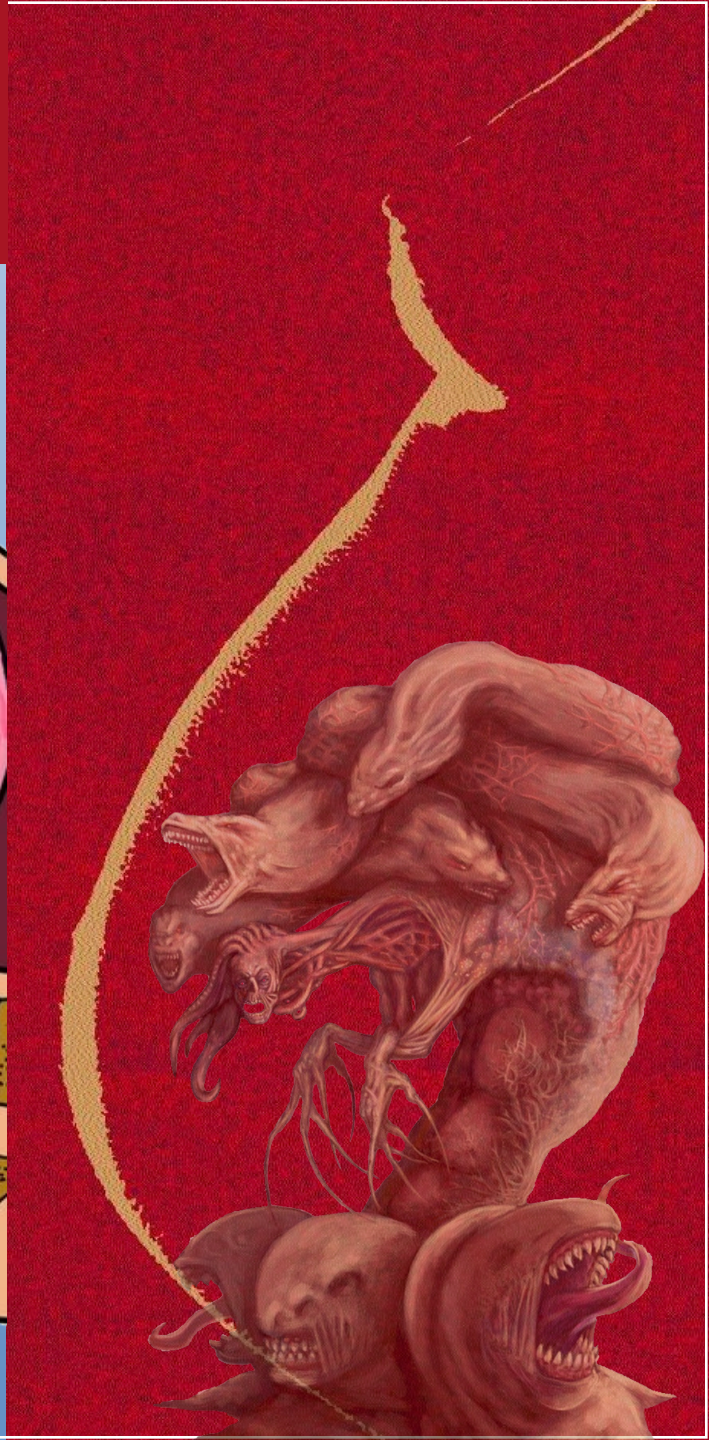


Применение утеротоников при операции кесарево сечения: между Сциллой и Харибдой

Е. М. Шифман

В 75–90% случаях послеродовое кровотечение – это гипо- или атоническое маточное кровотечение!!!





Клинический случай

- Спинальная анестезия для кесарева сечения в связи со слабостью родовой деятельности
- Высокий спинальный блок
- Гипотония
- Placenta accreta – кровопотеря
- Окситоцин 10 ЕД болюсно
- Немедленная остановка сердца
- Безуспешная реанимация

JAMA

Неблагоприятные явления при применении окситоцина

- **Смерть матери** → **легочная гипертензия**, **стеноз аорты**

(Robinson M. et al., JAMA 1967;200:378:378-381)

- **Желудочковая тахикардия** → **продленный синдром QT**
- **Инфаркт миокарда** → **у здоровых**

JAMA Network

May 1, 1967

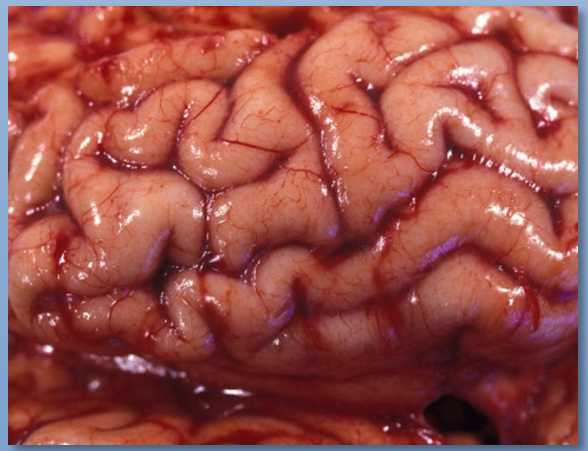
Congenital Aortic Stenosis in Pregnancy
Ventricular Fibrillation Induced by Oxytocin

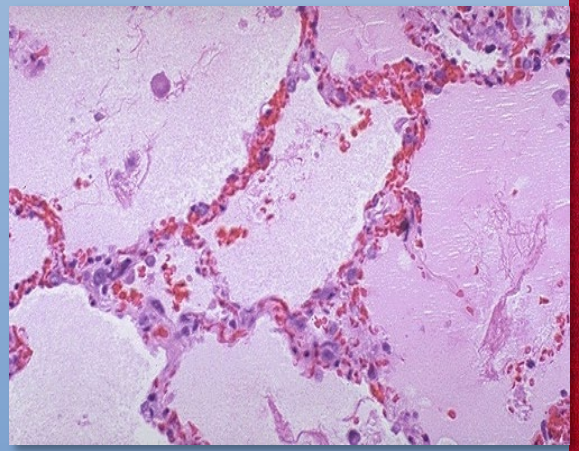
Martin Robinson, MD; Donald C. Greevy, MD; Jordan Katz, MD; et al

JAMA. 1967;200(5):378-381. doi:10.1001/jama.1967.03120180066009

Окситоцин – задержка жидкости

Реабсорбция свободной жидкости из дистальных извитых канальцев и собирательных протоков



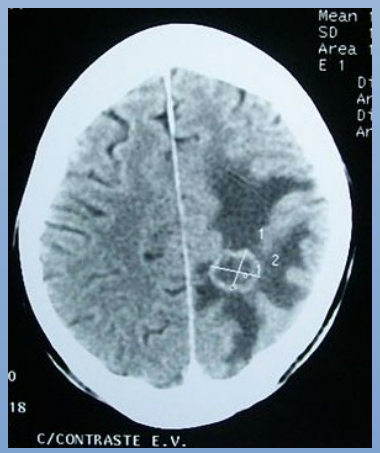


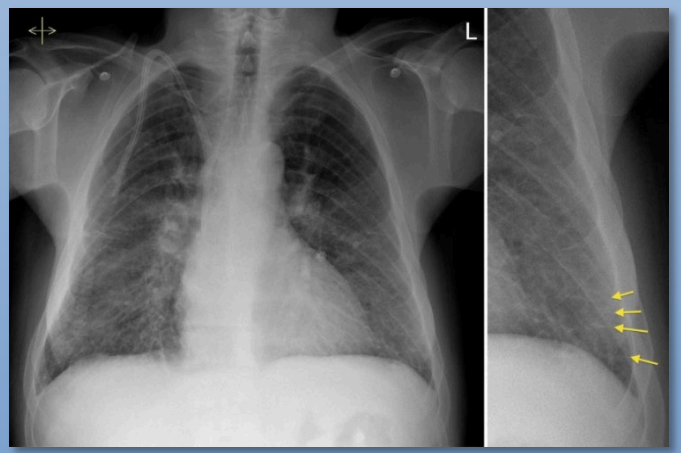
- **Интоксикация жидкостью** *(Водная интоксикация)*
  - ✓ Отек мозга
  - ✓ Судороги

✓ Отек легких

Окситоцин – задержка жидкости

Реабсорбция свободной жидкости из дистальных извитых канальцев и собирательных протоков





- **Интоксикация жидкостью**
  - ✓ Отек мозга
  - ✓ Судороги

✓ Отек легких

Многочисленные исследования реакции рожениц на назначение больших доз окситоцина (10 ЕД внутривенно капельно после извлечения плода), показали различные проявления гемодинамических и других эффектов **мимикрии с анафилактоидными реакциями**. Необходим срочный пересмотр протоколов назначения окситоцина во время операции кесарево сечения.

Acta Anaesthesiologica Scandinavica
AN INTERNATIONAL JOURNAL OF ANAESTHESIOLOGY AND INTENSIVE CARE, PAIN AND EMERGENCY MEDICINE

ORIGINAL ARTICLE

Oxytocin use during Caesarean sections in Denmark – are we getting the dose right?

B. N. Kjær[1], M. Krøigaard[2] and L. H. Garvey[2]

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Conflicts of interest
The authors have no conflicts of interest.

Funding
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Citation
Kjær BN, Krøigaard M, Garvey LH. Oxytocin use during Caesarean sections in Denmark – are we getting the dose right? Acta Anaesthesiologica Scandinavica 2015

doi: 10.1111/aas.12603

Background: In Denmark, an iv bolus of 10 IU oxytocin was traditionally given after delivery to prevent atony during caesarean sections. Randomized controlled trials have shown that lower iv bolus doses have same efficacy with fewer side effects and many countries now recommend a 5 IU maximum dose. The aims of this study were to investigate whether patients referred for allergy testing after oxytocin exposure had dose-related side effects to oxytocin rather than true allergic reactions and to investigate whether updated international recommendations on lower bolus doses had been implemented in practice.
Methods: Medical notes of patients tested with oxytocin as part of investigations in the Danish Anaesthesia Allergy Centre from May 2004 to January 2014 were reviewed retrospectively. A telephone survey of on-duty obstetricians at all Danish obstetric departments was performed and most recent online recommendations from the Danish societies of obstetrics and anaesthesia about the use of oxytocin were identified.
Results: In total 30 women were tested with oxytocin as part of investigations. None were allergic to oxytocin but 19 had symptoms consistent with dose-related side effects on iv provocation. The telephone survey revealed that iv doses of 10 IU oxytocin were still used and recommendations on the websites were not updated.
Conclusion: Too high oxytocin doses are still used in Denmark leading to dose-related side effects mimicking allergic reactions. Coordination between obstetricians and anaesthesiologists on producing common updated guidelines on the administration of oxytocin and dissemination of this information to obstetric and anaesthetic departments in Denmark is needed.

Editorial comments: what this article tells us
Major adverse responses to oxytocin in obstetric anaesthesia use were examined in this study in a Danish cohort, with a focus on possible allergic responses. None were found to have demonstrated allergies at later testing. High doses of oxytocin seem to remain common, with predictable adverse effects.

Acta Anaesthesiologica Scandinavica 60 (2016) 18–25

B. N. Kjær, M. Krøigaard and L. H. Garvey.
Oxytocin use during Caesarean sections in Denmark – are we getting the dose right?//
Acta Anaesthesiologica Scandinavica 60 (2016) 18–25.

УДК 615.217.03:618.714-005.1-084

Шифман Е.М.[1], Куликов А.В.[2], Кругова Л.В.[3], Вартанов В.Я.[3], Маршалов Д.В.[4]

БЕЗОПАСНОСТЬ ПРИМЕНЕНИЯ УТЕРОТОНИКОВ: ЧТО ДОЛЖЕН ЗНАТЬ АНЕСТЕЗИОЛОГ-РЕАНИМАТОЛОГ?

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[2]ГБОУ ВПО «Уральский государственный медицинский университет» Минздрава РФ, 620028, Екатеринбург;
[3]ГБУЗ СО «Тольяттинская городская клиническая больница № 5», 4450030, Тольятти;
[4]ГБОУ ВПО «Саратовский государственный медицинский университет им. В.И. Разумовского» Минздрава РФ, 410017, Саратов

Важнейшим аспектом профилактики и лечения послеродовых кровотечений является применение утеротоников. В обзоре внимание сфокусировано на надлежащем использовании окситоцина. Анализ литературы баз данных Scopus, Web of Science, MedLine, The Cochrane Library, EMBASE, Global Health, CyberLeninka, РИНЦ использовал материалы ведущих мировых организаций: World Health Organization, American Academy of Family Physicians, Royal College of Obstetricians and Gynaecologists (RCOG), International Federation of Obstetrics and Gynecology (FIGO), Collège National des Gynécologues et Obstétriciens Français, American College of Obstetricians and Gynecologists (ACOG), Cochrane Reviews. Показано, что окситоцин остается препаратом первой линии как для профилактики, так и лечения послеродовых маточных кровотечений. При плановом кесаревом сечении использование 5 МЕ окситоцина в качестве стандартной дозы является чрезмерной и требует переоценки. Адекватное сокращение матки может быть достигнуто более низкими дозами окситоцина (0,5–3 ЕД). Медленное болюсное введение окситоцина может эффективно минимизировать сердечно-сосудистые побочные эффекты без ущерба для терапевтического эффекта, так как побочные эффекты окситоцина зависят от дозы и представляется целесообразным вводить его медленно в виде инфузии. При гипотонии матки, если нет адекватного ответа на начальной стадии лечения с окситоцином, внимание должно быть уделено использованию утеротоников 2-й линии. У гемодинамически нестабильных пациенток при использовании окситоцина необходимо проявлять предельную осторожность. Считаем, что необходима дальнейшая работа по изучению и внедрению безопасных схем интраоперационного применения утеротоников.

Ключевые слова: *обзор; утеротоники; побочные действия; осложнения.*

Для цитирования: Шифман Е.М., Куликов А.В., Кругова Л.В., Вартанов В.Я., Маршалов Д.В. Безопасность применения утеротоников: что должен знать анестезиолог-реаниматолог? *Анестезиология и реаниматология.* 2017; 62(3): 220-224. DOI: http://dx.doi.org/10.18821/0201-7563-2017-62-3-220-224

Shifman E.M.[1], Kulikov A.V.[2], Krugova L.V.[3], Vartanov V.Ya.[3], Marshalov D.V.[4]

SAFETY OF UTEROTONICS: WHAT ANAESTHESIOLOGIST SHOULD KNOW ABOUT THEM?

[1]Moscow Regional Research and Clinical Institute ("MONIKI"), 129110, Moscow, Russian Federation;
[2]Department of anesthesiology and critical care medicine, Ural State Medical University, 620028, Yekaterinburg, Russian Federation;
[3]Department of Anesthesiology and Intensive Care, Togliatti City Clinical Hospital № 5, 4450030, Togliatti, Russian Federation;
[4]Department of Obstetrics and Gynecology, Medical Faculty, V.I. Razumovsky Saratov State Medical University, 410017, Saratov, Russian Federation

The most important aspect of the prevention and treatment of postpartum hemorrhage is the use of uterotonics. The review focused attention on the proper use of oxytocin. The analysis of literature, Scopus databases, Web of Science, MedLine, The Cochrane Library, EMBASE, Global Health, CyberLeninka, RISC, used materials leading organizations: World Health Organization, American Academy of Family Physicians, Royal College of Obstetricians and Gynaecologists (RCOG), International Federation of Obstetrics and Gynecology (FIGO), Collège National des Gynécologues et Obstétriciens Français, American College of Obstetricians and Gynecologists (ACOG), Cochrane Reviews has shown that oxytocin remains the drug of first-line, both for prevention and treatment of postpartum uterine bleeding. When a planned Caesarean section 5 IU oxytocin use as a standard dose is excessive and requires re-evaluation. Adequate uterine contractions can occur with lower doses of oxytocin (0,5–3 units). A slow bolus administration of oxytocin can effectively minimize the cardiovascular side effects without compromising the therapeutic effect. Since the side effects of oxytocin dose dependent, is expedient oxytocin administered as a slow infusion. If hypotension uterus, if there is no adequate response to initial treatment with oxytocin, attention should be paid to the use of second-line uterotonic. In hemodynamically unstable patients should be using oxytocin is necessary to exercise the utmost restraint. We believe that further work is needed on the study and implementation of security schemes intraoperative use of uterotonics.

Keywords: *review; uterotonics; side effects; complications.*

For citation: Shifman E.M., Kulikov A.V., Krugova L.V., Vartanov V.Ya., Marshalov D.V. Safety of uterotonics: what anaesthesiologist should know about them? *Anesteziologiya i reanimatologiya (Anaesthesiology and Reanimatology, Russian journal).* 2017; 62(3): 220-224. (In Russ.). DOI: http://dx.doi.org/10.18821/0201-7563-2017-62-3-220-224

Conflict of interest. The authors declare no conflict of interest.
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Accepted 2017

Шифман Е. М.,
Куликов А. В.,
Кругова Л. В.,
Вартанов В. Я.,
Маршалов Д. В.

Безопасность применения утеротоников: что должен знать анестезиолог-реаниматолог?

Анестезиология и Реаниматология. 2017. 62 (3). С. 220–224

Боли за грудиной и отек легких – встречаются редко и также связаны с быстрым и болюсном введении 10 ЕД окситоцина

International Journal of Obstetric Anesthesia (2008) 17, 247–254
0959-289X/$ - see front matter
doi:10.1016/j.ijoa.2008.03.003

ELSEVIER
www.obstetanesthesia.com

CASE REPORT

The hemodynamics of oxytocin and other vasoactive agents during neuraxial anesthesia for cesarean delivery: findings in six cases

T. L. Archer,* K. Knape, D. Liles, A. S. Wheeler, B. Carter
Department of Anesthesiology, University of Texas Health Science Center, San Antonio, Texas, USA

ABSTRACT
Oxytocin is a commonly used uterotonic that can cause significant and even fatal hypotension, particularly when given as a bolus. The resulting hypotension can be produced by a decrease in systemic vascular resistance or cardiac output through a decrease in venous return. Parturients with normal volume status, heart valves and pulmonary vasculature most often respond to this hypotension with a compensatory increase in heart rate and stroke volume. Oxytocin-induced hypotension at cesarean delivery may be incorrectly attributed to blood loss. Pulse power analysis (also called "pulse contour analysis") of an arterial pressure wave form allows continuous evaluation of systemic vascular resistance and cardiac output in real time, thereby elucidating the causative factors behind changes in blood pressure. Pulse power analysis was conducted in six cases of cesarean delivery performed under neuraxial anesthesia. Hypotension in response to oxytocin was associated with a decrease in systemic vascular resistance and a compensatory increase in stroke volume, heart rate and cardiac output. Pulse power analysis may be helpful in determining the etiology of and treating hypotension during cesarean delivery under neuraxial anesthesia.

Keywords: Oxytocin; Obstetrical hemorrhage; Pulse power analysis; Pulse contour analysis; PulseCO; LiDCO; Systemic vascular resistance; Cardiac output; Stroke volume; Hemodynamics of pregnancy

Archer TL, Knape K, Liles D, Wheeler AS, Carter B. The hemodynamics of oxytocin and other vasoactive agents during neuraxial anesthesia for cesarean delivery: findings in six cases. Int J Obstet Anesth 2008;17:247–54

Применение метилэргометрина увеличивает риск развития ОИМ

Метилэргометрин должен вводиться строго по показания, с обязательным информированием анестезиолога-реаниматолога.

Тактика ведения акушерских пациенток с ОИМ зависит от его патогенеза. В описанном нами случае, при вазоспастическом (нетромботическом патогенезе) ОИМ, проведение тромболизиса или экстренной коронароангиографии нецелесообразно… .

УДК 617-089.844+ 615.211:616-089.888.61

ИНФАРКТ МИОКАРДА ПОСЛЕ ОПЕРАЦИИ КЕСАРЕВА СЕЧЕНИЯ ПРИ СПИНАЛЬНОЙ АНЕСТЕЗИИ НА ФОНЕ ПРИМЕНЕНИЯ МЕТИЛЭРГОМЕТРИНА И ОКСИТОЦИНА (КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ)

С.В. Письменский, А.В. Пырегов

Федеральное Государственное Бюджетное Учреждение «Научный Центр Акушерства, Гинекологии и Перинатологии имени академика В.И.Кулакова» Минздравсоцразвития России. Москва, Россия.

MYOCARDIAL INFARCTION AFTER CESAREAN SECTION UNDER SPINAL ANESTHESIA DURING TREATMENT WITH OXYTOCIN AND METILERGOMETRIN (CLINICAL OBSERVATION)

S.V. Pismensky, A.V. Pyregov

Резюме

В статье приводится клиническое наблюдение инфаркта миокарда после операции кесарево сечение, выполненного под спинальной анестезией с применением утеротоников. Считаем, что использование метилэргометрина увеличивает риск развития острого инфаркта миокардка (ОИМ), а назначение препарата должно осуществляться строго по показания, с обязательным информированием анестезиолога-реаниматолога. Тактика ведения акушерских пациенток с ОИМ зависит от его патогенеза. В описанном нами случае, при вазоспастическом (нетромботическом патогенезе) ОИМ, проведение тромболизиса или экстренной коронароангиографии нецелесообразно, в остальном терапия стандартная.

***Ключевые слова:** острый инфаркт миокарда, метилэргометрин, тромболизис*

Abstract

The article presents a clinical observation of myocardial infarction after cesarean section performed under spinal anesthesia with the use of uterotonics. We believe that the use of metilergometrina increases the risk of acute myocardial miokardka (AMI), and use of the drug should be carried out strictly according to the testimony, with the obligatory informing Anaesthetist. Management of obstetric patients with AMI depends on its pathogenesis. In the case described by us, in vasospastic (netromboticheskom pathogenesis) of AMI, thrombolysis or emergency coronary angiography is impractical in the rest of the standard therapy.

***Keyworlds:** acute myocardial, metilergometrin, thrombolysis*

Введение

У женщин детородного возраста острый инфаркт миокарда случается достаточно редко. Частота его развития во время беременности не превышает от 2 до 5 случаев на 100 000 женщин [1, 2]. Принимая во внимание тенденцию к увеличению среднего возраста беременных, а также воздействия таких распространенных ныне факторов риска, как курение, сахарный диабет и стресс, можно ожидать возрастание удельного веса данной патологии. Напомним, что беременность сама по себе способна увеличивает вероятность развития ОИМ в несколько раз [3].

Известно, что ОИМ может развиться на любой стадии беременности. Наиболее распространенная локализация инфаркта - передняя стенка и верхушка левого желудочка. Частая причина возникновения ИМ в пред- и послеродовом периоде - спонтанное расслоение стенки проксимального отдела левой передней венечной артерии. Считают, что в основе этого процесса лежат структурные и биохимические изменения стенки сосуда, обусловленные избытком прогестерона, а также эозинофилия и недостаточность плазматического фактора, стимулирующего синтез простациклина и увеличение концентрации липопротеинов [4, 5, 6]. Литературные данные свидетельствуют, что до введения в рутинную практику первичных интервенционных методик лечения, смертность в остром периоде заболевания (преимущественно в III

Письменский С.В., Пырегов А.В. Инфаркт миокарда после операции кесарева сечения при спинальной анестезии на фоне применения метилэргометрина и окситоцина (клиническое наблюдение) // ТОЛЬЯТТИНСКИЙ МЕДИЦИНСКИЙ КОНСИЛИУМ. 2015. №5-6.59-63.

OBSTETRICS & GYNECOLOGY

- **Мизопростол показал утеротонический эффект**
- **Менее ясна роль мезопростола как дополнения к окситоцину:**
  - ✓ **Widmer с соавторами,** *Lancet. 2010 May 22; 372 (9728): 1808-13*
- **Уменьшает ли добавление мезопростола к окситоцину** *(как составляющая активной профилактики 3-ей стадии родов)* **послеродовое кровотечение?**

Thibaud Quibel, MD, Idir Ghout, MSc, François Goffinet, MD, Laurent J. Salomon, MD, Julie Fort, MSc, Sophie Javoise, Laurence Bussieres, MD, Philippe Aegerter, MD, and Patrick Rozenberg, MD) Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage: A Randomized Controlled Trial Obstet. Gynecol. 2016; 128 (4): 805-811

Original Research

Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage

A Randomized Controlled Trial

Thibaud Quibel, MD, Idir Ghout, MSc, François Goffinet, MD, Laurent J. Salomon, MD, Julie Fort, MSc, Sophie Javoise, Laurence Bussieres, MD, Philippe Aegerter, MD, and Patrick Rozenberg, MD, for the Groupe de Recherche en Obstétrique et Gynécologie (GROG)

OBJECTIVE: To evaluate the effectiveness and safety of misoprostol administered simultaneously with oxytocin as part of the active management of the third stage of labor.

METHODS: This multicenter, double-blind, randomized, placebo-controlled trial recruited women in the first stage of labor with expected vaginal deliveries at 36–42 weeks of gestation. Exclusion criteria were multiple pregnancies, hypersensitivity to misoprostol, and cesarean delivery. Participants received routine intravenous oxytocin and were randomly allocated to receive 400 micrograms misoprostol or placebo orally immediately after delivery of the newborn. The primary outcome was postpartum hemorrhage (500 mL or greater within 2 hours of birth). Secondary outcomes included severe postpartum hemorrhage (1,000 mL or greater) and adverse maternal events such as fever, shivering, and nausea. Two groups of 1,550 women were required to demonstrate a 33% decrease of postpartum hemorrhage according to a two-tailed α at 0.05 with 80% power. An interim analysis was planned after 50% enrollment.

RESULTS: Participant enrollment occurred from April 2010 to September 2013. Baseline characteristics were similar in the two groups. The study was discontinued after the planned interim analysis including 1,721 patients showed that misoprostol was not effective and was associated with significantly more adverse effects. The rate of postpartum hemorrhage was 8.4% (68/806) in the misoprostol and 8.3% (66/797) in the placebo group (P=.98), and rates of severe postpartum hemorrhage were 1.8% and 2.4%, respectively (P=.57). Maternal adverse events occurred significantly more frequently in the misoprostol group (for fever 30.4% in the misoprostol group compared with 6.3% in the placebo group, P<.001; for shivering 10.8% in the misoprostol group compared with 0.6% in the placebo group, P<.001).

CONCLUSION: Misoprostol administered with prophylactic routine oxytocin did not reduce the rate of postpartum hemorrhage risk and increased the rate of adverse events.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, https://clinicaltrials.gov, NCT01113229.

(Obstet Gynecol 2016;128:805–11)

DOI: 10.1097/AOG.0000000000001626

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Financial Disclosure

The authors did not report any potential conflicts of interest.

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OBSTETRICS & GYNECOLOGY

- **Приведено, чтобы показать снижение частоты послеродового кровотечения с 7,5 до 5,0%**
  - ✓ **N = 3,100**
- **Запланированный промежуточный анализ остановлен после набора 1 721 пациентки по причине**
  - ✓ **Бесперспективности**
  - ✓ **Неожиданно высокой частоты неблагоприятных явлений**

Original Research

Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage

A Randomized Controlled Trial

Thibaud Quibel, MD, Idir Ghout, MSc, François Goffinet, MD, Laurent J. Salomon, MD, Julie Fort, MSc, Sophie Javoise, Laurence Bussieres, MD, Philippe Aegerter, MD, and Patrick Rozenberg, MD, for the Groupe de Recherche en Obstétrique et Gynécologie (GROG)

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RESULTS: Participant enrollment occurred from April 2010 to September 2013. Baseline characteristics were similar in the two groups. The study was discontinued after the planned interim analysis including 1,721 patients showed that misoprostol was not effective and was associated with significantly more adverse effects. The rate of postpartum hemorrhage was 8.4% (68/806) in the misoprostol and 8.3% (66/797) in the placebo group ($P=.98$), and rates of severe postpartum hemorrhage were 1.8% and 2.4%, respectively ($P=.57$). Maternal adverse events occurred significantly more frequently in the misoprostol group (for fever 30.4% in the misoprostol group compared with 6.3% in the placebo group, $P<.001$; for shivering 10.8% in the misoprostol group compared with 0.6% in the placebo group, $P<.001$).

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OBSTETRICS & GYNECOLOGY

- **Накопленные данные позволяют предположить низкую эффективность добавления мизопростола**
- **Неблагоприятные побочные явления**
- **Вероятно, имеет ограниченную роль в предупреждении/лечении послеродового кровотечения в условиях высоких ресурсов**

Thibaud Quibel, MD, Idir Ghout, MSc, François Goffinet, MD, Laurent J. Salomon, MD, Julie Fort, MSc, Sophie Javoise, Laurence Bussieres, MD, Philippe Aegerter, MD, and Patrick Rozenberg, MD. Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage: A Randomized Controlled Trial
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OBSTETRICS & GYNECOLOGY

	Мизопростол	Плацебо	P-значение
Лихорадка	30.4%	6.3%	<0.001
Озноб	10.8%	0.6%	<0.001
Тошнота	2.7%	1.0%	0.01
Рвота	2.2%	0.8%	0.02
Диарея	0.7%	0%	0.03

Thibaud Quibel, MD, Idir Ghout, MSc, François Goffinet, MD, Laurent J. Salomon, MD, Julie Fort, MSc, Sophie Javoise, Laurence Bussieres, MD, Philippe Aegerter, MD, and Patrick Rozenberg, MD. **Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage: A Randomized Controlled Trial Obstet. Gynecol. 2016; 128 (4): 805-811**

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OBSTETRICS & GYNECOLOGY

	Мизопростол	Плацебо	P-значение
Послеродовое кровотечение	8.4%	8.3%	0.98
Тяжелое послеродовое кровотечение	1.8%	2.4%	0.57
Подгруппа высокого риска	11.5%	11.4%	0.95

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Еще одна трагедия…

- **Во время операции кесарево сечения не проводился должный мониторинг.**

В частности, не проводился интраоперационный мониторинг ЭКГ *(стандарт мониторинга, зафиксированный документах МЗ РФ).*

Учитывая, что в клиническом описании симптомов и патологоанатомическом заключении присутствуют

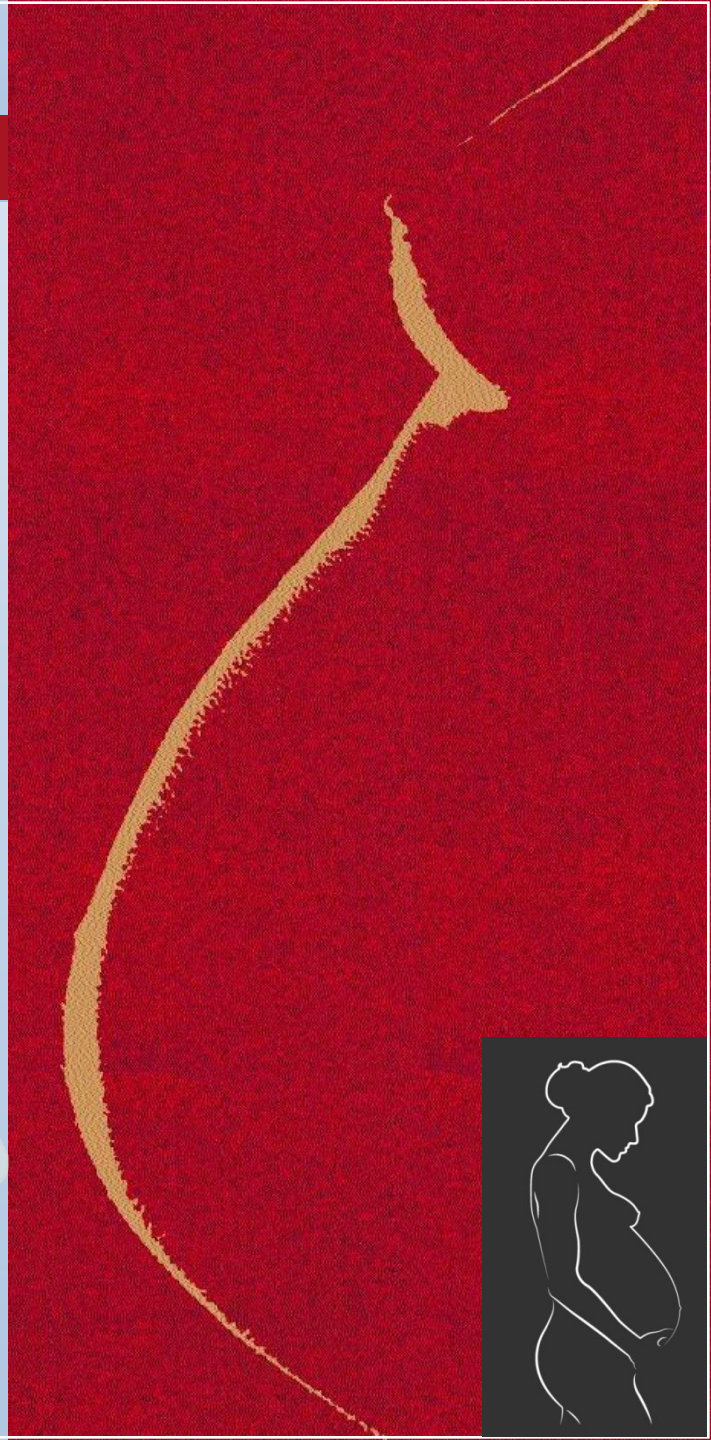
«острая сердечная недостаточность

… при отсутствии признаков исходной соматической патологии

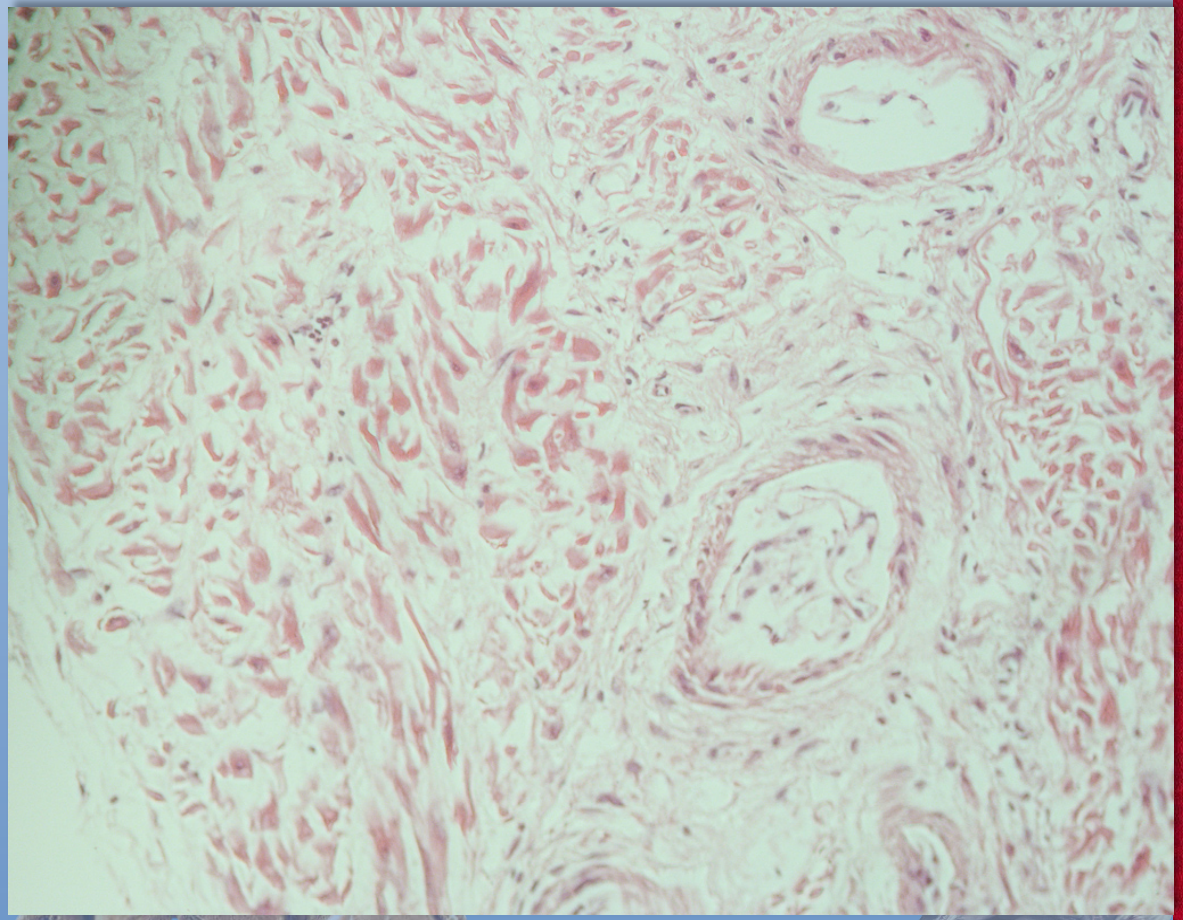
… острый коронароспазм

… с отёком стромы миокарда»,

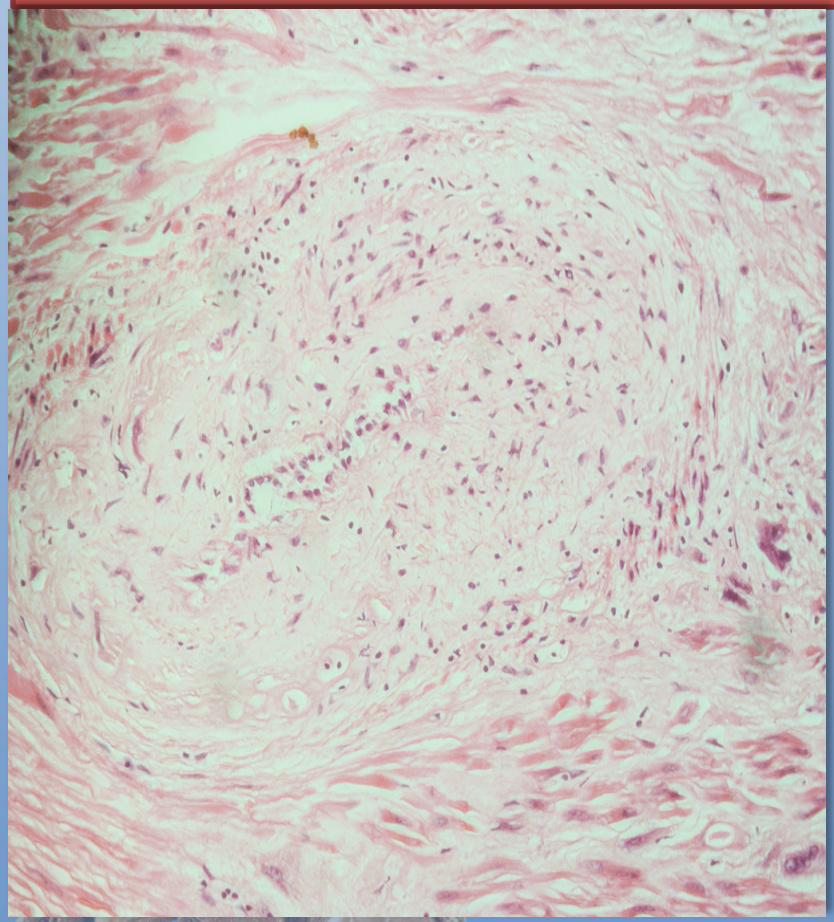
следует, что с высокой долей вероятности эти явления наступили вследствие прямого нарушения инструкции по режиму введения окситоцина для профилактики и лечения послеродовых кровотечений.



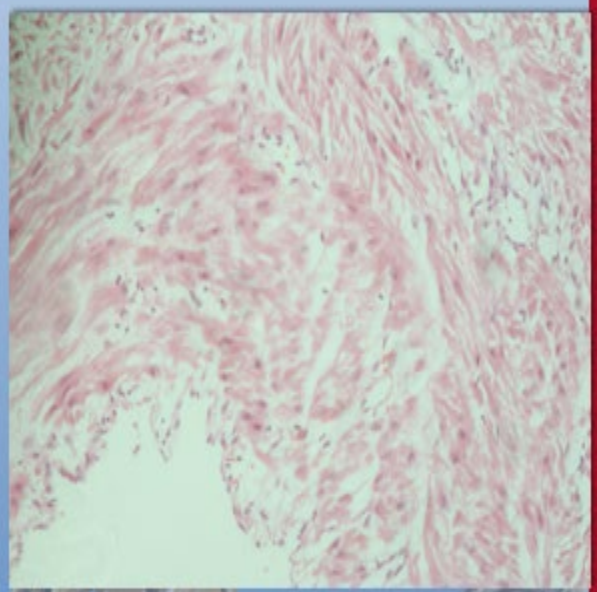
Норм-сосуды, фрагментация-КМЦ, отек-стромы



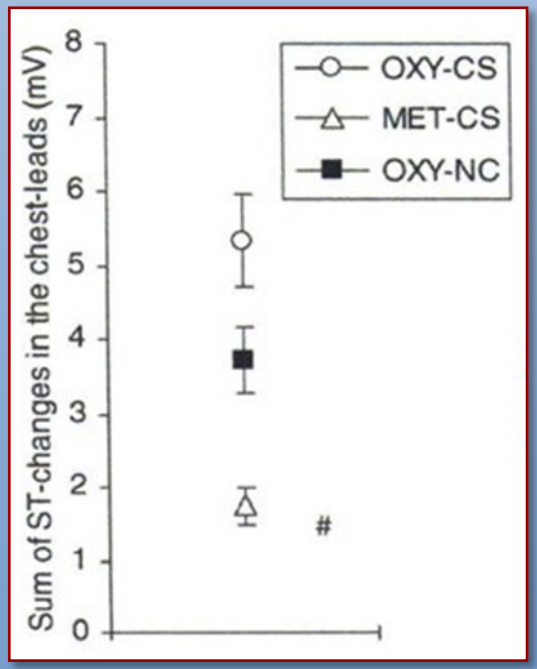
Спазмированный сосуд, периориентация ядер

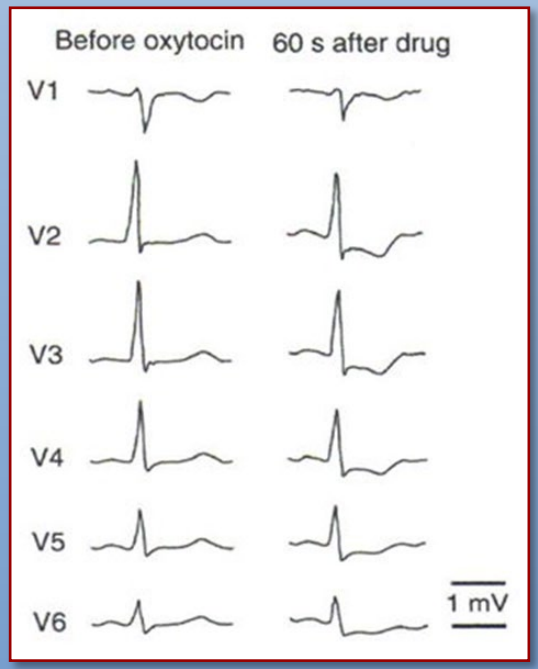


Фрагментация-кардиомиоцитов

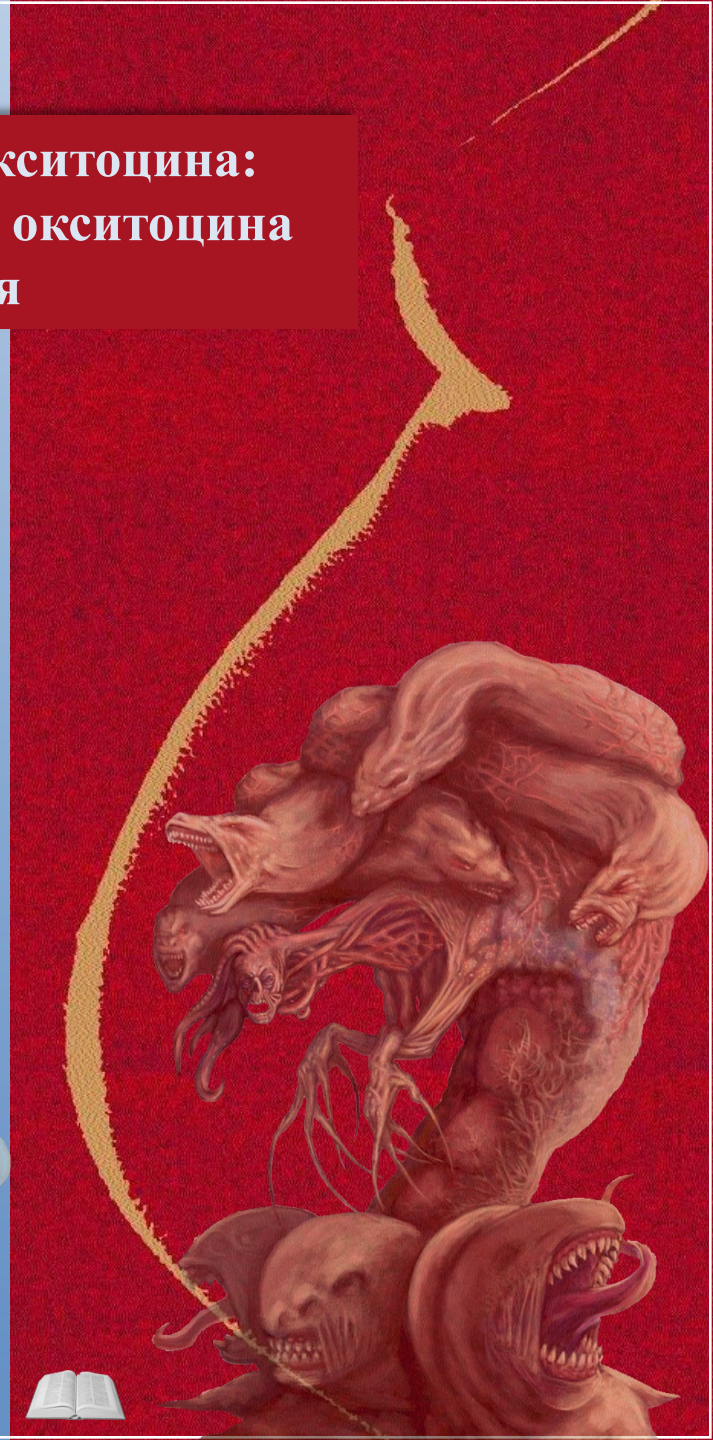


Признаки ишемии миокарда после введения окситоцина: рандомизированное, двойное слепое сравнение окситоцина и метилэргометрина во время кесарева сечения





Средняя сумма изменений ST в скалярных грудных отведениях mV.



Svanstrom et al. Brit Anaesth 2008; 100, 683–689

Цитирую:

1.1 ***Профилактика и лечение гипотонических кровотечений в послеродовом периоде:***

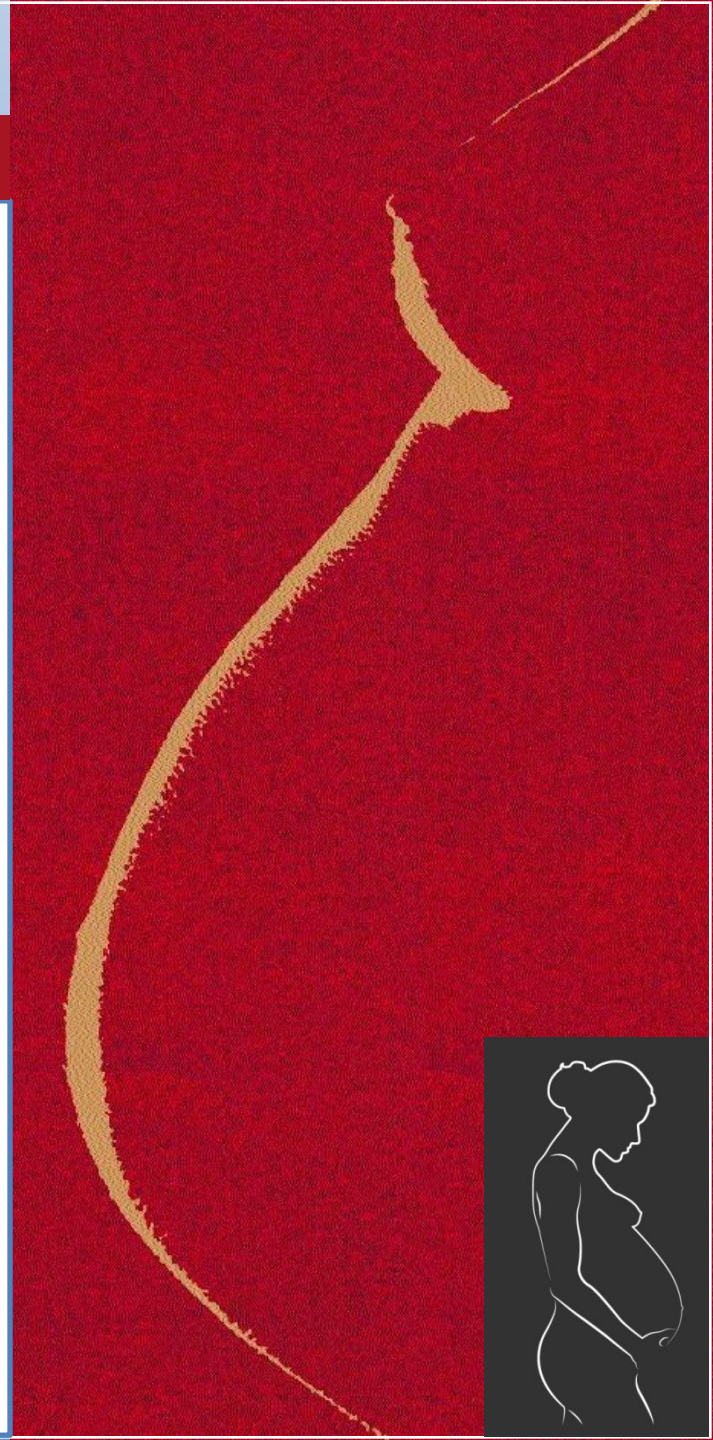
1. **В/в капельная инфузия — в 1000 мл негидратирующей жидкости растворить 10–40 МЕ окситоцина; для профилактики маточной атонии обычно необходимо 20–40 мЕД/мин окситоцина.**

2. **В/м введение — 5 МЕ/мл окситоцина после отделения плаценты**

1.2 6.2 Для приготовления стандартной инфузии окситоцина в 1000 мл негидратирующей жидкости растворить 1 мл (5 МЕ) окситоцина и тщательно перемешать, вращая флакон.

В 1 мл приготовленной таким образом инфузии содержится 5 мЕД окситоцина.

Для точного дозирования инфузионного раствора следует применять инфузионную помпу или другое подобное приспособление.



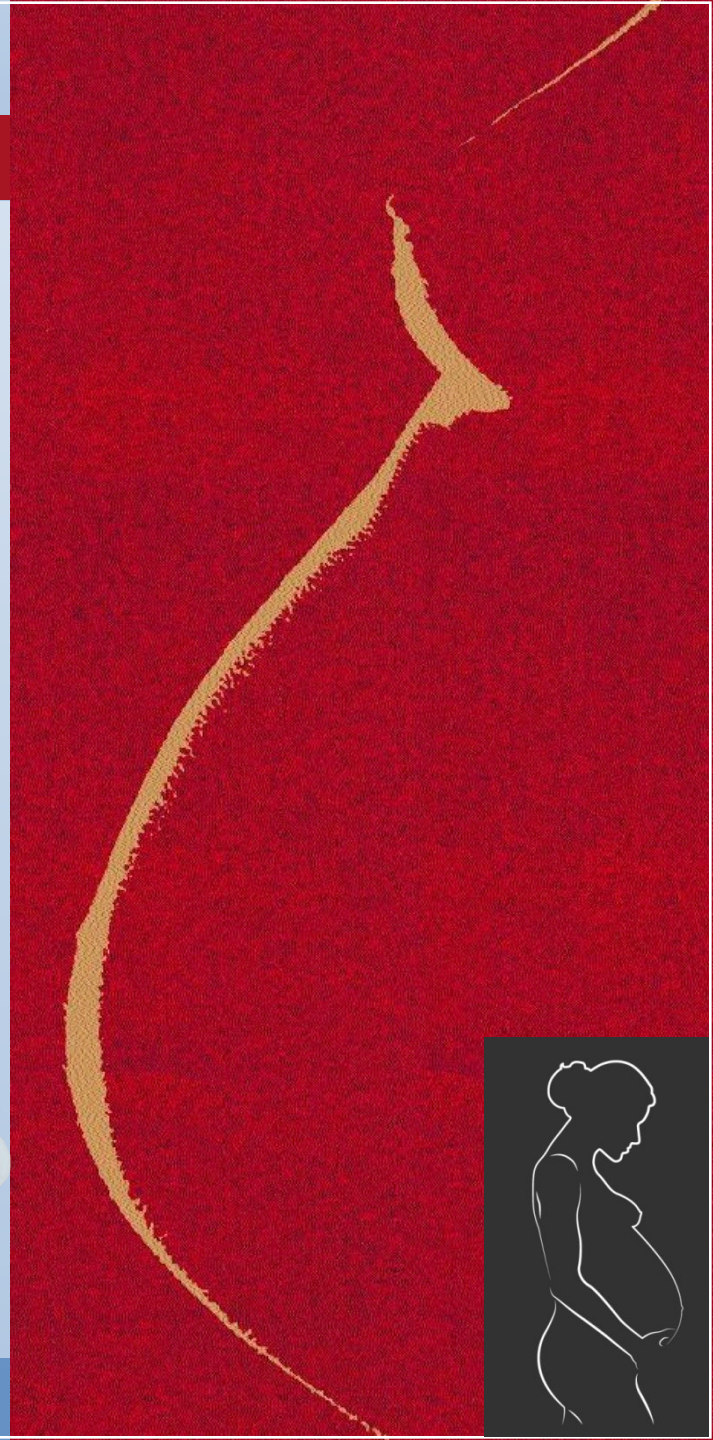
Еще одна трагедия…

Беременна Х., 35-ти лет с четвертой настоящей беременностью на сроке 38–39 недель, состоявшая на диспансерном наблюдении в группе высокого риска (кесарево сечение в 2000 г, 2015 г., 2003 г мед. аборт), доставлена фельдшером в ГУЗ … ЦРБ в (**04:00 17.07.2017**),

Через 2 часа с момента манифестации боли внизу живота, пояснице, усиливающимися во время схватки с диагнозом: Предвестники родов на сроке 38–39 недель беременности.

Через 3 часа 20 мин. (**07:40 17.07.2017**) с момента госпитализации: присоединились боли схваткообразного характера и диагностирован «Первый период родов на сроке 38–39 недель в ножном предлежании. Несостоятельный рубец на матке».

Через 2 часа 35 мин. (**09:55 17.07.2017**) пациентка взята в операционную, где выполнена «нижнесрединная лапаротомия с иссечение кожного рубца, с разведением спаек. Корпоральное кесарево сечение продольным разрезом при беременности 38–39 недель», на 15 минуте от начала операции извлечена живая доношенная девочка (*массой 3140 гр, длиной 52 см, по шкале Апгар 7–9 баллов*). **Во время операции 10 ЕД окситоцина на 200 мл физраствора, прокапано в течении 20 минут.**

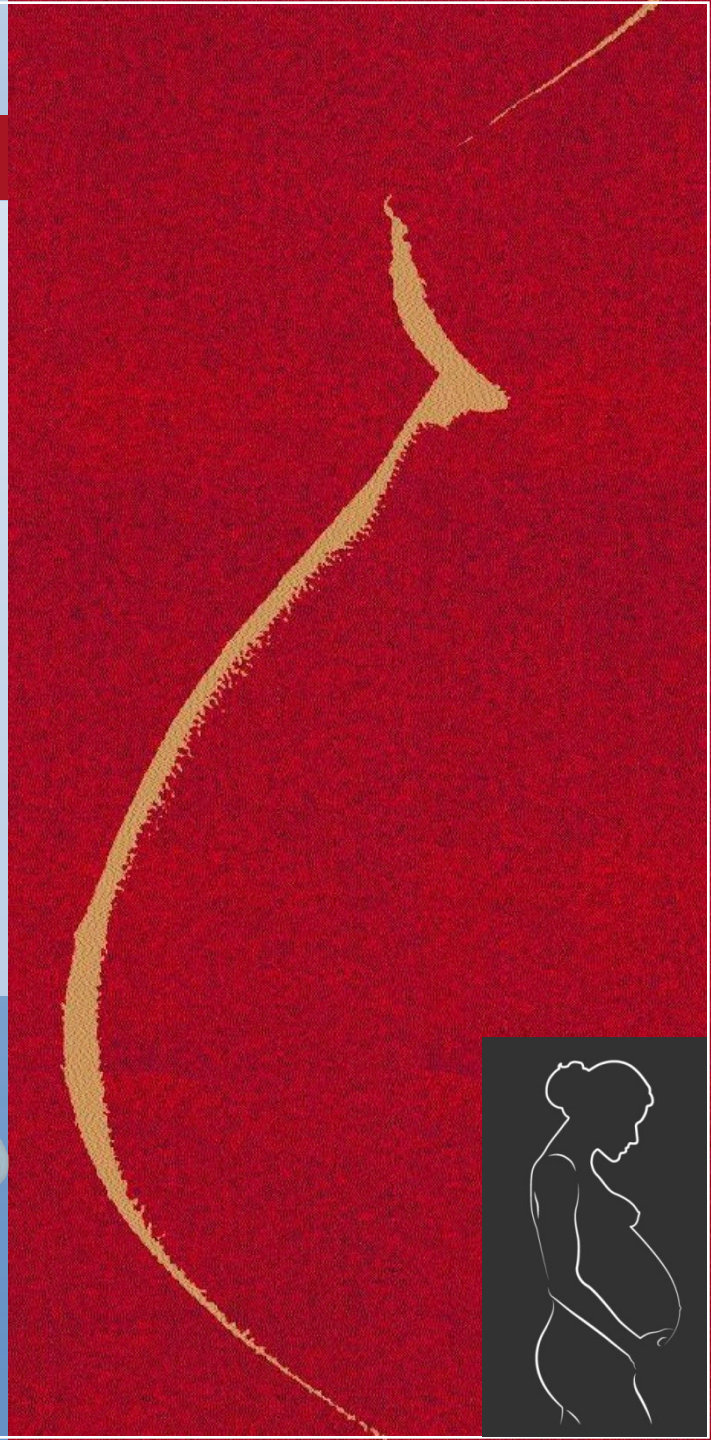


Еще одна трагедия…

Вследствие выявленной в ходе операции «Аневризмы матки» при врастании плаценты (**placenta increta** 27,5 %) и опасности массивного маточного кровотечения, принято решением о расширение объема операции «экстирпации матки»

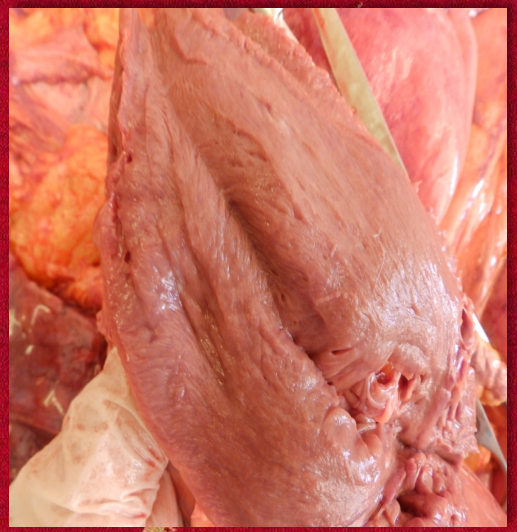
Введено дополнительно 5 ЕД окситоцина в/в болюсно и 5 ЕД инфузия окситоцина на 20 мл раствора кристаллоида.

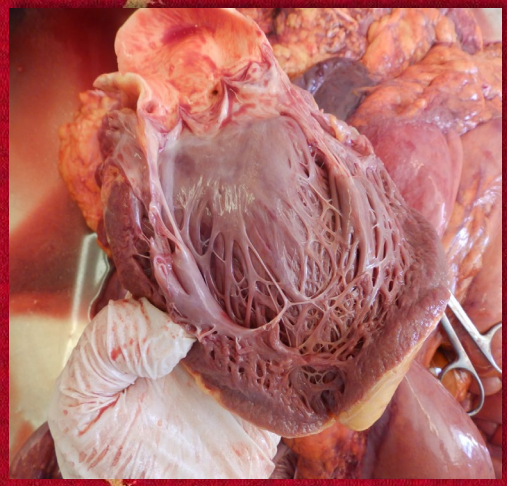
В 10:45 переход на общую анестезию интубация трахеи, ИВЛ. На этапе выделения мочевого пузыря в 10:50 зафиксирована остановка сердечной деятельности, начаты реанимационные мероприятия.
Без эффекта



Еще одна трагедия…

- **Полости дилатированы, пустые.**
  В магистральных сосудах темная жидкая кровь.
  Пристеночный эндокард гладкий, бледный.
  Сосочковые мышцы не утолщены,
  хордальные нити в норме.
- **На разрезе миокард дряблой консистенции, волокнистый, бледно-коричневый.**
  Клапаны сердца тонкие, гладкие;
  аортальный клапан – периметр 7 см,
  митральный – 10 см,
  трехстворчатый клапан – 10.5 см,
  клапан легочной артерии – 7 см.
  В правом желудочке добавочная хорда.
- **Коронарные сосуды с гладкой интимой.**
  Аорта, магистральные сосуды,
  с гладкой желтой интимой.



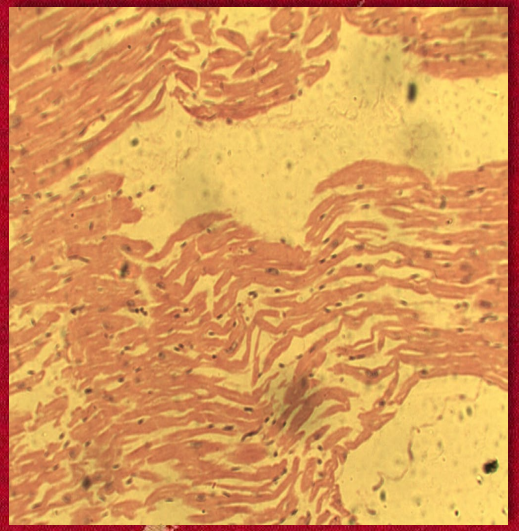


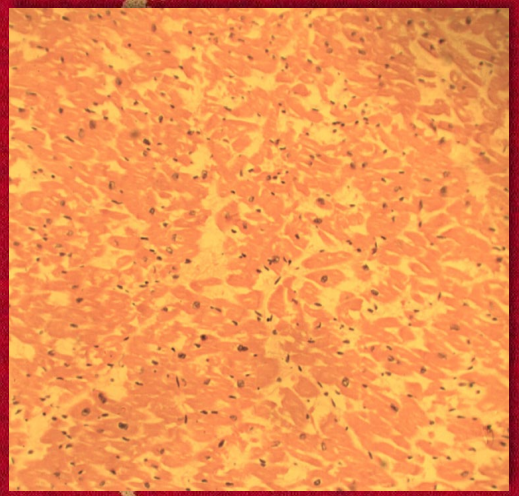
Еще одна трагедия…

- **Миокард:** выраженный межуточный и межклеточный отек, периваскулярные кровоизлияния; зернистая дистрофия саркоплазмы ардиомиоцитов, отмечается очаги дискоидного распада с фрагментацией мышечных волокон, очаговыми кровоизлияниями в эпи- мио- и эндокард.

  Эндотелий мелких артерий и артериол набухший с сочным эндотелием выступает в просвет сосуда.

  Местами потеря поперечной исчерченности отдельных мышечных волокон.





РЕЦЕНЗИЯ Еще одной трагедии

- **Хронология событий**
  - ✓ *Из индивидуальной карты беременной:*

В 29 нед. пациентка ночью поступила
в экстренном порядке в акушерское отделение
1-го уровня с жалобами на головокружение,
тошноту, рвоту. При поступлении АД 210/110 мм рт. ст.
В 00 час. 10 мин. за паховые сгибы согласно
биомеханизму родов в тазовом предлежании извлечен
плод женского пола массой 1100 гр.,
ростом 35 см в асфиксии 3 степени
с оценкой по Апгар 3 балла,
передана неонатологу.

Для профилактики кровотечения в/в введено 10 МЕ окситоцина.

Введение окситоцина продолжено в течение 5 суток в послеродовом периоде в/м 2 раза в сутки.

РЕЦЕНЗИЯ Еще одной трагедии

По заключению СКТ подтвержден геморрагический инсульт в СМА справа с прорывом крови в желудочковую систему, с формированием гематомы, без дислокации срединных структур, с кровоизлиянием в ствол мозга, отек мозга.

Заключение нейрохирурга при повторном осмотре консультантами санавиации: оперативное лечение (наложение вентрикулярного дренажа) не показано.

- **Хронология событий**
  - ✓ *Из индивидуальной карты беременной:*

Carvalho et al. В своих исследованиях показали, что ED90 окситоцина составляет 0.35 IU (95% ДИ, 0.18 до 0.52 ДИ).

Carvalho JC, Balki M, Kingdom J, Windrim R: Oxytocin requirements at elective cesarean delivery: A dose-finding study. Obstet Gynecol 2004; 104 (5 Pt 1):1005–10.

OBSTETRICS & GYNECOLOGY
Wolters Kluwer

Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study

José C. A. Carvalho, MD, PhD, Mrinalini Balki, MD, John Kingdom, MD, and Rory Windrim, MD

OBJECTIVE: Oxytocin is frequently used by intravenous bolus and infusion to minimize blood loss and prevent postpartum hemorrhage at cesarean delivery. Current dosing regimens are arbitrary whereas large doses may pose a serious risk to the mother. The purpose of this study was to estimate the minimum effective intravenous bolus dose of oxytocin (ED_{90}) required for adequate uterine contraction at elective cesarean in nonlaboring women.

METHODS: A randomized, single-blinded study was undertaken in 40 healthy term pregnant women presenting for elective cesarean under spinal anesthesia. Oxytocin was administered by bolus according to a biased coin up-and-down sequential allocation scheme with increments or decrements of 0.5 IU. Uterine contraction was assessed by the obstetrician, who was blinded to the dose of oxytocin, as either satisfactory or unsatisfactory. After achieving sustained uterine contraction, an infusion of 40 mU/min of oxytocin was started. Oxytocin-induced adverse effects and intraoperative complications were recorded and blood loss was estimated. Data were interpreted by parametric analysis based on logistic regression model and nonparametric analyses at 95% confidence intervals (CIs).

RESULTS: The ED_{90} of oxytocin as determined by logistic regression model fitted to the data was estimated to be 0.35 IU (95% CI 0.18–0.52 IU), with nonparametric estimates of 97.1% (95% CI 84.9–99.8%) response rate at 0.5 IU, and 100% (95% CI 92.2–100%) at 1.0 IU. The estimated blood loss was 693 ± 487 mL (mean ± standard deviation).

CONCLUSION: The bolus dose of oxytocin used at elective cesarean deliveries in nonlaboring women can be significantly reduced while maintaining effective uterine contraction. Alteration in practice will likely reduce the potential adverse effects of this drug when given in large bolus doses, but may require modification of the techniques to remove the placenta. (Obstet Gynecol 2004;104:1005–10. © 2004 by The American College of Obstetricians and Gynecologists.)

In many institutions, oxytocin is routinely administered by intravenous bolus and infusion at cesarean delivery after delivery of the fetus. Oxytocin promotes uterine contraction, thereby reducing blood loss from the placental site. However, when given in large doses and as a rapid bolus, oxytocin is associated with various adverse effects, including hypotension, nausea, vomiting, chest pain, headache, flushing, and myocardial ischemia.[1,2] For these reasons, the manufacturer's instructions do not recommend bolus administration.

A variety of regimens for administration of oxytocin have been described previously but appear to be empirical.[3–6] Furthermore, the minimum effective dose of oxytocin at cesarean delivery has not yet been established. The purpose of our study was therefore to estimate the minimum effective dose (ED_{90}) of oxytocin required to produce adequate uterine contraction at elective cesarean delivery in nonlaboring women.

From the Departments of Obstetrics and Gynecology and Anesthesia and Pain Management, Mount Sinai Hospital, Toronto, Ontario, Canada.

MATERIALS AND METHODS

After obtaining approval from the Research Ethics Board at Mount Sinai Hospital, a randomized, single-blinded study was performed with 40 healthy term pregnant women scheduled for elective cesarean delivery. Patients were recruited between October 1, 2003, and January 21, 2004, and 20 surgeons were involved in the study. All patients with conditions that predispose to uterine atony and postpartum hemorrhage such as placenta previa, multiple gestation, preeclampsia, macrosomia, hydramnios, uterine fibroids, history of uterine atony and postpartum bleeding, or bleeding diathesis were excluded from the study. A written informed consent was obtained from the patients before enrollment in the study. All patients received 30 mL of 0.3 mol/L sodium citrate orally, 30 minutes before the institution of spinal anesthesia. Baseline blood pressure (BP) and heart rate were calculated as the mean of 3 readings, 2 minutes apart, recorded in the admitting unit using an automated noninvasive BP device. An 18G peripheral intravenous line was inserted and 10 mL/kg of lactated Ringer's solution was given as preload.

After skin disinfection and local infiltration, a subarachnoid puncture was performed in the sitting position at L_{2-3} or L_{3-4} interspace using a 27G Whitacre needle. Anesthetic blockade of up to a T_4 dermatomal level was

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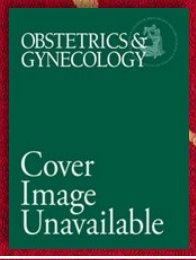

IOJA 2010 editorial
Oxytocin protocols during cesarean delivery: time to acknowledge the risk/benefit ratio?

L. Tsen & M. Balki

- 3 ед. ударная доза
- 3 мин. Оценка
- 3 ед. доза спасения
- 3 общих дозы (1 ударная, 2 спасения)
- 3 ед/л @ 100 мл/час поддержка

International Journal of Obstetric Anesthesia (2010) 19, 243–245
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doi:10.1016/j.ijoa.2010.05.001

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EDITORIAL

Oxytocin protocols during cesarean delivery: time to acknowledge the risk/benefit ratio?

A hormone discovered and synthesized over 50 years ago, oxytocin is currently used in the majority of births in developed countries and a growing number of births in the developing world.[1] Commonly employed to induce or augment the process of labor to effect vaginal delivery, oxytocin is also used as the first line drug to restore uterine tone and minimize postpartum blood loss following cesarean delivery. The purpose of this editorial, which is echoed in the review article by Dyer and colleagues in this issue of IJOA,[2] is to illuminate the risks associated with large intravenous (i.v.) bolus doses of oxytocin administered during cesarean delivery and to advocate an evidenced-based, infusion approach to dosing.

The administration of oxytocin is associated with significant maternal, fetal, and neonatal adverse events. Maternal arrhythmias, hypotension, uterine hyperstimulation and hyponatremia,[3,4] fetal decreases in oxygen saturation (SaO_2) related to contraction frequency,[5,6] and neonatal seizures, hyperbilirubinemia, or retinal hemorrhage[7,8] have been reported following oxytocin use. During cesarean delivery, with oxytocin administered following delivery, maternal morbidity and mortality are the most relevant concerns. The 1997–99 triennial audit of the Confidential Enquiries into Maternal Deaths in the United Kingdom (UK), reported the deaths of two women from cardiovascular instability following an i.v. bolus of oxytocin 10 IU.[9] Awareness of these deaths resulted in a dose reduction in the UK to an i.v. bolus of 5 IU;[9] however, even this dose, and the method of administration, may cause hypotension, tachycardia, decreased free water clearance, peripheral flushing, nausea, emesis and signs of myocardial ischemia.[10–13]

Although practitioners may be aware of these risks, the associated professional liability is the proverbial mountain hidden in plain sight: oxytocin remains *the* drug most commonly associated with preventable adverse events during childbirth, and *the* drug implicated in nearly half of all paid obstetric litigation claims.[14] Moreover, the United States Food and Drug Administration (FDA) has placed a black box warning restricting oxytocin use (during labor) to *medical* indications.[15] Furthermore, the Institute for Safe Medication Practices (ISMP), an independent, nonprofit organization whose recommendations are utilized by groups including the Joint Commission in evaluating medication safety, recently added oxytocin to the list of *high-alert* medications.[16] This distinction, which identifies drugs "bearing a heightened risk of harm when used in error" that may "require special safeguards to reduce the risk of error", has been applied to only 11 other specific drugs.[16]

In an effort to improve patient safety, the *cause célèbre* of the contemporary medical community, practitioners have questioned the high-dose, non-standardized oxytocin practices currently in use.[17–19] The re-evaluation of oxytocin acknowledges the unpredictable therapeutic index (in which a given dose can result in either hypertonic contractions or no discernable effect), use of excessive starting doses, lack of a predetermined, lock-step protocol that predicates increasing doses on determination of insufficient lower doses, and practices that contribute to normalization of deviance (degradation of professional or technical standards based on individual experience).[17–19] Interestingly, this call to action stops abruptly at the door of the operating room, despite literature demonstrating that common clinical practices result in unnecessary, excessive oxytocin doses. In non-laboring women undergoing cesarean delivery, a 'ceiling effect' of oxytocin 5 IU is witnessed, beyond which no further improvement in uterine tone and blood loss is observed;[20] in laboring women, high doses of oxytocin did not obviate the need for additional uterotonic agents.[21] Interestingly, a small loading dose of oxytocin (ED 90 = 0.35 IU) has been determined to be sufficient in producing adequate uterine contractions during elective cesarean deliveries in non-laboring women;[22] a similarly low loading dose (ED 90 = 2.99 IU) is required in laboring women.[23] Women who have received oxytocin augmentation for labor have greater blood loss despite higher oxytocin doses; this appears to originate from signal attenuation and desensitization of the oxytocin receptors, in a time and concentration dependent manner.[24–27] Similarly, continued high-dose oxytocin exposure in the postpartum period may also lead to acute receptor desensitization and render the myometrium less responsive to additional oxytocin.[27]

The current guidelines for the administration of oxytocin during cesarean delivery are diverse, empiric, and vague. The most recent editions of major obstetric

J Obstet Anesth. 2010 Jul;19(3):243-5

ANESTHESIOLOGY
The Journal of the American Society of Anesthesiologists, Inc.

From: Changes in Blood Pressure and Cardiac Output during Cesarean Delivery: The Effects of Oxytocin and Carbetocin Compared with Placebo

Anesthesiology. 2013; 119(3):541–551. doi:10.1097/ALN.0b013e31829416dd

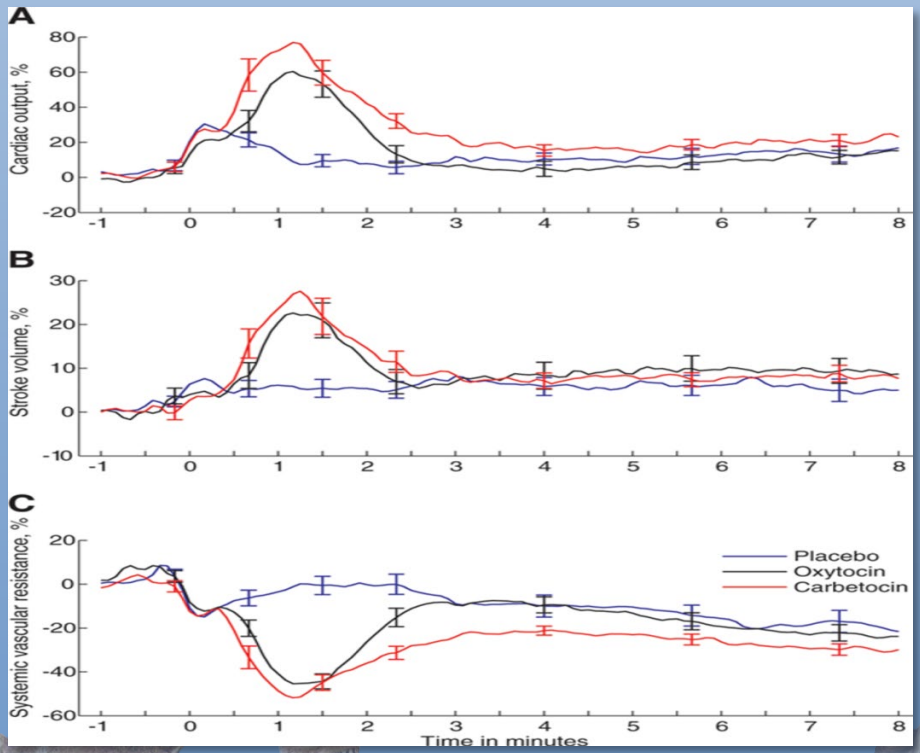


Figure Legend:

Estimated cardiac output (A), stroke volume (B), and systemic vascular resistance (C) in the three treatment groups the minute before and 8 min after intervention (intervention = time 0) presented as the percentage change from baseline representing measurements from the last 30 s before uterotomy.

ANESTHESIOLOGY
The Journal of the American Society of Anesthesiologists, Inc.

From: Changes in Blood Pressure and Cardiac Output during Cesarean Delivery: The Effects of Oxytocin and Carbetocin Compared with Placebo

Anesthesiology. 2013; 119(3):541–551. doi:10.1097/ALN.0b013e31829416dd

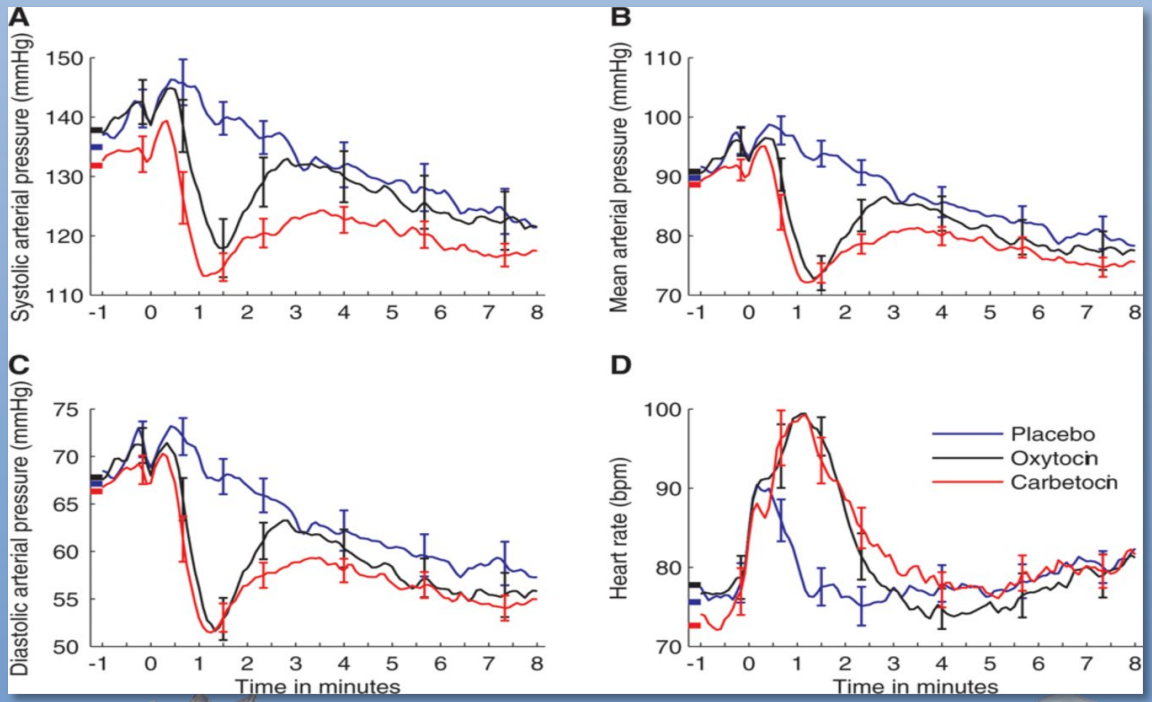
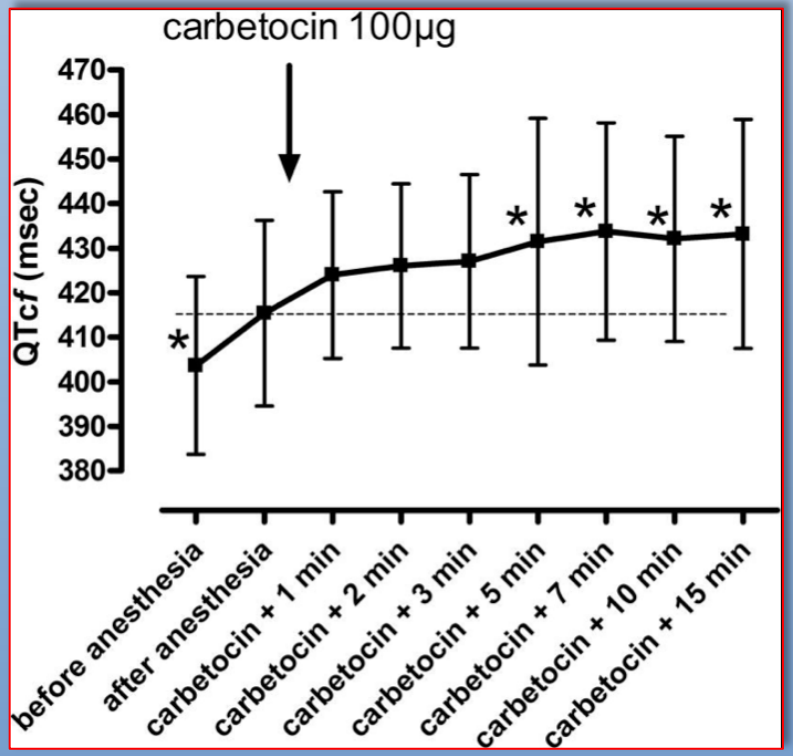


Figure Legend:

Invasive hemodynamic variables are presented as mean (SD) in the three treatment groups 1 min before and 8 min after intervention (intervention = time 0). The group means of the measurements in the last 30 s before uterotomy are indicated on the y-axis with horizontal lines. (A) Systolic arterial pressure, (B) mean arterial pressure, (C) diastolic arterial pressure, and (D) heart rate.



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0959-289X/$ - see front matter

http://dx.doi.org/10.1016/j.ijoa.2013.10.005

QT interval prolongation following carbetocin in prevention of post-cesarean delivery hemorrhage

Carbetocin is a new synthetic analog of human oxytocin that is used in the prevention of postpartum hemorrhage during cesarean delivery.[1] It is longer lasting than oxytocin;[2] however, it decreases arterial blood pressure and increases heart rate in similar proportions. Oxytocin has been shown to cause a transient increase in the QT interval,[3] and cause changes in T-wave morphology that may predispose to cardiac arrhythmia.[4] These effects may be caused by a direct action on conduction tissue but may also be related to indirect sympathetic effects such as a decrease in arterial blood pressure and an increase in heart rate.[3,5,6]

This observational study assessed the electrocardiographic and hemodynamic effects of carbetocin administered during cesarean delivery. After umbilical cord clamping, an intravenous bolus of carbetocin 100 µg (Pabal®, Ferring GmbH, Kiel, Germany) was administered over 10 s. A digital 12-lead electrocardiogram was obtained before induction of anesthesia, 3 min after stable anesthesia had been obtained, and then at 1, 2, 3, 5, 7, 10 and 15 min after carbetocin injection. The QT interval was measured semi-manually by a single observer and was corrected according to Fridericia's correction formula ($QTcf = QT/RR$). Sample size was calculated in order to detect a QT*cf* change >10 ms using a β risk at 0.20. QT*cf*, RR intervals and arterial blood pressure were compared by ANOVA for repeated measures and, if significant, using post-hoc analyses.

Among the 20 women enrolled (age: 31 ± 6 years, weight: 78 ± 14 kg), 85% underwent an elective procedure. Gestational age was 37 weeks and 3 days ± 7 days. Cesarean delivery was performed because of previous cesarean delivery ($n = 7$), placenta previa ($n = 3$), cervical dystocia ($n = 2$), twin pregnancy ($n = 2$), breech presentation ($n = 2$), intrauterine growth restriction ($n = 2$), fetal cardiac rhythm abnormality ($n = 1$) and HIV infection ($n = 1$). Spinal, combined spinal–epidural and epidural anesthesia were used in 10, five and five patients, respectively. Hyperbaric 0.5% bupivacaine was used in 15 cases, 2% lidocaine in four cases and both drugs combined in one case. Fifteen women required vasopressor support with ephedrine ($n = 10$, mean total dose 9 ± 11 mg) or phenylephrine ($n = 7$, mean total dose 60 ± 91 µg). Baseline hemodynamic characteristics before anesthesia were systolic blood pressure 134 ± 14 mmHg, diastolic blood pressure 79 ± 9 mmHg, heart rate 89 ± 14 beats/min and QT*cf* 403 ± 19 ms. Apgar scores were 10 in 75% [range 8–10] and 10 in 85% [range 9–10] at 1 and 5 min, respectively. Arterial blood gas measurement was obtained in 12 newborns: median pH was 7.31 [range 7.14–7.40]. Mean QT*cf* interval values over time are shown in Fig. 1. QT*cf* duration was significantly longer from the post-anesthesia measurement from 5 min until the last recorded value at 15 min after carbetocin administration. The maximal increase was observed at 7 min (+ 18 ± 4 ms, $P = 0.01$). Compared to the pre-anesthesia baseline measurements, all QT*cf* values were significantly prolonged with a maximal rise at 7 min (+ 30 ± 4 ms, $P < 0.0001$). No arrhythmia occurred during the study period. Carbetocin did not modify heart rate but was associated with a 19% drop of arterial blood pressure. Compared with post-anesthesia values, the nadir was found at 15 min after carbetocin administration: −23 ± 4 and −22 ± 3 mmHg for systolic and diastolic blood pressure, respectively (both $P < 0.0001$).

Although this observational study lacked a control group, the observed QT prolongation and hemodynamic changes following carbetocin are likely to be drug-related. Firstly, the observed decrease in arterial blood pressure is close to that reported in previous studies, supporting external validity;[7] secondly, data obtained in observational and placebo-controlled studies usually show similar drug-induced QT prolongation.[8] However, we cannot exclude that the prolongation in QT interval might have been related to other QT prolonging factors. Apart from case

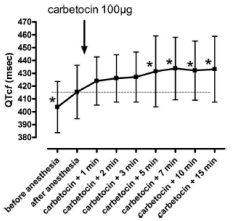


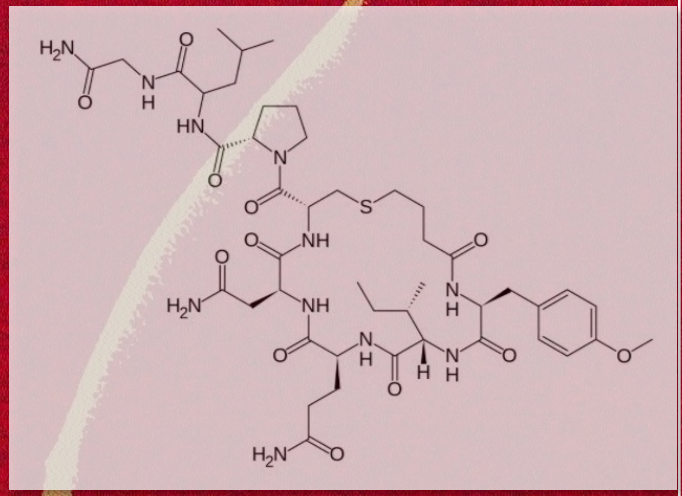
Fig. 1 Mean QT*cf* (±SD) during cesarean delivery. * $P < 0.05$ versus level after anesthesia.

M. Bruyere, N. Ait Hamou, D. Benhamou. QT interval prolongation following carbetocin in prevention of post-cesarean delivery hemorrhage. International Journal of Obstetric Anesthesia. 2016 Vol. 23, (1), P. 88–89

Заключение

Карбетоцин – многообещающий утеротоник

- Сходная эффективность с окситоцином в предупреждении послеродового кровотечения
- Лучший профиль безопасности по сравнению с окситоцином



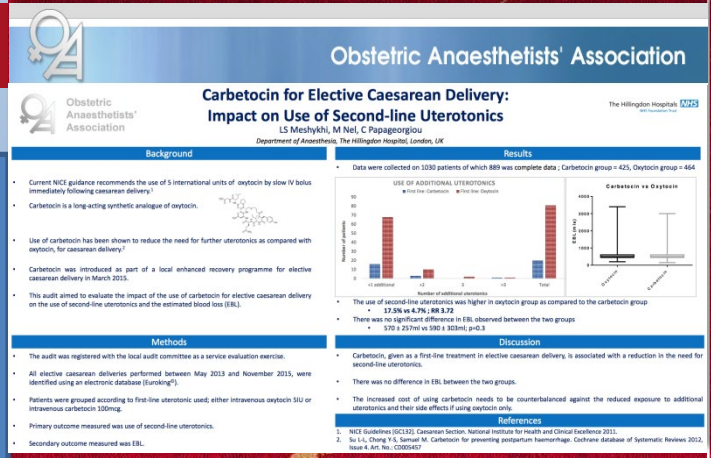
Выводы

- **Карбетоцин уменьшает частоту применения дополнительных доз окситоцина после КС по сравнению лицензированной дозой окситоцина (5МЕ)**

При введении **карбетоцина**, как препарата первой очереди при плановом КС, отмечалось снижении потребности в повторных введениях утеротоников

Не отмечено разницы по объему кровопотери в группах (*окситоцин* и *карбетоцин*)

Увеличение стоимости при лечении карбетоцином сопоставимо с уменьшением дополнительного применения утеротоников второй очереди и побочными эффектами применения только окситоцина


Obstetric Anaesthetists' Association

Carbetocin for Elective Caesarean Delivery:
Impact on Use of Second-line Uterotonics

LS Meshykhi, M Nel, C Papageorgiou

Department of Anaesthesia, The Hillingdon Hospital, London, UK

Background

- Current NICE guidance recommends the use of 5 international units of oxytocin by slow IV bolus immediately following caesarean delivery[1]
- Carbetocin is a long-acting synthetic analogue of oxytocin.
- Use of carbetocin has been shown to reduce the need for further uterotonics as compared with oxytocin, for caesarean delivery[2]
- Carbetocin was introduced as part of a local enhanced recovery programme for elective caesarean delivery in March 2015.
- This audit aimed to evaluate the impact of the use of carbetocin for elective caesarean delivery on the use of second-line uterotonics and the estimated blood loss (EBL).

Methods

- The audit was registered with the local audit committee as a service evaluation exercise.
- All elective caesarean deliveries performed between May 2013 and November 2015, were identified using an electronic database (Euroking®).
- Patients were grouped according to first-line uterotonic used; either intravenous oxytocin 5IU or intravenous carbetocin 100mcg.
- Primary outcome measured was use of second-line uterotonics.
- Secondary outcome measured was EBL.

Results

- Data were collected on 1030 patients of which 889 was complete data ; Carbetocin group = 425, Oxytocin group = 464

USE OF ADDITIONAL UTEROTONICS

Carbetocin vs Oxytocin

- The use of second-line uterotonics was higher in oxytocin group as compared to the carbetocin group
  - 17.5% vs 4.7% ; RR 3.72
- There was no significant difference in EBL observed between the two groups
  - 570 ± 257ml vs 590 ± 303ml; p=0.3

Discussion

- Carbetocin, given as a first-line treatment in elective caesarean delivery, is associated with a reduction in the need for second-line uterotonics.
- There was no difference in EBL between the two groups.
- The increased cost of using carbetocin needs to be counterbalanced against the reduced exposure to additional uterotonics and their side effects if using oxytocin only.

References

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Carbetocin for Elective Caesarean Delivery:
Impact on Use of Second-line Uterotonics
LS Meshykhi, M Nel, C Papageorgiou
Department of Anaesthesia, The Hillingdon Hospital, London, UK

Meshylhi L.S., Nel M., C. Papageorgiou. Carbetocin for Elective Caesarean Delivery: Impact on Use of Second –line Uterotonics. OAA meeting May 2016, P. 12

Заключение

- Окситоцин-ассоциированное влияние на гемодинамику включает:
  - ✓ *Вазодилатацию*
  - ✓ *Увеличение сердечного выброса*
  - ✓ *Снижение АД*
  - ✓ *Изменения на ЭКГ*

- У карбетоцина по сравнению с окситоцином отмечаются более краткосрочные гемодинамическое побочные эффекты, несмотря на больший период его полураспада.

Заключительные комментарии

- Для профилактики послеродового кровотечения карбетоцин эффективнее окситоцина
- Профиль побочных эффектов карбетоцина лучше, чем у синтометрина
- Период полураспада утеротоников отличается:
  - ✓ окситоцин – **3 мин.**
  - ✓ эргометрин – **12 мин.**
  - ✓ **карбетоцин** – **40 мин.**
- Не смотря на больший период полураспада, у карбетоцина более кратковременный период побочного влияния на гемодинамику