Drug Choices and Outcomes in Neuroanesthesia

or "Don't Touch That Vaporizer!"

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Objectives

- Be aware of the multiple goals to be met when providing anesthesia for patients with intracranial pathology
- Understand the effects of volatile and intravenous anesthetic agents on intracranial dynamics
- Be able to outline a rational choice of anesthetic when caring for patients with various intracranial situations

Overview

- Goals of anesthesia
- Effects of volatile anesthetics
- Effects of intravenous anesthetics
- Comparison of volatile anesthetics
- Comparison of intravenous anesthetics
- Volatile vs. intravenous anesthetics
- What's best?

Goals of Anesthetic Management

- Hemodynamic stability
- Maintenance of cerebral perfusion pressure
- Control of intracranial pressure
- Optimal surgical conditions (slack brain)
- Smooth emergence
- Rapid awakening for early neurologic assessment

Ideal Anesthetic Agent

- Maintain CBF without affecting autoregulation
- Minimize detrimental changes in Intracranial Pressure (ICP)
- Preserve reactivity of cerebral arterioles to \( P_{CO_2} \) changes
- Decrease CMRO\( _2 \) with cerebral protection effects
- Devoid of seizure activity
- Preserve hemodynamic stability, especially Cerebral Perfusion Pressure (CPP)
- Devoid of arrhythmogenic effect

Normal Values

<table>
<thead>
<tr>
<th>Table 21-1</th>
<th>Normal cerebral physiologic values</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF</td>
<td>Global ( 40-55 ) mL/100 g/min</td>
</tr>
<tr>
<td></td>
<td>Cortical (mostly) ( 55-70 ) mL/100 g/min</td>
</tr>
<tr>
<td></td>
<td>Subcortical (mostly white matter) ( 20-40 ) mL/100 g/min</td>
</tr>
<tr>
<td>CMRO( _2 )</td>
<td>2.5-3.5 mL/100 g/min</td>
</tr>
<tr>
<td>CVP</td>
<td>( 1.1-2.1 ) mm Hg/100 g/min/mL</td>
</tr>
<tr>
<td>Cerebral venous ( P_{O_2} )</td>
<td>35-45 mm Hg</td>
</tr>
<tr>
<td>Cerebral venous ( S_{O_2} )</td>
<td>55-70%</td>
</tr>
<tr>
<td>ICP (cerebral)</td>
<td>( 8-12 ) mm Hg</td>
</tr>
</tbody>
</table>

CBF, cerebral blood flow; CMRO\( _2 \), cerebral metabolic rate of oxygen; CVP, cerebral vascular resistance; ICP, intracranial pressure.

Patel PM and Drummond JC in Miller’s Anesthesia, 6th Ed, p. 104.
Determinants of ICP (and What We Can Control)

- Brain tissue
- Intra- and extracellular fluid (edema)
- CSF
- Blood (arterial/venous)
- Airway or intrathoracic pressure
- Jugular venous pressure
- \( P_{CO_2} \)
- \( P_{O_2} \)
- Anesthetics
- Vasodilators
- Seizures
- Temperature
- Arousal
- Pain

Why Does ICP Matter?

- Sustained ICP > 20 mm Hg is abnormal
- ICP 20 – 40 mm Hg is considered moderate intracranial hypertension
- ICP > 40 mm Hg is life-threatening
- Increased ICP results in secondary injury due to ischemia from reduced CPP and distortion of intracranial structures such as the brainstem

Effects of Volatile Agents (Are they all created equal?)

- Patel PM and Drummond JC in Miller's Anesthesia, 6th Ed; p. 817
- Patel PM and Drummond JC in Miller's Anesthesia, 6th Ed; p. 830

Janik, Daniel, MD Drug Choices and Outcomes in Neuroanesthesia
**Effects of Volatile Agents**

**Are They All Created Equal?**

- Isoflurane has been the “gold standard” of volatile agents for some time, but –
  - At both 0.5 and 1.5 MAC Sevoflurane increases \( V_{mca} \) less (4 and 17%) than Isoflurane (19 and 72%)
  - Sevoflurane preserves autoregulation better than Isoflurane

**Effects of Volatile Agents**

(Are they all created equal?)

- At both 0.5 and 1.5 MAC Sevoflurane increased \( V_{mca} \) less (max 7%) than Desflurane (max 65%)

**But What Happens During Brain Surgery?**

- In a study of patients with supratentorial mass lesions and mass effect on CT, in the presence of hyperventilation (\( P_{CO_2} = 25 \) mm Hg), 1 MAC Desflurane in air:O\(_2\) increased Cerebrospinal Fluid Pressure greater than Isoflurane (18 vs. 8 mm Hg)

**Effects of Volatile Agents**

(Comparative Studies, Intracranial Surgery)

- In a study of patients with intracranial mass lesions (with and without evidence of increased ICP, \( P_{CO_2} = 21 \) mm Hg), CBF was slightly higher at 1.0 MAC Isoflurane than Desflurane, but there were no differences at 1.25 and 1.5 MAC
- CBF under anesthesia was 17-35 ml/100g/min

**Effects of Volatile Agents**

(Comparative Studies, Intracranial Surgery)
Effects of Volatile Agents (Comparative Studies, Intracranial Surgery)

- In patients undergoing craniotomy with a background of Thiopental/Sufentanil and hyperventilation (P<sub>CO₂</sub>=30-35 mm Hg), Sevoflurane had earlier recovery profile than Isoflurane (moving feet: 24 minutes Sevo vs. 43 minutes Iso). Hemodynamic variables and brain relaxation scores were similar.

Gauthier A et al., Anesth Analg 2002; 95:1384-8

- In a study comparing 0.5, 1.0, or 1.5 MAC Isoflurane or Sevoflurane in air with Sufentanil (P<sub>CO₂</sub>=35-40 mm Hg) there was no change in ICP and a decrease in CBF with both agents; CPP decreased at 0.5 MAC with Sevoflurane and all levels of Isoflurane; MAP and CPP were lower with Isoflurane compared to Sevoflurane.

Artru AA et al., Anesth Analg 1997; 85:S87-82

- In a study of children (mean age 20 months) with suspected ICP above normal given a background of Fentanyl/ N₂O 60% and normocarbia, 0.5-1.0 MAC Isoflurane, Sevoflurane, and Desflurane similarly increased ICP and decreased MAP and CPP in a dose-dependent manner. ICP increased more (n.s.) with higher baseline values with Desflurane.

Sporheim S et al., Acta Anaesthesiol Scand 2003; 47:912-8

Effects of Intravenous Agents

- Patel PM and Drummond IC in Miller’s Anesthesia, 6th Ed., p. 821
But What Happens During Brain Surgery?

Effects of Intravenous Agents (Comparative Studies, Intracranial Surgery)

• In sedated patients with head trauma (GCS = 6-7) and $P_{\text{a}}CO_2 = 30-35$ mm Hg, Propofol (2mg/kg bolus with 150mcg/kg/min infusion) decreased ICP (11.3-9.2 mm Hg), decreased MAP (25%), decreased CBF (35-26 ml/100g/min), and decreased CPP (82-59 mm Hg)

Pinaud M et. al., Anesthesiology 1990; 73:404-9

Effects of Intravenous Agents (Comparative Studies, Intracranial Surgery)

• In patients with tumors and a background of isoflurane 0.3-0.8% in 66% $N_2O$ and $P_{\text{a}}CO_2 < 30$ mm Hg, boluses of Remifentanil (0.5 mcg/kg and 1.0 mcg/kg) or Alfentanil (10 mcg/kg and 20 mcg/kg), neither caused a change in ICP. Effects on MAP were similar (decreased)

Warner DS et. al., Anesth Analg 1996; 83:348-53

• In patients with tumors given isoflurane (low dose, unspecified)/66% $N_2O$ and $P_{\text{a}}CO_2 = 28$ mm Hg, Remifentanil and Fentanyl did not differ in ICP, CPP, MAP (except for intubation), brain condition, or recovery variables.

Guy J et. al., Anesthesiology 1997; 86:514-24

Effects of Intravenous Agents (Comparative Studies, Intracranial Surgery)

• In patients with tumors receiving Propofol or Isoflurane with or without $N_2O$, the use of Fentanyl (customary manner) was associated with delayed emergence (at 10 minutes but not 20) and greater Isoflurane use compared with Remifentanil (4/c at dressing)


• In patients for craniotomy with Propofol and $P_{\text{a}}CO_2 = 30-35$ mmHg, Remifentanil required less Propofol compared to Fentanyl and Alfentanil, and was associated with more rapid recovery than Alfentanil (but not Fentanyl). All agents decreased MAP post-induction


Effects of Intravenous Agents (Comparative Studies, Intracranial Surgery)

• In patients with tumors and a background of 60% $N_2O$ and normocarbia ($P_{\text{a}}CO_2 = 36$ mm Hg) Sufentanil (89%) and Alfentanil (22%) increased CSFP compared to Fentanyl, and all decreased CPP (Fentanyl=14%; Sufentanil 25%; Alfentanil 37%)


• In patients with tumors receiving 60-70% $N_2O$ with $P_{\text{a}}CO_2 = 25$ mm Hg and either Alfentanil, Fentanyl, or Sufentanil, although the Alfentanil group received ephedrine more frequently, there was no difference in recovery profiles or intraoperative brain conditions

From RF et. al, Anesthesiology 1990; 73:896-904
How do the Volatile Agents Compare to Intravenous Agents?

Volatile vs. Intravenous (Comparisons, Intracranial Surgery)

- In patients with tumors given either Propofol/Fentanyl, Isoflurane/N2O, or Fentanyl/N2O with PaCO2=30 mm Hg, there were no differences in mean CPP (81:89 vs. 102:0 mm Hg) or CPP (0.5% vs. 1.5%). Patients without signs of high ICP given either Isoflurane (0.5-1.5%) or Propofol infusion (N2O 50% given to both after dural opening) found lower CPP (81 vs. 70 mm Hg) at induction, lower CSFPr (15.2 vs. 11.6 mm Hg) and better recovery variables at 20-30 minutes with Propofol.

Rauvissin P et al., J Neurosurg Anesthesiol 1991; Vol 3(2):85-95
CBF, ICP, CBV, or CPP?

- CPP = MAP – ICP
- Want to maintain CPP = 70 – 90 mm Hg
- ICP affected by intracranial volume
- Intracranial volume has 4 components:
  - Tissue volume
  - CSF volume
  - Fluid compartment (edema)
  - Blood volume (arterial and venous)
- CBF reflects arterial volume – how much does this really affect total CBV?

Volatile vs. Intravenous Agents
(Is One Really Better?)

- It depends on how you define “better”
  - Quicker emergence (short term outcome)
  - Ease of titration/administration
  - Hemodynamic stability
  - Brain conditions
  - Long term outcomes (no data)
  - $ versus $ (cost containment)

One More Note

- In many of the studies comparing volatile agents, or volatile to intravenous agents, exclusion criteria included evidence of increased intracranial pressure such as mass shift, altered mental status, or abnormal measured ICP
My Opinion

• For all agents, the ultimate condition of the patient will be determined by the sum of the effects of the chosen agent on CBF, CMRO₂, vascular tone, MAP, CO, CSF formation/reabsorption, and CBV.
• The preponderance of evidence is that intravenous agents (Propofol, Barbiturates, Etomidate, Benzodiazepines, synthetic opiates (phenylpiperidine)) have less deleterious, and more salutary effects that are more predictable on intracranial dynamics than volatile agents, especially if MAP is maintained.
• Isoflurane, Sevoflurane, and Desflurane are similar, though the edge probably should go to Sevoflurane, and their ultimate effects on ICP/CPP are less predictable.
• There is no overwhelming evidence that one technique is superior to any other in terms of short term recovery profile, if the agents chosen are properly administered.
• Choose your poison (agents) wisely given the goals of anesthesia and surgery, and the condition of the patient such as........

My Opinion

• If the patient is wide awake, appearing for elective surgery, and is well-compensated in terms of intracranial dynamics:
  - Either volatile or TIVA are appropriate taking care to avoid bad things like –
    - Hypotension (remember CPP)
    - Hypertension
    - Hypoxemia
    - Hypercarbia
  - Inadequate anesthesia at critical points
  - Remember – It’s more important how you do it, than what you use.

My Opinion

• If the patient has signs or symptoms of high ICP (altered mental status, head injury, ventriculostomy/ICP monitor in place, midline shift on CT/MRI, etc.):
  - Management of the ICP/CBF/CBV/CPP is critical
  - TIVA is preferable, at least until the dura is opened and the effects of anesthetics on the brain bulk can be assessed directly
  - Keep a very close eye on CPP (>70 mm Hg)
  - Think/Think/Think: MAP-ICP

Comparative Costs

• 1993:
  - Propofol/Fentanyl = $152
  - Isoflurane/N₂O = $49
  - Fentanyl/N₂O = $15
• 2002:
  - Isoflurane/N₂O = $17
  - Propofol/Fentanyl/N₂O = $114
  - Isoflurane/N₂O then Propofol = $31

THE END