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DEXMEDETOMIDINE COMPARED TO VARIOUS METHODS OF SEDATIVE & ANALGESIC STRATEGY IN INTENSIVE CARE UNITS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background : Sedation and analgesia are essential for patients in critical care units who are critically ill and receiving mechanical ventilatory support. Sedation analgesia is routinely provided to prevent the pain, reduce their agitation and anxiety, improve the ventilation & synchronization. However, sedation plays a crucial role in critical care units, and the different methods of sedative analgesic therapies help to prevent the undersedation and oversedation.

Purpose : The purpose of this review is to assess the effectiveness of dexmedetomidine compared to various sedative and analgesic strategies in decreasing the adverse effects and enhancing patient outcomes in the intensive care units.

Materials & Methods: In this study, we conducted a systematic review and meta-analysis to collect relevant evidence for our recommendations and conclusions. We used powerful search engines, including PubMed, science direct, Cochrane Library, and, to gather information from 2014 to 2025. The primary outcome of this study is to identify the effectiveness of sedation and analgesic strategies compared to dexmedetomidine, as well as the duration of mechanical ventilation and length of stay in the intensive care unit. The secondary outcome includes the risk of adverse effects.

Results: A total of 18 studies were included in this review, comparing dexmedetomidine with other sedative and analgesic agents such as propofol, midazolam, fentanyl, clonidine, and remifentanil. The majority of studies demonstrated that dexmedetomidine was associated with shorter extubation times and reduced duration of mechanical ventilation compared to traditional sedatives. Several studies also indicated a decrease in ICU length of stay among patients receiving dexmedetomidine. In terms of safety, dexmedetomidine was generally well tolerated, with minimal respiratory depression. However, bradycardia and hypotension were noted as common adverse events, particularly at higher doses or in combination therapies. Comparisons with midazolam and fentanyl showed that dexmedetomidine had a lower incidence of delirium and improved patient-ventilator synchrony. Overall, dexmedetomidine consistently demonstrated favorable outcomes in terms of sedation quality, safety, and recovery compared to other sedative & analgesic strategies in ICU patient populations.

Conclusion : Dexmedetomidine offers effective sedation with faster extubation, reduced ICU stay, and minimal respiratory depression. Despite manageable cardiovascular effects, it remains a safe and beneficial option for critically ill patients requiring light, responsive sedation.

INTRODUCTION

Sedation and analgesia are essential for patients in critical care units who are critically ill and receiving mechanical ventilatory support. Sedation analgesia is routinely provided to prevent the pain, reduce their agitation and anxiety, improve the ventilation & synchronization. Pain can trigger catabolic hypermetabolism, which impacts wound healing, and risk of infections, hemodynamic instability, and prolongs the need for mechanical ventilation. Inadequate pain management can lead to psychological issues such as psychomotor agitation and delirium, and it can progress to coma. However, sedation plays a crucial role in critical care units, and the different methods of sedative analgesic therapies help to prevent the undersedation and oversedation. The goals of sedation are to reduce

agitation and ensure patient safety. [1 2] commonly used sedative drugs are benzodiazepines Midazolam, analgesic agents are fentanyl, anesthetic agents are propofol, dexmedetomidine.

Midazolam, a short-acting benzodiazepine, exerts its effects by binding to gamma-aminobutyric acid (GABA)_A receptors at the benzodiazepine binding site. These receptors are widely distributed in areas of the central nervous system, such as the reticular activating system (RAS), amygdala, medulla, cerebellum, and spinal cord, which are all involved in sedation, anxiety regulation, and muscle control. The drug enhances the inhibitory effects of GABA, leading to sedation, hypnosis, anxiolysis, anterograde amnesia, muscle relaxation, and anticonvulsant activity. Midazolam is typically administered as a continuous intravenous infusion at a dosage of 0.02 to 0.2 mg/kg/hour, depending on the patient's requirement. It is rapidly metabolized in the liver, primarily by the CYP3A4 enzyme system, and has an elimination half-life ranging from 1.5 to 2.5 hours. While effective, midazolam use can be associated with adverse effects, most notably respiratory depression and delirium, especially when used at high doses or in combination with other central nervous system depressants. [3]

Propofol has become a widely preferred sedative agent in intensive care units (ICUs) due to its favorable pharmacological action compared to benzodiazepines. The major advantages include rapid onset of action, ease of titration, rapid and smooth recovery, and complete elimination from the body within four hours. Additionally, propofol has antiemetic, antipruritic, and bronchodilator effects, making it highly suitable for short-term and procedural sedation. Propofol exerts its sedative and hypnotic effects primarily by enhancing the activity of GABA. One of the most common complications is hypotension, which results from systemic vasodilation and myocardial depression, especially in patients with preexisting cardiovascular instability. Bradycardia may also occur due to its depressant effects on the autonomic nervous system. [4]

Fentanyl is a potent synthetic opioid widely used for pain management in critical care settings, including the ICU. It acts primarily on mu-opioid receptors located in regions of the central nervous system such as the periaqueductal gray matter, the descending pain-modulating pathways of the midbrain, and the spinal cord. These sites play key roles in altering pain perception and response. Fentanyl is approximately 50 times more potent than morphine, providing powerful analgesic effects with a relatively rapid onset. It is commonly administered via intravenous infusion at doses of 1–2 mcg/kg/hour. The drug undergoes hepatic metabolism, and its elimination half-life ranges from 3 to 5 hours, though this may be prolonged in cases of organ dysfunction or with continuous use. Fentanyl is associated with adverse effects, including respiratory depression and hypotension. [5, 6]

Dexmedetomidine is a selective alpha-2 adrenergic receptor agonist that provides both sedative and analgesic effects primarily through its action on receptors located in the locus coeruleus, a region in the brainstem involved in arousal and alertness. One of its features is that patients receiving a dexmedetomidine infusion remain easily arousable, can follow commands, and often cooperate during mechanical ventilation, making it especially useful in ICU settings. The sedation produced by dexmedetomidine closely mimics non-rapid eye movement (NREM) sleep, which is thought to help preserve cognitive and immune functions in critically ill, sleep-deprived patients. Despite providing adequate levels of sedation, dexmedetomidine is associated with minimal respiratory depression, which offers a significant safety advantage over other sedative agents. However, hypotension and bradycardia are commonly reported cardiovascular side effects. Avoid the loading dosage to prevent the side effects. The standard maintenance infusion is 0.2–0.7 µg/kg/hour for ongoing sedation. Dexmedetomidine is widely used both in the operating room and intensive care unit for procedural and long-term sedation. [7 8]

The main objectives of this systematic review and meta-analysis are to critically evaluate and compare the dexmedetomidine versus various combinations of sedative and analgesic infusion strategies to decrease the adverse effects and increase the clinical outcomes.

MATERIAL AND METHODS

This systematic review and meta-analysis were carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The literature search covered studies published between 2014 and 2025. Utilizing the following keywords: "dexmedetomidine", fentanyl analgesia," "sedation therapy in ICU", propofol," "midazolam," "critically ill mechanical ventilated patients", "combination of sedative analgesia drugs", "intensive care unit," We systematically searched and screened articles from the following electronic databases: PubMed, ScienceDirect, Cochrane Library, and ClinicalTrials.gov. All retrieved records were evaluated based on predefined eligibility criteria, and duplicates were removed before screening.

Eligibility criteria

Only studies available as full-text articles were considered for inclusion, with no restrictions on language. Eligible studies met the following criteria: Evaluated and compared dexmedetomidine with either midazolam or in combination with fentanyl, propofol, or other sedative-analgesic regimens, including midazolam-fentanyl combinations or similar multimodal sedation strategies; Included adult patients admitted to the intensive care unit (ICU) who required mechanical ventilatory support; Reported at least one clinically relevant outcome such as ICU length of stay, duration of mechanical ventilation, time to extubation, or weaning time from ventilatory support; Employed a randomized controlled trial (RCT) design.

RESULTS

The selection process for eligible studies is outlined in Figure 1 (PRISMA flow diagram). Initially, 497 records were identified through database searches. After removing 383 records due to duplication and irrelevance based on title and abstract screening, 114 articles were identified as potentially relevant to the study objectives. During further screening, an additional 78 articles were excluded based on the title and abstract review. This left 36 full-text articles for eligibility assessment. Out of these, 18 studies were excluded for the following reasons: 12 were retrospective or non-randomized studies, and 6 were secondary analyses from previous trials that lacked clear methodological details. Ultimately, 18 studies were included in this systematic review, consisting of 17 randomized controlled trials (RCTs), and 1 clinical guideline. These selected studies met the inclusion criteria and were incorporated into the final qualitative synthesis

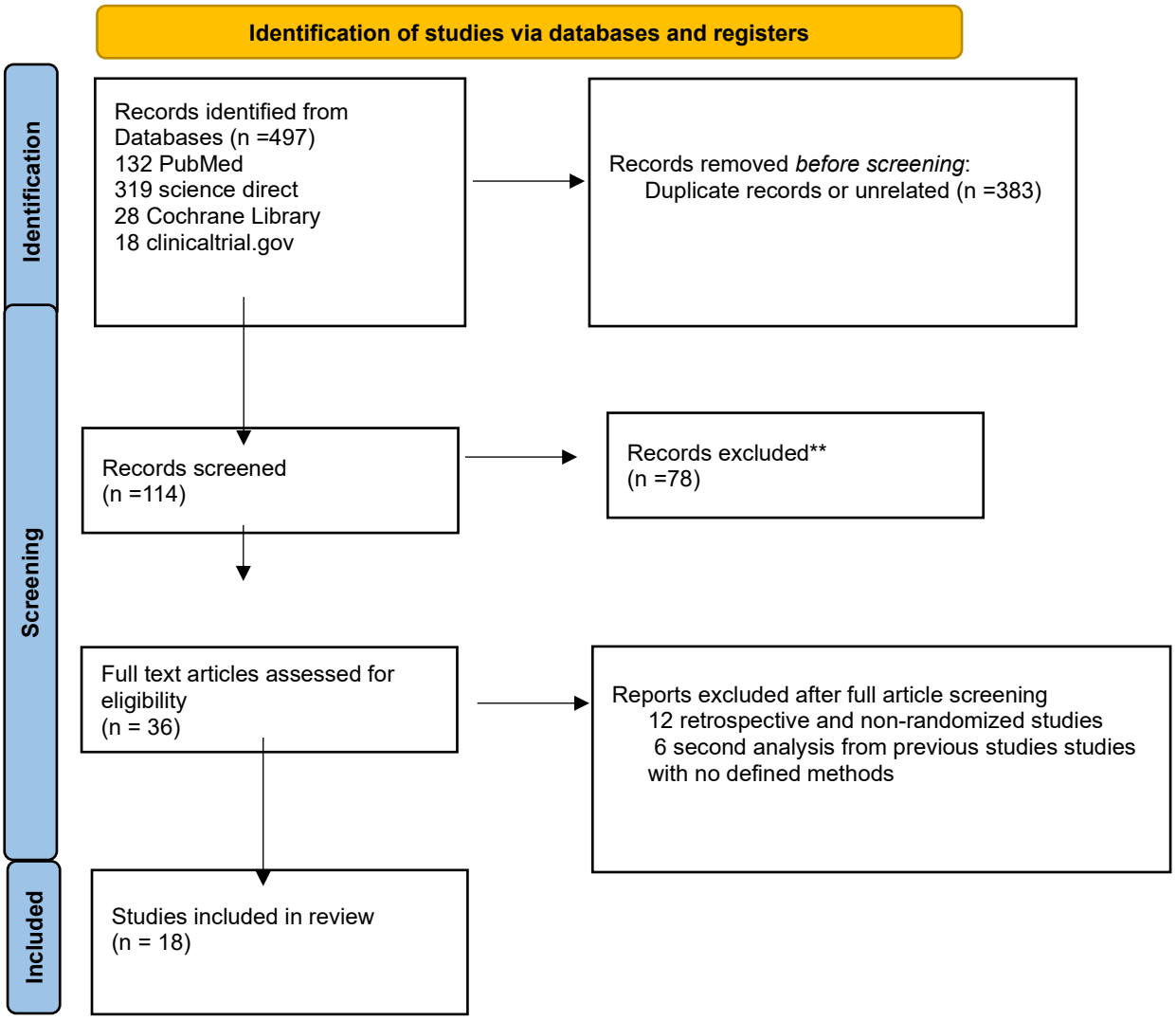

Figure: 1 PRISMA flow diagram for new systematic reviews

Table: 1 - Distribution of Sedation and Analgesic Regimens Evaluated in the Systematic Meta-analysis

Types of sedation & analgesic	No of Study
Dexmedetomidine infusion compared to propofol	**5**
Dexmedetomidine infusion clonidine compared to propofol	1
Dexmedetomidine compared to Fentanyl	3
Midazolam infusion compared to dexmedetomidine	3

dexmedetomidine and dexmedetomidine with ketamine	1
fentanyl combination with midazolam	1
dexmedetomidine	1
midazolam, compared to dexmedetomidine, and propofol	2
Intraoperative Infusion of Dexmedetomidine, Fentanyl, and Remifentanil	1
Number of studies	**18**

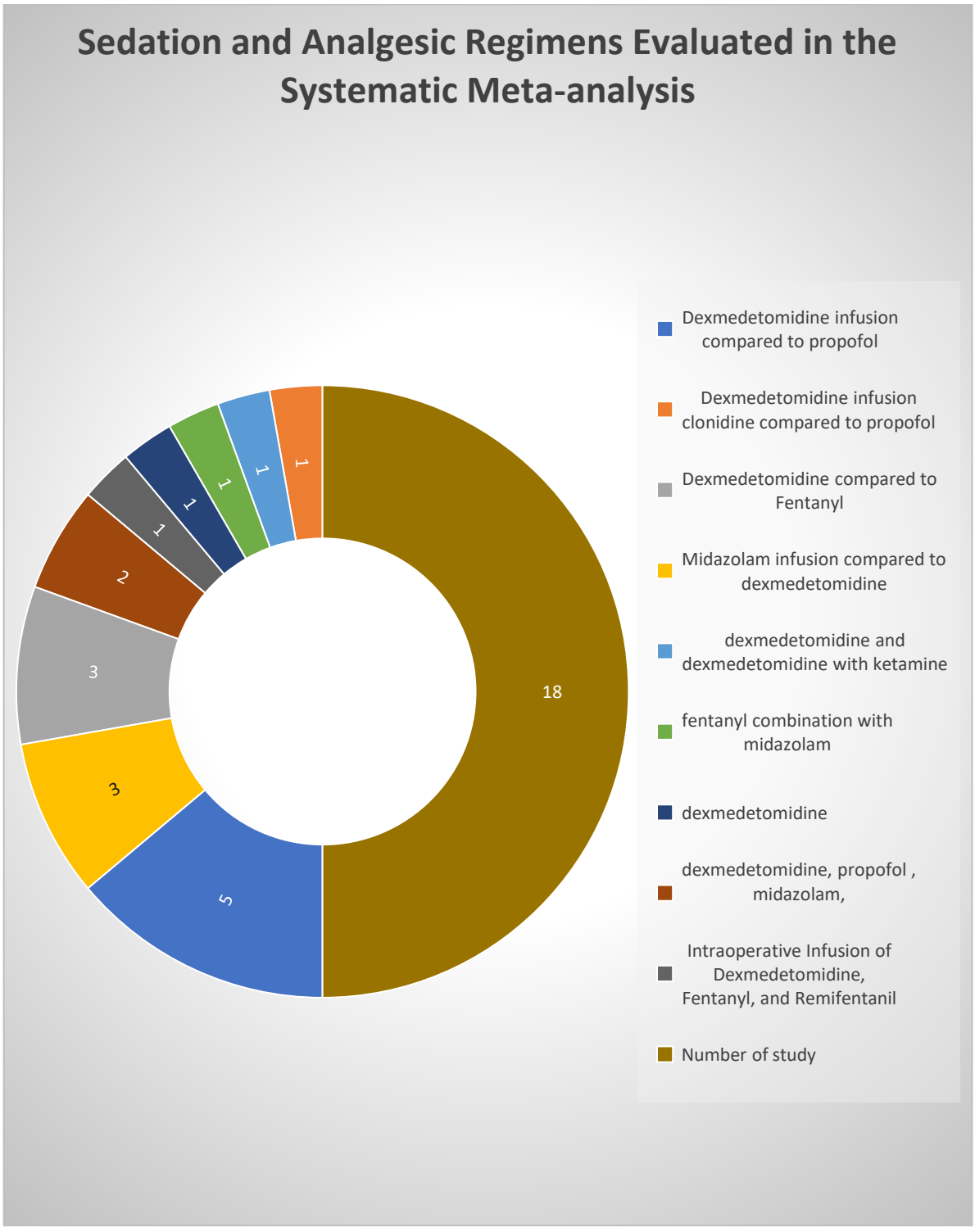

Figure. 2: Distribution of Sedation and Analgesic Regimens Evaluated in the Systematic Meta-analysis

Table: 2. Overview of the articles that contributed to the development of this systematic review and meta-analysis.

S.N	Authors and Publication Year	Study Title	study design	study participant	comparison / Interventions drugs	Results /conclusion
1	**Niharika Mustari et al., 2025 [9]**	Comparative study of efficacy of dexmedetomidine and propofol for sedation in intensive care unit	A prospective, randomized, double blinded and comparative study.	age 18- 60 years, patients who required mechanical ventilation sedation therapy	Group D: dexmedetomidine: 0.7 - 1mcg/kg/hr, Group P: Propofol: 25-75mcg/kg/hr	Dexmedetomidine serves as a highly effective alternative to conventional ICU sedatives like propofol and benzodiazepines. It enables conscious sedation without notable respiratory depression, supports hemodynamic stability, decreases the need for additional analgesics, allows for earlier patient discharge and may be more cost-effective.
2	**Timothy S. Walsh et al., 2025 [10]**	Dexmedetomidine-or Clonidine-Based Sedation Compared with Propofol in Critically Ill Patients TheA2B Randomized Clinical Trial	Pragmatic, open-label randomized clinical trial	Aged 18 years or older Receiving mechanical ventilation, Sedated with propofol, either alone or in combination with an opioid, following intubation Within 48 hours of the initiation of mechanical ventilation	dexmedetomidine 0.7-1.4µg/kg/h., clonidine- 1.0- 2 mcg/kg/h	Among critically ill patients, neither dexmedetomidine nor clonidine demonstrated a shorter duration to successful extubation compared to propofol

3	**Mohammed Sabir, Mirza Najeem Baig., 2023 [11]**	A better drug for extubation-dexmedetomidine or fentanyl	A randomized prospective double-blind study was conducted in a randomized open labeled manner	We selected forty adults, ages 18 to 60, of all genders, who had been mechanically ventilated for under 96 hours to participate in the study drug infusion	dexmedetomidine at a rate of 0.2-0.7 mcg/kg/h Fentanyl at the rate of 1-2 mcg/kg/h	Dexmedetomidine provided greater hemodynamic stability and a shorter extubation time compared to fentanyl. It also allowed for easier arousability and showed no significant respiratory depression

Table: 2 (continued)

S. N	**Authors and Publication Year**	**Study Title**	**study design**	**study participant**	**comparison / Interventions drugs**	**Results /conclusion**
4	**Yongfang Zhou et al., 2022 [12]**	Sequential use of midazolam and dexmedetomidine for long-term sedation may reduce weaning time in selected critically ill, mechanically ventilated patients: a randomized controlled study	This single-center, randomized, open-label, controlled trial	Age between 18 and 80 years Expected to need mechanical ventilation ≥ 72 hours Receiving fentanyl for pain management Receiving midazolam for sedation	Midazolam was administered at a rate of 0.04 to 0.20 mg/kg/h. midazolam was switched to propofol at 0.5 to 3.0 mg/kg/h or midazolam was switched to dexmedetomidine at 0.2 to 0.7 µg/kg/h.	The sequential use of midazolam and dexmedetomidine for long-term sedation was an effective and safe sedation strategy and might provide clinically relevant benefits for selected critically ill, mechanically ventilated patients.

5	**Bikram K et al., 2022 [13]**	A comparative study of sedo-analgesic effect of dexmedetomidine and dexmedetomidine with ketamine in postoperative mechanically ventilated patients	Prospective, randomized, interventional clinical trial	Patients aged 18 to 65 years who underwent major abdominal or head and neck oncological surgeries and were transferred to the ICU for postoperative mechanical ventilation support.	Group KD: Dexmedetomidine 0.5 mcg/kg/h + ketamine 0.5 mg/kg/h Group DEX: Dexmedetomidine 0.5 mcg/kg/h alone	The combination of dexmedetomidine and ketamine was associated with a reduced occurrence of hypotension and bradycardia. The combination therapy of dexmedetomidine and ketamine can be used safely and effectively as a sedo-analgesic agent.
6	**C.G. Hughes et al., 2021 [14]**	Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis	double-blind, randomized, controlled trial	Adults admitted to a medical or surgical ICU with suspected or confirmed infection and requiring continuous sedation during mechanical ventilation were included.	Dexmedetomidine was administered at a dose range of 0.2 to 1.5 µg/kg/h, propofol - 5 to 50 µg/kg/min.	There was no significant difference in outcomes between patients sedated with dexmedetomidine and those with propofol among mechanically ventilated individuals with sepsis managed under standard light-sedation protocols.

Table: 2 (continued)

S.N	**Authors and Publication Year**	**Study Title**	**study design**	**study participant**	**comparison / Interventions drugs**	**Results /conclusion**

7	**Yahya Shehabi et al., 2019** [15]	Early Sedation with Dexmedetomidine in Critically Ill Patients	open-label, randomized trial	critically ill adults who required mechanical ventilation for less than 12 hours and required sedatives and analgesic therapy	dexmedetomidine - 1mcg/kg/hr, max 1.5mcg/kg/hr	Dexmedetomidine was insufficient alone or as the primary agent to achieve clinically desired target sedation levels and was associated with more reported adverse events than usual care.
8	**Bongjin Lee et al., 2019 [16]**	Efficacy and Safety of Fentanyl in Combination with Midazolam in Children on Mechanical Ventilation	This double-blind, parallel, two-Group randomized controlled trial	Patients between 2 months and 18 years of age who were placed on mechanical ventilators at the PICU were included as participant.	midazolam and the experimental drug fentanyl were 0.06 mg/kg/hr and 0.05 mL/kg/ hr	Combining fentanyl with midazolam is safer and more effective than midazolam alone for sedating mechanically ventilated children. While hypotension occurred in both groups, serious adverse effects like coma and ileus were not observed.
9	**Ahmed Said Elgebaly et al., 2018 [17]**	Sedation Effects by Dexmedetomidine versus Propofol in Decreasing Duration of Mechanical Ventilation after Open Heart Surgery	Prospective, Randomized controlled trial	Patients between the ages of 18 and 55 years Required mechanical ventilation upon ICU admission	Group D: dexmedetomidine 0.8 µg/kg/h., Group P: propofol infusion rate :1.5 mg/kg/h.	For patients undergoing mechanical ventilation following cardiovascular surgery, dexmedetomidine is a safe and equally effective sedative compared to propofol. It provides stable hemodynamic parameters and a comparable time to extubation.

Table: 2 (continued)

S.N	Authors and Publication Year	Study Title	study design	study participant	comparison / Interventions drugs	Results /conclusion
10	**Malik Rameez Rashid., 2017 [18]**	Comparative evaluation of midazolam, dexmedetomidine, and propofol as Intensive Care Unit sedatives in postoperative electively ventilated eclamptic patients	a prospective, randomized, observational study	Patients diagnosed with eclampsia Underwent cesarean section under general anesthesia for pregnancy termination Required mechanical ventilation in the postoperative period	Midazolam: 0.05–0.3 mg/kg/h Propofol: 2–8 mg/kg/h Dexmedetomidine: 0.2–1.2 µg/kg/h	Propofol, midazolam, and dexmedetomidine are all effective agents for achieving adequate sedation in patients undergoing elective mechanical ventilation, dexmedetomidine, in comparison to midazolam and propofol, significantly lowers heart rate and mean arterial pressure, reduces the need for opioids and antihypertensive medications in eclamptic patients, and shortens the overall duration of ICU stay
11	**Riham Hussein Saleh et al., 2016 [19]**	Randomized controlled comparative trial between low dose dexmedetomidine sedation and that of fentanyl in children after surgical procedures in surgical Pediatric Intensive Care Unit	randomized double blinded study	age 1- 10 years Pediatric patients undergoing various surgical procedures Require postoperative mechanical ventilation, analgesia and sedation during the postoperative period	fentanyl at l mcg/kg/h (Fen Group), dexmedetomidine 0.3-lmcg/kg/h (Dex Group)	In mechanically ventilated pediatric patients, low-dose dexmedetomidine offers sufficient sedation and facilitates earlier extubation compared to fentanyl.

Table: 2 (continued)

S. N	Authors and Publication Year	Study Title	study design	study participant	comparison / Interventions drugs	Results /conclusion

12	**Jin Woo Choi et al., 2016 [20]**	Comparison of an Intraoperative Infusion of Dexmedetomidine, Fentanyl, and Remifentanil on Perioperative Hemodynamics, Sedation Quality, and Postoperative Pain Control	A prospective, randomized, double-blind study	Female patients between 18 and 60 years of age Classified as ASA physical status I or II Planned for laparoscopic total hysterectomy under general anesthesia	fentanyl: 0.4mcg/kg/hr, remifentanil: 0.08mcg/kg/min, dexmedetomidine: 0.5mcg/kg/hr	At sedative doses, dexmedetomidine provided superior postoperative hemodynamic stability compared to fentanyl or remifentanil, while offering comparable analgesic effects. Additionally, it allowed patients to remain aware during sedation in the post-anesthesia care unit (PACU).
13	**Giorgio Conti et al., 2016** [21]	Effects of dexmedetomidine and propofol on patient-ventilator interaction in difficult to-wean, mechanically ventilated patients: a prospective, open-label, randomized, multicenter study	prospective, open-label, randomized clinical trial	Adults admitted to the Intensive Care Unit (ICU) Had previously undergone one unsuccessful weaning attempt from mechanical ventilation	dexmedetomidine: 0.2–1.4 µg/kg/h., propofol: 0.3–4 mg/kg/h	In patients who failed their initial weaning trial, sedation using dexmedetomidine resulted in a significantly lower asynchrony index (AI) at 12 hours compared to propofol, despite similar RASS scores. These findings indicate that dexmedetomidine may improve patient-ventilator synchrony
14	**Xing Lu et al., 2016 [22]**	Clinical study of midazolam sequential with dexmedetomidine for agitated patients undergoing weaning to implement light sedation in intensive care unit	randomized, prospective study Using a computer-generated randomization	age from 18-80 years, patients who required sedatives or analgesics therapy	midazolam at a dose of 0.3- 3 mg/kg/hr., dexmedetomidine infusion rate: 0.2-1 mg/kg/hr	Sequential use of midazolam followed by dexmedetomidine effectively achieves targeted sedation in agitated ICU patients, while preserving respiratory and circulatory stability and minimizing adverse effects

Table: 2 (continued)

S.N	Authors and Publication Year	Study Title	study design	study participant	comparison / Interventions drugs	Results /conclusion
15	**Shikha Gupta et al., 2015 [23]**	Role of dexmedetomidine in early extubation of the intensive care unit patients	Randomized, open labeled manner	age 18- 60 years, post abdominal surgical patients who required mechanical ventilated support.	Group: I - dexmedetomidine infusion rate: 0.1-0.7mcg/kg/hr, Group: II- midazolam infusion rate: 0.04-02mg/kg/hr	Dexmedetomidine provides key advantages over midazolam for extubation, including faster extubation, better hemodynamic stability, easier arousal, and no respiratory depression.
16	**Shio Priye et al., 2015 [24]**	Dexmedetomidine as an adjunct in postoperative analgesia following cardiac surgery: A randomized, double-blind study	A prospective, randomized, double-blind clinical study	Patients aged above 18 years Underwent elective cardiac surgery Coronary artery bypass grafting (CABG) Valve repair or replacement Closure of atrial septal defect (ASD)	dexmedetomidine: 0.4 µg/kg/h., pain manage with IV fentanyl 25 µg	Continuous infusion of dexmedetomidine, even when administered without a loading dose, offers safe and effective supplemental analgesia. It lowers the need for opioid use and is associated with a reduced tendency for delirium, without causing adverse hemodynamic changes in patients undergoing cardiac surgery.

Table: 2 (continued)

S.N	Authors and Publication Year	Study Title	study design	study participant	comparison / Interventions drugs	Results /conclusion
17	**Prerana N Shah et al., 2014 [25]**	Comparison of post-operative ICU sedation between dexmedetomidine and propofol in Indian population	Phase III prospective, open-label, randomized clinical trial to evaluate the efficacy and safety of the intervention	Patients who require post-operative mechanical ventilator support or patients who require post-operative sedation and analgesic therapy	Dexmedetomidine-1 mcg/kg loading dose over 10 minutes, maintenance infusion of 0.2–0.7 mcg/kg/h propofol - 0.3mg/kg/hr	Patients on propofol produce more analgesics compared to those on dexmedetomidine. Dexmedetomidine infusion proved to be a safe and effective sedative-analgesic in the postoperative ICU setting.
18	**Vinit K. Srivastava et al., 2014 [26]**	Comparison of Dexmedetomidine, Propofol and Midazolam for Short-Term Sedation in Postoperatively Mechanically Ventilated Neurosurgical Patients	A prospective, randomized control, patient-blinded study	Adult patients aged between 20 and 65 years Classified as ASA physical status I, II, or III Scheduled for elective neurosurgical procedures patients who required mechanical ventilation in the postoperative period	dexmedetomidine 0.4-0.7 mcg/kg/h., propofol-1-3 mg/kg/h., Midazolam - 0.08 mg/kg/h.	Dexmedetomidine is a highly effective and safe sedative for neurosurgical patients on mechanical ventilation. It maintains excellent hemodynamic stability and offers an extubation time comparable to propofol, while also significantly reducing postoperative fentanyl requirements.

Table: 3 Summary of Comparison in Effects of dexmedetomidine versus other Sedative analgesic Strategies on Ventilation Duration and ICU Length of Stay

Study Author	Sedatives & analgesic Groups	Mean Time of Extubation / duration of ventilation	Mean Time of ICU Stay	P value

Niharika Mustari et al., 2025	Dexmedetomidine	N/A	N/A	N/A
	Propofol	N/A	N/A	N/A
Ahmed Said Elgebaly et al.2018	Dexmedetomidine (**n= 25)**	N/A	8.65±0.88	0.09
	Propofol **(n= 25)**	N/A	9.1±1.22	
C.G. Hughes et al., 2021	Dexmedetomidine	N/A	N/A	
	Propofol	N/A	N/A	
Giorgio Conti et al., 2016	Dexmedetomidine (N=16)	24.5- 118.7 hr	2.2–8.5 days	p= 0.958
	Propofol (N=10)	24.7–113.0 hr	5.0–24.8 days	
Vinit K. Srivastava et al., 2014	Dexmedetomidine (n=30)	12.03±3.13	N/A	0.6011
	Propofol (n=30)	12.86±3.52	N/A	
	Midazolam (n=30)	12.72±3.20	N/A	
Mohammed Sabir et al., 2023	Dexmedetomidine (n=20)	24.410±1.7731	N/A	0.0230
	Fentanyl (n=20)	31.33±3.2337	N/A	
Uma Srivastava et al., 2014	Dexmedetomidine (n=35	19 (14-28) hours	N/A	
	Clonidine (n=32)	20 (17-30) hours	N/A	
Xing Lu et al., 2016	Midazolam With Dexmedetomidine (N=40)	3.0 ± 1.5	5.4 ± 2.1	< 0.05
	Midazolam (N=40)	4.3 ± 2.2	8.0 ± 1.4	
Malik Rameez Rashid et al., 2017	Midazolam (n=32)	18 (6-67) hours	44.6 (33.5-52)	0.8203
	Propofol (p=34)	18.4 (7-91) hours	58.8 (41-73.25)	
	Dexmedetomidine(d=31)	16.9 (5-74) hours	52.5 (39.75-68)	
Vinit K. SriVastava et al., 2014	Dexmedetomidine (N=29)	N/A	N/A	
	Midazolam (N=29)	N/A	N/A	
	Propofol (N=29)	26.13±5.32	N/A	p<0.05
Jin Woo Choi et al., 2016	Fentanyl (n=30)	N/A	N/A	
	Remifentanil (n=30)	N/A	N/A	
	Dexmedetomidine (n=30)	N/A	N/A	
José Domingo López Castilla	Midazolam/fentanyl (N=43)	24.2 21 min	N/A	(P < .001)
	propofol/remifentanil(N=39)	230 102 min	N/A	
Riham Hussein Saleh et al., 2016	Fentanyl (n=25)	210–390 min	N/A	P value <0.001
	Dexmedetomidine (n=25)	85–265 min	N/A	N/A
Yong fang Zhou et al., 2022	Midazolam with Dexmedetomidine (N=77)	≥ 5 days 43 < 5 days 34	N/A	N/A
	Midazolam with propofol (n=78)	≥ 5 days 41 < 5 days 37	N/A	N/A
	Midazolam (n=73)	≥ 5 days 39 < 5 days 34	N/A	N/A

N/A: Not studied or not data available

Table: 4. Summary of Complications Related to Sedation Reported in Selected Clinical Studies

		Adverse effects			
Study	**sedatives**	**Hypotension**	**Bradycardia**	**Respiratory**	**Delirium**

				depression	
Uma Srivastava et al., 2014	Dexmedetomidine infusion (n =35)	3	3		N/A
	clonidine (n =35)	11	4		
Ahmed Said Elgebaly, Mohab Sabry et al., 2018	Dexmedetomidine **(n= 25)**	N/A	N/A	N/A	N/A
	Propofol **(n= 25)**	N/A	N/A	N/A	N/A
Xing Lu et al., 2016	Midazolam With Dexmedetomidine (N=40)	N/A	N/A	N/A	8
	Midazolam (N=40)	N/A	N/A	N/A	18
Prerana N Shah et al., 2014	Dexmedetomidine **(n= 15)**	91.46± 11.22	N/A	N/A	
	Propofol **(n= 15)**	88.36± 5.41	N/A	N/A	
Shio Priye et al., 2015	Dexmedetomidine (n=32)	N/A	N/A	N/A	1
	Fentanyl (n=32)	N/A	N/A	N/A	5
Giorgio Conti et al., 2016	Dexmedetomidine (N=16)	N/A	1	N/A	N/A
	Propofol (N=10)	N/A	1	N/A	N/A
Bongjin Lee et al., 2019	Midazolam (n=20)	2	N/A	N/A	N/A
	Midazolam combination with Fentanyl (n=18)	2	N/A	N/A	N/A
TimothyS.Walsh et al., 2025	Dexmedetomidine (n=457)	N/A	N/A	N/A	33%
	Clonidine (n=476)	N/A	N/A	N/A	33%
	Propofol (n=471)			N/A	20%
Jin Woo Choi et al., 2016	Fentanyl (n=30)	1	1	N/A	
	Remifentanil (n=30)	2	3	N/A	N/A
	Dexmedetomidine (n=30)	1	N/A	N/A	N/A
José Domingo López Castilla	Midazolam/fentanyl (N=43)	1	N/A	N/A	N/A
	propofol/remifentanil(N=39)	N/A	N/A	5	N/A
Yong fang Zhou et al., 2022	Midazolam with Dexmedetomidine (N=77)	4	1		15
	Midazolam with propofol (n=78)	2	1	N/A	23
	Midazolam (n=73)	0	0	N/A	32

N/A: Not studied or not data available

(Table:1) summarizes the meta-analysis incorporated a total of 18 studies evaluating different sedation and analgesic approaches in critical care settings. The most frequently assessed strategy was the comparison of dexmedetomidine infusion versus propofol, with six studies focusing on this contrast. Three studies examined dexmedetomidine in relation to fentanyl, while two studies each evaluated midazolam compared to dexmedetomidine, midazolam plus propofol, and dexmedetomidine used alone. Other strategies, including combinations such as dexmedetomidine with ketamine, fentanyl with midazolam, and intraoperative infusions

involving multiple agents like remifentanil, were each explored in one study. This distribution highlights the predominant research interest in dexmedetomidine-based sedation protocols, comparison to other sedative and analgesics in the intensive care units.

(Table 2) presents a comprehensive highlight the key studies that contributed to the formulation of this systematic review and meta-analysis. the findings reveal consistent patterns in the clinical performance of dexmedetomidine compared to other commonly used sedatives and analgesics in intensive care settings.

Dexmedetomidine versus Propofol: Research from Mustari et al. 2025 [9] and Elgebaly et al. 2018 [17] demonstrated that dexmedetomidine performs on par with propofol in maintaining adequate sedation. Additionally, dexmedetomidine was associated with advantages such as improved cardiovascular stability, reduced use of opioids, and the ability to maintain a lighter, more cooperative sedation state. In contrast, findings from Walsh et al. 2025 [10] and Hughes et al. 2021[14] indicated no meaningful difference in the time to extubation or overall clinical outcomes between the two agents, suggesting similar efficacy under standard care protocols.

Dexmedetomidine versus Midazolam: Studies conducted by Srivastava et al. 2014 [26] and Gupta et al. 2015 [23] found that dexmedetomidine allowed for quicker extubation and better patient responsiveness compared to midazolam. It was also associated with fewer respiratory complications. Furthermore, the sequential use of midazolam followed by dexmedetomidine, as investigated by Xing Lu et al. 2016[22], was found to enhance sedation effectiveness and maintain physiological stability in critically ill patients.

Dexmedetomidine versus Opioid Analgesics (Fentanyl/Remifentanil): Evidence from Sabir et al. 2023[11] and Saleh et al. 2016[19] showed that dexmedetomidine led to more favorable outcomes than fentanyl, including shorter ventilation times, greater hemodynamic control, and fewer side effects, particularly in pediatric and adult populations. Similarly, the study by Choi et al. 2016[20] revealed that dexmedetomidine offered improved postoperative stability compared to both fentanyl and remifentanil.

Dexmedetomidine in Combination Therapies: Combination approaches, such as the use of dexmedetomidine with ketamine as seen in the study by Bikram K et al. 2022[13], showed a reduction in side effects like bradycardia and hypotension, supporting its safety in postoperative settings. Moreover, multimodal sedation strategies incorporating dexmedetomidine, as supported by findings from Choi et al. 2016[20] and Priye et al.2015[24] contributed to better analgesic control and lower opioid requirements during the recovery period.

(Table: 3) This review out of 18 articles 14 studies specifically reported on comparing dexmedetomidine with various sedative and analgesic agents in terms of their impact on extubation time and ICU stay duration.

In the study by Niharika Musutari et al. 2025,[9] a comparison between dexmedetomidine and propofol was made; however, no relevant outcome data were reported. Similarly, C.G. Hughes et al. 2021[14] did not provide measurable results for comparison.

In the trial by Ahmed Said Elgebaly and Mohab Sabry (2018), ICU stay was slightly shorter in patients receiving dexmedetomidine (8.65 ± 0.88 days) compared to those on propofol (9.1 ± 1.22 days), although this difference did not reach statistical significance ($P = 0.09$).

Giorgio Conti et al. (2016) reported similar extubation durations between dexmedetomidine (24.5–118.7 hours) and propofol (24.7–113.0 hours), with ICU stay ranging from 2.2–8.5 days and 5.0–24.8 days, respectively ($P = 0.958$), showing no significant difference.

Vinit K. Srivastava et al. (2014) compared dexmedetomidine, propofol, and midazolam, observing comparable extubation times across all three agents (approximately 12–13 hours), with no significant difference ($P = 0.6011$). In another comparison within the same study, midazolam alone was associated with a significantly longer extubation time (26.13 ± 5.32 hours) than dexmedetomidine ($P < 0.05$).

Mohammed Sabir et al. (2023) found that dexmedetomidine resulted in significantly faster extubation (24.41 ± 1.77 hours) compared to fentanyl (31.33 ± 3.23 hours), with a P value of 0.0230.

Uma Srivastava et al. (2014) compared dexmedetomidine and clonidine, reporting median extubation times of 19 hours and 20 hours, respectively. No significant difference was noted.

In the study by Xing Lu et al. (2016), a combination of midazolam with dexmedetomidine significantly reduced both extubation time (4.3 ± 2.2 hours) and ICU stay (5.4 ± 2.1 days) when compared to midazolam alone (8.6 ± 4.1 hours and 8.0 ± 6.4 days, respectively) ($P < 0.05$).

According to Malik Rameez Rashid et al. (2017), dexmedetomidine (16.9 hours) and propofol (14.8 hours) provided shorter extubation durations than midazolam (18 hours). ICU stay was also shorter with dexmedetomidine (5.2 days) compared to midazolam (8.4 days), though no statistical analysis was reported.

In a separate trial by Srivastava et al., midazolam was again associated with a significantly longer extubation time compared to dexmedetomidine ($P < 0.05$).

Jin Woo Choi et al. (2016) found that patients sedated with propofol had a shorter ICU stay (130 minutes) than those given remifentanil (230 minutes), which was statistically significant ($P < 0.001$).

José Domingo López Castilla et al. demonstrated that a dexmedetomidine-fentanyl combination provided a much faster extubation (24.2 ± 2.1 minutes) than a propofol-remifentanil regimen (100 minutes) ($P < 0.001$).

Riham Hussein Saleh et al. (2016) also reported that remifentanil significantly shortened extubation time (130 ± 20 minutes) compared to fentanyl (252 ± 30 minutes) ($P < 0.001$).

Lastly, Yong Fang Zhou et al. (2022) observed that patients receiving midazolam combined with dexmedetomidine had shorter ICU stays (<5 days) than those receiving midazolam with propofol (<8 days) or midazolam alone (>8

days), indicating favorable outcomes with dexmedetomidine-based regimens, although statistical data were not provided.

(Table: 4) Out of the 18 studies analyzed in this systematic review, 14 provided specific data on the adverse effects associated with the use of various sedative and analgesic agents in critically ill patients. These agents included dexmedetomidine, propofol, midazolam, fentanyl, remifentanil, and clonidine. Across the studies, hypotension emerged as a common side effect, particularly with dexmedetomidine. For instance, Prerana N. Shah et al. (2014) documented significant hypotension associated with dexmedetomidine (91.46 ± 11.22), while Uma Srivastava et al. (2014) observed three instances of hypotension in their cohort. Clonidine also demonstrated a higher incidence, with 11 cases reported, and remifentanil was associated with two cases of hypotension, as noted by Jin Woo Choi et al. (2016). In contrast, fewer occurrences of hypotension were observed with propofol, midazolam, and fentanyl combinations. Bradycardia was more frequently reported in patients administered dexmedetomidine, with three cases in the study by Uma Srivastava et al. and two additional cases in the study by Jin Woo Choi et al. Midazolam, whether used alone or in combination, also caused bradycardia, though less frequently, as seen in the two cases reported by Lee et al. Clonidine was linked to four cases of bradycardia. Respiratory depression was most notably associated with midazolam, with 18 cases reported by Xing Lu et al. (2016) and 32 cases identified in the study by Yong Fang Zhou et al. (2022). Fentanyl and remifentanil were also associated with this complication, albeit to a lesser extent, with three cases linked to remifentanil. In contrast, dexmedetomidine was consistently associated with a low incidence of respiratory depression, suggesting a more favorable respiratory safety profile. Regarding neurocognitive complications, midazolam was associated with a higher incidence of delirium. Yong Fang Zhou et al. observed delirium in 23 patients treated with midazolam, compared to 15 patients who received dexmedetomidine. Similarly, Timothy S. Walsh et al. (2025) reported delirium in approximately one-third of patients who were administered dexmedetomidine or clonidine, whereas the incidence was lower (20%) in those receiving propofol. Additionally, Shio Priye et al. (2015) noted that five patients in the fentanyl group developed delirium compared to only one case in the dexmedetomidine group. Overall, the adverse effect profiles varied significantly across the different agents, with dexmedetomidine demonstrating a relatively safer profile concerning respiratory function and delirium, despite a higher tendency toward cardiovascular effects such as hypotension and bradycardia.

DISCUSSION:

The findings of this review highlight comparative evaluation of sedative agents in intensive care units, dexmedetomidine as a preferable alternative to conventional drugs such as propofol, midazolam, and fentanyl. Evidence from multiple clinical studies supports the effectiveness and safety of dexmedetomidine across diverse ICU populations, including pediatric, cardiac, neurosurgical, and septic patients.

A prominent advantage of dexmedetomidine is its ability to facilitate earlier extubation compared to other agents. Studies by Saleh et al. [19] and Sabir et al. [11] demonstrated that dexmedetomidine resulted in early extubation and better hemodynamic stability than fentanyl in both adult and pediatric patients. Gupta et al. [23] similarly found that it enabled faster extubation without inducing respiratory depression.

In terms of sedation depth and analgesic requirements, Mustari et al. [9] reported higher Ramsay Sedation Scores and lower pain scores in patients receiving dexmedetomidine compared to propofol, indicating improved sedation quality with reduced need for supplemental analgesics. However, findings by Hughes et al. [14] and Walsh et al. [10] suggest that in septic or critically ill patients, both dexmedetomidine and propofol showed comparable clinical outcomes, such as ventilator-free days and overall mortality, underscoring the importance of individualized sedation strategies.

Dexmedetomidine's hemodynamic effects also contribute to its appeal in specific populations. Elgebaly et al. [17]and Choi et al. [20] noted its ability to provide stable blood pressure and heart rate, even in patients recovering from cardiac surgery. Rashid et al. [18] and Srivastava et al. [26] further confirmed that dexmedetomidine reduced mean arterial pressure and heart rate more effectively than midazolam or propofol, potentially decreasing the need for antihypertensive medications.

Its use has also been supported in pediatric and agitated ICU patients due to minimal respiratory depression and preservation of airway reflexes. This makes it particularly beneficial in patients at risk of respiratory compromise or requiring frequent neurological assessments. Conti et al. [21] demonstrated that dexmedetomidine significantly reduced ventilator asynchrony compared to propofol, leading to smoother weaning. Zhou et al. [22] and Lu et al. [15] further noted that sedation protocols involving midazolam followed by dexmedetomidine improved weaning success and reduced ICU stays.

An additional benefit of dexmedetomidine lies in its opioid-sparing properties. Priye et al. [24] observed a reduction in postoperative opioid requirements and delirium incidence following cardiac surgery, while Srivastava et al. [26] and Shah et al. [25] reported decreased fentanyl and analgesic needs in patients treated with dexmedetomidine. Furthermore, combination therapy with agents such as ketamine has shown potential in enhancing the safety profile of dexmedetomidine by reducing the frequency of bradycardia and hypotension, as shown by Bikram et al. [13].

In terms of the primary outcomes evaluated in this review sedation quality, mechanical ventilation duration, and ICU stay. The dexmedetomidine consistently demonstrated positive effects. It was frequently associated with shorter

mechanical ventilation times, earlier extubation, and reduced ICU lengths of stay. These outcomes are not only clinically beneficial but may also improve ICU throughput and reduce healthcare costs.

Regarding safety, dexmedetomidine was generally well-tolerated. While hypotension and bradycardia were among the most commonly reported side effects, especially with higher doses or combination regimens, these effects were usually manageable with appropriate clinical monitoring. One of the most significant advantages of dexmedetomidine over opioids and benzodiazepines is its minimal impact on respiratory function, allowing for safer sedation in patients requiring ventilatory support.

Overall, the findings from this review provide the clinical utility of dexmedetomidine as a safe and effective sedative option in the ICU. Its favorable respiratory profile, hemodynamic stability, and ability to support early extubation make it a valuable tool in optimizing critical care sedation strategies.

CONCLUSION

Dexmedetomidine provides effective and safe sedation in ICU patients, promoting faster recovery, earlier extubation, and a reduced ICU stay, with minimal respiratory impact and manageable side effects.

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