Alpha-2 agonists for long-term sedation during mechanical ventilation in critically ill patients

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Authors' objectives

Background: Sedation reduces patient levels of anxiety and stress, facilitates the delivery of care and ensures safety. Alpha-2 agonists have a range of effects including sedation, analgesia and antianxiety. They sedate, but allow staff to interact with patients and do not suppress respiration. They are attractive alternatives for long-term sedation during mechanical ventilation in critically ill patients.

Objectives: To assess the safety and efficacy of alpha-2 agonists for sedation of more than 24 hours, compared with traditional sedatives, in mechanically-ventilated critically ill patients.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 10, 2014), MEDLINE (1946 to 9 October 2014), EMBASE (1980 to 9 October 2014), CINAHL (1982 to 9 October 2014), Latin American and Caribbean Health Sciences Literature (1982 to 9 October 2014), ISI Web of Science (1987 to 9 October 2014), Chinese Biological Medical Database (1978 to 9 October 2014) and China National Knowledge Infrastructure (1979 to 9 October 2014), the World Health Organization international clinical trials registry platform (to 9 October 2014), Current Controlled Trials metaRegister of controlled trials active registers (to 9 October 2014), the ClinicalTrials.gov database (to 9 October 2014), the conference proceedings citation index (to 9 October 2014) and the reference lists of included studies and previously published meta-analyses and systematic reviews for relevant studies. We imposed no language restriction.

Selection criteria: We included all randomized and quasi-randomized controlled trials comparing alpha-2 agonists (clonidine or dexmedetomidine) versus alternative sedatives for long-term sedation (more than 24 hours) during mechanical ventilation in critically ill patients.

Data collection and analysis: Two review authors independently assessed study quality and extracted data. We contacted study authors for additional information. We performed meta-analyses when more than three studies were included, and selected a random-effects model due to expected clinical heterogeneity. We calculated the geometric mean difference for continuous outcomes and the risk ratio for dichotomous outcomes. We described the effects by values and 95% confidence intervals (CIs). We considered two-sided P < 0.05 to be statistically significant.

Main results: Seven studies, covering 1624 participants, met the inclusion criteria. All included studies investigated adults and compared dexmedetomidine with traditional sedatives, including propofol, midazolam and lorazepam. Compared with traditional sedatives, dexmedetomidine reduced the geometric mean duration of mechanical ventilation by 22% (95% CI 10% to 33%; four studies, 1120 participants, low quality evidence), and consequently the length of stay in the intensive care unit (ICU) by 14% (95% CI 1% to 24%; five studies, 1223 participants, very low quality evidence). There was no evidence that dexmedetomidine decreased the risk of delirium (RR 0.85; 95% CI 0.63 to 1.14; seven studies, 1624 participants, very low quality evidence) as results were consistent with both no effect and appreciable benefit. Only one study assessed the risk of coma, but lacked methodological reliability (RR 0.69; 95% CI 0.55 to 0.86, very low quality evidence). Of all the adverse events included, the most commonly reported one was bradycardia, and we observed a doubled (111%) increase in the incidence of bradycardia (RR 2.11; 95% CI 1.39 to 3.20; six studies, 1587 participants, very low quality evidence). Our meta-analysis provided no evidence that dexmedetomidine had any impact on mortality (RR 0.99; 95% CI 0.79 to 1.24; six studies, 1584 participants, very low quality evidence). We observed high levels of heterogeneity in risk of delirium (I² = 70%), but due to the limited number of studies we were unable to determine the source of heterogeneity through subgroup analyses or meta-regression. We judged six of the seven studies to be at high risk of bias.

Authors' conclusions: In this review, we found no eligible studies for children or for clonidine. Compared with traditional sedatives, long-term sedation using dexmedetomidine in critically ill adults reduced the duration of mechanical ventilation and ICU length of stay. There was no evidence for a beneficial effect on risk of delirium and the heterogeneity was high. The evidence for risk of coma was inadequate. The most common adverse event was bradycardia. No evidence indicated that dexmedetomidine changed mortality. The general quality of evidence ranged from very low to low, due to high risks of bias, serious inconsistency and imprecision, and strongly suspected publication bias. Future studies could pay more attention to children and to using clonidine.


Bibliographic details

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