Uterotonic agents for caesarean section

Thierry Girard
Basel, Switzerland
Conflict of interest
Medical methods for preventing blood loss at caesarean section (Protocol)

Connell JE, Mahomed K
Uterotonic agents for caesarean section

• Why ?

• Which ?

• How ?

• When ?
Why?

>50%
Uterotonic agents for caesarean section

• Why?
• Which?
• How?
• When?
Which?

- Oxytocic
- Prostaglandins
- Ergot alkaloids
Which?

- Oxytocic
  - Oxytocin
  - Carbetocin
- Prostaglandins
- Ergot alkaloids
Which?

- Oxytocic
  - Oxytocin
  - Carbetocin

- Prostaglandins
  - PGE$_1$: misoprostol
  - PGE$_2$: dinoprostone, prostin, sulprostone
  - PGF$_{2\alpha}$: dinoprost, carboprost, hemabate

- Ergot alkaloids
Which?

- Oxytocic
  - Oxytocin
  - Carbetocin
- Prostaglandins
  - PGE$_1$: misoprostol
  - PGE$_2$: dinoprostone, prostan, sulprostone
  - PGF$_{2\alpha}$: dinoprost, carboprost, hemabate
- Ergot alkaloids
  - Methylergometrine, methergine
Uterotonic agents for caesarean section

• Why?

• Which?

• How?

• When?
How?

Ca\textsuperscript{2+}

MLCK

Myometrial contraction

PIP\textsubscript{2}

IP\textsubscript{3}

IP\textsubscript{3}

ER

DAG

PG synth

Calmodulin

Ca\textsuperscript{2+}

Ca\textsuperscript{2+}

R

G

PLC
Which?

- Oxytocin
- Prostaglandins
- Ergot alkaloids
Oxytocin

- Adverse effects
- Receptor desensitisation
- Down regulation
Oxytocin - adverse effects

- Cardiovascular
  - Hypotension
  - Arrhythmias
  - Myocardial ischemia
  - Increased pulmonary artery pressure
- Nausea & vomiting
- Headache
- Flushing
A RELATIONSHIP BETWEEN ADRENALINE AND THE MODE
OF ACTION OF OXYTOCIN AND OESTROGEN
ON VASCULAR SMOOTH MUSCLE

BY A. L. HAIGH, SYBIL LLOYD AND MARY PICKFORD

From the Departments of Veterinary Physiology, and of
Physiology, The University, Edinburgh

(Received 30 October 1964)

Papers already published report that in the normal mammals so far
examined (man, dog and rat, both sexes) oxytocin dilates a number of
vascular beds (Lloyd, 1959a, b; Lloyd & Pickford, 1961; Haigh,
ST depression at caesarean section and the relation to oxytocin dose. A randomised controlled trial

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Objective
To investigate whether there is a difference in occurrence of electrocardiogram changes suggestive of myocardial ischaemia between two different doses of oxytocin.

Design
Double-blind randomised controlled trial

Setting
University hospital in Sweden.

Population
A total of 103 healthy women undergoing elective caesarean section under spinal anaesthesia.

Methods
The participants were randomised to 5 or 10 units of oxytocin, given as an intravenous bolus. A Holter monitor was used to record electrocardiograms and non invasive blood pressure and heart rate (HR) was monitored. A blood sample was obtained 12-hour postoperatively.

Main outcome measures
Depression of the ST segment.

Secondary outcomes: symptoms, Troponin I levels, mean arterial pressure (MAP), HR and blood loss.

Results
There was a significant difference in occurrence of ST depressions associated with oxytocin administration, 4 (7.7%) with 5 and 11 (21.6%) with 10 units, \( P < 0.05 \). The absolute risk reduction was 13.9% (95% confidence interval, 0.5–27.3).

Decrease of mean MAP from baseline to 2 minutes differed, being 9 mmHg in the 5 unit group and 17 mmHg in the 10 unit group \( P < 0.01 \). The increase in mean HR did not differ. Troponin I levels were increased in four subjects (3.9%). There were no differences in occurrence of symptoms, Troponin I levels, or estimated blood loss.

Conclusion
ST depressions were associated with oxytocin administration significantly more often in subjects receiving 10 units compared with 5 units. Interventions to prevent hypotension during caesarean section may reduce the occurrence of ST depressions on electrocardiograms.

Keywords
Caesarean section, electrocardiography, heart, hypotension, ischaemia, oxytocin, regional anaesthesia.

Introduction
Electrocardiogram (ECG) changes, suggestive of myocardial ischaemia, have been observed in healthy women during elective caesarean section under regional anaesthesia and the incidence reported varies from 25% to 60.\(^1\)–\(^4\) An association with oxytocin administration has recently been described in a randomised trial using 10 units of oxytocin.\(^5\) Oxytocin, given as an intravenous bolus, causes transient hypotension, a reflex tachycardia and an increase in cardiac output, in healthy women undergoing caesarean section under spinal anaesthesia.\(^6\)–\(^8\) The magnitude of these effects is dose-related.\(^6,9\) Coronary vaso-constriction has also been described following oxytocin administration.\(^10\) Systemic haemodynamic changes and/or coronary vasospasm may impair the myocardial oxygen supply sufficiently to induce ischaemia, which could be an explanation for the ECG changes.\(^5,11\) The value of routine oxytocics in the third stage of caesarean delivery to prevent excessive bleeding has been well established and routine oxytocics are also recommended in patients with cardiac disease.\(^12\)–\(^14\) Doses of oxytocin, as well as route of administration, vary widely in clinical practice and many clinicians are not aware of all the adverse effects of oxytocin.\(^15,16\) Oxytocin could be detrimental to women who are hypovolemic and to women with cardiac disease.\(^11,15,17\)–\(^19\)
Cardiac Ischemia

- 10 IU: 22%
- 5 IU: 17%
- Total (n=103):
  - ST segment depression
Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing Caesarean section

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5 IU over 5 minutes
5 IU in 5ml as quickly as possible
Pulse rate changes with oxytocin

Study period (s)

Change in PR (beats min^-1)

-15 -10 -5 0 5 10 15 20 25 30

Bolus mean PR
Infusion mean PR

Fig 1
Heart rate before and after oxytocin administration (time 0). The data points shown are the mean (±SEM).

MAP changes with oxytocin

Study period (s)

Change of MAP (mm Hg)

-35 -30 -25 -20 -15 -10 -5 0 5 10 15

Bolus mean
Infusion mean

Fig 2
Mean arterial pressure recordings before and after oxytocin administration (time 0). The data points are mean (±SEM).
of HR in the infusion group is preferable clinically. It is reassuring to the anaesthetist who prefers to maintain cardiovascular equipoise that this physiological insult can be avoided simply by giving the oxytocin over 5 min. The decrease in MAP of 8 (8.7) mm Hg and the small increase in HR are certainly clinically preferable.
Hemodynamic Changes Associated with Spinal Anesthesia for Cesarean Delivery in Severe Preeclampsia

How-ever, this technique was associated with a 47% incidence of hypertension. In the current study, when target values of MAP for vasopressor administration (a 20% decrease in blood pressure) were reached, CO had not decreased significantly, and in many cases had increased (table 4). This suggests that maintaining blood pressure at the baseline level in this patient population during SA may be ineffective. (Fig. 3)
How-ever, this technique was associated with a 47% incidence of hypertension. In the current study, when target values of MAP for vasopressor administration (a 20% decrease in blood pressure) were reached, CO had not decreased significantly, and in many cases had increased (table 4). This suggests that maintaining blood pressure at the baseline level in this patient population during SA may...
delivery at a rate that maintains baseline MAP.

However, this technique was associated with a 47% incidence of hypertension. In the current study, when target values of MAP for vasopressor administration (a 20% decrease in blood pressure) were reached, CO had not decreased significantly, and in many cases had increased (table 4). This suggests that maintaining blood pressure at the baseline level in this patient population during SA may

Fig. 3. Ensemble of hemodynamic changes after the administration of oxytocin. (A) Heart rate (HR). At peak effect, HR increased from 84.7 (12.6) to 101.5 (15.9)* beats/min. (B) Mean arterial pressure (MAP). At peak effect, MAP decreased from 114.3 (15.0) to 80.6 (15.3)* mmHg. (C) Stroke volume (SV). At peak effect, SV increased from 82.9 (15.9) to 89.1 (17.3) (not significant). (D) Cardiac output (CO). At peak effect, CO increased from 7.0 (1.5) to 9.1 (2.3)* l/min. (E) Systemic vascular resistance (SVR). At peak effect, SVR decreased from 1,295 (252) to 718 (282)* dyn/cm5. * Value significantly different from baseline and postdelivery; P < 0.01.
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


**Figure 1.** Logistic response curve. Total response at each dose level.

- **ED$_{90}$**: 0.35 IU
- **100%**: 1 IU
Minimum Oxytocin Dose Requirement After Cesarean Delivery for Labor Arrest

Mrinalini Balki, MD, Michael Ronayne, MD, Sharon Davies, MD, Shafagh Fallah, PhD, John Kingdom, MD, Rory Windrim, MD, and José C. A. Carvalho, MD, PhD

ED90: 2.99 IU
EDITORIAL

Oxytocin protocols during cesarean delivery: time to acknowledge the risk/benefit ratio? L. Tsen & M. Balki

3 U loading dose (slow !)
3 minutes assessment
3 U rescue dose
3 total doses (1 loading, 2 rescue)
3 U/L @ 100 ml/h maintenance
Carbetocin

- Oxytocin receptor agonist
- Duration of action: 60-120 min
Changes in Blood Pressure and Cardiac Output during Cesarean Delivery

The Effects of Oxytocin and Carbetocin Compared with Placebo

Leiv Arne Rosseland, M.D., Ph.D.,* Tor Hugo Hauge, Ph.D.,† Guro Grindheim, M.D., Ph.D.,‡ Audun Stubhaug, M.D., Ph.D.,§ Eldrid Langesæter, M.D., Ph.D.||
Uterine tone

- Placebo
- Carbetocin
- Oxytocin

Previous studies have shown that oxytocin and carbetocin have hemodynamic side effects of comparable magnitude and duration, whereas the uterotonic effect of carbetocin is documented to be significantly longer than that of oxytocin. In this study, we found that the HR elevation after carbetocin lasted slightly longer than after oxytocin (fig. 2D), which may be of clinical interest for pregnant women with increased risk of cardiac events. Apart from this, none of our observed differences between carbetocin and oxytocin, even those that were statistically significant, have obvious clinical impact or relevance in healthy pregnant women. The hemodynamic side effects of carbetocin and oxytocin were compared previously in a randomized study. That study measured noninvasive blood pressure, HR, and hemodynamic variables estimated by impedance cardiography. Due to technical problems with the monitoring device, the dropout rate was substantial, and only 56 of 84 included patients were analyzed. There was an increase in HR of 18 and 14 beats/min after 10-s injections of oxytocin 5 U or carbetocin 100 µg, respectively. The HR declined below baseline 200 s after injection in their oxytocin group, and to a lesser extent, 270 s after injection in the carbetocin group. Systolic blood pressure decreased by 27 and 23 mmHg, respectively, with no statistically significant differences in the hemodynamic variables. Overall, their results were comparable with ours. The strengths of our trial are that we measured blood pressure and hemodynamic variables invasively and continuously, we analyzed all included patients, and the statistical power was greater. In addition, we included a placebo group. Compared with placebo, the differences in the hemodynamic effects of carbetocin and oxytocin were both statistically and clinically significant (fig. 3). The women that were randomized to placebo were hemodynamically more stable, and the observed increase in blood pressure and HR may be due to the placebo effect.
Carbetocin at elective Cesarean delivery: a randomized controlled trial to determine the effective dose

Carbétocine et césarienne programmée: étude randomisée contrôlée pour la détermination de la dose efficace

Daniel Cordovani, MD · Mrinalini Balki, MD · Dan Farine, MD · Gareth Seaward, MD · Jose C. A. Carvalho, MD, PhD

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of similar efficacy within the dose range of 80-120 µg. Further studies with doses lower than 80 µg are warranted to assess the balance of efficacy and side effects, namely, hypotension. However, our data may not be extrapolated to
Carbetocin at elective Cesarean delivery: a randomized controlled trial to determine the effective dose, part 2

La carbétocine lors d’un accouchement par césarienne programmé: une étude randomisée contrôlée pour déterminer la dose efficace, 2e partie

Suresh Anandakrishnan, MD · Mrinalini Balki, MD · Dan Farine, MD · Gareth Seaward, MD · Jose C. A. Carvalho, MD, PhD

20 µg
40 µg
60 µg
80 µg
100 µg
effective in women at low risk for PPH undergoing elective Cesarean deliveries. The incidence of side effects associated with these doses, notably hypotension, remains high and similar across all doses. Further dose-finding studies, including doses lower than 20 μg, are warranted to determine efficacy and side effects.
Carbetocin at elective Cesarean delivery: a sequential allocation trial to determine the minimum effective dose

La carbétocine lors d’un accouchement par césarienne programmé: une étude d’attribution séquentielle afin de déterminer la dose efficace minimale

Mubeen Khan, MD · Mrinalini Balki, MD · Iram Ahmed, MD · Dan Farine, MD · Gareth Seaward, MD · Jose C. A. Carvalho, MD, PhD
The overall rates of hypotension and hypertension were 37.5% and 12.5%, respectively, while nausea occurred in 27.5% of patients.

Discussion
For routine elective CD, we found that the ED$_{90}$ for carbetocin is 14.8 µg (95% CI 13.7 to 15.8). This dose is less than one-fifth of the recommended dose of 100 µg according to the current SOGC guidelines. These results further refine two previous dose-finding studies of carbetocin at elective CD conducted at our institution. Cordovani et al. compared carbetocin in doses of 80, 90, 100, 110, and 120 µg and observed similar efficacy in uterine contraction across all groups. Subsequently, Anandakrishnan et al. compared carbetocin in doses of 20, 40, 60, 80, and 100 µg and again found similar efficacy for uterine contraction across all treatment groups. The overall success rates of the carbetocin treatments in those studies were 87% and 94.5%, respectively. Given the monotonic distribution of results in both studies, it was not possible to calculate the ED$_{90}$; however, those findings involving a total of 200 females suggested that the ED$_{90}$ could be equal to or lower than 20 µg. That assumption has now been confirmed with the current study.

The effective dose obtained in the current study contrasts with the doses of carbetocin commonly reported and recommended in the literature. In a recent systematic review, Su et al. concluded that the risk of PPH in females undergoing CD was lower in the group receiving carbetocin compared with those receiving oxytocin (RR 0.55; 95% CI 0.31 to 0.95). It is noteworthy that all trials included in this systematic review studied carbetocin 100 µg, while the dosage of the oxytocin intravenous bolus varied from 5-32.5 IU over 16 hr. The fact that we found an ED$_{90}$ for carbetocin to be considerably lower than the recommended dose may not be all that surprising. Our group has described similar findings for oxytocin. Carvalho et al. determined the ED$_{90}$ of oxytocin at elective CD to be 0.35 IU (95% CI 0.18 to 0.52), almost ten times lower than a routinely recommended 5 IU bolus dose. Butwick et al. have subsequently confirmed these results. Our findings may be explained in different ways. The initial recommendation for a 100 µg bolus dose of carbetocin may have originated from animal studies suggesting carbetocin 100 µg is equivalent to oxytocin 5 IU. Animal data may not be readily transferable to humans, particularly in the case of carbetocin, as it has been suggested that the human myometrium is much more sensitive to carbetocin than the rat myometrium.
Which?

- Oxytocin
- Prostaglandins
- Ergot alkaloids
Prostaglandins
Prostaglandin E and F receptors in the uterus

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secretion and the role of various enzymes in their conversions, we have not yet fully understood the role of PG receptors, their regulation and molecular mechanisms.
Prostaglandins - side effects

- Nausea & vomitus
- Shivering
- Fever
- Diarrhoea
Prostaglandins

- PGE$_1$: misoprostol
- PGE$_2$: dinoprostone, prostin, sulprostone
- PGF$_{2\alpha}$: dinoprost
- 15-Methyl PGF$_{2\alpha}$: carboprost, hemabate
PGE$_1$: misoprostol

- Cheap
- No cooling needed
- Dose: 400 - 600 (-800) µg
- Route: vaginal, rectal oral
CORRESPONDENCE

Unexpected tracheal tube blockage from a semi-dissolved misoprostol tablet

In obstetric patients, difficulty with tracheal intubation has an incidence of approximately 1 in 30. We report a case where a sublingual misoprostol tablet inadvertently blocked the lumen of a tracheal tube during intubation in a pregnant patient with an unexpected difficult airway.

A 29-year-old, 65 kg nulliparous woman at term presented for an urgent caesarean section for fetal distress following non-progressive labour. The patient was extremely distressed and airway assessment by the anaesthesia resident revealed adequate mouth opening and a Mallampati class III airway. The patient refused neuraxial anaesthesia, so general anaesthesia with a rapid-sequence induction was performed using thiopental, succinylcholine and cricoid pressure. The first attempt at intubation failed because of an anteriorly-placed larynx (Cormack and Lehane grade 3). After another attempt using a stylet, the trachea was successfully intubated with a 7.0 mm internal diameter tracheal tube (Portex, Smiths Medical, Hythe, UK) with moderate difficulty. With cricoid pressure maintained, there was unusual resistance to bag ventilation associated with high peak airway pressures of 45–50 cmH₂O. Breath sounds and capnographic trace were absent. A check of the breathing circuit revealed no malfunction. A 12 French suction catheter was passed through the lumen of the tube and resistance was encountered at around 30 cm. The tube was removed immediately with cricoid pressure maintained. When the tube was examined, a semi-dissolved tablet was occluding the lumen above the Murphy eye (Fig. 1). The patient started to desaturate (SpO₂
Prostaglandins

- $\text{PGE}_1$: misoprostol
- $\text{PGE}_2$: dinoprostone, prostin, sulprostone
- $\text{PGF}_{2\alpha}$: dinoprost
- 15-Methyl $\text{PGF}_{2\alpha}$: carboprost, hemabate
PGE$_2$: prostin, sulprostone (Nalador®)

- France, Netherlands, Belgium, D-A-CH...
- Intravenous
- 500 µg in 1$^{st}$ hour (controlled!), then 500 µg / 8h
- Hypotension
- Bronchoconstriction
- Nausea, Shivering, Fever

Asthma!
VIII. Management of worsening PPH

- This section provides guidelines for treating bleeding that persists for more than 15-30 minutes (agreement among professionals). The time before taking further action depends on the amount of bleeding, its haemodynamic impact, and on the measures taken to maintain haemodynamic status (see Fig. 1).

- As for initial care, the best management is by a multidisciplinary team working closely together. Time is yet again crucial to the prognosis (agreement among professionals).

- The obstetrics team should re-investigate any obstetric cause for the bleeding by inspecting the cervix and vagina (if this has not already been done) and by exploring the uterine cavity, if necessary. However, these procedures should not delay the next stage of management.

- Sulprostone should be given by intravenous infusion with a syringe pump within 15-30 min of onset of bleeding (grade C). The intramuscular and intramyometrial routes are contraindicated (grade C). The starting dose should be 100-500 µg/hour. This dose
Women with atonic postpartum hemorrhage

- n=4,038; 2.8%
- Received sulprostone
  - n=1,370; 33.9% (of 4,038)

Women with atonic postpartum hemorrhage after vaginal delivery

- n=3,570; 88.4% (of 4,038)
- Received sulprostone
  - n=995; 27.9% (of 3,570)

Women with atonic postpartum hemorrhage after cesarean delivery

- n=468; 11.6% (of 4,038)
- Received sulprostone
  - n=375; 80.1% (of 468)

Women with severe atonic postpartum hemorrhage after vaginal delivery

- n=983; 24.3% (of 4,038)
- Received sulprostone
  - n=448; 45.6% (of 983)

Women with severe atonic postpartum hemorrhage after cesarean delivery

- n=244; 6.0% (of 4,038)
- Received sulprostone
  - n=211; 86.5% (of 244)
Table 4. Side Effects Among the 1,370 Women Treated With Sulprostone

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>n*</th>
<th>% (95% Confidence Interval) of the Women Treated With Sulprostone</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one side effect</td>
<td>51</td>
<td>3.7 (2.7–4.7)</td>
</tr>
<tr>
<td>Digestive</td>
<td>34</td>
<td>2.5 (1.7–3.5)</td>
</tr>
<tr>
<td>Hyperthermia, chills</td>
<td>7</td>
<td>0.5 (.2–1.0)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>5</td>
<td>0.4 (.1–0.8)</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>2</td>
<td>0.1 (.02–0.5)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>2</td>
<td>0.1 (.02–0.5)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2</td>
<td>0.1 (.02–0.5)</td>
</tr>
<tr>
<td>Severe cardiovascular or respiratory symptoms†</td>
<td>7</td>
<td>0.5 (.2–1.0)</td>
</tr>
</tbody>
</table>

* One woman experienced two side effects.
† Classified as severe—the five cases of cardiac side effects, one case of acute high blood pressure more than 200/110 mm Hg, and one case of acute cyanosis in a woman with asthma.
Prostaglandins

- $\text{PGE}_1$: misoprostol
- $\text{PGE}_2$: dinoprostone, prostin, sulprostone
- $\text{PGF}_{2\alpha}$: dinoprost
- 15-Methyl $\text{PGF}_{2\alpha}$: carboprost, hemabate
15-Methyl PGF$_{2\alpha}$: carboprost, hemabate

- 200 µg im, repeatable @15 min max 8 doses (1.6 mg)
- 250 µg intramyometrically (off-label)
- Bronchospasm
- Systemic and pulmonary hypertension
- Do not administer intravenously

Asthma !
Preeclampsia !
Which?

- Oxytocin
- Prostaglandins
- Ergot alkaloids
Ergot alkaloids: Methergine

http://www.herbmuseum.ca/content/upjohn-fluid-extract-ergot
Ergot alkaloids - side effects

- Nausea & vomitus
- Mean arterial pressure +11%
- Pulmonary artery pressure +30%
- Coronary artery spasm

Preeclampsia!
Ergot alkaloids - dosage

- RCOG: 0.5 mg slowly iv
- WHO: 0.2 mg iv or im
  - repeatable @15 minutes up to 1 mg
Uterotonic agents for caesarean section

• Why?
• Which?
• How?
• When?
When?

- First line
- Second line
- Third line
When?

- First line
  - Oxytocin, Carbetocin, (Misoprostol)
- Second line
- Third line
Treatments for secondary postpartum haemorrhage (Review)

Alexander J, Thomas PW, Sanghera J
ABSTRACT

Background
Secondary postpartum haemorrhage is any abnormal or excessive bleeding from the birth canal occurring between 24 hours and 12 weeks postnatally. In developed countries, 2% of postnatal women are admitted to hospital with this condition, half of them undergoing uterine surgical evacuation. Data are not available from developing countries.

Objectives
To evaluate the relative effectiveness and safety of the treatments used for secondary postpartum haemorrhage.

Search methods
We searched the Cochrane Pregnancy and Childbirth Group’s Trials Register (31 January 2008), the reference lists of trial reports and reviews and sought further sources from the first named authors of the papers identified.

Selection criteria

Main results

Of the 47 papers (36 studies) identified, none met the inclusion criteria.

Authors’ conclusions
No information is available from randomised controlled trials to inform the management of women with secondary postpartum
The use of uterotonic drugs during caesarean section

R.A. Dyer, D. van Dyk, A. Dresner
Department of Anaesthesia, University of Cape Town, South Africa
C/S: A protocol (Dyer)

- $\leq 3$ U oxytocin iv over 3-5 min.

- PPH:
  - Repeat 3 U oxytocin after 3-5 min
  - Beware: cardiac disease, preeclampsia, pulmonary hypertension
C/S: A protocol (Dyer)

- ≤ 3 U oxytocin iv over 3-5 min.

PPH:

- Repeat 3 U oxytocin after 3-5 min
- Beware: cardiac disease, preeclampsia, pulmonary hypertension

- 100 µg carbetocin slow iv
Maintain uterine tone

- Oxytocin 40 U in 500 ml => 125 ml/h
- Beware: hemodynamically unstable patients!

Down-regulation of oxytocin-receptors:

1. Ergometrin 0.2-0.5 mg slowly iv or im
   Beware: contraindications!

2. PGF$_2\alpha$ 250-500 µg intramyometrically (off label)

- Oxytocin 40 U in 30 min.
  or
  100 µg carbetocin slow iv

- PGE$_2$: 500 µg / 1h
  followed by 500 µg/8h
  (max 1500 µg/24h)