APPENDIX II: CHARACTERISTICS OF THE INCLUDED STUDIES

Table 2. Characteristics of the Included Systematic Reviews and Meta-analyses

Objectives/Scope	Type of primary studies	Population/ Medical context	Intervention	Comparator	Outcomes	Notes
1/5. Frazer et al. 2013[7] – USA						
To evaluate the differences in clinical outcomes between benzodiazepine and non-benzodiazepine sedation in mechanically ventilated adult ICU patients. Systematic review and meta-analysis of randomized controlled trials	RCTs only • A total of 6 trials, were included in the review; of which, 4 trials evaluated dexmedetomidine • Trials were published between 1997 and 2012 • A total of 1,235 patients contributed to mortality analysis	The review included trials on adult medical or surgical ICU patients receiving invasive mechanical ventilation and administration of IV sedation. Studies on cardiac or critically ill patients were excluded	• Non-benzodiazepine: o Dexmedetomidine (4 trials) o 1% propofol (2 trials)	Benzodiazepine: • Midazolam (4 trials) • Lorazolam (2 trials)	• ICU length of stay • Duration of mechanical ventilation • Delirium prevalence • All-cause mortality	The review included two studies that are common with other systematic reviews (Ruokonen et al. 2013[17] and Jakob et al. 2012[18])
2/5. Mo et al. 2013[6] – UK						
To evaluate the role of dexmedetomidine in the prevention and treatment of delirium in ICU patients. Systematic review of clinical trials	The review included 8 studies • 5 double-blind RCTs • 2 open-label RCTs • 1 observational study • Studies were published between 2007 and 2012	The review included only studies that used dexmedetomidine continuously for sedation in mechanically ventilated patients for at least 6 hours. Three studies were conducted on cardiac surgery patients	• Dexmedetomidine (various doses and regimens)	• Lorazepam (1 study) • Propofol or midazolam (3 studies) • Midazolam (2 studies) • Haloperidol (1 study) • Morphine (1 study)	• Delirium (incidence and/or duration)	The review included six studies that are common with other systematic reviews (Ruokonen et al. 2013[17], Jakob et al. 2012[18], Yapici et al. 2011[19], Reade et al. 2009[20], and Shehabi et al. 2009[21]).
3/5. Xia et al. 2013[8] – China						
To evaluate the difference between dexmedetomidine	RCTs only • A total of ten trials were included	The review included studies conducted in ICU settings and	• Dexmedetomidine (various doses and regimens)	• Propofol	• ICU length of stay • Duration of mechanical	The review included one study that are common with other

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Objectives/Scope	Type of primary studies	Population/ Medical context	Intervention	Comparator	Outcomes	Notes
and propofol for adult ICU sedation. Systematic review and meta-analysis of randomized controlled trials	• Trials were published between 2003 and 2012 • A total of 1,202 patients contributed to mortality analysis	compared dexmedetomidine with propofol			ventilation • Delirium prevalence • All-cause mortality • Hypotension • Bradycardia • Hypertension	systematic reviews Jakob et al. 2012[18]
4/5. Lin et al. 2012[9] – China						
To evaluate the clinical safety and efficacy of dexmedetomidine for sedation in post-cardiac surgery patients. Systematic review and meta-analysis of controlled studies	The review included 11 studies • 4 double-blind RCTs • 1 open-label RCT • 2 prospective observational studies • 4 retrospective studies • Studies were published between 2003 and 2011	The review included studies conducted in ICU setting with cardiac surgery patients	• Dexmedetomidine (various doses and regimens)	• Propofol_5 trials • Propofol or midazolam_1 trial • Propofol, lorazepam, or midazolam_1 trial • Midazolam_1 trial • Morphine_2 trials • Propofol and midazolam_1 trial	• ICU length of stay • Hospital stay • Duration of mechanical ventilation • Delirium • Hospital mortality • Hypotension • Bradycardia • Hypertension	The review included two studies that are common with other systematic reviews (Abd Aziz et al. 2011,[22] and Shehabi et al. 2009[21]).
5/5. Tan et al. 2010[10] – Australia						
To evaluate the clinical outcome when using dexmedetomidine as a sedative and analgesic agent in adult ICU patient. Meta-analysis of RCTs	The review included 24 RCTs • 12 double-blinded • 1 single-blinded • 11 open-label • 1 blinding wasn't known	15 studies included high-risk elective surgery, and nine studies included non-elective critically ill patients	• Dexmedetomidine (various doses and regimens)	• Placebo_7 trials • Propofol_9 • Midazolam_5 • Lorazepam_3 • Morphine or haloperidol_2	• ICU length of stay • Hospital stay • Duration of mechanical ventilation • Delirium • Mortality • Hypotension • Bradycardia • Vomiting	The review included three studies that are common with other systematic reviews (Ruokonen et al. 2013,[17] Reade et al. 2009,[20] and Shehabi et al. 2009[21]).

Characteristics of the Included Randomized Controlled Trials

Study Objectives and Design	Inclusion Criteria, Sample Size, and Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
1/5. Aydogan et al. 2013[11] – Turkey			
To compare the sedation efficacy of dexmedetomidine versus midazolam. Parallel design RCT	• Pediatric patients between 12 and 18 years operated for scoliosis and admitted to the ICU • Patients were included if they required mechanical ventilation • Patient with history of delirium were excluded • A total of 32 patients were randomized	**Intervention:** • Dexmedetomidine (N =16) • 0.4 mcg/k/h **Comparator:** • Midazolam (N = 16) • 0.1 mg/kg/h	• Duration of ICU stay • Duration of mechanical ventilation • Pain • Fentanyl consumption
2/5. MacLaren et al. 2013[12] – USA			
To evaluate the efficacy of dexmedetomidine as transitioning agent from benzodiazepine when ICU patients are qualified for daily awakening. Parallel design RCT	• The trial included patients requiring mechanical ventilation and receiving a benzodiazepine infusion with an anticipated need of at least 12 additional hours of sedation. • Patient were qualified for daily awakenings • Exclusion criteria included: use of benzodiazepines for purposes other than sedation; use of neuromuscular blockers for more than 12 hours; use of epidural medications; active myocardial ischemia; second- or third-degree heart block; hemodynamic instability; active neuromuscular disease; Childs-Pugh class C liver disease; alcohol abuse within 6 months of study eligibility; baseline dementia; solid organ transplant; pregnancy; moribund state with planned withdrawal of life support.	**Intervention:** • Dexmedetomidine (N = 11) • started at 0.15 mcg/kg/ h and adjusted by 0.15 mcg/kg/h to a maximum of 1.5 mcg/kg/h, **Comparator:** • Midazolam (N = 12) • started at 1 mg/h and adjusted by 1 mg/h to a maximum of 10 mg/h.	Evaluation after at least 72 hours after extubation or tracheostomy, but before hospital discharge: • Post-ICU anxiety • Post-ICU depression • Acute stress disorder manifestation

Characteristics of the Included Randomized Controlled Trials

Study Objectives and Design	Inclusion Criteria, Sample Size, and Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
3/5. Prasad et al. 2012[13] – India			
To compare the sedation with dexmedetomidine and fentanyl in post-operative pediatric cardiac surgical patients. Parallel design RCT	• Patients between one and fourteen years operated for congenital cardiac conditions were included. • The included patients had an anticipated overnight ventilation • Exclusion criteria prevented the participation of patients undergoing re-operation or surgeries done under deep hypothermia. Patients were excluded also if they had severe liver dysfunction, second and third degree heart block, and if they potentially needed ventilation for more than 24 hours.	**Intervention:** • Dexmedetomidine (N = 30) • 0.5 mcg/kg/ h **Comparator:** • Fentanyl (N = 30) • 1 mcg/kg/ h	• Time to extubation • Ramsay sedation score
4/5. Huang et al. 2012[14] – China			
To compare the use of dexmedetomidine with midazolam for the sedation of patient with acute cardiogenic pulmonary edema and hypoxemia. Parallel design RCT	• The trial included patient with acute cardiogenic pulmonary edema and hypoxemia. • Patients were treated with non-invasive ventilation • Exclusion criteria prevented the participation poor respiratory state requiring immediate intubation; a clear alternative primary diagnosis; severely altered consciousness; patients requiring an immediate lifesaving intervention such as cardiopulmonary resuscitation, airway control, cardioversion or inotropic support; any patient requiring thrombolysis or percutaneous coronary intervention for acute ST-segment elevation myocardial infarction.	**Intervention:** • Dexmedetomidine (N = 33) • started at 0.2-0.7 mcg/kg/h **Comparator:** • Midazolam (N = 29) • started at 0.05 mg/kg/h and adjusted by 0.05-0.1 mg/kg/h	• Need for endotracheal intubation • Mean time to endotracheal intubation • Length of ICU stay • ICU mortality
5/5. Mirski et al. 2010[15] and Goodwin et al. 2013[16] – USA			
To compare the sedative efficacy of dexmedetomidine and propofol in ICU patients Cross-over design	• The trial included ICU patients who were awake, able to follow commands, and displaying restlessness or agitation. • Patients were included if they required new implementation of continuous i.v. sedation or an increase in opioid above analgesic dosing	**Intervention:** • Dexmedetomidine • Titrated to 0.2-0.7 mcg/kg/h **Comparator:** • Propofol • Titrated to 20-70 mcg/kg/min	• Change in the cognitive functions • Incidence of delirium • Need for adjunctive fentanyl