


**SOCIETY FOR SAMBA**  
ANESTHESIA  
Outpatient • Office Based • Non-Operating Room

**2022 SAMBA ANNUAL MEETING**  
MAY 11 - 14, 2022

## Midazolam for No One




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## Midazolam

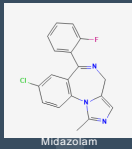
- Anxiolytic introduced into practice 1982
- Short-acting benzodiazepine
  - Enhances the effect of GABA on the GABA<sub>A</sub> receptors producing sedation/anxiolysis
- Elimination half-life of 1.8-6.4 hours
- Onset 1-5 minutes, up to 9-11 minutes to reach full clinical effect
- Poor oral absorption-50% bioavailability



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## Disadvantages/Side Effects

- Anterograde amnesia, sometimes profound
- Respiratory depression
- Psychomotor dysfunction, especially in elderly
- Increased time to discharge
- Delirium/post-operative cognitive dysfunction (POCD)

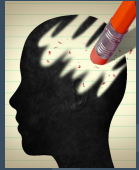


Midazolam

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## Anterograde Amnesia

- Some patients relate amnesic periods of hours to days. Is it good for patients to be amnesic for the better part of a day?
- We know that few patients follow our directions about having someone stay with them for 24 hours
- Will patients forget perioperative instructions given to them, undertake a task where recall is critical?
- Some patients uncomfortable with not remembering the entire events of the day



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## Respiratory Depression

- Even with low doses, some hypopnea and low saturations in patients administered midazolam
- Doses of 0.5 mg or 2 mg pre-op increased incidence of O<sub>2</sub> sats <94% in pre-op period
- Respiratory depression exacerbated by intra- or post-op opioids

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**Midazolam sedation for upper gastrointestinal endoscopy in older persons: a randomized, double-blind, placebo-controlled study**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**The effect of midazolam premedication on mental and psychomotor recovery in geriatric patients undergoing brief surgical procedures**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**Frequent hypoxemia and apnea after sedation with midazolam and fentanyl**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

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## Psychomotor Dysfunction

- Psychomotor function impaired by midazolam in young healthy volunteers for up to 60 min
  - Impaired driving ability
- Persistent decrease in alertness in 36% of study subjects 60 min after administration
- Benzodiazepine use in elderly increases risk for falls, hip fractures

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**The effects of midazolam and flumazenil on psychomotor function and alertness in human volunteers**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**Sedation and recovery of psychomotor function after intravenous administration of various doses of midazolam and diazepam**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

Clinical Study: J. Lee, et al. 2008. Anesth Analg 107:1001-1005.  
**Association between use of benzodiazepines and risk of fractures: a meta-analysis**  
J. Lee, et al. 2008. Anesth Analg 107:1001-1005.

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## Delayed Recovery and Discharge when Combined with GA

- Time to discharge 20-30 min longer in elderly patients administered midazolam as pre-med (0.5, 2.0 mg)
- Time to discharge increased in children given oral midazolam as premed (0.5 mg/kg)
- No improvement in post-op recovery satisfaction with midazolam

**The effect of midazolam premedication on mental and psychomotor recovery in geriatric patients undergoing brief surgical procedures**

**Premedication with midazolam delays recovery after ambulatory sevoflurane anesthesia in children**

**The effect of midazolam as premedication on the quality of postoperative recovery after laparotomy: randomized clinical trial**

- Association of delirium with post-op administration of benzodiazepines
- Post op delirium associated with increased risk of subsequent diagnosis of cognitive decline or dementia

**Association Between Perioperative Medication Use and Postoperative Delirium and Cognition in Older Adults Undergoing Elective Noncardiac Surgery**

> Br J Anaesth. 2017 Aug 1;119(2):316-323. doi: 10.1093/bja/aex130.

### Postoperative delirium in elderly patients is associated with subsequent cognitive impairment

Several groups have released recommendations about optimizing perioperative brain health.

- Fifth International Perioperative Neurotoxicity Working Group
- American Society for Enhanced Recovery and Perioperative Quality Initiative
- Perioperative Brain Health Expert Panel
- ASA Perioperative Brain Health Initiative

Miles Berger<sup>1</sup>, Katie J. Henning<sup>2</sup>, Charles H Brown 4th<sup>3</sup>, Stacie G Deiner<sup>4</sup>, Robert A Whittington<sup>5</sup>, Roderic G Eckenhoff<sup>6</sup>, Martin S Angst, Sinziana Avramescu, Alex Bekker, Marek Brzezinski, Greg Crosby, Deborah J Culley, Maryellen Eckenhoff, Lars I Eriksson, Lis Evered, Jim Ibinson, Richard P Kline, Andy Kofke, Daqing Ma, Joseph P Mathew, Mervyn Maze, Beverley A Orser, Catherine C Price, David A Scott, Brendan Silbert, Diansan Su, Niccolò Terando, Dian-Shi Wang, Huafeng Wei, Zhongcong Xie, Zhiyi Zuo, Perioperative Neurotoxicity Working Group

Medication or Class of Medication	Examples	Rationale for Avoiding
General anesthetic induction agents	Etomidate Propofol Thiopental	Central anesthetic effects
Anticholinergics/antispasmodics	Atropine, scopolamine Isosulfated	Central anticholinergic effects
Antidepressants (first and second generation)		Risk of cognitive impairment, delirium, neurotoxic multifactorial causes, tardive dyskinesia
Benzodiazepines	Midazolam, diazepam Alprazolam, lorazepam, clonazepam	Risk of cognitive impairment, delirium Risk of cognitive impairment, delirium, psychosis
1 $\alpha$ -receptor antagonists	Roxatidine	Risk of cognitive impairment, delirium
Antipsychotics		Central anticholinergic effects
Morphine		Neurotoxic effects
Statistical misadventures	Cyclophosphamide	Anticholinergic effects

Christopher G Hughes<sup>1</sup>, Christina S Boncyk<sup>1</sup>, Deborah J Culley<sup>2</sup>, Lee A Fleisher<sup>3</sup>,  
Jacqueline M Leung<sup>4</sup>, David L McDonagh<sup>5</sup>, Tong J Gan<sup>6</sup>, Matthew D McEvoy<sup>7</sup>, Timothy E Miller<sup>8</sup>,  
Perioperative Quality Initiative (POQI) 6 Workgroup

Table 3. Precipitating Factors Associated With Postoperative Delirium

Identified Precipitating Factors		
Intraoperative Aspects	Postoperative Issues	Medication Exposure
Surgical complexity	Anemia	Benzodiazepines
Surgical duration	Pain	Diphenhydramine
Surgical approach	Sleep disturbances	Scopolamine
Cardiopulmonary bypass	Renal insufficiency	Ketamine
Transfusion	Atrial fibrillation	Meperidine
Blood pressure	Infection	Morphine
Glycemic control	Hypoxemia	Zolpidem
Depth of sedation/ burst suppression	Mechanical ventilation	Histamine-receptor antagonists

Carol J Peden<sup>1</sup>, Thomas R Miller<sup>2</sup>, Stacie G Deiner<sup>3</sup>, Roderic G Eckenhoff<sup>4</sup>, Lee A Fleisher<sup>4</sup>,  
Members of the Perioperative Brain Health Expert Panel

*"Routine cognitive screening raises awareness amongst the perioperative care team and can result in some simple changes in behaviour such as reduced use of benzodiazepines."*

## Alternatives to Midazolam

- Propofol/Lidocaine
- Dexmedetomidine
- Non-pharmacologic therapies
- Remimazolam?



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## Propofol

- Inadequate doses of propofol often used
- Propofol 20 mg as effective as midazolam for premedication/anxiolysis
- Psychomotor reflexes for driving return to baseline 60 min after discontinuation of propofol infusions

**Propofol versus midazolam for premedication: a placebo-controlled, randomized double-blinded study**  
 Choudhry S, Laro T, Patel P, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.  
**Comparative Study** | *Journal of Clinical Pharmacy and Therapeutics*. 2020;45(1):1-11. doi: 10.1111/jcpt.12345.  
**Safety and driving ability following low-dose propofol sedation**  
 Akita H, et al. *Journal of Clinical Pharmacy and Therapeutics*. 2020;45(1):1-11. doi: 10.1111/jcpt.12345.

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## Lidocaine

- IV lidocaine 1.5 mg/kg improves success of LMA placement and decreases coughing and airway obstruction
- During bronchoscopy, IV lidocaine 1.5 mg/kg suppresses cough better than LT lidocaine
- Decreases dose of propofol needed for sedation in endoscopies

**Facilitation of laryngeal mask insertion. Effects of lignocaine given intravenously before induction with propofol**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.  
**Comparison of intravenous and topical lidocaine as a suppressant of coughing after bronchoscopy during general anesthesia**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.  
**Efficacy and safety of supplemental intravenous lidocaine for sedation in gastrointestinal endoscopic procedures: systematic review and meta-analysis of randomized controlled trials**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.

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## Dexmedetomidine

- Anxiolysis without respiratory depression
- May be organ protective
- Associated with less POCD
- Especially useful in children
  - Can be given intranasally, orally, IM or IV
  - May also prevent emergence delirium
- Can cause bradycardia and rare sinus arrest, hypotension
- Longer time of onset and offset

**Dexmedetomidine in anaesthesia**  
 Andrew Davis, Peter H. Turner.  
**Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations**  
 A comparison of oral dexmedetomidine and oral midazolam as premedicants in children

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## Non-pharmacologic Therapies

- Verbal reassurance/distraction
- Relaxation techniques
  - Cognitive behavioral therapy
  - Biofeedback
  - Hypnosis
- Acupuncture
- Music

**Effects of non-pharmacological interventions on preoperative anxiety and postoperative pain in patients undergoing breast cancer surgery: A systematic review**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.  
**The effectiveness of interventions aimed at reducing anxiety in health care waiting spaces: a systematic review of randomized and nonrandomized trials**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.  
**Dealing with Anxious Patients: A Systematic Review of the Literature on Nonpharmacological Interventions to Reduce Anxiety in Patients Undergoing Medical or Dental Procedures**  
 Li J, et al. *British Journal of Anaesthesia*. 2019;123(4):681-687. doi: 10.1016/j.bja.2019.05.011.

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## Remimazolam?

- Ultra-short acting benzodiazepine
- Faster time of onset and recovery profile than midazolam
- Organ-independent metabolism to inactive metabolites
- Whether better than propofol remains to be seen

**Remimazolam for anaesthesia or sedation**  
 Richard D. George, et al.  
**Remimazolam: Pharmacologic Considerations and Clinical Role in Anesthesiology**  
 Richard D. George, et al.

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Sometimes it's better to keep  
it simple...



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