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Question: Remimazolam compared to propofol for sedation and anesthesia in adult intubated patients.
Setting: Hospital/clinical setting for patients requiring sedation or anesthesia
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	remimazolam	propofol	Relative (95% CI)	Absolute (95% CI)		
***QoR-15, P=0.0007 (assessed with: scores; Scale from: 0 to 150)[a]**												
4	randomised trials	not serious	not serious	not serious	not serious	none	143	144	-	MD **6.89 lower** (10.89 lower to 2.89 lower)	⨁⨁⨁⨁ High	IMPORTANT
Delirium, P=0.85 (assessed with: Nu-DESC/CAM-ICU)												
6	randomised trials	not serious	not serious	not serious	not serious	none	73/621 (11.8%)	75/622 (12.1%)	**RR 0.97** (0.72 to 1.13)	**4 fewer per 1,000** (from 34 fewer to 16 more)	⨁⨁⨁⨁ High	CRITICAL
***Hypotension, P=0.04 (assessed with: multiple definition standards)**												
6	randomised trials	not serious	serious[b]	not serious	not serious	none	73/215 (34.0%)	114/216 (52.8%)	**RR 0.63** (0.40 to 0.99)	**195 fewer per 1,000** (from 317 fewer to 5 fewer)	⨁⨁⨁◯ Moderate[b]	CRITICAL
Postoperative nausea and vomiting, P=0.12												
7	randomised trials	not serious	not serious	not serious	not serious	none	31/351 (8.8%)	20/349 (5.7%)	**RR 1.52** (0.89 to 2.61)	**30 more per 1,000** (from 6 fewer to 92 more)	⨁⨁⨁⨁ High	IMPORTANT
Extubation time (min), P=0.88												
4	randomised trials	not serious	very serious[c]	not serious	serious[c]	none	216	213	-	MD **0.4 lower** (5.74 lower to 4.94 higher)	⨁◯◯◯ Very low[c]	IMPORTANT
***Extubation time (s), P=0.01**												
3	randomised trials	not serious	not serious[d]	not serious	not serious	none	122	125	-	MD **104.63 lower** (184.07 lower to 25.18 lower)	⨁⨁⨁⨁ High[d]	NOT IMPORTANT[d]

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. "*" denotes statistical significance.
b. Substantial heterogeneity was observed (I^2 = 69%, P = 0.01). The main sources of inconsistency can be attributed to: 1. Different surgical settings: Some studies involved day surgery (Wenchen Luo et al.), while others included one-lung ventilation (Q.Kuang et al.), bronchoscopy (Yafei Pan et al.), elderly laparoscopic surgery (Yeong-Gwan Jeon et al.), and breast cancer surgery (Yaqi Huang et al.). 2. Population diversity: Studies enrolled different types of patients, ranging from general surgical patients to specific populations (e.g., elderly patients, cancer patients). 3. Methodological variations: - Different definitions of hypotension across studies - Variations in hemodynamic monitoring methods - Potential differences in anesthetic protocols and drug administration Despite this heterogeneity, the direction of effect remained largely consistent, and subgroup analyses (e.g., by age) demonstrated robust results. The heterogeneity likely reflects the clinical diversity
c. Extreme heterogeneity (I^2 = 99%, P <0.00001) with completely opposite effect directions across studies. Effect sizes varied substantially, ranging from -6.00 to +7.20 minutes. While heterogeneity might be explained by different flumazenil usage (Zhuxin Luo et al. did not use flumazenil while the other three studies did), the inconsistency is too severe to make reliable clinical inferences.
d. Moderate heterogeneity (I^2 = 56%, P = 0.10) with consistent effect direction across all studies. All studies used flumazenil antagonism and showed remimazolam reduced extubation time (mean difference -104.63 seconds, 95% CI [-184.07, -25.18]). While statistically significant (P = 0.01), the clinical significance of a ~2-minute difference in extubation time is limited.