

Vasopressor Choice for Spinal Hypotension

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	2020	Anaesthesia	Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,
Randomised trial	2015	Anesthesiology	Given by infusion, norepinephrine held systolic pressure as well as phenylephrine
Meta-analysis	2020	British journal of anaesthesia	Norepinephrine, metaraminol
Randomised trial	2019	Anesthesia and analgesia	Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6
Meta-analysis	2024	Anaesthesia	Phenylephrine raises blood pressure while lowering cardiac output
Randomised trial	2017	Anesthesiology	Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a

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.

ANAESTHESIA 2020

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol, norepinephrine and phenylephrine were the most effective at...

BRITISH JOURNAL OF ANAESTHESIA 2020

Norepinephrine, metaraminol

Norepinephrine, metaraminol

ANAESTHESIA 2024

Phenylephrine raises blood pressure while lowering cardiac output

Phenylephrine raises blood pressure while lowering cardiac output

WHERE THE GUIDANCE SITS

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,

Meta-analysis · Anaesthesia

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol, norepinephrine and phenylephrine were the most effective at preventing hypotension, while crystalloid given before induction was no better than control.

Prevention of Hypotension After Spinal Anaesthesia for Caesarean Section: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials, Anaesthesia 2020 · PMID 31531852

WHERE THE GUIDANCE SITS

Norepinephrine, metaraminol

Meta-analysis · British journal of anaesthesia

Norepinephrine, metaraminol, and mephentermine may have a lower probability of adversely affecting fetal acid-base status (umbilical arterial base excess) compared to phenylephrine during Caesarean delivery under neuraxial anesthesia.

Vasopressor Drugs for the Prevention and Treatment of Hypotension During Neuraxial Anaesthesia for Caesarean Delivery: A Bayesian Network Meta-Analysis of Fetal and Maternal Outcomes, British journal of anaesthesia 2020 · PMID 31810562

WHERE THE GUIDANCE SITS

Phenylephrine raises blood pressure while lowering cardiac output

Meta-analysis · Anaesthesia

Phenylephrine raises blood pressure while lowering cardiac output, and although it increases cerebral blood flow it decreases cerebral tissue oxygen saturation.

Effects of Phenylephrine on Systemic and Cerebral Circulations in Humans: A Systematic Review With Mechanistic Explanations, Anaesthesia 2024 · PMID 37948131

WHAT THE TRIALS FOUND

Where randomised evidence moved the question

3 findings, each on the slide that follows.

ANESTHESIOLOGY 2015

Given by infusion, norepinephrine held systolic pressure as well as phenylephrine

Given by infusion, norepinephrine held systolic pressure as well as phenylephrine but with a higher heart rate and cardiac output, lower systemic...

ANESTHESIA AND ANALGESIA 2019

Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6

Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6 micrograms versus 38% with phenylephrine 100 micrograms

ANESTHESIOLOGY 2017

Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a

Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a potency ratio near 13 to 1, so the two cannot be swapped at the...

WHAT THE TRIALS FOUND

Given by infusion, norepinephrine held systolic pressure as well as phenylephrine

Randomised trial · Anesthesiology

Given by infusion, norepinephrine held systolic pressure as well as phenylephrine but with a higher heart rate and cardiac output, lower systemic vascular resistance and less bradycardia.

Randomized Double-Blinded Comparison of Norepinephrine and Phenylephrine for Maintenance of Blood Pressure During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2015 · PMID 25635593

WHAT THE TRIALS FOUND

Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6

Randomised trial · Anesthesia and analgesia

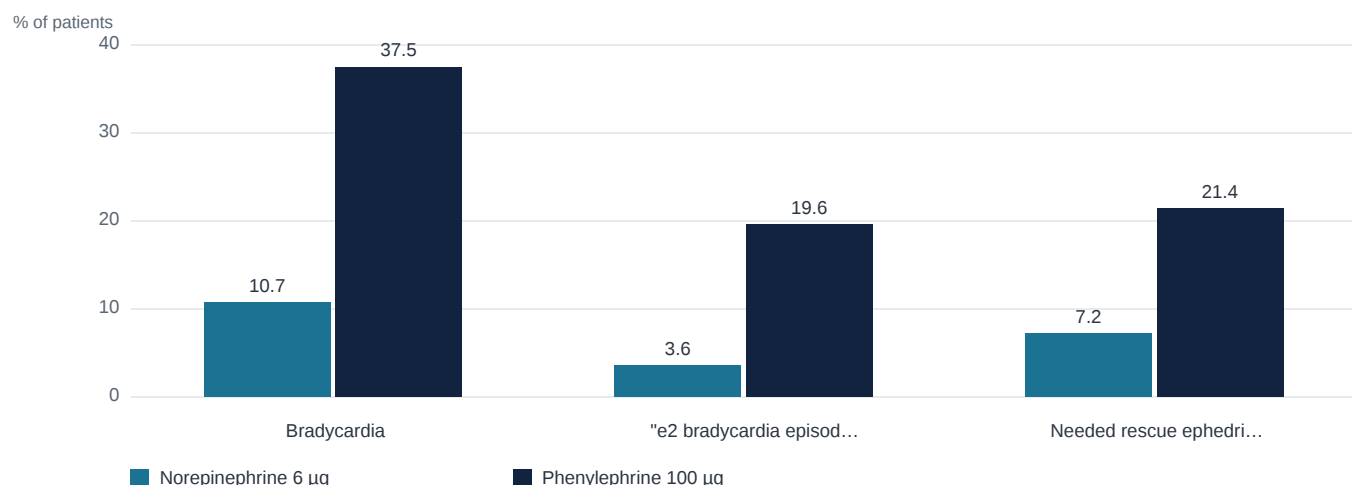
Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6 micrograms versus 38% with phenylephrine 100 micrograms, and fewer patients needed rescue ephedrine.

Comparison of Intermittent Intravenous Boluses of Phenylephrine and Norepinephrine to Prevent and Treat Spinal-Induced Hypotension in Cesarean Deliveries: Randomized Controlled Trial, Anesthesia and analgesia 2019 · PMID 30113395

THE NUMBERS

Norepinephrine boluses cause far less bradycardia

Equipotent boluses: norepinephrine 6 µg vs phenylephrine 100 µg.



At equipotent doses the bradycardia burden is roughly a quarter that of phenylephrine.

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WHAT THE TRIALS FOUND

Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a

Randomised trial · Anesthesiology

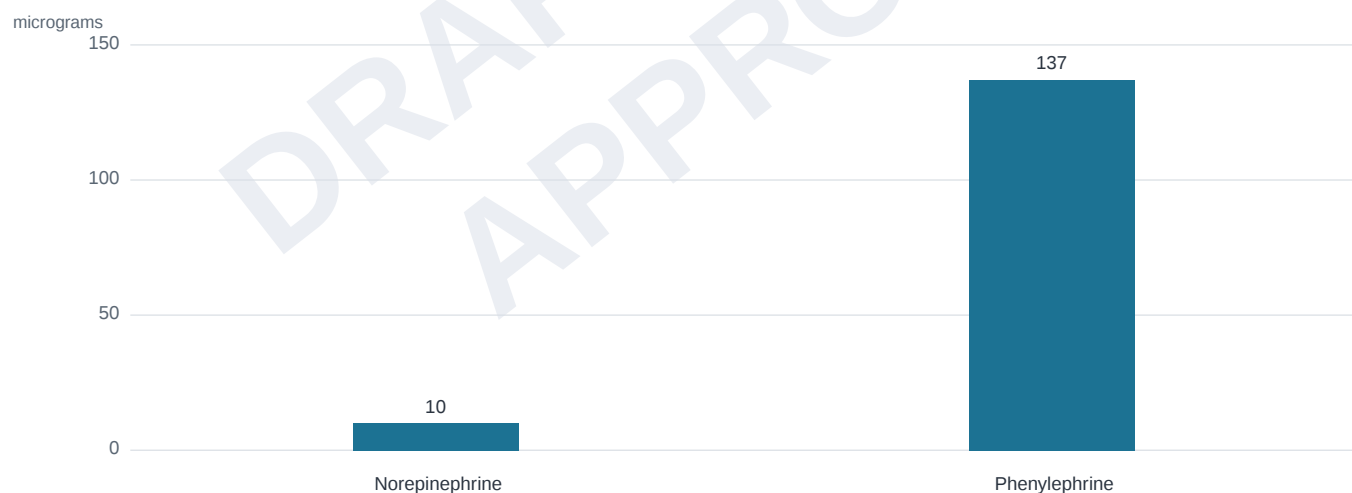
Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a potency ratio near 13 to 1, so the two cannot be swapped at the same numerical dose.

A Random-Allocation Graded Dose-Response Study of Norepinephrine and Phenylephrine for Treating Hypotension During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2017 · PMID 28872480

THE NUMBERS

The two drugs are not interchangeable by number

Dose giving a 50% response, from a graded dose-response study.



Norepinephrine 8 µg "H phenylephrine 100 µg — a potency ratio near 13 to 1.

A Random-Allocation Graded Dose-Response Study of Norepinephrine and Phenylephrine for Treating Hypotension During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2017 · PMID 28872480

IN THE ROOM

What this changes about the next case

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

- 1 Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol, norepinephrine and phenylephrine were the most effective at preventing hypotension, while crystalloid given before induction was no better than control.
- 2 Norepinephrine, metaraminol, and mephentermine may have a lower probability of adversely affecting fetal acid-base status (umbilical arterial base excess) compared to phenylephrine during Caesarean delivery under neuraxial anesthesia.
- 3 Phenylephrine raises blood pressure while lowering cardiac output, and although it increases cerebral blood flow it decreases cerebral tissue oxygen saturation.
- 4 Given by infusion, norepinephrine held systolic pressure as well as phenylephrine but with a higher heart rate and cardiac output, lower systemic vascular resistance and less bradycardia.
- 5 Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6 micrograms versus 38% with phenylephrine 100 micrograms, and fewer patients needed rescue ephedrine.

KEY TAKEAWAYS

What to carry into the next case

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,
Anaesthesia 2020

Given by infusion, norepinephrine held systolic pressure as well as phenylephrine
Anesthesiology 2015

Norepinephrine, metaraminol
British journal of anaesthesia 2020

Using equipotent boluses, bradycardia occurred in 11% with norepinephrine 6
Anesthesia and analgesia 2019

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,

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

Ten minutes after a spinal for a total knee replacement, the blood pressure falls from 148/82 to 84/44 with a heart rate of 52. You reach for a vasopressor and the resident asks which one and why.

BOARD QUESTIONS

1. State the approximate equipotent dose relationship between norepinephrine and phenylephrine for treating spinal hypotension, and the practical consequence for dosing.
2. Comparing norepinephrine and phenylephrine given by infusion during spinal anaesthesia, describe how they compare for systolic pressure control and for heart rate, cardiac output, systemic vascular resistance and bradycardia.
3. You give phenylephrine for hypotension. Describe its effect on blood pressure and cardiac output, and what happens to cerebral blood flow and to cerebral tissue oxygen saturation.
4. A network meta-analysis of 109 trials ranked strategies for preventing post-spinal hypotension. Which agents ranked most effective, what did it find about crystalloid given before induction, and what feature of the included trials limits how directly you can apply the ranking to a patient having a knee replacement?

ANSWER KEY

1. Norepinephrine 8 micrograms is about equivalent to phenylephrine 100 micrograms, a potency ratio near 13 to 1, so the two drugs cannot be swapped at the same numerical dose.

Roughly 13 to 1 — if you carry a phenylephrine microgram number over to norepinephrine, you are an order of magnitude off.

A Random-Allocation Graded Dose-Response Study of Norepinephrine and Phenylephrine for Treating Hypotension During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2017 · PMID 28872480

2. Given by infusion, norepinephrine held systolic pressure as well as phenylephrine, but with a higher heart rate and cardiac output, a lower systemic vascular resistance, and less bradycardia.

Both agents defend the systolic pressure — the difference is what sits behind it, with norepinephrine preserving more heart rate and cardiac output and less bradycardia.

Randomized Double-Blinded Comparison of Norepinephrine and Phenylephrine for Maintenance of Blood Pressure During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2015 · PMID 25635593

3. Phenylephrine raises blood pressure while lowering cardiac output, and although it increases cerebral blood flow it decreases cerebral tissue oxygen saturation.

A better cuff number and even a higher cerebral blood flow can still come with a fall in cerebral tissue oxygen saturation — the pressure is not the tissue.

Effects of Phenylephrine on Systemic and Cerebral Circulations in Humans: A Systematic Review With Mechanistic Explanations, Anaesthesia 2024 · PMID 37948131

4. Metaraminol, norepinephrine and phenylephrine were the most effective at preventing hypotension, and crystalloid given before induction was no better than control. All 109 trials were of spinal anaesthesia for caesarean section, so the ranking comes from an obstetric population rather than from non-obstetric surgical patients.

The vasopressor ranking is strong, but it is obstetric data — and note that in it, crystalloid before induction did not beat control.

Prevention of Hypotension After Spinal Anaesthesia for Caesarean Section: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials, Anaesthesia 2020 · PMID 31531852

Ranked across 109 trials of spinal anaesthesia for caesarean section, metaraminol,

SOURCES

[1] Prevention of Hypotension After Spinal Anaesthesia for Caesarean Section: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials, Anaesthesia 2020 · PMID 31531852

[2] Randomized Double-Blinded Comparison of Norepinephrine and Phenylephrine for Maintenance of Blood Pressure During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2015 · PMID 25635593

[3] Vasopressor Drugs for the Prevention and Treatment of Hypotension During Neuraxial Anaesthesia for Caesarean Delivery: A Bayesian Network Meta-Analysis of Fetal and Maternal Outcomes, British journal of anaesthesia 2020 · PMID 31810562

[4] Comparison of Intermittent Intravenous Boluses of Phenylephrine and Norepinephrine to Prevent and Treat Spinal-Induced Hypotension in Cesarean Deliveries: Randomized Controlled Trial, Anesthesia and analgesia 2019 · PMID 30113395

[5] Effects of Phenylephrine on Systemic and Cerebral Circulations in Humans: A Systematic Review With Mechanistic Explanations, Anaesthesia 2024 · PMID 37948131

[6] A Random-Allocation Graded Dose-Response Study of Norepinephrine and Phenylephrine for Treating Hypotension During Spinal Anesthesia for Cesarean Delivery, Anesthesiology 2017 · PMID 28872480