

Inhaled Anesthetics: Sevoflurane, Isoflurane, Nitrous Oxide

Inhalation Anesthesia 2411

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	1993	British Journal of Anaesthesia	The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years was 1.48%, lower than the values for adults and children
Other	1996	Acta Anaesthesiologica Scandinavica	In patients with coronary artery disease, isoflurane and desflurane given in rising concentrations up to 1 MAC each lowered mean arterial pressure by...
Other	1996	Drugs	Sevoflurane has lower blood solubility than isoflurane and negligible airway irritant effects, which is exactly why it is the agent you can use for a...
Other	2003	Anesthesia and Analgesia	During inhalational induction the alveolar concentration of nitrous oxide rises towards the inspired concentration faster than sevoflurane's does,...
Other	2007	Anesthesiology	In ENIGMA, avoiding nitrous oxide during major surgery lowered the rate of major complications
Other	2014	Lancet	In ENIGMA-II, 7,112 patients with known or suspected coronary disease had the

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.

BRITISH JOURNAL OF ANAESTHESIA 1993

The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years

The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years was 1.48%, lower than the values for adults and children

ACTA ANAESTHESIOLOGICA SCANDINAVICA 1996

In patients with coronary artery disease, isoflurane and desflurane given in rising concentrations up to 1 MAC each

In patients with coronary artery disease, isoflurane and desflurane given in rising concentrations up to 1 MAC each lowered mean arterial pressure by...

DRUGS 1996

Sevoflurane has lower blood solubility than isoflurane and negligible airway irritant effects, which is exactly why it is the agent you can use for a...

Sevoflurane has lower blood solubility than isoflurane and negligible airway irritant effects, which is exactly why it is the agent you can use for a...

ANESTHESIA AND ANALGESIA 2003

During inhalational induction the alveolar concentration of nitrous oxide rises towards the inspired concentration faster than sevoflurane's does,...

During inhalational induction the alveolar concentration of nitrous oxide rises towards the inspired concentration faster than sevoflurane's does,...

IN PRACTICE

The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years

Other · British Journal of Anaesthesia

The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years was 1.48%, lower than the values for adults and children, and the concentration needed to stop 95% of patients moving was 1.98% - so MAC is a half-of-patients dose and it falls with age.

Nakajima et al., British Journal of Anaesthesia 1993 · PMID 8471368

IN PRACTICE

In patients with coronary artery disease, isoflurane and desflurane given in r

Other · *Acta Anaesthesiologica Scandinavica*

In patients with coronary artery disease, isoflurane and desflurane given in rising concentrations up to 1 MAC each lowered mean arterial pressure by about 16 to 18%, and that fall came primarily from a 21 to 26% drop in systemic vascular resistance rather than from any change in cardiac index.

Grundmann et al., *Acta Anaesthesiologica Scandinavica* 1996 · PMID 8933850

IN PRACTICE

Sevoflurane has lower blood solubility than isoflurane and negligible airway i

Other · *Drugs*

Sevoflurane has lower blood solubility than isoflurane and negligible airway irritant effects, which is exactly why it is the agent you can use for a smooth mask induction and isoflurane is not.

Patel et al., *Drugs* 1996 · PMID 8706599

IN PRACTICE

During inhalational induction the alveolar concentration of nitrous oxide rise

Other · *Anesthesia and Analgesia*

During inhalational induction the alveolar concentration of nitrous oxide rises towards the inspired concentration faster than sevoflurane's does, consistent with their blood/gas partition coefficients, and raising the inspired nitrous oxide concentration shifts the whole equilibration curve leftward - the concentration effect, with a brief second gas effect on the sevoflurane.

Goldman, *Anesthesia and Analgesia* 2003 · PMID 12538185

IN PRACTICE

In ENIGMA, avoiding nitrous oxide during major surgery lowered the rate of maj

Other · *Anesthesiology*

In ENIGMA, avoiding nitrous oxide during major surgery lowered the rate of major complications (odds ratio 0.71) and severe nausea and vomiting (odds ratio 0.40), though it did not shorten hospital stay.

Myles et al., *Anesthesiology* 2007 · PMID 17667565

IN PRACTICE

In ENIGMA-II, 7,112 patients with known or suspected coronary disease had the

Other · *Lancet*

In ENIGMA-II, 7,112 patients with known or suspected coronary disease had the same rate of death and cardiovascular complications with or without nitrous oxide (8% in both groups) and no excess risk at one year, but severe nausea and vomiting rose from 11% to 15% - so the case against nitrous oxide is emetogenic, not cardiac.

Myles et al., *Lancet* 2014 · PMID 25142708

IN THE ROOM

What this changes about the next case

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

- 1 The minimum alveolar concentration of sevoflurane measured in patients averaging 71 years was 1.48%, lower than the values for adults and children, and the concentration needed to stop 95% of patients moving was 1.98% - so MAC is a half-of-patients dose and it falls with age.
- 2 In patients with coronary artery disease, isoflurane and desflurane given in rising concentrations up to 1 MAC each lowered mean arterial pressure by about 16 to 18%, and that fall came primarily from a 21 to 26% drop in systemic vascular resistance rather than from any change in cardiac index.
- 3 Sevoflurane has lower blood solubility than isoflurane and negligible airway irritant effects, which is exactly why it is the agent you can use for a smooth mask induction and isoflurane is not.
- 4 During inhalational induction the alveolar concentration of nitrous oxide rises towards the inspired concentration faster than sevoflurane's does, consistent with their blood/gas partition coefficients, and raising the inspired nitrous oxide concentration shifts the whole equilibration curve leftward - the concentration effect, with a brief second gas effect on the sevoflurane.
- 5 In ENIGMA, avoiding nitrous oxide during major surgery lowered the rate of major complications (odds ratio 0.71) and severe nausea and vomiting (odds ratio 0.40), though it did not shorten hospital stay.

KEY TAKEAWAYS

What to carry into the next case

The minimum alveolar concentration of sevoflurane measured in patients averaged

British Journal of Anaesthesia 1993

In patients with coronary artery disease, isoflurane and desflurane given in r

Acta Anaesthesiologica Scandinavica 1996

Sevoflurane has lower blood solubility than isoflurane and negligible airway i

Drugs 1996

During inhalational induction the alveolar concentration of nitrous oxide rise

Anesthesia and Analgesia 2003

MAC is the currency of every volatile - it is the dose, it falls with age, and every volatile buys its depth partly by dropping the systemic vascular resistance and with it the blood pressure.

QUESTIONS I'LL ASK YOU IN THE ROOM

1. What does one MAC actually mean, and in what fraction of patients?
2. This patient is 80 rather than 30 - does the number on the dial change?
3. Where is the blood pressure going as you deepen, and through which mechanism?
4. What would nitrous oxide add here, and in which patient would you leave it off?

ORAL BOARDS STEM

You are maintaining a healthy 30-year-old for a knee arthroscopy on sevoflurane in oxygen and air. Your attending reaches over, taps the vaporiser dial, and asks what one MAC actually means, what it means for this particular patient, and what would change if you added 60% nitrous oxide or swapped the sevoflurane for isoflurane.

MAC is the currency of every volatile - it is the dose, it falls with age, and every volatile buys its depth partly by dropping the systemic vascular resistance and with it the blood pressure.

SOURCES

- [1] Nakajima et al., British Journal of Anaesthesia 1993 · PMID 8471368
- [2] Grundmann et al., Acta Anaesthesiologica Scandinavica 1996 · PMID 8933850
- [3] Patel et al., Drugs 1996 · PMID 8706599
- [4] Goldman, Anesthesia and Analgesia 2003 · PMID 12538185
- [5] Myles et al., Anesthesiology 2007 · PMID 17667565
- [6] Myles et al., Lancet 2014 · PMID 25142708
- [7] Leslie et al., Anesthesiology 2015 · PMID 26501387