

## Comparison of Dexmedetomidine versus Propofol for Sedation In Mechanically Ventilated ICU Patients, Articles Review

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### ABSTRACT:

**Background:** sedating mechanically ventilated patients is an important pharmacologic therapy in ICU. Various sedative agents are available, propofol and dexmedetomidine could be mentioned.

**Objective:** This article was aimed to evaluate the comparison of dexmedetomidine and propofol for sedation of mechanically ventilated ICU patients.

**Methods:** survey of different published articles on the topic.

**Results:** Major results of the articles showed that length of hospital stay, time to extubation, arousability, delirium effects, analgesic requirement and hemodynamic instability was generally low in dexmedetomidine infused patients than patients infused with propofol.

**Conclusion:** Dexmedetomidine could be more advantageous than propofol for sedating mechanically ventilated ICU patients.

**Keywords:** Dexmedetomidine; Intensive care unit; Propofol; Sedation, mechanical ventilation

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### I. Introduction

The goal of sedation in critically ill patients under mechanical ventilation is to keep them calm and without agitation to maximize patient comfort and ventilator synchrony. There are several different classes of sedative medications available, each with distinct pharmacokinetic and pharmacodynamics properties, and different side-effect profiles that may limit their use. Therefore careful drug selection is helpful to improve patient outcomes and decrease overall time on sedation. Dexmedetomidine (Precedex™) and propofol (Diprivan™) have very different mechanisms of action and pharmacokinetic profiles that make them attractive sedative agents in this patient population (Wanat, Fitoussis, Boston et al., 2014).

The  $\alpha_2$  agonist, centrally acting dexmedetomidine is a new sedative and analgesic agent which is licensed and approved in 1999 in USA for post-operative intensive care sedation (Venn & Grounds, 2001). Dexmedetomidine was the first and only  $\alpha_2$  agonist drug approved for sedation in mechanically ventilated patients during the first 24 hours and in non-intubated patients prior to and/or during surgical or nonsurgical procedures. Lacking respiratory depression even with accidental over dosage gave it the advantage over other sedatives as benzodiazepines, opioids and propofol as all of them cause dose dependent respiratory depression (Ashraf & Ahmad, 2014).

Propofol is a sedative-hypnotic agent used mainly for induction or maintenance of anesthesia or sedation. Its rapid onset, short duration of action, and relatively low cost had made it to be the standard medication for sedation for long time, but it has an adverse effect profile that may be concerning in cardiovascular patients (Wanat et al., 2014). In developing countries like my country Eritrea, comparative analysis between old and new drugs is among the ignored areas in ICU. Judging the effectiveness of drugs will be impossible without comparative analysis especially in critical settings. It is therefore important to compare the new drug (dexmedetomidine) with relatively the old drug (propofol), so that effective drug will be advocated for sedating ICU patients.

### Objective

The aim of this article was to conduct articles review for evaluating the comparative sedative effects of dexmedetomidine versus propofol in mechanically ventilated ICU patients.

### II. Materials And Methods

Data was collected from different published articles which evaluated the comparative sedative effects of dexmedetomidine and propofol in ICU patients under mechanical ventilation. Internet assistance was the main source for collecting the articles especially websites like Pub Med and NCBI. Printed version articles were also utilized. Articles which were strictly adherent to the title were only included. Though there was difference

in sample size (study participants) between the articles, most of the articles used case-control study or clinical trials. Most of the articles are therefore related in methodological approach. More than forty-five articles were revised out of which nineteen were the most adherent to reflect the topic under review. Articles which were slightly far from the topic were not considered as priority for evaluation due to the fear of biasedness.

**Measurements/outcomes**

Most of the articles had focused in comparing effects of the drugs in reference to the following outcomes: ICU length of stay (LOS), requirement of a second sedative/analgesic agent, hemodynamic stability of patients and other related effects.

**III. Results And Discussion**

**3.1 Length of hospital/ICU stay, delirium effect and time to extubation,**

According to research by Wanat et al. (2014), Sedation with dexmedetomidine resulted in a significant reduction in time on mechanical ventilation than propofol; but, no difference was seen in ICU or hospital LOS and delirium effect between the two groups. When compared with propofol, dexmedetomidine sedation reduced incidence, delayed onset, and shortened duration of post-operative delirium(George, Natalie, Ludwik, et al.,2016).In contrast, similar study by Xia, Chen, Yao, et al. (2013), and Eremenko and Chemova (2014), have concluded that; for ICU patient sedation, dexmedetomidine may offer advantages over propofol in terms of decrease in the length of ICU stay and the risk of delirium. Similarly infusion of dexmedetomidine compared with propofol was found to have shorter duration and diminished

Severity of delirium in a study reported by Hollinger et al., 2017. Most of the studies collected are generally consistent in the better clinical benefits of dexmedetomidine over propofol in reference to length of hospital stay, time of extubation, duration of mechanical ventilation which is explanatory for the effectiveness of the drug and its early wash out. Dexmedetomidine was also found to have decreased incidence of delirium which explains its slight anxiolytic behaviour.

*Table 1. Tabular summary of comparing dexmedetomidine versus propofol as per year of study with respect to length of stay, Extubation time and Delirium effects.*

Year of study	Author(s)	Length of stay		Extubation time		Delirium effects	
		dexmedetomidine	propofol	dexmedetomidine	propofol	dexmedetomidine	propofol
2017	Hollinger et al					shorter	Longer
2016	Liu et al.	Better	Poorer				
2016	George et al.					lower	higher
2015	Karaman et al.			Faster	Delayed		
2014	Eremenko&Chemova	Lower	Higher			Low risky	higher
2014	Vinit et al.			Same	Same		
2014	Wanat et al.					No difference	No- d/ce
2013	Torbic et al.			Faster	Delayed		
2013	Xia, et al.	Lower	Higher			Low risky	higher
2001	Venn&Grounds			Faster	Delayed		

**3.2 Extra Sedative and/or Analgesic Consumption**

Higher incidence of analgesic consumption was seen with propofol-based sedation therapy compared to therapy with dexmedetomidine (Anger, Szumita, Baroletti et al., 2010). Conversely no statistically significant differences were noted between the drugs when assessing the outcomes of analgesic consumption (Marc, Whitney, Roger, et al., 2011). Another study has also revealed that Dexmedetomidine patients required significantly less analgesics for pain relief compared to propofol (Martin, Ramsay, Mantz et al., 2003 and Eremenko&Chemova, 2014).Venn and Grounds (2001) has also showed more than three times alfentanil to be consumed on the propofol received group compared with patients sedated with dexmedetomidine. Herr, Sum-Ping and England (2003) also indicated that, the extent of morphine use to be significantly low in the dexmedetomidine group. Only 28% of the dexmedetomidine patients required morphine for pain relief while ventilated versus 69% of propofol-based patients (p < 0.001). To maintain analgesia, Propofol patients required 4 times the mean dose of morphine(need more analgesics)than those of dexmedetomidine group throughout the study period in ICU,(Shah,Dongre,Patil,et al., 2014).The need for a second sedative agent to achieve optimal sedation was similar between both groups((24% of dexmedetomidine patients vs. 27% of propofol patients, P = .737(Wanat et al. , 2014). But in another similar study no extra sedation was required (Martin et al., 2003).In case of extra need of sedative and/or analgesics, though extra researches are needed to compare the sedative potency difference, current studies are conclusive enough for dexmedetomidine on its lower consumption of analgesics and this could probably be due to the intrinsic analgesic effect of the drug.

### 3.3 Hemodynamic & ventilatory stability and arousability

A research done on “Impact of a Protocol Advocating Dexmedetomidine Over Propofol Sedation” have found dexmedetomidine to have faster discontinuation of mechanical ventilation and is associated with greater hemodynamic stability and arousability, as such they advocated for the use of dexmedetomidine to be promoted than propofol. (Torbic, Papadopoulos, Manjourides, et al. 2013). Dexmedetomidine infused patients had low extubation times and high hemodynamic and respiratory functions stability as compared to propofol infused patients (Karaman, Abud & Tekgul, 2015, & Venn & Grounds, 2001). In other study done by Ashraf and Ahmad (2014) also, dexmedetomidine sedation provided more respiratory safety and heart rate stability as such they recommended it as a suitable alternative agent especially for the relatively longer procedures. Dexmedetomidine sedation was found to reduce the incidence of new-onset postoperative atrial fibrillation as compared to propofol (Liu et al. 2016)

Ufuk and his followers (2015) indicated in their study on obstructive sleep apnea patients that, Dexmedetomidine could be preferred as a safer agent with respect to respiratory function compared to propofol, especially in patients who are known to be susceptible to hypoxia and hypercarbia.

Blood pressure was maintained within normal range and respiratory rate and oxygen saturation was normal in dexmedetomidine given patients than propofol in which case patients had hypotension, tachycardia and unarousability (Martin et al., 2003, & Torbic et al., 2013). Using dexmedetomidine at a dose of 0.2 to 1.4 mg/kg/hour for intravenous sedation is safe in terms of hemodynamic stability and blood oxygenation for sedation during mechanical lung ventilation (Tarabrin, Shcherbakov, Gavrychenko, et al. 2014). Despite ventilation and intubation, patients sedated with dexmedetomidine could be easily roused to cooperate with procedures (e.g. physiotherapy, radiology) without showing irritation as compared to propofol (Venn & Grounds, 2001). These properties of maintained blood pressure and quick arousability, combined with the analgesic qualities and lack of respiratory depression seen with dexmedetomidine, have made it advantageous for patients at risk from myocardial ischemia. Sedation with dexmedetomidine was found to offer some advantages in terms of patient-ventilator synchrony compared to propofol in a study done by Conti and his colleagues in 2016. As expected studies are consistent on the hemodynamic stability of dexmedetomidine and the lack of respiratory depressions which are unlike in case of propofol. Little respiratory effect with dexmedetomidine explains its great importance in ventilation.

### 3.4 Patient and clinician satisfaction

Dexmedetomidine was found to be a safe and acceptable sedative agent for those requiring intensive care as per clinician’s and patient’s perspectives (Venn & Grounds, 2001). Similarly in a study by Martin et al. (2003) nurses judged that dexmedetomidine patients were easier to manage. This area of satisfaction is mostly ignored in clinical practice in our area as a tool for measuring effectiveness but yet it is an important parameter for evaluation.

**Table 2.** Tabular summary of comparing dexmedetomidine versus propofol as per year of study with respect to Hemodynamic stability, extra need of analgesics and arousability.

Year of study	Author(s)	Hemodynamic & ventilatory stability		Extra need of analgesics		arousability	
		dexmedetomidine	propofol	dexmedetomidine	propofol	dexmedetomidine	propofol
2017	Hollinger et al	Same	Same				
2016	Liu et al.	Better	Poorer				
2016	Conti et al.	Better	Poorer				
2015	Ufuk et al.	<b>Better</b>	<b>Poorer</b>				
2015	Karaman et al.	Better	Poorer				
2014	Ashraf & Ahmad	Better	Poorer				
2014	Eremenko & Chermova			Lower	Higher		
2014	Vinit et al.	Better	Poorer	Lower	Higher		
2014	Tarabrin et al.	Better	Poorer				
2014	Shah et al.			Lower	Higher		
2014	Wanat et al.			Lower	Higher		
2013	Torbic et al.	Better	Poorer			Better	poorer
2011	Marc et al.			No d/ce	No d/ce		
2010	Anger et al.			Lower	Higher		
2003	Herr et al.			Lower	Higher		
2003	Martin et al.			No d/ce	No d/ce	Fast	Delayed
2001	Venn & Grounds	Better	Poorer	Lower	Higher	Better	Poorer

#### IV. Conclusion and Recommendation

Even though further studies and systematic reviews are recommended for conclusive evidence, dexmedetomidine seems to be more advantageous than propofol for sedating mechanically ventilated patients in ICU.

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