Prolonged use of intravenous clonidine for sedation and analgesia in critically ill adult patients

M. Zeeman1,4, H.L.A. van den Oever2, M. Arbouw3, J. van der Valk2, C. Kramers4,5,6
Departments of 1Clinical Geriatrics, 2Intensive Care Medicine, 3Clinical Pharmacy, Deventer Hospital, Deventer, the Netherlands, Departments of 4Pharmacology-Toxicology and 5Internal Medicine Radboud University Medical Center Nijmegen, the Netherlands, Department of Clinical Pharmacy, CWZ Nijmegen, the Netherlands

Correspondence
M. Zeeman – m.zeeman@dz.nl

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Abstract
Background: Clonidine is used in critically ill patients for sedative and analgesic purposes.
Objectives: 1) to review, systematically, the literature on prolonged intravenous (iv) clonidine for sedation in critically ill patients; 2) to evaluate the evidence from related fields of medicine on the use of clonidine for sedative or analgesic purposes, and; 3) to investigate prescribing practices of clonidine.
Methods: We searched the literature for: 1) the use of prolonged iv clonidine for sedation in adult critically ill patients; 2) evidence of iv clonidine in the perioperative setting and in patients suffering from alcohol withdrawal; 3) information on haemodynamic side effects of clonidine. We performed a telephone and email enquiry to investigate dosing schemes.
Results: Three published prospective trials were found. Clonidine shortened the duration of ventilation. Clonidine also had an analgesic and opioid-sparing effect. The cardiovascular events reported included bradycardia and first-degree atrioventricular block. Clonidine doses in the literature varied from 50 to 3360 µg/70 kg/day. All of the 14 responding intensive care units (ICUs) confirmed the prolonged use of iv clonidine. Doses varied from 240 to 2400 µg/70 kg/day and loading doses varied from 0 to 150 µg.
Conclusion: Prolonged use of iv clonidine is common in critically ill patients, but the evidence is limited. Clonidine can decrease postoperative opioid consumption and pain intensity and can produce dose-dependent sedation. Dosing schemes varied considerably between the surveyed ICUs as well as in the literature. Cardiovascular side effects were reported. Clonidine should be used cautiously in high-risk cardiovascular patients.

Introduction
Clonidine is an alpha-2 adrenoceptor agonist. It was developed in the 1960s for the treatment of hypertension, which is currently the only approved indication in most countries. Soon after its introduction, sedation and reduction of anxiety became recognised as side effects. These sedative effects were illustrated in an experiment by Hall et al. who administered different doses of intravenous (iv) clonidine to healthy volunteers.1 Dose-dependent sedation was observed in all subjects. The authors remarked that subjects remained rousable throughout the experiment, even at higher doses of clonidine. A condition in which patients are comfortably asleep, but can easily be roused, is often desired in ventilated critically ill patients. This may explain why clonidine has found use as a sole sedative or as an adjunct to sedation in many intensive care units (ICUs).

Clonidine is used for many indications in the ICU, such as hypertension, substance withdrawal, adjunct and alternative for sedation and analgesia, and prevention of delirium. In critical care settings, clonidine is often administered over a prolonged period of time, with continuous iv infusion or intermittent bolus injections, whilst most of the studies investigating the safety and effectiveness of clonidine were performed with a single oral dose. There are no dosing recommendations for prolonged use of iv clonidine for the different indications in the ICU. Clonidine has an elimination half-life of approximately 12-14 hours, which can increase to 42 hours in patients with renal insufficiency.2 Therefore, dosing effects and side effects of clonidine in studies...
Prolonged use of intravenous clonidine for sedation and analgesia in critically ill adult patients

The objectives of this study were: 1) to systematically review the existing literature of prolonged iv administration of clonidine for sedation of critically ill patients; 2) to evaluate circumstantial evidence from related fields of medicine on the use of clonidine for sedative or analgesic purposes; and 3) to investigate current prescribing practices of clonidine in Dutch ICUs.

Methods

We did an extensive literature search in Medline, PubMed, Embase, Cochrane library, and TRIP database with the following free text and MESH terms: “clonidine” AND “intensive care” OR “ICU” OR “critical care” AND “sedation” OR “hypnotics and sedatives” OR “alpha-2-agonists” AND “delirium” OR “side effects” OR “hemodynamic” OR “adverse events”. Included were original articles of any type, experimental or observational, concerning adult patients. All articles were written in English in the period 1946 to March 2014. The references from retrieved reviews and original articles were also manually searched. We excluded studies of interventions in which an oral, transdermal, nasal or single iv dose of clonidine was administered, because the aim of our study was to collect evidence from prolonged iv use of clonidine. The following primary outcomes and measures were extracted from the literature survey: 1) level of sedation, 2) delirium, 3) prescribing practices/dosing, and 4) nature and incidence of adverse events.

To gather circumstantial evidence of prolonged iv clonidine as a sedative, we searched for randomised, controlled trials which investigated the use of clonidine in a perioperative setting. The chosen trials reported at least on sedation, postoperative cumulative opioid consumption or pain intensity. We also searched for randomised, controlled trials which investigated the prolonged use of iv clonidine to treat alcohol withdrawal syndrome. The chosen trials reported at least on withdrawal symptoms, sedation or delirium.

All selected articles were specifically scanned for adverse events associated with clonidine. We also included recent original articles in which side effects of clonidine were reported. Finally, we performed an email and telephone enquiry addressed to 25 Dutch ICUs. Respondents were interviewed about current prescribing practices with clonidine in critically ill patients.

Results

Records identified through database searching (n = 478) Records after duplicates removed (n = 480)

Records included in qualitative synthesis (n = 3)

Studies included in qualitative synthesis (n = 3)

Studies excluded, with reasons (n = 2)

Full-text articles assessed for eligibility (n = 72)

Full-text articles excluded, with reasons (n = 48)

Additional records identified through other sources (n = 2)

Intravenous clonidine as a sedative in critically ill patients

The flowchart of inclusion is shown in figure 1. We included three prospective studies, of which only one was blinded.7,9,10

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>Intervention/clonidine dose</th>
<th>Outcome</th>
<th>Main findings</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubino 2010 (30)</td>
<td>Bolus 0.5 µg/kg followed by 1-2 µg/kg/h continuous, or placebo 1680-3360 µg/70kg/24 h</td>
<td>Neurological outcome and respiratory function</td>
<td>Lower DDS, shorter weaning and shorter period of ICU stay in clonidine group</td>
<td>RCT, blinded pilot study</td>
</tr>
<tr>
<td>Liatsi 2009 (30)</td>
<td>900-1800 µg in two doses with 10 min interval, when effective: 1800-2500 µg/24 h continuous infusion Vs remifentanyl-propofol</td>
<td>Respiratory, metabolic and haemodynamic effects</td>
<td>25/30 pts responded to clonidine; mild sedation, better ventilation weaning No severe hypotension or bradycardia</td>
<td>Prospective intervention study, not blinded</td>
</tr>
<tr>
<td>Fauler and Verner 1993 (11)</td>
<td>Bolus 150 µg; mean dose 720 (290-2370) µg/24 h</td>
<td>Kinetic parameters, side effects</td>
<td>Lowering MAP and heart rate not clinically significant</td>
<td>Pharmacokinetic study</td>
</tr>
</tbody>
</table>

ns: not significant

DDS: delirium detection scale

MAP: mean arterial pressure
A wide variety of dosing schedules were used (table 1).

In a blinded, prospective study with 30 patients undergoing surgery for acute type A aortic dissection, patients were randomised to receive either iv clonidine (0.5 μg/kg bolus, followed by a continuous infusion at 1-2 μg/kg/h) or placebo. The delirium detection score was lower in the clonidine group (p < 0.001). Patients with clonidine showed different ventilation parameters: higher PaO\(_2\)/FiO\(_2\), higher PaCO\(_2\) (p < 0.001), lower ratio of frequency and tidal volume, and lower pressure-frequency product (p < 0.001), suggesting better respiratory conditions and a more relaxed pattern of breathing in the weaning phase. Despite a limited study size, there were also significant differences in clinically relevant endpoints: Patients who received iv clonidine required a shorter period of weaning and showed a shorter ICU length of stay (p < 0.001).

In a small interventional cohort study of 30 ventilated patients who developed withdrawal symptoms in the weaning phase, patients were given 900-1800 μg clonidine iv divided into two doses, after termination of the sedation with remifentanyl-propofol. The investigators found decreased sedation when the initial sedation with remifentanyl-propofol was replaced with clonidine (Ramsay sedation score from 3.5 ± 0.5 to 2.2 ± 0.5), enabling patients to cooperate better with the weaning process. However, there was no randomisation and no blinding, and five non-responders to clonidine treatment were excluded from the analysis.

In an email survey among ICUs in Germany, the investigators found that clonidine was used for sedation duration for less than 24 hours in 35% of the hospitals. For sedation duration between 24 and 72 hours, clonidine was used in 48% of the hospitals. In the weaning phase, clonidine was used in 56% of the hospitals. No dosing information was given.

A Canadian group performed a chart review to analyse clonidine prescribing practices in an ICU of a tertiary care hospital. The investigators found that clonidine was used in 9% of patients admitted to the ICU. The average duration of clonidine use was nine days (range 1-34 days). Clonidine was prescribed for a variety of indications, mostly sedation, pain control, agitation, hypertension and withdrawal symptoms. The average daily dose was 260 μg (range 50-800 μg). A small pharmacokinetic study in 11 patients undergoing surgery for oesophagogastrectomy showed a linear relation between dosage and plasma concentration of iv clonidine. No effect on sedation or analgesia was reported.

In conclusion the prolonged administration of iv clonidine in critically ill patients was reported in two intervention studies; it was clearly associated with lower delirium scores in one and a suggestion of decreased delirium in the other. Clonidine provided mild, comfortable sedation in both studies, seemingly favourable for weaning purposes. Both trials used iv clonidine administration as an intervention to facilitate weaning, showing favourable results, though patient numbers were limited. Yet, at least in some institutions, clonidine seemed to be used liberally.

Table 2. Studies of intravenous clonidine as a sedative in perioperative situations

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>Intervention/clonidine dose / max daily dose</th>
<th>Outcome</th>
<th>Main findings</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernard 1991 (50)</td>
<td>Load 5 μg/kg/60 min 0.3 μg/kg/h during 11 h vs placebo 231 μg/70kg/11 h</td>
<td>Pain</td>
<td>Clonidine delayed onset of pain Lower pain score with clonidine 42±5 to 26±3 (scale 0 to 100)</td>
<td>Double-blind RCT</td>
</tr>
<tr>
<td>De Kock 1992 (187)</td>
<td>Load 4 μg/kg/30 min 2 μg/kg/h with anaesthesia vs anaesthesia alone 3360 μg/70kg/24 h</td>
<td>Number of analgesic demands Sedation scores</td>
<td>Reduction of analgesic demands 45±27 vs 81±60 (p = 0.0001) No difference in sedation scores</td>
<td>RCT, observer blinded</td>
</tr>
<tr>
<td>Striebel 1993 (60)</td>
<td>300 μg / 2 h vs placebo</td>
<td>Pain</td>
<td>No pain reduction</td>
<td>Double-blind RCT</td>
</tr>
<tr>
<td>Jeffs 2002 (60)</td>
<td>Load 4 μg/kg/20 min PCA clonidine 20 μg + morphine 1 mg vs placebo iv + morphine 1 mg</td>
<td>Pain, nausea</td>
<td>Clonidine: lower pain score in the first 12 h 1 (0-3) vs 3 (1-4) (p&lt;0.05) No reduction in morphine use Reduction in nausea</td>
<td>Double-blind RCT</td>
</tr>
<tr>
<td>Marinangeli 2002 (80)</td>
<td>Load 2,3,5 μg/kg/30 min 0.3 μg/kg/h during 12 h vs placebo 252 μg/70kg/12 h</td>
<td>Optimal dose when sedation and analgesia is required</td>
<td>3 μg/kg followed by 0.3 μg/kg/h during 12 h is optimal dose for sedation 2 μg/kg: 5±2 ds morphine 3 μg/kg: 11±3 ds morphine 5 μg/kg: 19±4 ds morphine Placebo: 29±8 ds morphine</td>
<td>Double-blind RCT, dose finding</td>
</tr>
</tbody>
</table>

ds: doses
PCA: patient-controlled analgesia
in ventilated patients to facilitate sedation and weaning. Studies were too few and too heterogeneous for meta-analysis.

**Clonidine as a sedative drug in perioperative situations**

We included five studies (Table 2),13-16 of which three were blinded, investigating the effect of intraoperative clonidine on postoperative pain. In four studies a loading dose of 2-5 µg/kg clonidine in 20-60 min was given, followed by a continuous infusion of 0.3-2 µg/kg/h.3,13-15 In an open-label randomised controlled trial (RCT), 300 µg/2h postoperatively was given.16 Four out of five studies concluded that clonidine had a significant morphine-sparing and analgesic effect.3,13-15 In one study no effect on pain reduction was demonstrated.16 In one of the studies a dose-dependent effect of clonidine on sedation and sleep was observed.15 In that study, the optimal balance between analgesia and side effects was achieved with a loading dose of 3 µg/kg. In conclusion, prolonged perioperative use of clonidine decreased postoperative opioid consumption and pain intensity, and produced dose-dependent sedation and sleep.

**Clonidine in alcohol withdrawal related agitation and delirium in ICU patients**

We found three RCTs which were all open label and performed by the same study group (Table 3). The first study was performed in 159 multiply injured alcohol-dependent patients.17 Patients were randomised to one of three iv regimens: flunitrazepam/clonidine, chlorpromazine/haloperidol or flunitrazepam/haloperidol. No differences in the primary outcomes, mechanical ventilation and major intercurrent complications were found. There was some advantage in the flunitrazepam/clonidine regimen with respect to pneumonia and the necessity for mechanical ventilation (p < 0.05). The second RCT included 197 alcohol-dependent patients who were admitted to the ICU after oesophageal tumour resection.18 They were randomised to iv flunitrazepam/clonidine, chlorpromazine/haloperidol, flunitrazepam/haloperidol or ethanol. No differences in duration of ICU treatment, prevention of alcohol withdrawal syndrome and rate of major intercurrent complications were found. In the third RCT, 44 patients with alcohol withdrawal syndrome were randomised to either a continuous infusion of iv flunitrazepam combined with clonidine or haloperidol, or the same medication bolus adjusted in response to the development of the signs and symptoms of alcohol withdrawal syndrome.19 In the bolus-titrated group, ICU treatment was significantly shorter due to a lower incidence of pneumonia. This study was not designed to specifically compare clonidine with other drugs.

**Table 3. Literature on clonidine used in alcohol withdrawal related agitation and delirium**

<table>
<thead>
<tr>
<th>Study (N)</th>
<th>Intervention/clonidine dose /max daily dose</th>
<th>Outcome</th>
<th>Main findings</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spies 1995 (197)</td>
<td>Load 150 (75-300) µg Max 0.83 (0.07-3.39) µg/kg/h iv flunitrazepam/clonidine 1394 (118-5695) µg/70kg/24h or chlorpromazine/haloperidol or flunitrazepam/haloperidol or ethanol</td>
<td>Duration of ICU stay prevention of AWS rate of major intercurrent complications</td>
<td>No difference between the groups</td>
<td>RCT, blinded</td>
</tr>
<tr>
<td>Spies 1996 (159)</td>
<td>Flunitrazepam /clonidine Max dose 0.88 (0.14-4.69) µg/kg/h 1478 (235-7879) µg/70kg/24h chlorpromazine/haloperidol or flunitrazepam/haloperidol or ethanol</td>
<td>Duration of ventilation major intercurrent complications</td>
<td>Some advantage (pneumonia)</td>
<td>RCT, partially Blinded (AWS score blinded)</td>
</tr>
<tr>
<td>Spies 2003 (44)</td>
<td>Bolus 150-300 µg Max infusion rate 5.5 (2.2-7.4) µg/kg/h 9240 (3696-12,432) µg/70kg/24 h clonidine or flunitrazepam bolus or haloperidol bolus or continuous infusion clonidine/flunitrazepam/haloperidol</td>
<td>Effect of bolus vs continuous infusion adjustment on severity and duration of AWS</td>
<td>Decreased severity of AWS with the bolus approach</td>
<td>RCT, blinded</td>
</tr>
</tbody>
</table>

AWS: alcohol withdrawal syndrome
In conclusion, prolonged iv clonidine treatment in patients suffering from alcohol withdrawal syndrome may lead to some advantage with respect to a lower degree of intercurrent complications such as pneumonia, and shorter duration of mechanical ventilation. The lack of difference in outcome between the flunitrazepam/clonidine and flunitrazepam/haloperidol groups suggested that clonidine was equally effective as haloperidol in treating withdrawal symptoms. However, because clonidine was not tested alone, no definitive conclusions about the effect of clonidine can be drawn.
Side effects of IV clonidine in critically ill patients

Studies of oral clonidine have shown side effects, such as hypotension, hypertension, bradycardia and dry mouth. It has been hypothesised that the cardiovascular effects depend on the dose.\textsuperscript{20-22} In the three studies of clonidine used in patients suffering from alcohol withdrawal syndrome, cardiovascular side effects were reported (table 4).\textsuperscript{17-19} In one of the studies, cardiac complications were significantly more frequent in the flunitrazepam/clonidine group (p = 0.0047).\textsuperscript{17} However, severe cardiac complications that led to withdrawal of patients from the study were observed with all three regimens and these complications did not significantly differ between groups (p = 0.6720). In another study, the authors reported bradycardia requiring positive chronotropic support in the clonidine group, but this was not compared with placebo or another treatment.\textsuperscript{19} In the third trial performed in patients suffering from alcohol withdrawal syndrome, severe cardiac complications which led to withdrawal from the study were reported, but there was no significant difference between groups (p = 0.3152). We found two other studies that looked specifically at the haemodynamic effects of oral clonidine during heart catheterisation.\textsuperscript{23,24} Effective sedation was achieved with clonidine and the haemodynamic side effects appeared to be comparable between clonidine and midazolam. Recently the results of the POISE-2 study were published, a large RCT including 10,010 surgical patients at risk of cardiovascular events.\textsuperscript{25} In order to investigate the cardioprotective effect of clonidine, patients were randomised to placebo or a single oral dose of 0.2 mg clonidine, and thereafter a transdermal patch of clonidine 0.2 mg/day for 72 hours. There was no significant difference between groups at the primary and secondary endpoints, death, myocardial infarction or stroke at 30 days. However, nonfatal cardiac arrest was increased in the clonidine group compared with placebo, although absolute numbers were low (16 vs 5, p = 0.02). Also clinically important hypotension and bradycardia occurred significantly more frequently in the clonidine group (p < 0.001).

A dose-finding study of IV clonidine for the treatment of postoperative pain demonstrated that a loading dose of 5 µg/kg caused hypotension and sedation that was more severe and longer lasting compared with a loading dose of 2 or 3 µg/kg.\textsuperscript{15} In all of the studies discussed in this article, except for the POISE-2 trial, no significant differences were found with respect to bradycardia or haemodynamic changes leading to withdrawal of one or more of the study participants. However, in these studies, high-risk patients with existing bradycardia, hypotension or second- or third-degree atrioventricular node block and acute angina were excluded at study entry, while the POISE-2 trial was specifically performed in patients at risk of cardiovascular events.

In conclusion, treatment with clonidine may lead to side effects such as hypotension, bradycardia and cardiac arrest, which is particularly relevant in patients with known risk factors for cardiovascular events. These side effects are likely to develop in a dose-dependent manner.

Clonidine in Dutch ICUs

We requested 25 Dutch ICUs to participate with an email and telephone enquiry to investigate prescribing practices of clonidine.\textsuperscript{26} Fourteen out of 25 (56%) ICUs responded to our enquiry (table 5).

Table 5. Clonidine use in Dutch ICUs

<table>
<thead>
<tr>
<th>IC level</th>
<th>Clonidine use</th>
<th>Indication</th>
<th>Loading dose (μg)</th>
<th>Continuous infusion dose (μg/70 kg/24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Often</td>
<td>Hypertension; Sedation</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>3</td>
<td>Often</td>
<td>Substance withdrawal; Hypertension; Delirium; Sedation</td>
<td>40-120</td>
<td>240-1920</td>
</tr>
<tr>
<td>3</td>
<td>Often</td>
<td>Substance withdrawal; Sedation</td>
<td>150</td>
<td>1200</td>
</tr>
<tr>
<td>3</td>
<td>Often</td>
<td>Substance withdrawal</td>
<td>75-150</td>
<td>1200</td>
</tr>
<tr>
<td>3</td>
<td>Sometimes</td>
<td>Delirium</td>
<td>No loading dose</td>
<td>720-2400</td>
</tr>
<tr>
<td>3</td>
<td>Sometimes</td>
<td>Hypertension; Delirium</td>
<td>150</td>
<td>960</td>
</tr>
<tr>
<td>3</td>
<td>Sometimes</td>
<td>Substance withdrawal; Delirium</td>
<td>960</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sometimes</td>
<td>Substance withdrawal; Delirium</td>
<td>480-1200</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sometimes</td>
<td>Hypertension; Sedation</td>
<td>150</td>
<td>960</td>
</tr>
<tr>
<td>2</td>
<td>Sometimes</td>
<td>Substance withdrawal; Hypertension; Delirium</td>
<td>150</td>
<td>450-1000</td>
</tr>
<tr>
<td>1</td>
<td>Sometimes</td>
<td>Hypertension; Delirium</td>
<td>150</td>
<td>No continuous infusion</td>
</tr>
<tr>
<td>1</td>
<td>Sometimes</td>
<td>Delirium</td>
<td>50</td>
<td>1200-2400</td>
</tr>
<tr>
<td>1</td>
<td>Sometimes</td>
<td>Delirium</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
In our opinion, the responding ICUs reflected the Dutch situation with respect to the level of ICU care and geographical location. In 100% of the ICUs that responded, iv clonidine was used for at least one off-label indication (sedation, withdrawal symptoms or agitation) in ventilated patients. A wide range of dosing regimens were reported: infusion regimens varied from 240-2400 µg/70 kg/h and loading doses varied from no loading to 150 µg.

Discussion

Prolonged administration of iv clonidine as a sedative is common in critically ill patients in the Netherlands and abroad. However, we found insufficient data, and data limited to small series of patients, supporting its prolonged iv use. Widening our search to circumstantial evidence such as perioperative care and prevention of alcohol withdrawal syndrome showed no evidence demonstrating any benefit from prolonged administration of iv clonidine with regard to sedation, reduction of alcohol withdrawal syndrome or delirium. However, small effects were seen on reduction of duration of ventilation, postoperative pain scores, and morphine use.

None of the studies performed in critically ill patients discussed in this article showed significant bradycardia or haemodynamic changes that led to withdrawal of one or more of the study participants, except for the POISE-2 trial. The POISE-2 trial showed significantly increased incidences of nonfatal cardiac arrest, hypotension and bradycardia in the study group, but this trial was specifically on high cardiovascular risk patients excluded from most of the other studies. Although side effects such as hypotension and bradycardia are of concern in an ambulant population, we believe that these side effects are of less concern in a controlled environment such as an ICU. However, given the results of the POISE-2 trial, our advice is to be cautious with the use of clonidine in patients with a high risk of cardiovascular events.

Most of the studies did not last longer than 24 hours and the maximum daily dose used was low compared with current practice in ICUs. The average elimination half-life of clonidine is 12-14 hours. It is unlikely that steady-state levels were reached in any of these short-term studies, as it takes at least three half-lives to reach steady state. Therefore, irrespective of the dose used, we assume that plasma levels of clonidine in these short-term studies were low compared with plasma levels reached when treatment duration is more than 24 hours. These shortcomings make it difficult to extrapolate the safety aspects of the short-term studies in comparison with current practice of prolonged iv clonidine infusion.

We found no consensus in the literature as to the best dosing practice. In the studies where a loading dose was followed by a continuous infusion, the dosing schemes varied more than 50-fold. In our telephone enquiry we found that in clinical ICU practice the same broad variety of dosing schedules was used as reported in the literature.

Conclusion

Based on widespread common practice and a limited number of trials, it seems plausible that clonidine could be a valuable additive to achieve 'comfortable sedation' in critically ill patients. However, the evidence to support the efficacy and safety of the prolonged use of iv clonidine in critically ill patients is limited. Published data suggest that the perioperative use of clonidine can decrease postoperative opioid consumption and pain intensity and can produce dose-dependent sedation. Dosing schemes varied considerably between the surveyed ICUs and between schemes published in the literature. Side effects reported during prolonged iv administration in critically ill patients were limited to the well-known cardiovascular effects of clonidine. Clinical studies are needed to establish the best dosing regimens of prolonged iv clonidine for sedation and studies are needed to investigate the effectiveness and safety of its use in ventilated patients. In the meantime, clonidine should be used cautiously in high-risk cardiovascular patients.

Disclosures

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The prolonged use of intravenous clonidine for sedation and analgesia in critically ill adult patients: a systematic review