

Table 1. General Characteristics of Common ICU Sedative Agents

Drug	Type of medication	Sedation	Analgesia	Mechanism of action	Advantages	ICP effects	Seizure threshold effect	Adverse events
Fentanyl	Opioid	+	+++	Mu receptor agonist	Reversible, rapid onset, short duration	Indirect elevation (hypercarbia)	Myoclonus, no seizures	Respiratory depression, chest wall rigidity, gastric dysmotility, hypotension
Remifentanyl	Opioid	+	+++	Mu receptor agonist	Reversible, rapid onset, short duration	Indirect elevation (hypercarbia)	Myoclonus, no seizures	Respiratory depression, chest wall rigidity, gastric dysmotility, hypotension
Morphine sulfate	Opioid	+	+++	Mu receptor agonist	Reversible	Elevates ICP	Myoclonus, no seizures	Respiratory depression, gastric dysmotility, hypotension, hallucinations
Diazepam	Benzodiazepine	+++	+	GABA _A receptor agonist	Reversible	Indirect elevation (hypercarbia)	Treat seizures	Respiratory depression, hypotension, confusion
Lorazepam	Benzodiazepine	+++	-----	GABA _A receptor agonist	Reversible	Indirect elevation (hypercarbia)	Treat seizures	Respiratory depression, hypotension, confusion
Midazolam	Benzodiazepine	+++	-----	GABA _A receptor agonist	Reversible, shorter duration, and titratable	No direct effect on ICP. Indirect elevation (hypercarbia and hypotension)	Treat seizures	Respiratory depression, hypotension, confusion
Thiopental	Barbiturate	+++	-----	GABA _A receptor agonist	-----	ICP reduction	Treat seizures	Respiratory depression, hypotension, gastric dysmotility, bronchospasm, angioedema
Pentobarbital	Barbiturate	+++	-----	GABA _A receptor agonist	-----	ICP reduction	Treat seizures	Respiratory depression, hypotension, gastric dysmotility, bronchospasm, angioedema
Phenobarbital	Barbiturate	+++	-----	GABA _A receptor agonist	-----	ICP reduction (large doses)	Treat seizures	Respiratory depression, hypotension, gastric dysmotility, bronchospasm, angioedema
Haloperidol	Neuroleptic (butyrophenone)	+++	-----	Blocks dopamine, adrenergic, serotonin, acetylcholine, and histamine receptors	-----	Not studied	Unpredictable	Extrapyramidal signs; may lower seizure threshold

Droperidol	Neuroleptic (butyrophenone)	+++	-----	Blocks dopamine, adrenergic, serotonin, acetylcholine, and histamine receptors	-----	No effect	Unpredictable	Extrapyramidal signs; may lower seizure threshold; QT prolongation
Clonidine	Alpha-2 agonist	++	++	Alpha-2 receptor agonist (pre- and post-synaptic)	Useful in setting of alcohol or drug withdrawal	No effect	Little data: increases epileptiform activity in known focal seizures?	Dry mouth, bradycardia, hypotension, rebound hypertension
Dexmedetomidine	Alpha-2 agonist	++	++	Alpha-2 receptor agonist (pre- and post-synaptic)	Useful in setting of alcohol or drug withdrawal	No effect	No human studies	Dry mouth, bradycardia, hypotension, adrenal suppression, atrial fibrillation
Propofol		+++	-----	Unclear	Very short duration, easy titratability	Lowers ICP	Conflicting results but most likely treats seizures	Hypotension, respiratory depression, metabolic acidosis, rhabdomyolysis, anaphylaxis, sepsis, pain at venous site

+= mild; ++= moderate; +++= high

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Table 2: Pharmacokinetics & Dosing Parameters of Common ICU Sedatives

<i>Drug</i>	<i>Half-life</i>	<i>Starting dose</i>	<i>Titration</i>	<i>Protein binding</i>	<i>Metabolism</i>	<i>Active metabolite</i>
Fentanyl	30-60 min (single IV dose). Repeated is hours	12.5-50 mcg IV q 20-30 min	Infusion 0.01-0.03 mcg/kg/min and titrate q 15-30 min, up to 50-100 mcg/h	80-86%	Hepatic	-----
Remifentanyl	3-10 min after single dose	0.5-1.0 mcg/kg IV bolus	Infusion 0.05-0.2 mcg/kg/min	92%	Plasma esterases	-----
Morphine sulfate	1.5-4.5 hours IV, IM, SQ	5-20 mg IM q 4 hours 2-10 mg IV q 4 hours	Caution: metabolites may accumulate For post-operative pain (PCAP): 0.2-3.0 mg and 5-20 min lockout intervals	20-30%	Hepatic	Morphine-3-glucuronide Morphine-6-glucuronide
Diazepam	30-60 hours	2 mg IV q 30-60 min	-----	99%	Hepatic	Desmethyl-diazepam, oxazepam, hydroxydiazepam
Lorazepam	10-20 hours	0.25-0.5 mg IV q 1-2 hours	-----	91-93%	Hepatic	-----
Midazolam	1-2.5 hours	0.5-1 mg IV q 5-30 min	Infusion 0.25-1.0 mcg/kg/min	97%	Hepatic	1-Hydroxymethyl midazolam
Thiopental	8-12 hours	1-5 mg/kg IV	-----	30-40%	Mostly hepatic. Also kidney, brain	-----
Pentobarbital	15-50 hours	3-30 mg/kg IV	Infusion 1-2 mg/kg/h to burst-suppression EEG	35-45%	Mostly hepatic	-----
Phenobarbital	53-120 hours	1-3 mg/kg IV or IM (sedation). 15-20 mg/kg IV (status epilepticus)	-----	20-40%	Mostly hepatic and urine (unchanged)	-----
Haloperidol	12-36 hours	0.5-5.0 mg IV	-----	92%	Hepatic	-----
Droperidol	4-12 hours	0.625 -2.5 mg IV	-----	92%	Hepatic	-----
Clonidine	12-16 hours	0.1 mg PO q 8-24 hours. Increase 0.1 mg/d q 1-2 d up to 0.6 mg/d	-----	20-40%	Hepatic (50%) and urine (unchanged, 50%)	-----
Dexmedetomidine	2 hours	1 mcg/kg IV over 10 min	Infusion 0.2-0.7 mcg/kg/h	94%	Hepatic	-----
Propofol	4-10 min	1.0-2.5 mg/kg IV (anesthesia)	Increase infusion by 5-10 mcg/kg/min q 5-	Not found	Hepatic and extrahepatic	-----

		induction) 5 mcg/kg/min for 5 min IV (sedation)	10 min to maintenance 25- 100 mcg/kg/min up to 100-300 mcg/kg/min			
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ICP: intracranial pressure; IV: intravenous; IM: intramuscular; SQ: subcutaneous; PCAP: patient-controlled analgesia pump.