A1.9   Should opioid antagonists with heavy sedation or anaesthesia be used for opioid withdrawal?

GRADE evidence profile

Author(s):	Davoli M, Amato L
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Question:	Should opioid antagonist under heavy sedation be used for opioid withdrawal?
Patient or population:	opioid-dependent patients undergoing managed withdrawal
Settings:	inpatient
Systematic review:	Gowing L et al.; *Opioid antagonists under heavy sedation or anaesthesia for opioid withdrawal* (CLIB 2, 2006)[161].

Quality assessment						Summary of findings				Quality	Importance
						No of patients		**Effect**			
No. studies	**Design**	**Limitations**	**Consistency**	**Directness**	**Other considerations**	**Opioid antagonist under heavy sedation**	**Standard opioid withdrawal**	**Relative risk (RR) (95% CI)**	**Absolute risk (AR) (95% CI)**		
Completion of treatment⁵ (clonidine comparison)[163, 162] (Objective follow-up: 1-3 days[d])											
2[a]	Randomized trials	No limitations[b]	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)	74/86 (86%)	95/121 (78,5%)	RR 1.15[c] (0.79 to 1.68)	150/1 000 more (140 less to 350 more)	⊕⊕⊕◯ Moderate	7
Completion of treatment[e] (buprenorphine comparison)[163] (Objective follow-up: 1-3 days[d])											
1	Randomized trials	No limitations[b]	No important inconsistency	No uncertainty	Imprecise or sparse data (-2)	7/35 (20%)	9/37 (24,3%)	RR 0.82[c] (0.34 to 1.97)	50 less/1 000 (230less to 150 more)	⊕⊕◯◯ Low	7
Commencement of naltrexone (clonidine comparison)											
2	Randomized trials	No limitations	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)	73/86 (85%)	21/84 (25%)	RR 3.4[c] (2.32 to 4.98)		⊕⊕⊕◯ Moderate	5
Commencement of naltrexone (buprenorphine comparison)											
1	Randomized trials	No limitations	No important inconsistency	No uncertainty	Imprecise or sparse data (-2)	33/35 (94%)	36/37 (97%)	RR 0.97[c] (0.88 to 1.07)		⊕⊕◯◯ Low	5
Severity and duration of withdrawal[163] (subjective rating scales follow-up:)											
1[f]	Randomized trials	No limitations[g]	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)[h] High probability of reporting bias (-1)[i]	/	/	unable to compare scales	-	⊕⊕◯◯ Low	7
Adverse events (Objective follow-up: 1-4 days[d])											
2	Randomized trials	No limitations	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)	14/287 (5%)	4/285 (1.4%)	RR 3.41 (1.13 to 9.12)		⊕⊕⊕◯ Moderate	6
Life threatening adverse events[163] (Objective follow-up: 1-4 days[d])											
1[f]	Randomized trials	No limitations[g]	No important inconsistency	No uncertainty	Imprecise or sparse data (-2)[j]	3/35 (8,6%)	0/71 (0%)	RR 14[c] (0.74 to 263.78)	90/1 000 (10 less to 180 more)	⊕⊕◯◯ Low	9
Relapsed at follow-up (ITT analysis)[163, 162] (Objective (urine analysis) follow-up: 12 months)											
2[a]	Randomized trials	No limitations[b]	No important inconsistency	No uncertainty[m]	Imprecise or sparse data (-1)	74/86 (86%)	109/121 (90,1%)	RR 0.97³ (0.88 to 1.08)	30/1 000 less (110 less to 70 more)	⊕⊕⊕◯ Moderate	5
Retention at 12 months[163, 162] (Objective follow-up: 12 months)											
2[a]	Randomized trials	No limitations[b]	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)	35/86 (40,7%)	43/121 (35,5%)	RR 0.95[c] (0.69 to 1.30)	20/1 000 less (110 less to 110 more)	⊕⊕⊕◯ Moderate	5

[a]   The countries in which the 2 studies were conducted are: USA (1), Australia (1), both trials were conducted with inpatients.
[b]   In both studies method of allocation concealment was not stated, 1 study was single blind (patients blind) and the other one no blindness
[c]   Fixed effect model
[d]   Length of treatment
[e]   The outcome is not relevant in this context
[f]   The study was conducted in the USA in inpatient setting
[g]   Method of allocation concealment not stated, no blindness
[h]   Only one study and data based on self-reporting
[i]   Based on self-reporting and no dose response effect shown by other 2 RCTs for withdrawal symptoms and duration
[j]   Only one study and few participants (106)
[k]   This is a relevant outcome
[l]   Dose response effect shown by other 2 RCTs comparing different doses
[m]   Data based on study with very high proportion of patients lost to follow-up
[n]   Only two studies, few participants (78)