INTRAOPERATIVE TEACHING

Oxytocin Dosing and Uterotonic Escalation

Intraoperative teaching · CA-2

THE QUESTION

Where the evidence disagrees

This topic was selected because an evidence synthesis beats a textbook on it: the trials disagree, or the guidance has moved recently.

THE EVIDENCE

What each source contributes, and how strong it is

Study design first — a cohort and a randomised trial do not carry the same weight.

Design	Year	Journal	What it found
Meta-analysis	2022	American journal of obstetrics and	In a network meta-analysis of 46 trials, carbetocin probably reduced the need for
Cohort	2017	Journal of physiology and pharmaco	A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at
Review	2011	Current opinion in anaesthesiology	Prior exposure to oxytocin desensitises the uterine oxytocin receptor
Guideline	2019	Anaesthesia	The international consensus recommends a small initial bolus of oxytocin followed by
Meta-analysis	2021	American journal of obstetrics and	Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial
Randomised trial	2004	Obstetrics and gynecology	The ED90 for adequate uterine contraction at elective caesarean in non-labouring

6 resolved citations behind this deck; every point above traces to one of them.

WHERE THE GUIDANCE SITS

What the guidelines and pooled evidence say

3 findings, each on the slide that follows.

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 2022

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for additional uterotonics by 185 per 1000 cases versus oxytocin

ANAESTHESIA 2019

The international consensus recommends a small initial bolus of oxytocin followed by

The international consensus recommends a small initial bolus of oxytocin followed by a titrated infusion, because standard recommended doses are…

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 2021

Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial

Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial boluses under 5 IU reduced nausea

WHERE THE GUIDANCE SITS

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for

Meta-analysis · American journal of obstetrics and

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for additional uterotonics by 185 per 1000 cases versus oxytocin, and oxytocin worked best when started as a bolus.

Preventing Postpartum Hemorrhage After Cesarean Delivery: A Network Meta-Analysis of Available Pharmacologic Agents, American journal of obstetrics and gynecology 2022 · PMID 34534498

WHERE THE GUIDANCE SITS

The international consensus recommends a small initial bolus of oxytocin followed by

Guideline · Anaesthesia

The international consensus recommends a small initial bolus of oxytocin followed by a titrated infusion, because standard recommended doses are higher than required and risk acute cardiovascular effects.

International Consensus Statement on the Use of Uterotonic Agents During Caesarean Section, Anaesthesia 2019 · PMID 31347151

WHERE THE GUIDANCE SITS

Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial

Meta-analysis · American journal of obstetrics and

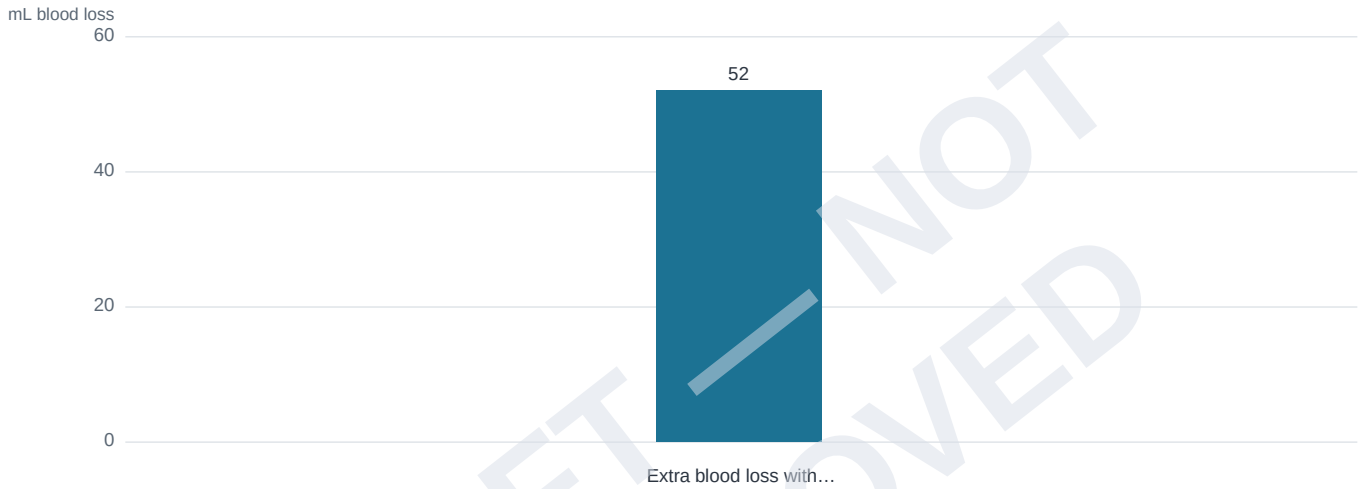
Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial boluses under 5 IU reduced nausea, and total doses of 5-9 IU increased the need for additional uterotonics versus 10-19 IU.

Intravenous Oxytocin Dosing Regimens for Postpartum Hemorrhage Prevention Following Cesarean Delivery: A Systematic Review and Meta-Analysis, American journal of obstetrics and gynecology 2021 · PMID 33957113

THE NUMBERS

Bolus plus infusion beats bolus alone

35 studies, 7,333 women, intravenous regimens compared.



Bolus-only regimens lost about 52 mL more than bolus-plus-infusion; initial boluses under 5 IU reduced nausea.

Intravenous Oxytocin Dosing Regimens for Postpartum Hemorrhage Prevention Following Cesarean Delivery: A Systematic Review and Meta-Analysis, American journal of obstetrics and gynecology 2021 · PMID 33957113

WHAT THE TRIALS FOUND

The ED90 for adequate uterine contraction at elective caesarean in non-labouring

Randomised trial · Obstetrics and gynecology

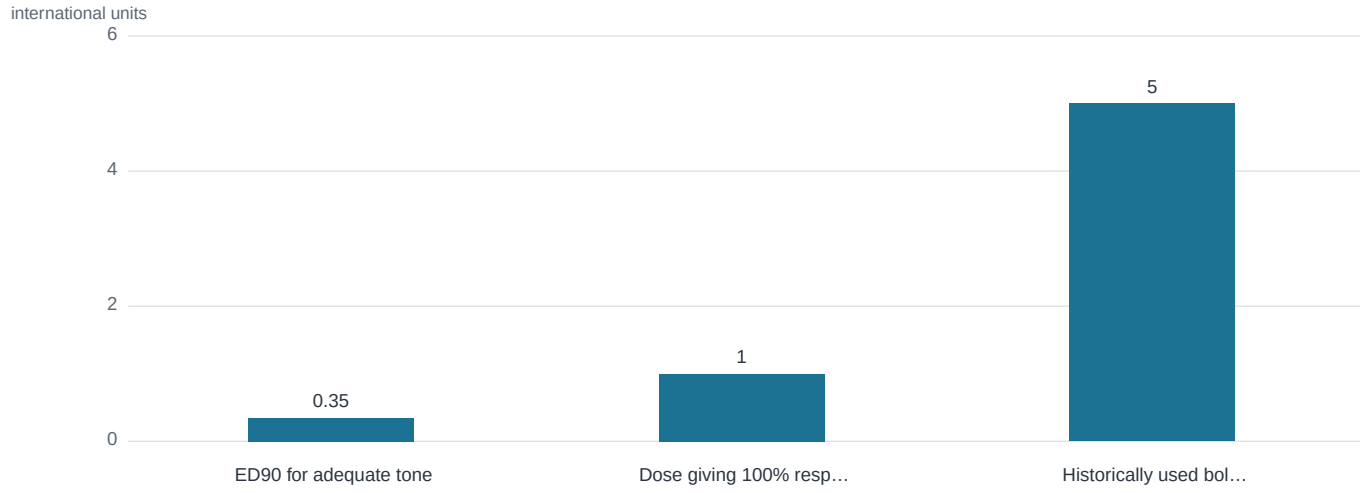
The ED90 for adequate uterine contraction at elective caesarean in non-labouring women was 0.35 IU — a fraction of the 5 IU historically given — with 100% response by 1.0 IU.

Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study, Obstetrics and gynecology 2004 · PMID 15516392

THE NUMBERS

The effective dose is a fraction of what is traditionally given

40 women, elective caesarean, dose-finding study.



0.35 IU produced adequate uterine contraction in 90% — the traditional 5 IU bolus is an order of magnitude above it.

Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study, Obstetrics and gynecology 2004 · PMID 15516392

IN PRACTICE

What the cohorts and reviews add

2 findings, each on the slide that follows.

A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at

A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at elective caesarean

CURRENT OPINION IN ANAESTHESIOLOGY 2011

Prior exposure to oxytocin desensitises the uterine oxytocin receptor

Prior exposure to oxytocin desensitises the uterine oxytocin receptor, so a woman already on an oxytocin infusion in labour will need different…

IN PRACTICE

A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at

Cohort · Journal of physiology and pharmaco

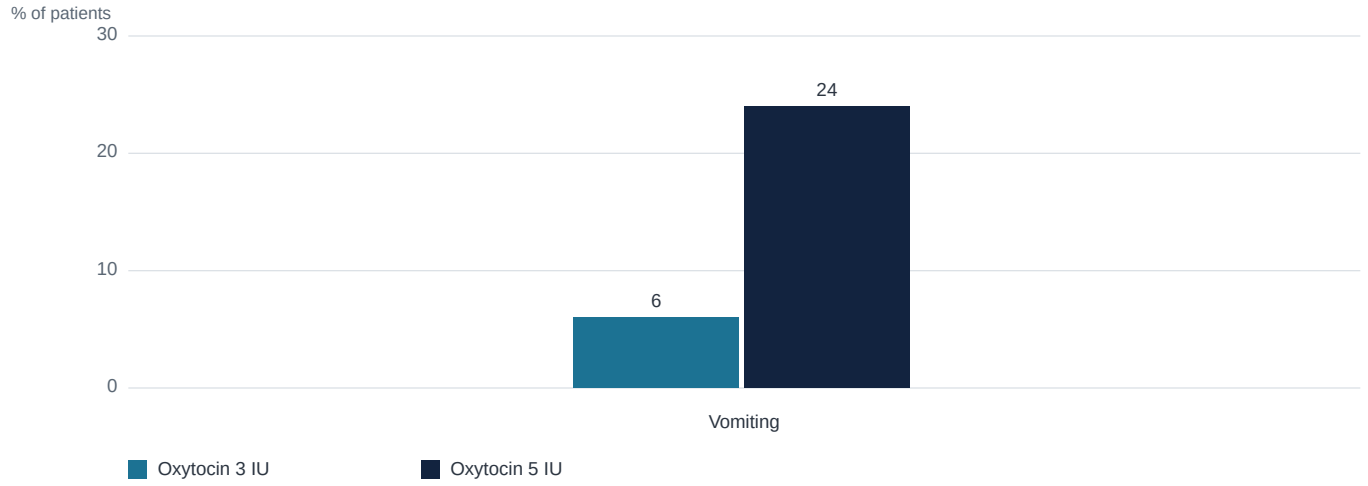
A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at elective caesarean, and produced less vomiting (6% versus 24%).

An Observational Cohort Study of 3 Units Versus 5 Units Slow Intravenous Bolus Oxytocin in Women Undergoing Elective Caesarean Delivery, Journal of physiology and pharmacology : an official journal of the Polish Physiological Society 2017 · PMID 29151071

THE NUMBERS

3 IU was noninferior to 5 IU, with less vomiting

73 women, elective caesarean under spinal.



Same blood loss, a quarter of the vomiting.

An Observational Cohort Study of 3 Units Versus 5 Units Slow Intravenous Bolus Oxytocin in Women Undergoing Elective Caesarean Delivery, Journal of physiology and pharmacology : an official journal of the Polish Physiological Society 2017 · PMID 29151071

IN PRACTICE

Prior exposure to oxytocin desensitises the uterine oxytocin receptor

Review · Current opinion in anaesthesiology

Prior exposure to oxytocin desensitises the uterine oxytocin receptor, so a woman already on an oxytocin infusion in labour will need different dosing than an elective case.

Oxytocin for Labour and Caesarean Delivery: Implications for the Anaesthesiologist, Current opinion in anaesthesiology 2011 · PMID 21415725

IN THE ROOM

What this changes about the next case

Colour is the strength of the evidence behind each step, not the urgency.

1. **1**
   The international consensus recommends a small initial bolus of oxytocin followed by a titrated infusion, because standard recommended doses are higher than required and risk acute cardiovascular effects.
2. **2**
   In a network meta-analysis of 46 trials, carbetocin probably reduced the need for additional uterotonics by 185 per 1000 cases versus oxytocin, and oxytocin worked best when started as a bolus.
3. **3**
   Bolus-plus-infusion regimens gave slightly less blood loss than bolus alone, initial boluses under 5 IU reduced nausea, and total doses of 5-9 IU increased the need for additional uterotonics versus 10-19 IU.
4. **4**
   The ED90 for adequate uterine contraction at elective caesarean in non-labouring women was 0.35 IU — a fraction of the 5 IU historically given — with 100% response by 1.0 IU.
5. **5**
   A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at elective caesarean, and produced less vomiting (6% versus 24%).

KEY TAKEAWAYS

What to carry into the next case

> **In a network meta-analysis of 46 trials, carbetocin probably reduced the need for**
> American journal of obstetrics and gynecology 2022

> **A 3 IU slow bolus was noninferior to the standard 5 IU for 24-hour blood loss at**

> **Prior exposure to oxytocin desensitises the uterine oxytocin receptor**
> Current opinion in anaesthesiology 2011

> **The international consensus recommends a small initial bolus of oxytocin followed by**
> Anaesthesia 2019

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for

QUESTIONS I'LL ASK YOU IN THE ROOM

1. How does your plan change if the patient is not optimised?
2. What is the physiology behind what we just did?
3. Talk me through the trade-off you made there.
4. What would make you abandon this plan and do something else?

ORAL BOARDS STEM

> *After delivery at an elective caesarean the uterus remains boggy despite an oxytocin bolus and infusion, and the obstetrician asks what you are giving next.*

BOARD QUESTIONS

1. In the dose-finding study of oxytocin at elective caesarean delivery in non-labouring women, what was the ED90 for adequate uterine contraction, how does it compare with the dose historically given, and at what dose did every woman respond?
2. A woman who has been on an oxytocin infusion through labour now needs a caesarean. Explain the receptor-level reason her oxytocin dosing cannot be assumed to be the same as for an elective non-labouring patient.
3. State what the international consensus statement recommends for how oxytocin should be administered at caesarean section, and give the two reasons it gives for that approach.
4. In the network meta-analysis of pharmacologic agents for preventing postpartum haemorrhage after caesarean delivery, state the comparison made between carbetocin and oxytocin, the specific outcome and the size of the effect, the certainty language used, and what it concluded about how oxytocin is best started.

ANSWER KEY

1. The ED90 was 0.35 IU — a fraction of the 5 IU historically given — with 100% response by 1.0 IU.

The ED90 in a non-labouring elective caesarean is 0.35 IU, which is why the historical 5 IU was always more than the uterus needed.

Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study, Obstetrics and gynecology 2004 · PMID 15516392

2. Prior exposure to oxytocin desensitises the uterine oxytocin receptor, so a woman already on an oxytocin infusion in labour will need different dosing than an elective case.

The receptor she has been bathing in oxytocin all day is desensitised, so her dosing is a different problem from the elective case.

Oxytocin for Labour and Caesarean Delivery: Implications for the Anaesthesiologist, Current opinion in anaesthesiology 2011 · PMID 21415725

3. It recommends a small initial bolus of oxytocin followed by a titrated infusion. The two reasons are that standard recommended doses are higher than required, and that they risk acute cardiovascular effects.

Small bolus then titrate — the standard recommended doses are more than you need and carry acute cardiovascular risk for no added benefit.

International Consensus Statement on the Use of Uterotonic Agents During Caesarean Section, Anaesthesia 2019 · PMID 31347151

4. Across 46 trials, carbetocin probably reduced the need for additional uterotonics by 185 per 1000 cases versus oxytocin, and oxytocin worked best when started as a bolus. The effect is stated as 'probably', which is graded certainty short of certain, and it applies to the single outcome of needing additional uterotonics — not to blood loss, transfusion, or any other endpoint.

Carbetocin probably spares 185 additional-uterotonic doses per 1000 cases versus oxytocin — 'probably', and only for that one outcome.

Preventing Postpartum Hemorrhage After Cesarean Delivery: A Network Meta-Analysis of Available Pharmacologic Agents, American journal of obstetrics and gynecology 2022 · PMID 34534498

In a network meta-analysis of 46 trials, carbetocin probably reduced the need for

SOURCES

[1] Preventing Postpartum Hemorrhage After Cesarean Delivery: A Network Meta-Analysis of Available Pharmacologic Agents, American journal of obstetrics and gynecology 2022 · PMID 34534498

[2] An Observational Cohort Study of 3 Units Versus 5 Units Slow Intravenous Bolus Oxytocin in Women Undergoing Elective Caesarean Delivery, Journal of physiology and pharmacology : an official journal of the Polish Physiological Society 2017 · PMID 29151071

[3] Oxytocin for Labour and Caesarean Delivery: Implications for the Anaesthesiologist, Current opinion in anaesthesiology 2011 · PMID 21415725

[4] International Consensus Statement on the Use of Uterotonic Agents During Caesarean Section, Anaesthesia 2019 · PMID 31347151

[5] Intravenous Oxytocin Dosing Regimens for Postpartum Hemorrhage Prevention Following Cesarean Delivery: A Systematic Review and Meta-Analysis, American journal of obstetrics and gynecology 2021 · PMID 33957113

[6] Oxytocin Requirements at Elective Cesarean Delivery: A Dose-Finding Study, Obstetrics and gynecology 2004 · PMID 15516392