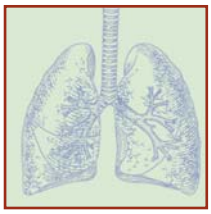

Safety and Acceptability of Patient-Administered Sedatives During Mechanical Ventilation

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Background Safety and acceptability of sedative self-administration by patients receiving mechanical ventilation is unknown.

Objectives To determine if self-administration of dexmedetomidine by patients is safe and acceptable for self-management of anxiety during ventilatory support.

Methods In a pilot trial in 3 intensive care units, 17 intubated patients were randomly assigned to dexmedetomidine and 20 to usual care. Dexmedetomidine was administered via standard pumps for patient-controlled analgesia, with a basal infusion (0.1-0.7 μg/kg per hour) titrated by the number of patient-triggered doses (0.25 μg/kg per dose). Safety goals were heart rate greater than 40/min, systolic blood pressure greater than 80 mm Hg, and diastolic blood pressure greater than 50 mm Hg. Acceptability was based on patients' self-reported satisfaction and ability to administer the sedative. A 100-mm visual analog scale was used daily to assess patients' anxiety.

Results The sample was 59% male and 89% white. Mean values were age, 50.6 years; score on the Acute Physiology and Chronic Health Evaluation, 60.1; and protocol duration, 3.4 days. Five dexmedetomidine patients had blood pressure and/or heart rate lower than safety parameters, necessitating short-term treatment. Nurses' adherence to reporting of safety parameters was 100%; adherence to the dexmedetomidine titration algorithm was 73%. Overall baseline anxiety score was 38.4 and did not change significantly (β_{day}=2.1; SE, 2.5; P=.40). Most dexmedetomidine patients (92%) were satisfied or very satisfied with their ability to self-administer medication.

Conclusions For select patients, self-administration of dexmedetomidine is safe and acceptable. (*American Journal of Critical Care.* 2017;26:288-296)

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Administration of sedatives to critically ill patients receiving mechanical ventilation is a common practice in intensive care units (ICUs). These medications are administered for numerous reasons, including to reduce anxiety and to promote patients' comfort with mechanical ventilator breaths. Recent practice guidelines[1] suggest that administration of these medications be targeted to achieve a "lightly sedated, interactive patient" when medically feasible. Scales to guide sedation levels rely on clinicians to administer medications on the basis of subjective assessment and observation of a patient's arousal and motor activity. Although clinicians want patients to remain comfortable and in synchrony with ventilator breaths, the ideal method to achieve this goal is not consistent across providers.

Patient-controlled analgesia (PCA) has been used for many years to promote effective self-management of pain by patients; PCA is superior to clinician-administered analgesics, and patient satisfaction is high.[2] The existence of a similar parallel between PCA and sedative self-administration by patients receiving mechanical ventilation is not known. Findings from our previous proof-of-principle study[3] indicate that patients receiving mechanical ventilation are willing, able, and satisfied with their ability to self-administer sedative medications to manage anxiety. However, in the proof-of-principle study, a highly selective group of patients was recruited whose self-administration of sedatives was limited to 24 hours. The next logical step was to build on these promising findings by examining whether self-management of sedative therapy in a larger group of patients for longer than 24 hours is safe. Thus, our aims in the study reported here were to determine whether self-administered sedative therapy with dexmedetomidine is a safe and acceptable sedation option for patients receiving mechanical ventilation.

Methods

Study Aims

Our primary goal was to establish the safety and acceptability of patients' self-administration of dexmedetomidine compared with standard, nurse-administered sedative in a small randomized pilot trial for up to 5 days. Safety was determined by the occurrence of study-defined adverse events, adverse hemodynamic effects, or self-extubations. Deviations from protocol related to the study drug, research protocol, or infusion pump were also collated. Acceptability was defined as the patient's appraisal of his or her ability to self-administer the medication for relaxation, including level of relaxation, and anxiety. Secondary aims were to determine adherence to the notification parameters in the dexmedetomidine safety alert and the adherence of patients' bedside nurses to the infusion titration algorithm. Approval for the use of human subjects in research was obtained from the University of Minnesota institutional review board and included limitations on proxy consent.

Self-administration of sedatives by patients receiving mechanical ventilation is novel.

Patients and Setting

Adult intubated patients expected to require mechanical ventilation for at least an additional 48 hours were screened at 3 ICUs in the Minneapolis, Minnesota, area. The ICUs consisted of a medical ICU (14 beds) and a surgical ICU (21 beds) at the University of Minnesota Medical Center in Minneapolis and a 24-bed community medical-surgical ICU at Fairview-Southdale Hospital, Edina, Minnesota. The ICUs used the same electronic medical records, ventilator management, weaning, and order sets for selection of sedatives. Nursing care was typically provided by bedside nurses in a ratio of 1 nurse to 2 patients. Medical care was provided by faculty intensivists across units. Standard practices on the ICUs consisted of daily assessment by a respiratory therapist of patients' readiness for weaning and attainment of criteria for a spontaneous breathing trial.

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Screening and enrollment by trained research personnel followed a rigorous, 3-step procedure to ensure that only those patients receiving mechanical ventilation who were willing and able to self-manage sedative therapy were appropriately offered participation in the study.

Step 1: Prescreening. Research personnel initially screened via electronic medical records to determine the presence of exclusion criteria: (1) aggressive ventilatory support (eg, positive end-expiratory pressure > 15 cm H_2O, prone positioning, high-frequency oscillator ventilation); (2) condition potentially worsened by dexmedetomidine (eg, systolic blood pressure < 85 mm Hg, second- or third-degree heart block, or bradycardia with heart rate < 50/min); (3) condition preventing use of the push-button device (eg, paralysis); (4) positive test results for pregnancy; (5) acute hepatitis or liver failure; (6) general anesthesia within the preceding 24 hours; (7) acute stroke or uncontrolled seizures; (8) acute myocardial infarction; (9) receipt of medications known to interact with dexmedetomidine (eg, isoniazid, clonidine, fluoxetine, hydrocodone); and (10) severe cognition or communication problems (eg, coma, deafness without signing literacy, physician-documented dementia).

Only patients receiving mechanical ventilation who were willing and able to self-manage sedative therapy were eligible for the study.

Step 2: Screening of Patients. Eligible patients were next assessed for their ability to communicate, follow commands, and depress the push button on the medication infusion device. The Confusion Assessment Method for the ICU (CAM-ICU) was used to determine the presence of delirium. The CAM-ICU is a widely used, valid, and reliable assessment tool for the presence (CAM-ICU positive) or absence (CAM-ICU negative) of delirium.[4-8] Interrater reliability[5] (κ)is from 0.92 to 0.99; sensitivities and specificities are high, and differences between subgroups are not significant.[4,6] Patients were required to be CAM-ICU negative for enrollment.

Step 3: Informed Consent. If step 2 was passed and the attending physician approved enrollment, the study was explained to the patient in greater detail, and he or she was offered the opportunity to enroll. Consent was acquired directly from the patient when possible. The content of the consent form was read verbatim to the patient by research personnel. A list of yes-no questions about the consent process was used to ensure understanding. If a patient correctly answered the questions and agreed to participate, he or she then signed the consent form. In specific cases in which a patient was unable to provide consent, a proxy consent procedure with the legally authorized representative was implemented. Proxy consent was obtained when patients were too fatigued or weak to participate in a lengthy consent process, had decreased ability to maintain concentration, or were more sedated for a short duration for a bedside procedure such as bronchoscopy. If proxy consent was necessary, the legally authorized representative provided written consent with the patient's assent.

Data Collection

Demographic and descriptive data were recorded at enrollment and included age, sex, race, ethnicity, weight, medical diagnoses, comorbid conditions, indication for ventilatory support, all medications, and ventilator settings. Scores on the Acute Physiology and Chronic Health Evaluation III were calculated on the basis of data in the electronic medical record during the first 24 hours of ICU admission.

Daily Measures Included in the Protocol. Research personnel assessed all patients daily for delirium by using the CAM-ICU, and positive findings were reported to the primary care team. Anxiety, defined as a state marked by apprehension, agitation, arousal, increased motor activity, and fearful withdrawal,[9,10] was assessed daily by using a 100-mm vertical visual analog scale (VAS-A). All patients responded to the question "How anxious are you feeling today?" by marking their current level of anxiety from 0 (not anxious at all) to 100 (most anxious ever). Scores were calculated on the basis of the distance in millimeters from the bottom anchor to the mark placed by the patient.[11-14] The vertical presentation of the VAS-A is more sensitive and easier than other versions for patients to use, particularly patients who have a narrowed visual field or are under stress.[15-17] The VAS-A is an accurate and sensitive measure of the anxiety state, is a reliable measure of anxiety in patients receiving mechanical ventilation,[12] and can easily be completed by patients receiving mechanical ventilation.[18]

Duration of Mechanical Ventilation and ICU Stay. Duration of mechanical ventilation was defined as the time (in days) from intubation to clinician-ordered extubation, withdrawal of ventilatory support, or death. Unplanned self-extubations and reintubations were recorded. Length of ICU stay was defined as the time (in days) from ICU admission to ICU discharge or death.

Study Treatments

In order to prevent any unconscious selection bias by preferentially recruiting only those patients who were thought to be ideal for self-administration of dexmedetomidine, patients were randomly allocated via consecutive opaque envelopes to either the experimental dexmedetomidine protocol or usual ICU care. Because of the necessity to first establish the safety of dexmedetomidine, clinicians were not blinded to the experimental treatment. Likewise, the medical safety officers needed to know which medications a patient was receiving in order to address any acute changes in the patient's condition. Further, medical staff not affiliated with the study team were concerned that blinding was possibly unsafe because of the limited knowledge on dexmedetomidine. Patients remained in the study for up to 5 days or until they withdrew, were extubated, transferred from the ICU, or died.

Experimental Dexmedetomidine Protocol. We selected dexmedetomidine (Precedex; Hospira, Inc) because of its pharmacokinetic profile, including light sedation, whereby patients can easily be awakened, and its successful use in our preliminary proof-of-principle study.[3] Dexmedetomidine is approved by the Food and Drug Administration for continuous infusion for up to 24 hours. It has a rapid distribution half-life of 6 minutes, a terminal elimination half-life of 2 hours, and linear kinetics in dosages of 0.2 to 0.7 μg/kg per hour, the maximum approved dose.[19] This study was done under the approval of the Food and Drug Administration Investigational New Drug number 111693 (C.R.W.). Preparation and distribution of the drug were the responsibility of the University of Minnesota Medical Center Investigational Drug Services pharmacy.

Dexmedetomidine Administration Protocol. We used the LifeCare PCA Infusion System (model 20709-04, Hospira, Inc) to administer the dexmedetomidine in the PCA and continuous infusion mode. The pharmacy prepared bar-coded syringes for this infusion device. We used the same dosing algorithm for patient-controlled sedation that we used in our preliminary study[3]: a loading dose (0.5 μg/kg) followed by a continuous basal infusion of 0.2 μg/kg per hour, up to a maximum infusion of 0.7 μg/kg per hour. Patients were allowed 3 self-administered boluses of dexmedetomidine per hour (0.25 μg/kg) with a 20-minute lockout.[3] Dexmedetomidine patients were instructed to depress the push button when they felt anxious or if they desired medication for relaxation.

Nurses increased or decreased the basal infusion rate according to the number of bolus attempts by the patient in the preceding 2 hours. Details of the protocol have been published elsewhere.[3] Because the study aims were to evaluate the safety and acceptability of self-administration of dexmedetomidine, patients in the dexmedetomidine group did not have daily sedative reduction trials. If a patient continued to receive mechanical ventilation after 5 days, the dexmedetomidine protocol was discontinued, and the sedative regimen reverted to medications ordered by the primary care team.

Dexmedetomidine Safety Monitoring. An extensive safety monitoring plan was required for this pilot trial. Research personnel abstracted every-4-hour heart rate and blood pressure recordings from the medical records. Research personnel or nurses reported study-defined adverse events (adverse hemodynamic effects: systolic blood pressure < 80 or > 180 mm Hg, diastolic blood pressure < 50 or > 100 mm Hg; heart rate < 40 or > 120 beats/min), persistent inability to understand rationale for triggering the push button, or marked worsening of respiratory status requiring aggressive ventilatory support. Any safety issues, change in a patient's medical status, or adverse events were first reported to the attending physician and then to a study medical safety officer; both were available at all times by pager and participated in decisions to immediately modify or suspend the protocol. The study physician made the final decision on restarting the protocol or withdrawing a patient from the study.

> Patients who were assigned to the experimental group self-administered dexmedetomidine.

Protocol Deviations. Research personnel reviewed the electronic medical records daily for protocol deviations related to the study drug, infusion pump, or any cause for dexmedetomidine patients.

Protocol Adherence. A daily checklist was used to monitor the abilities of the patients' nurses on all shifts to adhere to the infusion algorithm.

Acceptability of Dexmedetomidine. At completion of the dexmedetomidine protocol, an investigator-created 5-choice Likert-scale questionnaire was used to query patients randomized to the dexmedetomidine group about their ability to self-administer the medication for relaxation, ability to control anxiety, and level of relaxation experienced.

Usual Care

Patients randomized to usual care continued on their current sedative regimen with doses and frequencies of medications ordered by the primary care team and administered per standard practice

Table 1
Demographic and clinical characteristics of patients by group (n = 37)

Characteristic	PST-DEX (n = 17)	Usual care (n = 20)	*P*
Age, mean (SD), y	53.4 (15.3)	48.3 (14.9)	.31
Male sex, No. (%) of patients	9 (53)	13 (65)	.46
APACHE III score, mean (SD)	65.6 (32.0)	55.2 (33.3)	.34
Total days in ICU, mean (range)	16.5 (3-40)	15.5 (3-45)	.16
Total days of mechanical ventilation, mean (range)	3.9 (1-12)	6.7 (1-24)	.08
Days in ICU before study enrollment, mean (range)	8.1 (1-36)	9.9 (0-32)	.77
Days of ventilator support before study enrollment, mean (range)	3.9 (0-20)	7.8 (0-25)	.18
Days enrolled in study, mean (range)	3.1 (1-5)	3.6 (1-5)	.99

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; PST-DEX, patient self-administered sedative therapy with dexmedetomidine.

by the nurses. For usual care, administration of sedative therapy consisted of physician orders with parameters to titrate continuous infusions up or down on the basis of a prescribed target Minnesota Sedation Assessment Tool[20] or Motor Activity Assessment Scale.[21] A majority of patients also had orders for bolus doses of sedatives and/or opioids as needed. Continuous infusions of sedatives and/or as-needed bolus doses were titrated at the nurses' discretion on the basis of physician-ordered parameters. If feasible and appropriate, patients who received usual care had reduction or interruption in the continuous sedative infusion to increase wakefulness and reevaluate sedative requirements.

In addition, patients in both groups were evaluated each morning by a respiratory therapist for readiness for a spontaneous breathing trial. No data were gathered on differences between groups on daily screening and reduction of sedatives or spontaneous breathing trials.

Statistical Analysis

Descriptive statistics and graphing were used for summary statistics and illustrated the distribution of the interval measures. Comparisons between patients' demographic and clinical characteristics were accomplished by using *t* tests for normally distributed interval data and Mann-Whitney tests for skewed distributions. Categorical data were compared by using χ^2 tests of association. Mixed models were fit to detect any change in anxiety levels over time by group. Analysis was performed by using SPSS, version 19 (IBM SPSS Statistics) and SAS, version 9.3 (SAS Institute Inc), software. Results were considered significant at *P* less than .05.

Results

Demographic and Clinical Characteristics

Of the 37 enrolled patients, 59% were male, 89% were white, 3% were Asian, 5% were black, and 3% were native Hawaiian or Pacific Islander. The mean age was 50.6 (SD, 15) years. Mean illness severity (Acute Physiology and Chronic Health Evaluation III) was 60.1 (SD, 32.6; Table 1). A majority of patients had a respiratory-related diagnosis at the time of ICU admission and a number of comorbid conditions (Table 2).

Among the 522 patients eligible after the first chart review screening, 81 remained eligible after secondary screening. A total of 37 participants were enrolled (46% consent rate); 2 of the 37 provided consent by proxy (5%) (see Figure). The main exclusions were aggressive ventilatory support, use of vasopressors, chemical paralysis, stroke, myocardial infarction, and delirium. More than half of the patients (56%) who passed the prescreening were assessed as CAM-ICU positive on the secondary screening. Further, patients often lacked adequate hand strength to depress the push button. Patients approached for consent who declined to participate indicated that they were too tired, were not interested, or thought they had too much going on.

Of the 37 patients, 17 were assigned to the experimental dexmedetomidine group (46%) and 20 to usual care (54%), resulting in an unbalanced randomization. The 2 groups did not differ significantly on baseline variables (Table 1).

Patients were enrolled for a mean of 3.4 days (SD, 1.6 days; median, 4 days; range, 1-5 days). Mean duration of treatment according to the study protocol was 3.1 days (SD, 1.5 days; median, 2.0 days) for patients in the dexmedetomidine group and 3.6 days (SD, 1.7 days; median, 4.0 days) for patients in the usual-care group. In the usual-care group, 3 patients were extubated during their enrollment in the study. A total of 7 patients received a tracheostomy while enrolled: 4 in the usual-care group and 3 in the dexmedetomidine group. No patients died during the study period. A total of 4 patients were assessed as CAM-ICU positive (delirium present) during the study: 0 patients in the dexmedetomidine group and 4 in the usual-care group (*P* = .06).

Daily Anxiety Ratings. Overall mean anxiety ratings at enrollment were 38.4 (SD, 28). Mixed models analyses were fit to determine any changes in anxiety scores over the 5-day protocol. No significant

change occurred in VAS-A ratings during the 5-day study period (β_{day} = 2.1; SE, 2.5; P = .40).

Supplemental Medications. During the 5-day study period, 59% of dexmedetomidine patients received a mean of 3.75 (SD, 7.2; mode, 0; median, 1) bolus doses of medications. Medications included bolus doses of midazolam, fentanyl, and hydromorphone.

Safety

Study-Defined Hemodynamic Effects or Adverse Events. Five dexmedetomidine patients (29%) experienced study-defined hemodynamic alterations. In all instances, the hypotension and/or bradycardia resolved after the infusion was temporarily decreased or suspended or fluids were administered (Table 3). No dexmedetomidine patient was removed from the study because of safety concerns. Among the patients receiving usual care, 1 self-extubated and required reintubation. No dexmedetomidine patient self-extubated.

Safety Alert Notification. Patients' nurses appropriately made calls to the medical safety officer for patients' needs 100% of the time and made recommended changes in the drug infusion rate or care interventions 100% of the time.

Protocol Deviations. The deviations in protocol that occurred were related to the infusion pump. In the first case, the patient's nurse documented that the infusion pump ceased infusing for an unknown period; the patient had no adverse effects. In the second case, the drug library of the infusion pump did not recognize the medication syringe bar code, preventing initiation of the infusion. This patient was removed from the study, and the primary care team reinstituted the previous sedative therapy without incident.

Patients' Acceptability of Dexmedetomidine

Acceptability of dexmedetomidine was evaluated via 3 investigator-created questions (Table 4). A total of 13 of the 17 dexmedetomidine patients (76%) responded; the 4 nonresponses were due to extubation and transfer from the ICU, change in medical condition, or the patient's decision to withdraw ventilatory support. A majority of dexmedetomidine patients were satisfied or very satisfied with their ability to self-administer medication (92%) and control anxiety (62%).

Adherence to Medication Algorithm Protocol

Patients' bedside nurses, not research nurses, adhered to the previously published titration algorithm[3] 78% of the time on day shifts, 75% on evening shifts, and 65% on night shifts. Adherence to the dexmedetomidine basal infusion titration algorithm across all shifts was 73%.

Table 2
Primary admission diagnosis, comorbid conditions, and indication for mechanical ventilation (n = 37)

Feature	No. (%) of patients	
	PST-DEX (n = 17)	Usual care (n = 20)
Primary ICU admission		
CABG	0 (0)	1 (5)
Hypotension	1 (6)	0 (0)
ARDS	1 (6)	1 (5)
COPD	3 (18)	0 (0)
Pneumonia	4 (24)	3 (15)
Pulmonary fibrosis	1 (6)	2 (10)
Shortness of breath	1 (6)	6 (30)
Respiratory failure	2 (12)	4 (20)
Cancer	2 (12)	1 (5)
Sepsis	2 (12)	1 (5)
Abdominal pain	0 (0)	2 (10)
Gastrointestinal bleeding	0 (0)	2 (10)
Pancreatitis	1 (6)	0 (0)
Acute renal failure	2 (12)	0 (0)
Surgery	2 (12)	3 (15)
Comorbid conditions		
Cardiovascular	7 (41)	11 (55)
Respiratory	10 (59)	11 (55)
Neurological	5 (29)	4 (20)
Renal	3 (18)	3 (15)
Gastrointestinal	5 (29)	7 (35)
Metabolic or endocrine	9 (53)	7 (35)
Malignant neoplasia	3 (18)	5 (20)
Infection	4 (24)	0 (0)
Hematologic	3 (18)	3 (15)
Musculoskeletal	3 (18)	5 (20)
Transplant	5 (29)	1 (5)
Obesity	2 (12)	2 (10)
Indication for mechanical ventilation		
Airway protection	0 (0)	2 (10)
ARDS	2 (12)	1 (5)
COPD	1 (6)	0 (0)
Hypoxia	2 (12)	2 (10)
Pneumonia	3 (18)	4 (20)
Respiratory arrest	1 (6)	1 (5)
Shortness of breath	8 (47)	10 (50)
Respiratory failure	9 (53)	8 (40)
Tachypnea	1 (6)	1 (5)

Abbreviations: ARDS, adult respiratory distress syndrome; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; PST-DEX, patient self-administered sedative therapy with dexmedetomidine.

Discussion

Our aims in this randomized clinical pilot study were to determine safety and acceptability of self-administration of dexmedetomidine in patients receiving mechanical ventilation. Findings indicate that dexmedetomidine is safe as defined by a priori

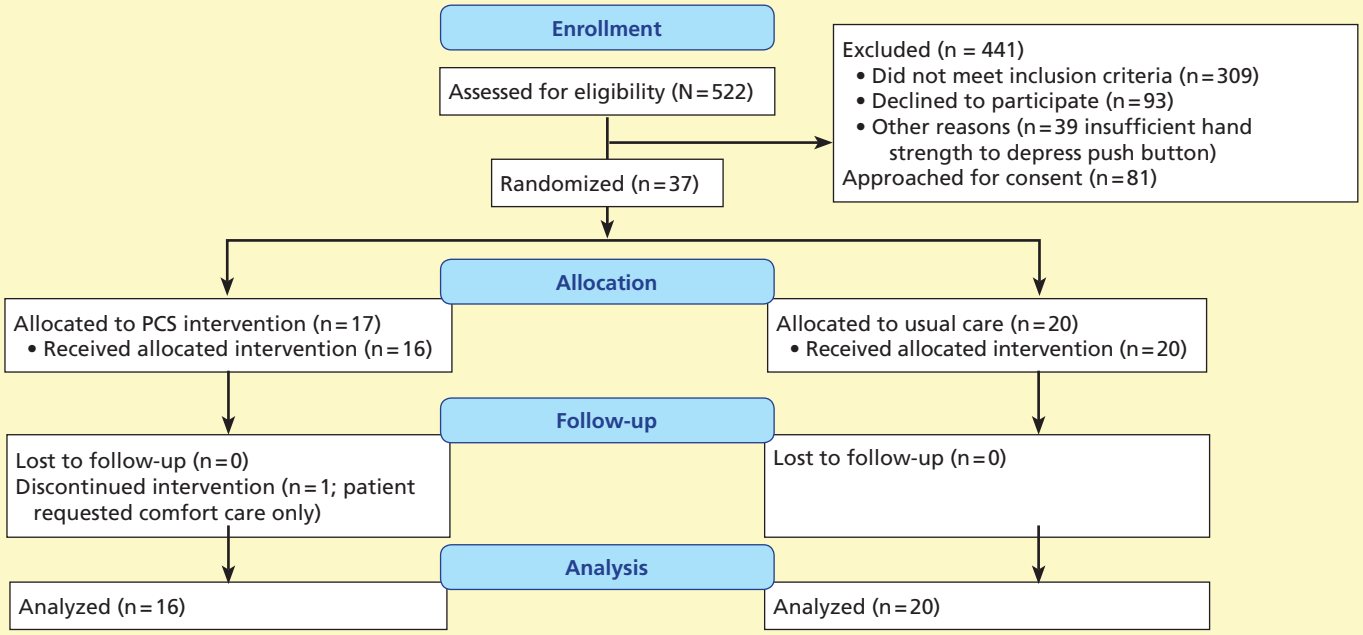

Figure Flow diagram of the trial.

Table 3
Dexmedetomidine protocol hemodynamic alterations: interventions and outcomes

Patient	Hypotension	Bradycardia	Intervention	Outcome
1	During night shift, BP decrease triggered alert parameter notification		Dexmedetomidine infusion suspended overnight for approximately 8 hours; restarted in morning	No further hemodynamic alterations; continued in the study
2	During night shift, BP decrease triggered alert parameter notification	During night shift, HR decrease triggered alert parameter notification	Patient remained in stable condition and did not require any additional intervention other than continued observation	No further hemodynamic alterations; continued in the study
3	During night shift, BP decrease triggered alert parameter notification		Dexmedetomidine infusion suspended for approximately 1.5 hours; restarted without incident	No further hemodynamic alterations; continued in the study
4		HR decreased >30%, triggered alert parameter notification	Patient remained in stable condition and did not require any additional intervention other than continued observation	No further hemodynamic alterations; continued in the study
5	Diastolic BP consistently <50 mm Hg overnight triggered alert parameter notification		500-mL saline bolus plus dexmedetomidine infusion suspended for approximately 2 hours; restarted without incident	No further hemodynamic alterations; continued in the study

Abbreviations: BP, blood pressure; HR, heart rate.

Table 4
Acceptability of patient-managed sedative therapy with dexmedetomidine (n=13)[a]

Question	Very satisfied	Satisfied	Neutral	Unsatisfied	Very unsatisfied
Ability to self-administer medication	6 (46)	6 (46)	1 (8)	0 (0)	0 (0)
Ability to control anxiety	6 (46)	3 (23)	3 (23)	1 (8)	0 (0)
Ability to achieve relaxation	5 (39)	3 (23)	2 (15)	2 (15)	1 (8)

[a] Three patients did not complete the satisfaction survey at the conclusion of the protocol; 1 patient did not receive the intervention because of problems with the infusion pump. Values are number (percentage) of patients. Because of rounding, not all percentages total 100.

criteria for a select sample of patients during the later, more stable part of mechanical ventilation. We observed changes in heart rate and mild hypotension during the dexmedetomidine infusion comparable to changes noted with clinician-administered sedatives.[22-24] These hemodynamic alterations resolved with minor clinical interventions; no dexmedetomidine patients were removed from the study for safety reasons. The patients' bedside nurses were able to adhere to the protocol's safety alert parameters and correctly adhered to the dexmedetomidine titration algorithm a majority of the time. No self-extubations occurred in patients randomized to the dexmedetomidine group.

Likewise, a majority of patients were satisfied with their ability to self-administer dexmedetomidine to control anxiety and achieve relaxation. Patients were able to use dexmedetomidine according to the patients' individual needs under the conditions and limited duration of this trial. Although no significant change in anxiety over time occurred for either group, our findings suggest that the ability of patients randomized to the dexmedetomidine group to manage anxiety with self-administration of a sedative was comparable to that of patients who received clinician-administered sedative therapy. This result is congruent with the finding that most dexmedetomidine patients were satisfied with their ability to control anxiety. These pilot data can be used to adequately power future clinical trials of dexmedetomidine to determine if sedative self-administration is efficacious for symptom management in patients receiving mechanical ventilation.

Interestingly, no patients in the dexmedetomidine group experienced delirium after enrollment, whereas 4 patients in the usual-care group did. This post hoc finding requires confirmation in larger studies. Because our dexmedetomidine protocol involves a medication, the intervention is not drug-free. However, dexmedetomidine can accelerate the resolution of delirium[22] and allow patients to be more interactive with caregivers.[23] Compared with other commonly used ICU sedatives such as midazolam or propofol, use of dexmedetomidine is consistent with the goals of the 2013 clinical practice guidelines[23] for interactive, more alert patients during mechanical ventilation.

Limitations

Because of the requirement that patients be awake enough to understand the sedation self-management concept, dexmedetomidine was not appropriate for many patients receiving mechanical ventilation, especially in the first few days of respiratory failure. Thus, the generalizability of the study findings is limited to patients treated with mechanical ventilation whose clinical characteristics are similar to those of our participants. On the other hand, as ICUs increasingly adopt a "lightly sedated strategy," more patients would be eligible for a sedation self-management protocol similar to the one used in this trial. A patient receiving mechanical ventilation whose treatment included an early mobility protocol most likely would be appropriate for a sedation self-management protocol.

We compared usual care with a combined experimental arm of dexmedetomidine delivered by continuous infusion plus patient self-initiated boluses. A study design of self-administered dexmedetomidine vs nurse-directed sedation with dexmedetomidine was considered. However, such a trial would have limited generalizability because dexmedetomidine is not a first-line sedative in usual clinical practice.[25,26] Because of resource limitations, we did not assess patients for physical or mental limitations after they left the ICU. Last, we did not evaluate the satisfaction of patients' bedside nurses with dexmedetomidine because we previously documented overall satisfaction of nursing staff with patient self-administration of sedative therapy.[3]

> Patients were satisfied with their ability to self-administer dexmedetomidine.

Conclusions

Self-administration of sedative therapy by patients receiving mechanical ventilation is safe. Patients are satisfied and able to self-administer dexmedetomidine to manage anxiety and achieve relaxation. Patient self-administration of sedative therapy logically fits in the contemporary practice of sedation management to have patients more alert and participating in their care. Only a larger, adequately powered study can determine whether patient-controlled sedation can achieve clinically relevant outcomes such as shorter duration of mechanical ventilation, decreases in patients' symptoms such as anxiety, prevention of delirium, and improved recovery after critical illness.

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