

Induction Drugs: Propofol, Ketamine, Fentanyl, Midazolam

Induction Drug Learning 100-1

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	2000	Current Medicinal Chemistry	Propofol produces unconsciousness by positively modulating the inhibitory action of GABA at the GABA-A receptor
Other	1986	Anaesthesia	Patients under 60 needed 2.25 to 2.5 mg/kg of propofol to lose consciousness while those over 60 needed only 1.5 to 1.75 mg/kg
Other	2011	BMJ	About 60% of adults have pain when propofol is injected
Other	2006	Seminars in Cardiothoracic and Vascular Anesthesia	Ketamine's central sympathetic stimulation and its blockade of neuronal catecholamine uptake normally mask its direct negative inotropic effect
Other	1982	Acta Anaesthesiologica Scandinavica	Fentanyl 2 micrograms/kg given before induction significantly attenuated the respiratory depression caused by propofol
Other	2008	Handbook of Experimental Pharmacology	Midazolam works by potentiating GABA at the GABA-A receptor and buys you time

7 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.

CURRENT MEDICINAL CHEMISTRY 2000

Propofol produces unconsciousness by positively modulating the inhibitory action of GABA at the GABA-A receptor

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ANAESTHESIA 1986

Patients under 60 needed 2.25 to 2.5 mg/kg of propofol to lose consciousness while those over 60 needed only 1.5 to 1.75 mg/kg

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BMJ 2011

About 60% of adults have pain when propofol is injected

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SEMINARS IN CARDIOTHORACIC AND VASCULAR ANESTHESIA 2006

Ketamine's central sympathetic stimulation and its blockade of neuronal catecholamine uptake normally mask its direct negative inotropic effect

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IN PRACTICE

Propofol produces unconsciousness by positively modulating the inhibitory action of GABA at the GABA-A receptor

Other · Current Medicinal Chemistry

Propofol produces unconsciousness by positively modulating the inhibitory action of GABA at the GABA-A receptor, and the price it charges for that is a relatively high incidence of apnoea together with a fall in blood pressure.

Trapani et al., Current Medicinal Chemistry 2000 · PMID 10637364

IN PRACTICE

Patients under 60 needed 2.25 to 2.5 mg/kg of propofol to lose consciousness w

Other · Anaesthesia

Patients under 60 needed 2.25 to 2.5 mg/kg of propofol to lose consciousness while those over 60 needed only 1.5 to 1.75 mg/kg, and in the elderly doses above 1.75 mg/kg caused significant hypotension and apnoea - so age changes the dose before anything else does.

Dundee et al., Anaesthesia 1986 · PMID 3487990

IN PRACTICE

About 60% of adults have pain when propofol is injected

Other · BMJ

About 60% of adults have pain when propofol is injected, and across 177 trials the two most effective preventives were using an antecubital rather than a hand vein (relative risk 0.14) and pretreating with lidocaine under venous occlusion (relative risk 0.29).

Jalota et al., BMJ 2011 · PMID 21406529

IN PRACTICE

Ketamine's central sympathetic stimulation and its blockade of neuronal catech

Other · Seminars in Cardiothoracic and Vas

Ketamine's central sympathetic stimulation and its blockade of neuronal catecholamine uptake normally mask its direct negative inotropic effect, but in a failing myocardium that direct depression is unmasked and cardiac performance deteriorates.

Bovill, Seminars in Cardiothoracic and Vascular Anesthesia 2006 · PMID 16703233

IN PRACTICE

Fentanyl 2 micrograms/kg given before induction significantly attenuated the r

Other · Acta Anaesthesiologica Scandinavica

Fentanyl 2 micrograms/kg given before induction significantly attenuated the rise in arterial pressure and heart rate at laryngoscopy and intubation, and 6 micrograms/kg abolished the response altogether.

Kautto, Acta Anaesthesiologica Scandinavica 1982 · PMID 7113629

IN PRACTICE

Midazolam works by potentiating GABA at the GABA-A receptor and buys you sedat

Other · Handbook of Experimental Pharmacol

Midazolam works by potentiating GABA at the GABA-A receptor and buys you sedation, anxiolysis and anterograde amnesia, along with dose-dependent ventilatory depression and a modest fall in arterial pressure with a rise in heart rate driven by falling systemic vascular resistance.

Olkola et al., Handbook of Experimental Pharmacology 2008 · PMID 18175099

IN THE ROOM

What this changes about the next case

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

- 1** Propofol produces unconsciousness by positively modulating the inhibitory action of GABA at the GABA-A receptor, and the price it charges for that is a relatively high incidence of apnoea together with a fall in blood pressure.
- 2** Patients under 60 needed 2.25 to 2.5 mg/kg of propofol to lose consciousness while those over 60 needed only 1.5 to 1.75 mg/kg, and in the elderly doses above 1.75 mg/kg caused significant hypotension and apnoea - so age changes the dose before anything else does.
- 3** About 60% of adults have pain when propofol is injected, and across 177 trials the two most effective preventives were using an antecubital rather than a hand vein (relative risk 0.14) and pretreating with lidocaine under venous occlusion (relative risk 0.29).
- 4** Ketamine's central sympathetic stimulation and its blockade of neuronal catecholamine uptake normally mask its direct negative inotropic effect, but in a failing myocardium that direct depression is unmasked and cardiac performance deteriorates.

Fentanyl 2 micrograms/kg given before induction significantly attenuated the rise in arterial pressure and heart rate at laryngoscopy and intubation, and 6 micrograms/kg abolished the response altogether.

KEY TAKEAWAYS

What to carry into the next case

Propofol produces unconsciousness by positively modulating the inhibitory acti

Current Medicinal Chemistry 2000

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Anaesthesia 1986

About 60% of adults have pain when propofol is injected

BMJ 2011

Ketamine's central sympathetic stimulation and its blockade of neuronal catech

Seminars in Cardiothoracic and Vascular Anesthesia 2006

Each induction drug has a predictable haemodynamic signature, and knowing which direction each one pushes the blood pressure is what separates giving a recipe from making a plan.

QUESTIONS I'LL ASK YOU IN THE ROOM

1. Which of these four drugs will drop his pressure, and is it the vessels, the heart, or the sympathetic tone doing it?
2. Why does the fentanyl go in before the propofol rather than after it?
3. He grimaces as the propofol runs in - what caused that, and what would have prevented it?
4. If this were a hypotensive trauma patient instead, which syringe would you reach for first, and what would still worry you about that choice?

ORAL BOARDS STEM

A 62-year-old man is on your table for an open cholecystectomy. He is hypertensive on lisinopril, has taken nothing by mouth since midnight, and arrives at 148/86 with a heart rate of 74. Four syringes are laid out in front of you - propofol, ketamine, fentanyl, midazolam - and your attending asks which ones you are giving, in what order, and what you expect each of them to do to his blood pressure over the next three minutes.

Each induction drug has a predictable haemodynamic signature, and knowing which direction each one pushes the blood pressure is what separates giving a recipe from making a plan.

SOURCES

- [1] Trapani et al., Current Medicinal Chemistry 2000 · PMID 10637364
- [2] Dundee et al., Anaesthesia 1986 · PMID 3487990
- [3] Jalota et al., BMJ 2011 · PMID 21406529
- [4] Bovill, Seminars in Cardiothoracic and Vascular Anesthesia 2006 · PMID 16703233
- [5] Peltoniemi et al., Clinical Pharmacokinetics 2016 · PMID 27028535
- [6] Kautto, Acta Anaesthesiologica Scandinavica 1982 · PMID 7113629
- [7] Olkkola et al., Handbook of Experimental Pharmacology 2008 · PMID 18175099