Anesthésie-Réanimation et dysfonction neurologique

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Perioperative ketamine administration to prevent postoperative delirium and neurocognitive disorders: A systematic review and meta-analysis.

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Position du problème et objectif(s) de l'étude:

Surgery induces high rates of cognitive disorders, persisting for up to 12 months in elderly adults. Preventive effects of ketamine on these disorders remain debated. This review aimed to assess the potential preventive effects of perioperative ketamine on postoperative delirium and postoperative neurocognitive disorders (POND).

Matériel et méthodes:

Systematic review and meta-analysis was performed including all randomized controlled trials investigating the effects of perioperative ketamine administration in adult patients compared to placebo or no intervention on postoperative delirium and/or POND between January 2007 and April 2022.

Database searches were conducted in PubMed Medline, Embase, Scopus, Central. The primary outcomes were the incidences of postoperative delirium and of POND, separately explored, with no restriction on definition or on mode of measurement of either outcome. Random effects models were used to pool overall estimates. To combine results, the Mantel-Haenszel method was used. Results were expressed as oddsratio (OR) with a 95% confidence interval (95% CI). Comparisons for rare events were made using the Peto OR method. The GRADE approach was used to assess the quality of evidence. This

meta-analysis is registered in PROSPERO (CRD42022324856).

Résultats & Discussion:

Among 1379 publications, 14 RCTs (n=1618 patients) were included; 50% were at low-moderate risk of bias. No difference in the incidences of postoperative delirium and POND separately was reported between the ketamine and placebo groups (respectively 8 trials, 1265 patients, OR 0.93, 95%CI [0.51; 1.70], I2=28%, and 5 trials, 494 patients, OR 0.52, 95%CI [0.15; 1.80]; I2=78%). No significant differences in

postoperative psychological adverse effects (6 trials, 1260 patients, OR 1.19, 95%CI [0.91; 1.55]; I2=0%), in level of pain (3 trials, 1035 patients, SMD 0.06, 95%CI [-0.33; 0.44]; I2=0%), hospital length ofstay (4 trials, 486 patients, SMD 0.01, 95%CI [-1.14; 1.16]; I2=67%), or mortality (2 trials, 363 patients, OR 1.19, 95%CI [0.14; 9.78]; I2=0%) were observed. Subgroup analyses showed no difference in delirium/POND incidences based on surgical setting, ketamine dose, mode of administration, combination with other drug(s), or assessment timing, or definition of cognitive disorders.

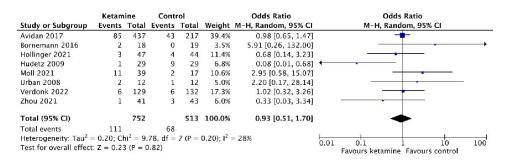
Conclusion:

Perioperative ketamine does not prevent postoperative delirium or POND. Significant heterogeneity between studies suggests that standardized measures for POND assessment and a specific focus on

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patients at high-risk for POND should be used to improve the comparability of future studies. Our findings support the safety of perioperative intravenous ketamine.

(a)



(b)

	Ketamine		Control		Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
Hollinger 2021	10	47	6	44	23.2%	1.71 [0.56, 5.19]		
Hudetz, 2009	7	26	21	26	21.6%	0.09 [0.02, 0.32]		
Lee 2015	1	25	0	26	9.6%	3.24 [0.13, 83.47]	- •	-
Verdonk 2022	26	125	23	115	26.5%	1.05 [0.56, 1.97]	-	
Zhu 2015	2	30	10	30	19.1%	0.14 [0.03, 0.72]	-	
Total (95% CI)		253		241	100.0%	0.52 [0.15, 1.80]		
Total events	46		60					
Heterogeneity: $Tau^2 = 1.40$; $Chi^2 = 18.46$, $df = 4$ (P = 0.001); $I^2 = 78\%$							0.005 0.1 1 10	200
Test for overall effect	Z = 1.0	3 (P = 0)	0.31)				Favours [Ketamine] Favours [Control]	200

Figure 1

- (a). Forest plot of incidence of postoperative delirium and
- (b). Forest plot of incidence of POND. Random effects model.

POND: Post-operative neurocognitive disorders CI, confidence interval; df, degrees of freedom

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