SUPPLEMENTARY TABLES

TABLE 1. Manual Infusion Combinations of Propofol + Opioid for TIVA

Suggested combination infusion regimens required to maintain ±15% of the effect site concentrations associated with a 50% and 95% probability of no response to surgical stimuli and the most rapid possible return of consciousness after termination.

MEDICATIONS	PROPOFOL + REMIFENTANIL	PROPOFOL + FENTANYL	PROPOFOL + SUFENTANIL
PROPOFOL	**Propofol EC_{50}–EC_{95} (2.5–2.8 µg/ml)**	**Propofol EC_{50}–EC_{95} (3.4–5.4 µg/ml)**	**Propofol EC_{50}–EC_{95} (3.3–4.5 µg/ml)**
BOLUS + INFUSION	1.5 mg/kg IV over 30 sec + 115-130 mcg/kg/min for 40 min 100-110 mcg/kg/min for 150 min 80-100 mcg/kg/min thereafter	2.0–3.0 IV over 30 sec + 150-250 mcg/kg/min for 40 min 115-200 mcg/kg/min for 150 min 110-180 mcg/kg/min thereafter	2.0–2.8 IV over 30 sec + 150-200 mcg/kg/min for 40 min 115-170 mcg/kg/min for 150 min 110-130 mcg/kg/min thereafter
	+	**+**	**+**
OPIOID	**Remifentanil EC_{50}–EC_{95} (4.7–8.0 ng/ml)**	**Fentanyl EC_{50}–EC_{95} (1.1–1.6 ng/ml)**	**Sufentanil EC_{50}–EC_{95} (0.14–0.20 ng/ml)**
BOLUS + INFUSION	1.5–2 mcg/kg IV over 30 sec + 0.1-0.2 mcg/kg/min for 20 min 0.05-0.2 mcg/kg/min thereafter	3 mcg/kg IV over 30 sec + 1.5–2.5 mcg/kg/hr for 30 min 1.3–2 mcg/kg/hr up to 150 min 0.7–1.4 mcg/kg/hr thereafter	0.15–0.25 mcg/kg IV over 30 sec + 0.15–0.22 mcg/kg/hr thereafter

- EC_{50} and EC_{95} are the dose combinations needed to keep 50% and 95% of the patients nonmoving all the time, respectively.
- Consider 25-50% of the dose recommended in older patients, severe hemodynamic compromise, or ASA status > 3
- Lean body weight or adjusted body weight is recommended in obese patients

TABLE 2. Dosing Ranges for Common TIVA Adjunctive Agents: dexmedetomidine, ketamine, lidocaine

DOSING	Dexmedetomidine	Ketamine	Lidocaine
BOLUS + INFUSION	0.25 mcg/kg IV bolus + 0.1 – 0.5 mcg/kg/hr	0.25 -35 mg/kg IV bolus + 0.1 mg/kg/hr – 0.5mg/kg/hr	1-1.5 mg/kg* IV bolus + 0.5-2 mg/kg/hr*
CLINICAL PEARLS	May increase risk of bradycardia and hypotension.	Dose dependent psychological manfiestions such as emergence reactions, hallucincations and psychotomimetic effects may occur. May cause hypertension, tachycardiac and increase salivation production	Allow 8h for steady-state serum levels to be achieved before making dosage adjustments

*Lean or adjusted body weight

- Addition of such adjuncts are thought to reduce the need for sedatives/hypnotic agents and/or opiods due to syngergistic mechanisms
- Data are sparse regarding specific combinations of agents and specific dosing when used in combination with other general anesthetic agents and/or opioids

TABLE 3. Relevant Pharmacokinetic & Pharmacodynamic Principles: Propofol, Dexmedetomidine, Ketamine, Lidocaine

	PROPOFOL	DEXMEDETOMIDINE	KETAMINE	LIDOCAINE
MECHANISM	Mainly $GABA_A$ & glycine agonism	Selective α_2 agonist	NMDA receptor antagonist	Blocks pain transmission in the spinal cord
ONSET OF ACTION	~30 seconds	5-10 minutes	30 seconds	2-5 minutes
DURATION	3-15 minutes	60-240 minutes	Anesthetic effect: 5-10 minutes Recovery: 1-2 hours	1-2 hours
ADULT VOLUME OF DISTRIBUTION	2-10 L/kg (lower in older patients)	~118L	2.1-3.1 L/kg	91 L/kg
PROTEIN BINDING	99%	~94%	27%	60-80%
METABOLISM	Hepatic	Hepatic	Hepatic	Hepatic
CONTEXT-SENSITIVE HALF TIME	< 30 minutes for infusions up to about 2 hours	Variable ~75 minutes after 2 hour infusion ~250 minutes after 8 hour infusion	~ 30 minutes	30-40 minues
EXCRETION	Urine primarily	Urine primarily	Urine primarily	Urine primarily
ADDITIONAL CONSIDERATIONS	▪ With increasing age, the dose requirement decreases because of occurrence of higher peak plasma concentrations. ▪ Accumulation in tissues and redistribution into plasma occurs with prolonged use.	▪ Clearance and plasma protein binding are decreased in hepatic impairment. ▪ Duration of action depends on dose and duration of continuous infusion	▪ Analgesia outlasts the general anesthetic component.	▪ Half life is prolonged with heart failure, hepatic impairment, renal impairment ▪ Narrow therapeutic index, toxicities may occur with plasma levels> 5 mcg/ml

TABLE 4. Relevant Pharmacokinetic & Pharmacodynamic Principles: Remifentanil, Fentanyl, Sufentanil

	REMIFENTANIL	FENTANYL	SUFENTANIL
MECHANISM	Binds opioid receptors at sites within the CNS		
ONSET OF ACTION	1-3 minutes	3 minutes	1-3 minutes
DURATION	3-10 minutes	0.5 – 1 hour	varies
ADULT VOLUME OF DISTRIBUTION	Initial 100 mL/kg V_{dss} 350 mL/kg	V_{dss} 4-6 L/kg	V_{dss} ~1.7 L/kg
PROTEIN BINDING	70%	80-87%	91-93%
METABOLISM	Blood & Tissue Esterases	Hepatic	Hepatic
CONTEXT-SENSITIVE HALF TIME	< 5 minutes	> 100 minutes continues to increase as infusion increases	20-45 minutes
EXCRETION	Urine primarily	Urine primarily	Urine
ADDITIONAL CONSIDERATIONS	▪ Clearance in older adults is reduced ~25%	▪ Half-life is infusion duration dependent ▪ Advanced age, renal & hepatic impairment alter clearance and plasma proteins	▪ If > 20% IBW, use lean body weight to determine dosage

V_{DSS} = STEADY STATE VOLUME OF DISRIBUTION

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