That Sums It Up

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Inhalational anesthetics, additive minimum alveolar concentration (MAC)

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Abstract

This case discusses the additive nature of the minimum alveolar concentration (MAC) for volatile anesthetics.

Case

On Monday, at 6:25 AM, an anesthesia resident was running late with his room setup for his 7 AM start for an elective surgical case under general anesthesia for an otherwise healthy college student. He performed an appropriate machine check-out, set up his airway equipment, and drew up his drugs, but did not have time to go back to the anesthesia workroom.

After an uncomplicated induction and intubation, the patient was started on isoflurane. Approximately 1 hour into the case, the anesthesia machine indicated "Low Isoflurane: Refill Reservoir." There was no additional isoflurane in the room. The resident called the anesthesia technician to request more isoflurane but the support personnel were all called to two simultaneous traumas and forgot about the request for isoflurane. The isoflurane became depleted.

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Instinctively, the resident changed to the sevoflurane vaporizer. After a few minutes, the sevoflurane end-tidal concentration was 1% and the isoflurane end-tidal concentration was still 1.1%. The gas analyzer displayed a minimum alveolar concentration (MAC) of 1.5%.

Discussion

This is an example of additive synergistic pharmacodynamic drug effects.

MACs of inhalational gases are additive.[1,2]

One MAC is the percent volume of expired inhalational anesthetic that prevents movement in 50% of patients to surgical stimulus. The MACs for desflurane, sevoflurane, isoflurane, and nitrous oxide are roughly 6%, 2%, 1.2%, and 105% respectively. Other MACs have been defined and determined as well. "MAC-awake" is the end-tidal anesthetic concentration at which 50% of patients respond to commands. It is widely believed that an end-tidal anesthetic concentration greater than the MAC-awake value will prevent patients from remembering intraoperative events. This value varies for each agent, but is approximately one-third of MAC for isoflurane, desflurane, and sevoflurane.[3] Like MAC, this value decreases with age, but not with opioids (at lower doses). Additionally, "MAC-BAR" is the concentration that blocks autonomic response to any surgical stimulation. This is approximately 1.3 (for isoflurane and desflurane) to 2.2 (sevoflurane) times their respective MAC concentrations.[3]

The MACs of inhalational anesthetics are additive. Gas analyzers sample the end-tidal gas mixture to determine the MAC of each inhalational gas present during exhalation. For example, adding 0.5 MAC of desflurane (3%) and 0.5 MAC of nitrous oxide (52%) results in approximately 1 MAC.

Based on this, combining desflurane, sevoflurane, or isoflurane with nitrous oxide may be beneficial for patients without contraindications who are having inhalational agent-induced intraoperative hypotension, but for whom reducing the depth of anesthesia is not an option. Nitrous oxide tends to stimulate the sympathetic nervous system causing minimal or slight increase in arterial blood pressure, heart rate, and cardiac output. Other anesthetic agents like inhalational gases, opioids, and propofol can cause hypotension; adding nitrous oxide can decrease the percentage of other inhalational anesthetics required and may decrease their side effects while keeping the MAC the same.[3] This is not meant to imply that nitrous oxide is free from side effects; indeed nitrous oxide can cause nausea and vomiting, myocardial depression, and decreased tidal volumes just as the other inhalational agents can.

Additionally, nitrous oxide can cause the rapid (and potentially dangerous) expansion of closed air spaces.

Inhalational MACs are decreased with the addition of opioids.

MACs of anesthetic inhalational agents are reduced when used in conjunction with opioids. For example, a 50% reduction in the MAC of isoflurane can be achieved by reaching a fentanyl blood level of 1.7 ng/mL.[4] Studies have verified that other opioids such as alfentanil, sufentanil, and remifentanil also decrease the MAC of isoflurane, albeit at different respective plasma concentrations.[5–7]

Table 22.1 lists common opioids used during anesthesia. The target plasma concentration of opioids used to reduce inhalation anesthetics to their respective MAC concentrations has been studied. The opioid bolus and infusion rates to achieve these plasma levels are also listed but must be used with clinical discretion for each patient.

The use of multiple agents relies on the principle of MAC addition to decrease the dose-dependent side effects of each specific agent.

In general, the inhalational agents cause decreases in the cerebral metabolic rate of oxygen utilization ($CMRO_2$), an increase in cerebral blood flow (CBF) and intracranial pressure (ICP), and a decrease in the amplitude of sensory evoked potentials. These occur in a dose-dependent manner, so the addition of other agents, such as remifentanil, allows for a reduction in the inhaled agent's concentration and creates a more favorable monitoring situation. For example, it is recommended that isoflurane be limited to 0.5 MAC when evoked potentials are to be monitored[1].

Table 22.1 Target Plasma Concentration Parameters for Common Opioids

Opioid	Target Plasma Concentration to Reduce Inhalation Agents to MAC Awake	Bolus and Infusion Rate to Achieve Target Plasma Concentration
Fentanyl	1–4 ng/mL	Bolus: 3–10 μg/kg Infuse: 0.02–0.07 μg/kg/min
Alfentanil *	40–160 ng/mL	Bolus: 20–80 μg/kg Infuse: 0.25–1 μg/kg/min
Sufentanil	0.15–0.5 ng/mL	Bolus: 0.15–0.5 μg/kg Infuse: 0.003–0.01 μg/kg/min
Remifentanil[a]	1–(5–15) ng/mL	Bolus: 0.25–1 μg/kg Infuse: 0.025–(0.2–1.0) μg/kg/min

[Based on data from Ref. [8]]

[a]Remifentanil and alfentanil bolus should be given as a rapid infusion over 1 to 2 minutes

Take-Home Points

- The minimum alveolar concentration (MAC) of inhalational gases can be summed together.
- The MAC requirement can be decreased by the concurrent use of opioids.
- Using adjunctive therapy can decrease the MAC requirement while also decreasing the side effects of anesthetic gases.

Summary

Interaction: pharmacodynamic
Substrates: inhalational anesthetics, opioids
Mechanism/site of action: various
Clinical effect: anesthetic depth is increased by additive fractional dosing

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