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Hemodynamic Adverse Effects of Dexmedetomidine and Propofol in a Critically Ill Trauma and Surgical Population: A Retrospective Cohort

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ABSTRACT

Background: Propofol and dexmedetomidine may cause hemodynamic adverse effects (AEs) and more data are needed in a trauma and surgical population.

Objective: The objective of this study was to evaluate the rate of hemodynamic AEs requiring an intervention between dexmedetomidine and propofol in a critically ill trauma and surgical population.

Methods: This was a retrospective cohort study at a Level 1 trauma center. Intensive care unit patients admitted from October 1, 2017, through October 31, 2018, were divided into two groups: dexmedetomidine or propofol. The primary end point was the proportion of patients who required a therapeutic intervention for a hemodynamic AE within the first 24 hr of initiation of dexmedetomidine or propofol.

Results: A total of 800 charts were reviewed and 85 patients (dexmedetomidine [$n = 35$] and propofol [$n = 50$]) were included. The study population consisted of Caucasian (86%) males (61%) with a median age of 61 [interquartile range—IQR 48, 72], and 18% and 24% required antihypertensive and vasopressor agents, respectively. No difference in the primary outcome was observed (17 [49%] vs. 27 [54%], $p = .624$). There was no difference in the overall incidence of hemodynamic AE (18 [51%] vs. 30 [60%], $p = .433$). Dexmedetomidine patients had a greater decrease in median heart rate (HR) compared with the propofol (23 [IQR 16, 41] vs. 14 [IQR 5, 24] beats/min, $p = .002$).

Conclusions: The rate of hemodynamic AEs requiring therapeutic interventions was similar between dexmedetomidine and propofol in a critically ill trauma and surgical population; however, dexmedetomidine may be associated with a larger decrease in HR.

Key Words

Adverse effects, Dexmedetomidine, Hemodynamics, Propofol, Sedation

BACKGROUND

Critically ill patients on mechanical ventilation may require sedative agents for indications such as agitation, anxiety, and to relieve the stress of mechanical ventilation. Critically ill patients are more at risk for hemodynamic adverse effects (AEs) due to underlying disease-related processes, along with alterations in medication pharmacokinetics and pharmacodynamics and drug accumulation (Devlin et al., 2018). Based on the current clinical practice guidelines, both dexmedetomidine and propofol are recommended over benzodiazepines for agitation in mechanically ventilated adult intensive care unit (ICU) patients (Devlin et al., 2018). However, both propofol and dexmedetomidine are associated with hemodynamic AEs, such as hypotension and bradycardia (Erdman et al., 2014).

Direct comparisons between the two sedatives have not demonstrated a significant difference in the incidence of hemodynamic AEs (Chang et al., 2018; Elbaradie, El Mahalawy, & Solyman, 2004; Erdman et al., 2014; Nelson, Patel, & Hammond, 2020; Venn & Grounds, 2001). The PRODEX study showed a similar incidence of hypotension in patients sedated with propofol or dexmedetomidine, as well as a similar incidence of bradycardia (Jakob et al., 2012). Erdman et al. (2014) conducted a retrospective study assessing the hemodynamic AEs of

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C.R.N., M.D.C., L.A.F., and C.M. designed the study. C.R.N. performed literature search and data collection. C.M. completed statistical analysis. C.R.N,. M.D.C., L.A.F, and C.M. contributed to data interpretation. C.R.N. wrote the manuscript with input from all authors. M.D.C. and C.M. provided critical revisions of the manuscript. All authors approved the final version of the manuscript.

The authors declare no conflicts of interest.

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dexmedetomidine and propofol in neurocritical care patients. The primary outcome of incidence of a hemodynamic AE, defined as systolic blood pressure (SBP) <90 mmHg, mean arterial pressure (MAP) <65 mmHg, or heart rate (HR) <50 beats per minute (bpm), was 30% in each group. However, an intervention necessary to treat the hemodynamic AE was higher in the dexmedetomidine group than in the propofol group (84% vs. 62%) (Erdman et al., 2014).

To our knowledge, few studies have evaluated hemodynamic AEs of dexmedetomidine compared with propofol in trauma and surgical ICU patients. Chang et al. (2018) evaluated the difference in hemodynamics between dexmedetomidine and propofol in a randomized controlled trial of 60 surgical ICU patients. Cardiac index did not differ between groups, nor did the incidence of bradycardia or hypotension (Chang et al., 2018). In retrospective study, trauma ICU patients receiving higher doses of dexmedetomidine (>0.7 μg/kg/hr) experienced a higher rate of hypotension but no difference in bradycardia compared with standard doses of dexmedetomidine (≤0.7 μg/kg/hr) and propofol. This study also recorded hemodynamic AEs that required interventions and found a greater proportion of patients receiving standard doses of dexmedetomidine required a decrease or discontinuation of concomitant analgesic therapy compared with propofol (Devabhakthuni et al., 2011). In other studies of surgical and trauma patients, the incidence of hemodynamic AEs has only been measured as secondary end points with no significant differences (Venn & Grounds, 2001; Winings et al., 2020).

Objective

Although the literature to date indicates there may not be a difference in the overall incidence of hemodynamic AEs, it is still unknown whether there is a difference in the AEs serious enough to require an intervention. Therefore, the objective of this study was to evaluate hemodynamic AEs that require therapeutic interventions between dexmedetomidine and propofol in a critically ill trauma and surgical population.

METHODS

This was a retrospective, observational cohort study of critically ill trauma and surgical patients admitted to an ICU between October 1, 2017, and October 31, 2018, who received at least 4 hr of a continuous infusion of dexmedetomidine or propofol. This study was approved by the Institutional Review Board and the requirement for informed consent was waived. The institution is a 511-bed, Level 1 trauma center with four ICUs, including medical, surgical, neuroscience, and cardiovascular.

A source population included patients admitted to any ICU with an order for dexmedetomidine or propofol by a query of the electronic medical records (EMRs). After the source population list was obtained, charts were randomly selected using a random number generator for manual chart review based on a convenience sample and feasibility. Patients were excluded for the following: (1) not admitted to the surgical ICU service, (2) lack of intra-arterial blood pressure monitoring, (3) loading dose of dexmedetomidine or propofol, (4) procedural or intraoperative sedation, (5) agents given for less than 4 hr, (6) history of heart block, (7) coadministration of dexmedetomidine and propofol for more than 24 hr, (8) active treatment for status epilepticus, (9) mechanical ventilation for less than 24 hr, (10) permanent pacemaker, (11) younger than 18 years, or (12) pregnancy. Patients deemed eligible for inclusion were divided into two groups: patients who received dexmedetomidine and patients who received propofol.

Because the practice pattern at the institution is to use propofol for sedation initially, any patient who received propofol and was then transitioned to dexmedetomidine within 24 hr was assigned to the dexmedetomidine group (Erdman et al., 2014). The institution's default titration parameters allow propofol to be initiated at 5–10 μg/kg/min and titrated by 2–5 μg/kg/min every 2–5 min to target the desired level of sedation up to a maximum rate of 60 μg/kg/min. Dexmedetomidine may be initiated at 0.2–0.4 μg/kg/hr and titrated by 0.1–0.2 μg/kg/hr every 15–30 min to target the desired level of sedation up to a maximum rate of 1.5 μg/kg/hr. The default orders for both dexmedetomidine and propofol do not suggest a loading dose, and therefore this is not typical practice at the institution.

Data were abstracted by one investigator trained in data collection using Research Electronic Data Capture (REDCap) (Harris et al., 2009). Admission baseline demographics including age, biologic sex, race, weight, body mass index (BMI), and Glasgow Coma Scale were obtained directly from the EMR query. The institutional Acute Physiology and Chronic Health Evaluation (APACHE) III scores were determined on day 1 of the ICU encounter by trained clinical abstractors. Other data were abstracted from the EMR via manual chart review. Comorbid conditions, such as chronic kidney disease, diabetes, hypertension, atrial fibrillation, heart failure, and hepatic impairment, were collected. Other medications administered during the first 24 hr of sedation were evaluated, including other sedative, antihypertensive, and vasopressor agents. Patient outcomes were evaluated, including ICU length of stay, hospital length of stay, and in-hospital mortality. The primary list of included patients was then cross-referenced to the institution's trauma registry to determine the trauma subgroup. Injury Severity Scores (ISS) and Abbreviated Injury Scale (AIS) scores were obtained from the trauma registry database.

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The primary outcome of the study was the proportion of patients who required at least one therapeutic intervention for a hemodynamic AE within the first 24 hr of dexmedetomidine or propofol initiation. The need for a therapeutic intervention was determined at the discretion of the treating physician and/or bedside nursing staff for changes with the sedative dose. Therapeutic interventions were defined as one or more of the following: fluid bolus (consisted of crystalloid fluid of at least 250 ml or colloid of any amount), dose reduction of the sedative by at least 20%, initiation of a vasoactive agent, uptitration of a vasoactive agent by at least 20%, and/or discontinuation of the sedative agent. Hemodynamic AEs were defined as at least one of the following in the first 24 hr of sedation: MAP <65 mmHg, SBP <90 mmHg, or HR <50 bpm. Blood pressure and HR readings were collected from intra-arterial line measurements. These readings were collected at baseline, or immediately prior to the initiation of the sedative agent, and each hour for the first 24 hr of sedation. Secondary outcomes of the study were the proportion of patients who required at least one therapeutic intervention for a hemodynamic AE within the first 6 or 12 hr of sedation, the proportion of patients who experienced any hemodynamic AE, the proportion of patients who experienced a hypotensive episode (MAP <65 mmHg or SBP <90 mmHg), the proportion of patients who experienced an episode of bradycardia (HR <50 bpm), the proportion of patients who required each of the individual therapeutic interventions, and the measurement of change in MAP, SBP, and HR from baseline to lowest point in the first 24 hr of sedation.

Based on the lack of literature evaluating hemodynamic AEs requiring a therapeutic intervention, a power analysis could not be performed and a convenience sample was used. Categorical variables are reported as *n* (%) and analyzed by χ^2 or Fisher's exact test as appropriate. Continuous variables are reported as mean with standard deviation or median with interquartile range (IQR) and analyzed by Student's *t* test or the Mann–Whitney *U* test based on normality of data distribution. Normality was determined by a significant Shapiro–Wilk test ($p > .05$). Statistical analysis was performed using IBM SPSS statistics, Version 24.0 (SPSS Inc, Chicago, IL), and the level of significance set a *p* less than .05 (two sided).

RESULTS

Figure 1 depicts the flow diagram of included and excluded patients. A total of 1,375 patients were identified for screening and 800 patient charts were randomly selected for review. The majority of patients were excluded for lack of surgical ICU admission ($n = 617$). Other exclusion criteria included a lack of intra-arterial blood pressure monitoring ($n = 17$), loading dose of sedative ($n = 17$), procedural or intraoperative sedation ($n = 14$),

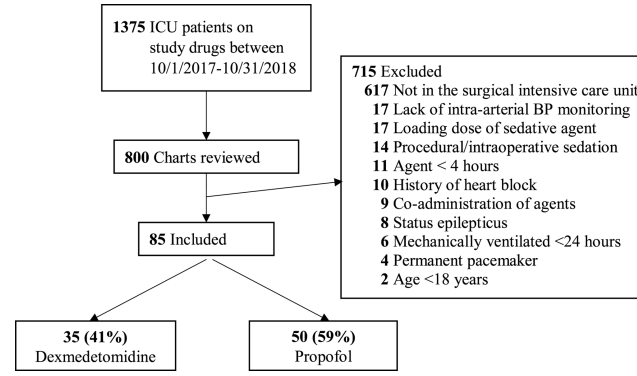

Figure 1. Flow diagram depicting inclusion and exclusion criteria for study cohort. BP = blood pressure.

sedative agent administered for less than 4 hr ($n = 11$), history of heart bock ($n = 10$), coadministration of dexmedetomidine and propofol for more than 24 hr ($n = 9$), status epilepticus ($n = 8$), mechanical ventilation for less than 24 hr ($n = 6$), permanent pacemaker ($n = 4$), and younger than 18 years ($n = 2$). A total of 85 patients were included (dexmedetomidine [$n = 35$] and propofol [$n = 50$]) for analysis.

Baseline demographics are described in Table 1. The study population was primarily composed of Caucasian (86%) males (61%) with a median age of 61 [IQR 48, 72] years. Baseline demographics were similar between the two groups with a few exceptions. There were more males in the dexmedetomidine group (29 [83%] vs. 23 [46%], $p < .001$). There was a statistically significant greater median duration of mechanical ventilation (139 hr [IQR 75, 222] vs. 64 hr [IQR 38, 162], $p = .018$), ICU length of stay (275 hr [IQR 167, 453] vs. 138 hr [IQR 88, 233], $p < .001$), and hospital length of stay (425 hr [IQR 296, 664] vs. 317 hr [IQR 233, 396], $p = .013$) in the dexmedetomidine versus the propofol group. There was no difference in baseline hemodynamic parameters, including the average baseline HR (93 [*SD* 17] vs. 96 [*SD* 23] bpm, $p = .513$), SBP (127 [*SD* 22] vs. 128 [*SD* 29] mmHg, $p = .663$), or MAP (91 [*SD* 15] vs. 91 [*SD* 19] mmHg, $p = .948$) between the dexmedetomidine versus the propofol groups. There was no difference between the two groups for simultaneous medication use, including sedative, antihypertensive, and vasopressor agents during the 24-hr study timeframe. Blood transfusions during the first 24 hr of sedation also did not differ between the groups.

Table 2 describes the primary and secondary outcomes between the study groups. There was no statistically significant difference in the primary outcome of proportion of patients who required at least one therapeutic intervention for a hemodynamic AE within the first 24 hr of sedation with dexmedetomidine compared with propofol (17 [49%] vs. 27 [54%], $p = .624$). No difference was observed in the proportion of patients who experienced

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TABLE 1 Baseline Demographic Information for Dexmedetomidine and Propofol Groups

	Total $n = 85$	Dexmedetomidine $n = 35$	Propofol $n = 50$	p Value
Baseline characteristics				
Age (years)[a]	61 [48, 72]	59 [46, 73]	62 [48, 70]	.886
Sex, male[b]	52 (61)	29 (83)	23 (46)	<.001
Race[b]				.652
African American	11 (13)	4 (11)	7 (14)	
Caucasian	73 (86)	31 (43)	42 (84)	
Other/undocumented	1 (1)	0 (0)	1 (2)	
Weight (kg)[a]	83 [68, 96]	83 [73, 100]	82 [64, 95]	.379
BMI (kg/m^2)[a]	27 [23, 32]	27 [24, 31]	27 [23, 34]	.947
APACHE III score[a], $n = 64$	57 [39, 83]	57 [31, 83]	53 [41, 77]	.782
GCS score[a], $n = 51$	10 [7, 14]	9 [6, 14]	10 [7, 14]	.494
Comorbidities[b]				
Hypertension	39 (46)	13 (37)	26 (52)	.176
Diabetes	20 (24)	6 (17)	14 (28)	.245
Heart failure	9 (11)	3 (9)	6 (12)	.731
Atrial Fibrillation	8 (9)	3 (9)	5 (10)	1.000
Chronic kidney disease	7 (8)	2 (6)	5 (10)	.695
Hepatic impairment	5 (6)	2 (6)	3 (6)	1.000
Clinical data				
Renal replacement therapy[b]	11 (13)	5 (14)	6 (12)	.755
CRRT	7 (8)	3 (9)	4 (8)	1.000
IHD	4 (6)	2 (6)	2 (4)	
Mechanical ventilation (hours)[a]	97 [44, 193]	139 [75, 222]	64 [38, 162]	.018
Length of stay (hours)[a]				
ICU	190 [105, 337]	275 [167, 453]	138 [88, 233]	<.001
Hospital	338 [250, 484]	425 [296, 664]	317 [233, 396]	.013
In-hospital mortality[b]	15 (18)	6 (17)	9 (18)	.919
Baseline hemodynamics[c]				
HR (bpm)	94 (21)	93 (17)	96 (23)	.513
SBP (mmHg)	127 (26)	125 (22)	128 (29)	.663
DBP (mmHg)	73 (16)	74 (16)	73 (17)	.809
MAP (mmHg)	91 (17)	91 (15)	91 (19)	.948
Sedative agents[b]	68 (80)	28 (80)	40 (80)	1.000
Fentanyl	67 (79)	27 (77)	40 (80)	.751
Lorazepam	11 (13)	7 (20)	4 (8)	.187
Midazolam	3 (4)	1 (3)	2 (4)	1.000
Antihypertensive agents[b]	15 (18)	8 (23)	7 (14)	.292
Beta-blockers	10 (12)	7 (20)	3 (6)	.084
Diuretics	4 (5)	2 (6)	2 (4)	1.000
Calcium channel blockers	3 (4)	0 (0)	3 (6)	.265
Alpha-1 blockers	1 (1)	1 (3)	0 (0)	.412
Vasodilator	1 (1)	0 (0)	1 (2)	1.000

(*continues*)

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TABLE 1 Baseline Demographic Information for Dexmedetomidine and Propofol Groups (*Continued*)

	Total *n* = 85	Dexmedetomidine *n* = 35	Propofol *n* = 50	*p* Value
Vasopressor agents[b]	20 (24)	9 (26)	11 (22)	.691
Norepinephrine	19 (22)	8 (23)	11 (22)	.926
Vasopressin	5 (6)	1 (3)	4 (8)	.644
Dobutamine	1 (1)	1 (3)	0 (0)	.412
Blood transfusions[b]	20 (24)	8 (23)	12 (24)	.903
Packed red blood cells	17 (20)	7 (20)	10 (20)	1.000
Platelets	3 (4)	1 (3)	2 (4)	1.000
Fresh frozen plasma	1 (1)	1 (3)	0 (0)	.412
Units of blood products[a], *n* = 20	1.5 [1, 3]	1.5 [1, 2.5]	1.5 [1, 3.5]	.734
Sedative rate prior to event[a], *n* = 48		0.4 [0.3, 0.5][d]	10 [5, 20][e]	

Note. AKI = acute kidney injury; APACHE = Acute Physiology and Chronic Health Evaluation score; BMI = body mass index; bpm = beats per minute; CRRT = continuous renal replacement therapy; DBP = diastolic blood pressure; GCS = Glasgow Coma Scale; HR = heart rate; ICU = intensive care unit; IHD = intermittent hemodialysis; MAP = mean arterial pressure; SBP = systolic blood pressure.

[a]*Mdn [interquartile range].*

[b]*n (%).*

[c]*M (SD).*

[d]*μg/kg/hr.*

[e]*μg/kg/min.*

TABLE 2 Primary and Secondary Outcomes: Hemodynamic Adverse Effects and Therapeutic Interventions in Dexmedetomidine and Propofol Groups

Outcome Variables	Total *n* = 85	Dexmedetomidine *n* = 35	Propofol *n* = 50	*p* Value
Primary outcome: Intervention for hemodynamic AE within 24 hr[a]	44 (52)	17 (49)	27 (54)	.624
Type of intervention within 24 hr[a]				
Dose reduction of sedative	32 (38)	13 (37)	19 (38)	.920
Fluid bolus	29 (34)	9 (26)	20 (40)	.171
Initiation of vasoactive agent	11 (13)	5 (14)	6 (12)	1.000
Uptitration of vasoactive agent	9 (11)	2 (6)	7 (14)	.296
Discontinuation of sedative	4 (5)	4 (11)	0 (0)	.026
Hemodynamic AE within 24 hr[a]	48 (57)	18 (51)	30 (60)	.433
Type of hemodynamic AE within 24 hr[a]				
Hypotension	43 (51)	15 (43)	28 (56)	.233
Bradycardia	6 (7)	4 (11)	2 (4)	.224
Hemodynamic changes within 24 hr[b]				
Decrease in MAP (mmHg)	25 [13, 41]	23 [12, 40]	25 [13, 44]	.588
Decrease in SBP (mmHg)	29 [22, 56]	29 [23, 51]	31 [22, 66]	.460
Decrease in HR (bpm)	17 [10, 29]	23 [16, 41]	14 [5, 24]	.002
Intervention for hemodynamic AE[a]				
Within 12 hr	36 (42)	13 (37)	23 (46)	.417
Within 6 hr	24 (28)	9 (26)	15 (30)	.663

Note. AE = adverse effect; bpm = beats per minute; HR = heart rate; MAP = mean arterial pressure; SBP = systolic blood pressure.

[a]*n (%).*

[b]*Mdn [interquartile range].*

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any hemodynamic AE (18 [51%] dexmedetomidine vs. 27 [54%] propofol, $p = .4333$). The proportion of patients who required an intervention within the first 6 hr was not different between dexmedetomidine and propofol (9 [26%] vs. 15 [30%], $p = .662$), as well as within the first 12 hr (13 [37%] vs. 23 [46%], $p = .417$). The most common type of therapeutic intervention in the entire cohort was a dose reduction in the sedative (32 [38%]), followed by the administration of a fluid bolus (29 [34%]). More patients required a discontinuation of the sedative in the dexmedetomidine group than in the propofol group (4 [11%] vs. 0 [0%], $p = .026$), which was statistically significant.

The incidence of bradycardia was not statistically significant between groups; however the patients in the dexmedetomidine group experienced a statistically significant reduction in HR from baseline to the lowest point in the first 24 hr of sedation (median difference of 23 vs. 14 bpm, $p = .002$). Patients who received dexmedetomidine had consistently lower HR throughout the first 24 hr of sedation compared with patients who received propofol (Figure 2A). MAP and SBP for both groups were similar throughout the first 24 hr of sedation (Figures 2B and 2C). In both groups, MAP and SBP tended to reach their lowest point approximately 8 hr after the initiation of the sedative.

The trauma subgroup analysis is described in Table 3. Baseline demographics, such as BMI, comorbidities, mechanism and type of injuries, traumatic brain injuries, and ISS and AIS scores, were similar between the two groups, except there were statistically more males in the dexmedetomidine group (84% vs. 52%, $p = .015$). There was no difference in the primary outcome (9 [36%] dexmedetomidine vs. 11 [44%] propofol, $p = .564$). Similar to the overall cohort, the most common intervention was the dose reduction of the sedative dose (56%). There was also no difference in the overall incidence of hemodynamic AEs (10 [40%] dexmedetomidine vs. 14 [56%] propofol, $p = .258$). The patients in the dexmedetomidine group experienced a statistically significant reduction in HR from baseline to the lowest point in the first 24 hr of sedation (median difference of 22 vs.15 bpm, $p = .013$).

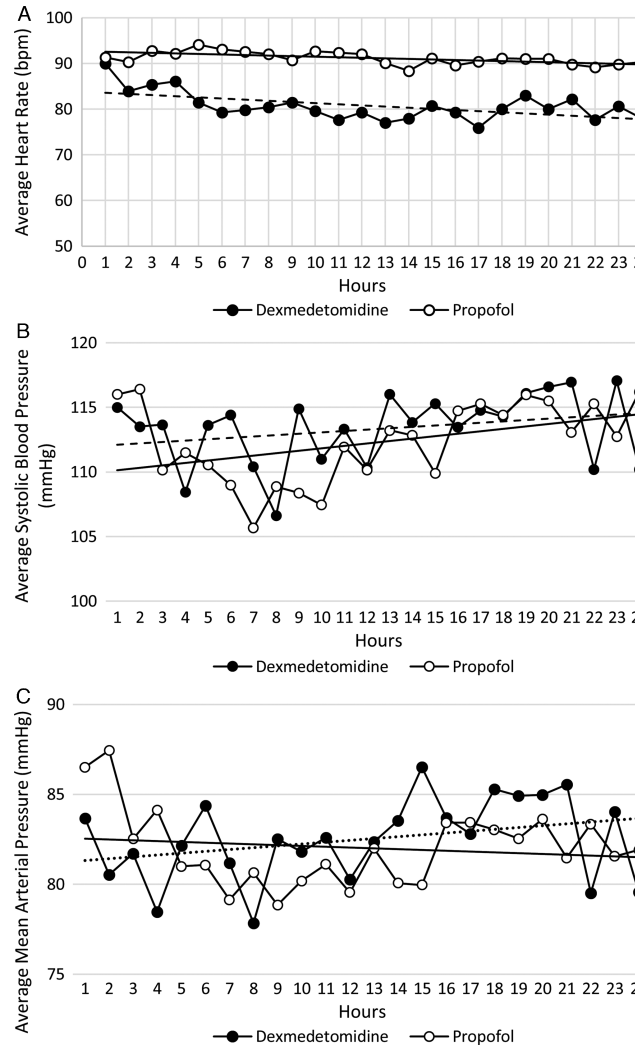

Figure 2. Average heart rate, systolic blood pressure, and mean arterial pressure in first 24 hr of sedation between dexmedetomidine and propofol. (A) Average heart rate. (B) Average systolic blood pressure. (C) Average mean arterial pressure.

DISCUSSION

This retrospective cohort study provided a comparison of hemodynamic AEs that required a therapeutic intervention in a critically ill trauma and surgical population. In this cohort, there was no statistically significant difference in the primary outcome of the proportion of patients who required at least one therapeutic intervention for a hemodynamic AE in the first 24 hr of dexmedetomidine compared with propofol. There was also no difference in the overall incidence of hemodynamic AEs between the two groups; however, there was a greater reduction in HR from baseline in the dexmedetomidine group.

The study by Erdman et al. (2014) was conducted in neurocritical care patients, who typically have strict hemodynamic monitoring parameters and blood pressure goals due to the nature of their conditions. Hemodynamic AEs were found to be similar between the dexmedetomidine and propofol groups. However, the incidence of using a therapeutic intervention for the hemodynamic AE was higher in the dexmedetomidine group, which may have alluded that AEs with dexmedetomidine may require treatment more often. However, up to 68% of all patients included in the study received antihypertensives, which may have confounded results (Erdman et al., 2014). This may not be as generalizable to other ICU populations, as only 18% of all patients received antihypertensive agents in the current study.

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TABLE 3 Baseline Characteristics and Hemodynamic Adverse Effects in Trauma Subgroup

Baseline Characteristics	Trauma *n* = 50	Dexmedetomidine *n* = 25	Propofol *n* = 25	*p* Value
Age[a]	55 [33,69]	53 [32, 69]	59 [34, 70]	.756
Sex, male[b]	34 (68)	21 (84)	13 (52)	.015
Race, Caucasian[b]	44 (88)	23 (92)	21 (84)	.667
BMI (kg/m^2)[a]	29 [24, 33]	29 [24, 31]	28 [24, 35]	.720
Comorbidities[b]				
Hypertension	21 (42)	9 (36)	12 (48)	.390
Diabetes	9 (18)	4 (16)	5 (20)	1.000
Heart failure	2 (4)	0 (0)	2 (8)	1.000
Atrial fibrillation	3 (6)	2 (8)	1 (4)	1.000
Chronic kidney disease	1 (2)	0 (0)	1 (4)	1.000
Hepatic impairment	2 (4)	2 (8)	0 (0)	.490
AKI	1 (2)	1 (4)	0 (0)	1.000
Mechanism of injury[b]				.110
Blunt	46 (92)	25 (100)	21 (84)	
Penetrating	4 (8)	0 (0)	4 (16)	
Type of injury[b]				.052
Motor vehicle crash	21 (42)	11 (44)	10 (40)	
Fall	17 (34)	8 (32)	9 (36)	
Gunshot wound	4 (8)	0 (0)	4 (16)	
Assault	1 (2)	0 (0)	1 (4)	
Other	7 (14)	6 (24)	1 (4)	
Traumatic brain injury[b], *n* = 22	22 (44)	11 (44)	11 (44)	1.000
Mild severity (GCS 13–15)	6 (27)	4 (36)	2 (18)	.420
Moderate severity (GCS 9–12)	6 (27)	2 (18)	4 (36)	
Severe severity (GCS 3–8)	10 (45)	5 (45)	5 (45)	
ISS[c]	20.1 (10.7)	21.6 (11.4)	18.6 (9.9)	.331
AIS maximal[a]	3.5 [3, 4]	4.0 [3, 4]	3.0 [2.5, 4.5]	.395
Head/neck, *n* = 38	3.0 [3, 4]	2.0 [2, 4]	3.0 [2, 5]	.352
Face, *n* = 30	1.0 [1, 2]	1.0 [1, 2]	1.0 [1, 2]	.854
Abdomen, *n* = 20	1.5 [1, 3]	1.0 [1, 2.5]	2.0 [1, 3]	.710
Spine, *n* = 18	2.0 [2, 2.25]	2.0 [2, 3]	2.0 [2, 2]	.211
Extremity, *n* = 36	2.0 [1, 2]	2.0 [1, 3]	2.0 [1, 2]	.505
Chest, *n* = 27	3.0 [2, 3]	3.0 [3, 4]	2.5 [2, 3]	.075
External, *n* = 8	1.0 [1, 1]	1.0 [1, 1]	1.0 [1, 1.25]	1.000
Hemodynamic AE with intervention within 24 hr[b]	20 (40)	9 (36)	11 (44)	.564
Type of intervention[b]				
Fluid bolus	16 (32)	6 (24)	10 (40)	.225
Dose reduction of sedative	28 (56)	13 (52)	15 (60)	.569
Initiation of vasoactive agent	6 (12)	2 (8)	4 (16)	.667
Uptitration of vasoactive agent	5 (10)	3 (12)	2 (8)	1.000
Discontinuation of sedative	4 (8)	4 (16)	0 (0)	.110
Hemodynamic AE[b]	24 (48)	10 (40)	14 (56)	.258

(*continues*)

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TABLE 3 Baseline Characteristics and Hemodynamic Adverse Effects in Trauma Subgroup (*Continued*)

Baseline Characteristics	Trauma *n* = 50	Dexmedetomidine *n* = 25	Propofol *n* = 25	*p* Value
Type of hemodynamic AE[b]				
Hypotension	19 (38)	7 (28)	12 (48)	.145
Bradycardia	6 (12)	4 (16)	2 (8)	.667
Decrease in MAP (mmHg)[a]	18 [6, 29]	17 [8, 25]	22 [6, 35]	.392
Decrease in SBP (mmHg)[a]	27 [12, 41]	24 [12, 33]	28 [11, 58]	.261
Decrease in HR (bpm)[a]	18 [10, 27]	22 [14, 44]	15 [6, 22]	.013

Note. AE = adverse effect; AIS = Abbreviated Injury Scale; AKI = acute kidney injury; BMI = body mass index; bpm = beats per minute; GCS = Glasgow Coma Scale; HR = heart rate; ISS = Injury Severity Score; MAP = mean arterial pressure; SBP = systolic blood pressure.

[a]*Mdn [interquartile range].*

[b]*n (%).*

[c]*M (SD).*

In the current study, there was also no statistically significant difference in the overall incidence of hemodynamic AEs between the two groups. This is consistent with previous literature evaluating the incidence of hemodynamic AEs in surgical ICU patients (Chang et al., 2018; Elbaradie et al., 2004; Venn & Grounds, 2001). This is also consistent with the previous study in trauma ICU patients. In the current study the median rate of dexmedetomidine was 0.4 μg/kg/hr prior to the AE, which is within the standard doses definition set in the previous study. There was no difference in the incidence of hemodynamic AEs between standard doses of dexmedetomidine and the propofol group in the previous study (Devabhakthuni et al., 2011). The significant reduction in HR as well as the consistently lower HR throughout the first 24 hr of dexmedetomidine initiation was consistent with previous literature (Chang et al., 2018; Elbaradie et al., 2004; Jakob et al., 2012; Venn & Grounds, 2001). Providers should be cautious when considering dexmedetomidine in patients with lower baseline HR or with an increased risk for bradycardia.

The incidence of hemodynamic AEs related to dexmedetomidine and propofol observed in this study is at the higher end of the range reported in the literature (Erdman et al., 2014; Gerlach, Dasta, Steinburg, Martin, & Cook, 2009; Ice et al., 2016; Jakob et al., 2012; Nelson et al., 2020; Shearin, Patanwala, Tang, & Erstad, 2014). A possible explanation for this may be the different definitions of hemodynamic AEs. Previous studies have used lower SBP and MAP thresholds than those used in this study (Ice et al., 2016; Shearin et al., 2014). Additionally, varied definitions were utilized, including hypotension defined as a decrease in SBP by 30 mmHg or MAP by 10 mmHg and bradycardia defined as a decrease in HR by 30 bpm from baseline (Nelson et al., 2020). The median observed decrease in SBP and HR in this study was less than 30 for both dexmedetomidine and propofol, which would have impacted results had an alternative definition of hemodynamic AE been used. Another explanation could be the different study populations. Previous studies in surgical and trauma ICU patients observed overall higher incidences of hypotension and bradycardia with both propofol and dexmedetomidine compared with studies of medical ICU or neurocritical care patients (Chang et al., 2018; Devabhakthuni et al., 2011). Hypotension and bradycardia in these patients can lead to decreased tissue perfusion to the surgical site or traumatic injury and be detrimental to recovery, making it essential to understand and anticipate the risks associated with these agents.

Although our investigation evaluated other clinical outcomes, these results should be interpreted with caution and remain hypothesis generating. Our study found a significant increase in the duration of mechanical ventilation, which corresponded with longer ICU and hospital length of stay. This is likely because of a transition period between the agents, along with greater difficulty with the sedation weaning and extubation process. These results were similar to Devabhakthuni et al., which also found an increased duration of mechanical ventilation, ICU and hospital length of stay (Devabhakthuni et al., 2011). Winings et al. (2020) did not find a statistical difference in the duration of mechanical ventilation, nor ICU or hospital length of stay. However, this was likely due to the differences in study design and assigning patients to the agent without a transition period (Winings et al., 2020).

Although both propofol and dexmedetomidine may contribute to hypotension and potentially require a therapeutic intervention, dexmedetomidine may be associated with a greater decrease in HR from baseline. Patients on these agents should be monitored closely for these AEs,

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especially for patients with lower BP or HR readings or those requiring vasoactive agents, such as vasopressors or antihypertensives. Additionally, loading doses, higher dosing ranges, or quick titrations may contribute to AEs, although these were not directly tested in this evaluation and warrant further investigation.

Limitations

There are limitations to this study worth noting. It was a small, retrospective study; however, the sample size was comparable or larger than previous literature (Chang et al., 2018; Devabhakthuni et al., 2011; Nelson et al., 2020; Winings et al., 2020). Data were abstracted from a single center, which may limit the external validity. Although the therapeutic interventions assessed are common and consistent with previous literature (Devabhakthuni et al., 2011; Erdman et al., 2014), the need for any intervention could have been used for indications other than hemodynamic AEs. Although there was not a significant difference in other sedative agents utilized between the groups, hemodynamic AEs from those agents may be possible depending on dose or route of administration. Additionally, compliance with the dexmedetomidine or propofol titration instructions was not evaluated, which may have further influenced the hemodynamic parameters. Other possible confounders were possible, including preexisting hypertension, sex, race, type of injury, or others; however, the only statistical difference between the groups at baseline was sex. Sedation assessment scores were not assessed in this study; however, these are routinely evaluated at least every 4 hr for patients in the ICU setting by trained nursing staff. It was possible that sedative discontinuation may be related to spontaneous awakening trials, which was not assessed in this cohort. However, this was not a standard institutional practice during the study timeframe and would be difficult to distinguish in a retrospective fashion. The practice pattern of the institution introduces a selection bias in that propofol is most often used at the initiation of mechanical ventilation and then the patient is transitioned to dexmedetomidine once clinical status is improving and the potential for extubation is higher. Therefore, there was no washout period between the agents. However, we attempted to account for this by minimizing the transition period to less than 24 hr similar to Erdman et al. (2014). Although there was likely a difference in the time to initiation of the sedative agent, this was not fully assessed in exact time points. However, the baseline demographics and hemodynamic parameters prior to the initiation of the sedative agent were similar between the two groups.

CONCLUSIONS

This study evaluated the requirement of therapeutic interventions for hemodynamic AEs of dexmedetomidine compared with propofol in a critically ill trauma and surgical population. There was no association in the overall rate of hemodynamic AEs that required therapeutic interventions. Dexmedetomidine was associated with a significant decrease in HR, which remained consistently lower throughout the first 24 hr of sedation. It should be anticipated that both dexmedetomidine and propofol may be associated with hemodynamic AEs in a critically ill trauma and surgical population and a smaller proportion may require treatment.

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