

Vasopressors and Inotropes: Phenylephrine, Ephedrine, Norepinephrine, Epinephrine,

Intraoperative Griefing CA-1

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
Other	2024	Anaesthesia	Phenylephrine raises blood pressure while simultaneously reducing cardiac output
Other	2015	Anesthesiology	Norepinephrine carries weak beta-adrenergic activity alongside its potent alph
Other	2017	Anesthesiology	In a graded dose-response study the ED50 for restoring blood pressure was 10 m
Other	2003	Anesthesia and Analgesia	Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine
Other	2005	Netherlands Journal of Medicine	Vasopressin raises mean arterial pressure through V1 receptors and lowers card
Other	2021	Journal of Anesthesia	Adrenaline is the first-line treatment for anaphylaxis and should be given int

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

IN PRACTICE

What the cohorts and reviews add

6 findings, each on the slide that follows.

ANAESTHESIA 2024

Phenylephrine raises blood pressure while simultaneously reducing cardiac output

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ANESTHESIOLOGY 2015

Norepinephrine carries weak beta-adrenergic activity alongside its potent alph

Norepinephrine carries weak beta-adrenergic activity alongside its potent alpha effect

ANESTHESIOLOGY 2017

In a graded dose-response study the ED50 for restoring blood pressure was 10 m

In a graded dose-response study the ED50 for restoring blood pressure was 10 micrograms of norepinephrine against 137 micrograms of phenylephrine, so...

ANESTHESIA AND ANALGESIA 2003

Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine

Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine out of sympathetic nerve terminals rather than from direct receptor...

IN PRACTICE

Phenylephrine raises blood pressure while simultaneously reducing cardiac output

Other · Anaesthesia

Phenylephrine raises blood pressure while simultaneously reducing cardiac output, and although it increases cerebral blood flow it lowers cerebral tissue oxygen saturation - so the number on the monitor improves while the flow behind it does not.

Meng et al., Anaesthesia 2024 · PMID 37948131

IN PRACTICE

Norepinephrine carries weak beta-adrenergic activity alongside its potent alpha

Other · Anesthesiology

Norepinephrine carries weak beta-adrenergic activity alongside its potent alpha effect, and given by infusion at caesarean delivery it held systolic pressure as well as phenylephrine while preserving a greater cardiac output.

Ngan Kee et al., Anesthesiology 2015 · PMID 25635593

IN PRACTICE

In a graded dose-response study the ED50 for restoring blood pressure was 10 m

Other · Anesthesiology

In a graded dose-response study the ED50 for restoring blood pressure was 10 micrograms of norepinephrine against 137 micrograms of phenylephrine, so these two drugs can never be exchanged at the same numerical dose.

Ngan Kee, Anesthesiology 2017 · PMID 28872480

IN PRACTICE

Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine

Other · Anesthesia and Analgesia

Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine out of sympathetic nerve terminals rather than from direct receptor activation, since destroying those terminals abolished the response, and in obstetric practice ephedrine has the highest probability of being the worst agent for fetal acid-base status.

Kobayashi et al., Anesthesia and Analgesia 2003 · PMID 14570629

IN PRACTICE

Vasopressin raises mean arterial pressure through V1 receptors and lowers card

Other · Netherlands Journal of Medicine

Vasopressin raises mean arterial pressure through V1 receptors and lowers cardiac output, has little effect in a healthy subject but potentiates norepinephrine in vasodilatory shock, and above 0.04 units per minute has been reported to cause cardiac arrest.

den Ouden et al., Netherlands Journal of Medicine 2005 · PMID 15719846

IN PRACTICE

Adrenaline is the first-line treatment for anaphylaxis and should be given int

Other · Journal of Anesthesia

Adrenaline is the first-line treatment for anaphylaxis and should be given intravenously in the perioperative setting, and anaphylaxis is exactly what you should suspect when hypotension persists despite inotropes and vasopressors even with no rash to look at.

Takazawa et al., Journal of Anesthesia 2021 · PMID 34651257

IN THE ROOM

What this changes about the next case

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

- 1 Phenylephrine raises blood pressure while simultaneously reducing cardiac output, and although it increases cerebral blood flow it lowers cerebral tissue oxygen saturation - so the number on the monitor improves while the flow behind it does not.
- 2 Norepinephrine carries weak beta-adrenergic activity alongside its potent alpha effect, and given by infusion at caesarean delivery it held systolic pressure as well as phenylephrine while preserving a greater cardiac output.
- 3 In a graded dose-response study the ED50 for restoring blood pressure was 10 micrograms of norepinephrine against 137 micrograms of phenylephrine, so these two drugs can never be exchanged at the same numerical dose.
- 4 Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine out of sympathetic nerve terminals rather than from direct receptor activation, since destroying those terminals abolished the response, and in obstetric practice ephedrine has the highest probability of being the worst agent for fetal acid-base status.
- 5 Vasopressin raises mean arterial pressure through V1 receptors and lowers cardiac output, has little effect in a healthy subject but potentiates norepinephrine in vasodilatory shock, and above 0.04 units per minute has been reported to cause cardiac arrest.

KEY TAKEAWAYS

What to carry into the next case

Phenylephrine raises blood pressure while simultaneously reducing cardiac output

Anaesthesia 2024

Norepinephrine carries weak beta-adrenergic activity alongside its potent alpha

Anesthesiology 2015

In a graded dose-response study the ED50 for restoring blood pressure was 10 mg

Anesthesiology 2017

Ephedrine's pressor effect in vivo comes from releasing stored norepinephrine

Anesthesia and Analgesia 2003

Choose the pressor by the receptor you actually need - squeeze the vessels, drive the heart, or both - and never forget that raising the pressure is not the same as raising the flow.

QUESTIONS I'LL ASK YOU IN THE ROOM

1. Which of these raises blood pressure while lowering cardiac output, and when is that trade worth making?
2. She is bradycardic as well as hypotensive - does that change your first choice, and why?
3. Ephedrine worked the first two times and did nothing the third time. What happened?
4. The patient takes an ACE inhibitor and phenylephrine is not holding her. What else is in the drawer, and why might it work when phenylephrine will not?

ORAL BOARDS STEM

Ten minutes into a laparoscopic hysterectomy in a healthy 45-year-old, the cuff reads 78/44 with a heart rate of 58. The drug drawer beside you holds phenylephrine, ephedrine, norepinephrine, epinephrine and vasopressin. Before you pick one up, your attending asks you to say out loud what each of them does to heart rate, to systemic vascular resistance, and to cardiac output.

Choose the pressor by the receptor you actually need - squeeze the vessels, drive the heart, or both - and never forget that raising the pressure is not the same as raising the flow.

SOURCES

- [1] Meng et al., Anaesthesia 2024 · PMID 37948131
- [2] Ngan Kee et al., Anesthesiology 2015 · PMID 25635593
- [3] Ngan Kee, Anesthesiology 2017 · PMID 28872480
- [4] Kobayashi et al., Anesthesia and Analgesia 2003 · PMID 14570629
- [5] Singh et al., British Journal of Anaesthesia 2020 · PMID 31810562
- [6] den Ouden et al., Netherlands Journal of Medicine 2005 · PMID 15719846
- [7] Takazawa et al., Journal of Anesthesia 2021 · PMID 34651257
- [8] Ma et al., Canadian Journal of Anaesthesia 2025 · PMID 40244358