

**SAFETY IN NURSING CARE WITH SEDATIVE,  
ANALGESIC, AND VASOACTIVE DRUGS: SCOPE REVIEW**

Melissa Carleti<sup>1</sup>; Djulia Andriele Wachter<sup>2</sup>; Juliana Neves Giordani<sup>3</sup>  
Rita Catalina Aquino Caregnato<sup>4</sup>; Carine Raquel Blatt<sup>5</sup>

**Highlight:** (1) Nursing is essential to the safe administration of medications. (2) Vasoactive drugs can be administered peripherally with special care. (3) Multiparametric monitoring is essential in the use of sedatives and analgesics.

PRE-PROOF

(as accepted)

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<sup>1</sup> Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA). Porto Alegre/RS, Brazil.  
<https://orcid.org/0000-0002-7150-6733>

<sup>2</sup> Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA). Porto Alegre/RS, Brazil.  
<https://orcid.org/0000-0002-9127-3164>

<sup>3</sup> Hospital de Clínicas de Porto Alegre. Porto Alegre/RS, Brazil.  
<https://orcid.org/0000-0003-2397-0109>

<sup>4</sup> Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA). Porto Alegre/RS, Brazil.  
<https://orcid.org/0000-0001-7929-7676>

<sup>5</sup> Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA). Porto Alegre/RS, Brazil.  
<https://orcid.org/0000-0001-5935-1196>

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### **ABSTRACT**

The objective of this study was to map the existing evidence on the safety of nursing care in the preparation and administration of sedative, analgesic, and vasoactive drugs in critically ill patients. This scoping review involved searching the following databases: EMBASE, SCOPUS, PubMed/MEDLINE, Cochrane Library, CINAHL, and Web of Science. The search was supplemented with gray literature. Thirty-two studies were selected for review, with the majority (12) from the USA and one from Brazil. Of these, 16 were published in the last five years, and 18 focused on vasoactive care, while 11 dealt with analgesics and sedatives. The literature was reviewed to identify care for invasive/painful procedures and the role of nurses in this practice for sedatives and analgesics. Regarding vasoactive drugs, the following key points emerged: administration via peripheral routes, care with infusion pumps, communication, physicochemical incompatibilities, benefits of ready-to-use or premanipulated drugs, and implementation of care protocols. The publications describe the complexity and various precautions taken by the care team to ensure the safety of these medications.

**Keywords:** Patient Safety; Hospital Medication Systems; Vasoactive Drugs; Analgesia; Hypnotics and Sedatives.

### **INTRODUCTION**

Recent decades have witnessed substantial advancements in the field of healthcare. These advancements have been marked by the emergence of sophisticated technological infrastructures, a broadening array of treatment modalities, and an expanding therapeutic repertoire. However, this paradigm shift has the potential to jeopardize the delivery of safe care. Medication errors stand as a primary contributor to preventable injuries and damage within healthcare services, accounting for approximately 50% of such incidents<sup>1</sup>.

Errors of this nature have been demonstrated to result in disability and death in as many as 6.5% of hospitalized patients, in addition to generating costs<sup>2</sup>. It has been estimated that

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errors related to pharmaceuticals have an annual financial impact of approximately US\$ 42 billion, which is equivalent to nearly 1% of the global health expenditure<sup>3</sup>.

The issue of patient safety gained worldwide repercussions following the report published by the *Institute of Medicine* in 1999, "To Err is Human - Building a Safer Health System", which reported that between 44,000 and 98,000 patients died as a result of adverse events, 7,000 of which were related to medication errors<sup>4</sup>. In 2006, the World Health Organization (WHO) established six international patient safety targets, one of which was entitled "Improving the Safety of Highly Monitored Medicines"<sup>1</sup>. Building upon this initiative, the third global patient safety challenge was launched in 2017. It was entitled "Medication Without Harm," which included three categories of priority actions, including high-risk situations, such as highly supervised medicines<sup>3</sup>. In 2013, the Brazilian Ministry of Health promulgated Ordinance No. 529, thereby instituting the National Patient Safety Program (NPSP). This program encompasses six fundamental protocols, one of which pertains to the safety of pharmaceuticals, encompassing their prescription, utilization, and administration<sup>5</sup>.

From this panorama, errors involving potentially dangerous drugs stand out, accounting for between 27% and 72% of these errors. Among medications that are subject to heightened surveillance, antibiotics, sedatives, analgesics, antithrombotic agents, anticoagulants, anesthetics, cardiovascular drugs, insulin, and albumin have been associated with 50% of the moderate to severe harm experienced by hospitalized patients<sup>6</sup>. This group of drugs includes analgesics, sedatives, and vasoactive amines. These medications are commonly administered to patients with critical illnesses<sup>7</sup>. The nursing team is responsible for the final phase of the medication process, which involves the preparation and administration of medication. This stage of the medication process is complex and essential, and errors can unfortunately occur.<sup>8</sup>

To address this need, a scoping review was undertaken to map the available evidence on the safety of nursing care in the preparation and administration of sedative, analgesic, and vasoactive drugs in critically ill patients. A preliminary search was conducted in March 2022 in PubMed/MEDLINE, EMBASE, SCOPUS, Cochrane Library, CINAHL, and Web of Science, and no reviews with this focus were identified.

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### METHOD

This is a *scoping review*, following the guidelines of the *Joanna Briggs Institute* (JBI), which establishes five stages<sup>9</sup>. The manuscript was written in accordance with the *Prisma Extension for Scoping Reviews* (Primas-ScR) checklist<sup>10</sup>. The review was registered on the Open Science Framework platform, DOI 10.17605/OSF.IO/3U8VX.

Stage 1: Identifying the research question:

The review question was formulated using the acronym PCC (Population, Concept and Context). The population was defined as critically ill patients. The concept was nursing care, specifically the preparation and administration of sedative, analgesic, and vasoactive drugs. The context was defined as intensive care unit, emergency and emergency room. The research question is therefore defined as follows: What evidence is available on the safety of nursing care in the preparation and administration of sedative, analgesic, and vasoactive drugs to critically ill patients in intensive care units, emergency rooms or emergency rooms?

Stage 2: Identification of relevant studies

The following inclusion criteria were established for the consideration of studies: addressing the issue of safety in the preparation and administration of sedatives, analgesics, and vasoactive drugs; focusing on adult patients; conducted in the emergency room, emergency department, intensive care unit, or a setting simulating these environments; available on the website of the journals and/or contact the authors in Portuguese, English, Spanish, or French, without limitation to the year of publication; irrespective of the study design. For studies that were not available in full, at least one attempt was made to contact the main author, and a search was also made in other databases. If there was no access or return, the articles were not included.

The first search took place in the SCOPUS and PubMed/MEDLINE databases with the descriptors *patient safety*, *nursing care*, *critical care*, *emergency care*, *vasoactive*, *analgesics*, *sedation* using the Boolean operators AND and OR to list the keywords most used in published research and map the context. In this way, it was possible to compose the specific search strategy, applied and consolidated in PubMed/MEDLINE and the other databases (EMBASE, SCOPUS, *Cochrane Library*, CINAHL and Web of Science): (*Safety management OR patient safety OR safe practices OR Security patient OR Security OR Medication safety OR drug safety*

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*OR Safety management OR safe practices OR safe process) AND (nursing intervention OR medication preparation OR medication administration OR Nursing care OR nursing OR nursing process OR nursing practice OR care planning) AND (Critical ill OR critical care OR intensive care units OR Critical Care OR emergency care OR emergency department) AND (vasoactive OR vasoactive drugs OR Vasoactive medication OR Vasoconstrictor Agents OR Vasodilator Agents OR Vasopressor OR Analgesics OR Sedation OR Sedation infusions OR Analgesia OR sedatives OR sedative drugs OR Analgosedation) NOT (pediatric patient OR child OR pediatrics OR neonate OR newborn OR newborn infants).*

In the gray literature, materials were selected from the websites of institutions, bodies and magazines focused on patient safety: Consensus Magazine, Institute for Safe Medication Use Practices - ISMP Brasil, Federal Nursing Council (COFEN), Brazilian Nursing and Patient Safety Network (REBRAENSP), Ministry of Health and on PROQUALIS and *greylit.org*.

Stage 3: Selection and initial assessment of studies

The data search took place in April 2022. The gray literature was stored in the *Microsoft Office Excel®* program. The studies were selected independently and blindly by two reviewers familiar with the subject, using *Rayyan®*. The studies were selected by reading the titles, abstracts and, finally, the full text. Studies that did not involve adults; critically ill patients in intensive care units, emergency rooms or emergency rooms; sedative, analgesic or vasoactive drugs were excluded. Disagreements were resolved by a third reviewer with experience in the subject, who independently decided whether to include or exclude the study.

The data from the selected studies was extracted using a specific form drawn up in *Microsoft Office Excel®*, previously tested on four articles.

Stage 4: Data analysis

The following data was collected: title, authors, year of publication, country, objective, design, study site (emergency, intensive care unit, emergency room), population, main outcome, drugs involved, description of safety, nursing care and main focus.

Stage 5: Grouping, summarizing and presenting the data.

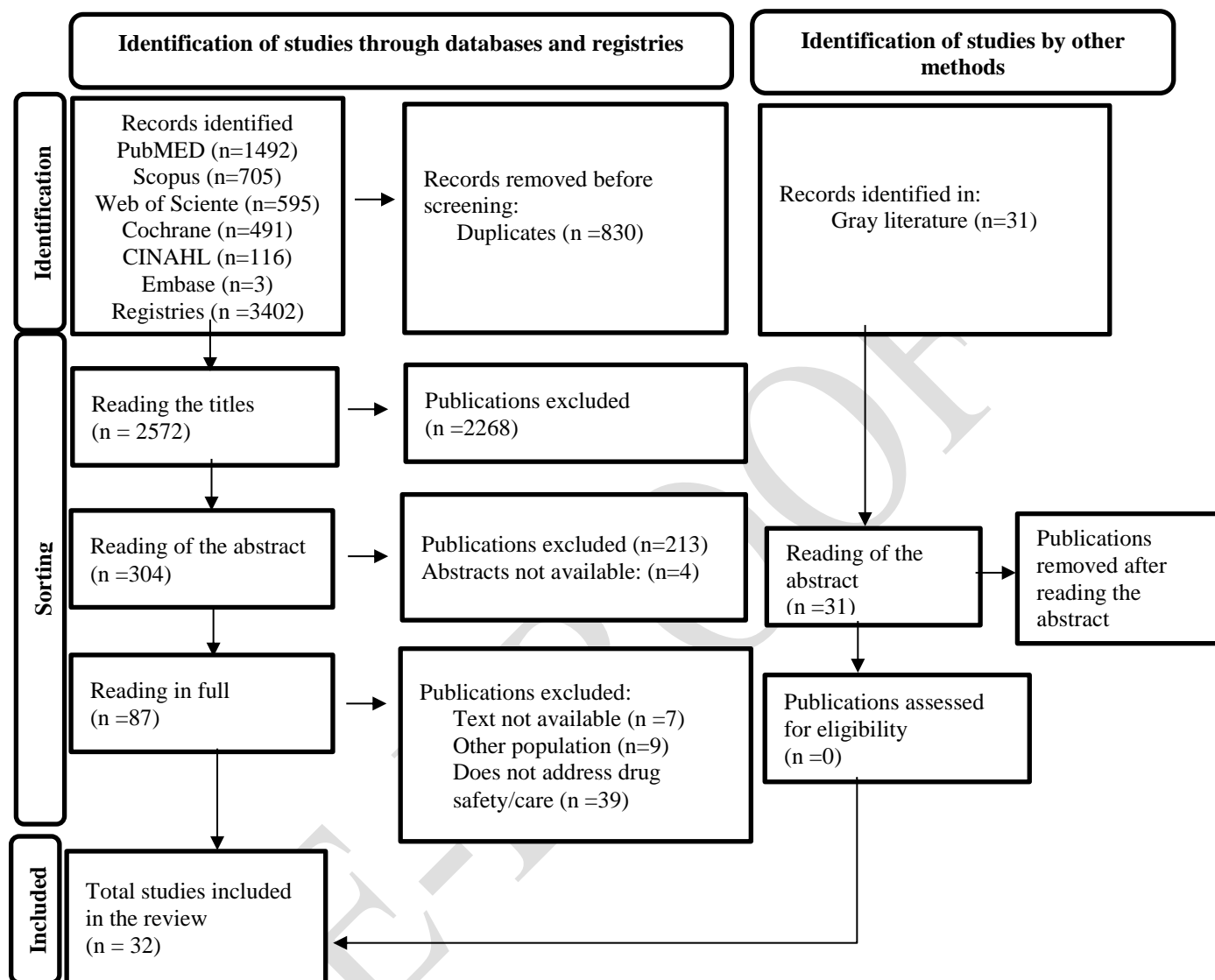
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The data from the selected studies was extracted using a specific form drawn up in *Microsoft Office Excel*®, previously tested on four articles. The results were then presented using descriptive statistics and discussed using the literature.

## **RESULTS**

As illustrated in Figure 1, the preliminary search yielded 3,402 publications, of which 2,572 were identified as duplicates and subsequently excluded. The titles of 3,045 publications were reviewed, and 87 articles were selected for full reading. The articles excluded during the full-text review included: articles not available in full (n = 7), articles on other populations (n = 9), and articles not addressing drug safety/care (n = 3). This resulted in a final selection of 32 articles. Initially, 31 publications from the gray literature were included. However, all of these were excluded because they did not address the topic, which did not change the number of articles included in the review.

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**Figure 1.** Flowchart adapted from the *Prisma Extension for Scoping Reviews (Primas-ScR)*<sup>10</sup>, which was used to select safety studies on nursing care in the preparation and administration of sedative, analgesic and vasoactive drugs in critically ill patients.

Table 1 presents a comprehensive overview of the study's geographical distribution, chronological framework, objectives, design, and location. Of the articles selected for inclusion, 34.3% were from the USA and 18.8% from the UK. The earliest articles date back to 2004, while the most recent date to 2021, with a preponderance of articles from 2017 (n = 5). The

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articles were classified into various categories, including twelve reviews, twenty-two studies focused on the ICU, eighteen articles dealing with care related to vasoactive drugs, eleven articles focusing on sedatives and analgesics, and three articles that highlighted the three groups of drugs.

**Table 1.** Description of the studies included in the review on safety in nursing care in the preparation and administration of sedative, analgesic and vasoactive drugs in critically ill patients.

Article/Country	Year	Objective	Design	Location
1 <sup>11</sup> United Kingdom	2004	Identify the risk factors and variables associated with the administration of epinephrine and norepinephrine.	Review	ICU
2 <sup>12</sup> United Kingdom	2004	Evaluate practice and identify the safest method for administering inotropes	Three audits	ICU
3 <sup>13</sup> France	2007	Evaluate the influence of the quality improvement program in reducing the number of incidents when changing vasoactive infusion pumps	Intervention	ICU
4 <sup>14</sup> USA	2007	Review the pharmacology and clinical usefulness of intravenous vasoactive agents	Review	ICU
5 <sup>15</sup> France	2011	Investigate and analyze catecholamine exchange techniques in syringe pumps	Review	ICU
6 <sup>16</sup> USA	2011	Review sedation and analgesia procedures	Review	Emergency
7 <sup>17</sup> Germany	2012	Analyze the effects on potential medication errors and address factors that have the potential to improve medication safety	Descriptive	ICU
8 <sup>18</sup> United Kingdom	2012	Investigate the extent and frequency of dose errors and delays as a consequence of preparing drug infusions at the bedside, instead of using prefilled syringes	Randomized clinical trial	Simulated environment
9 <sup>19</sup> Austria	2013	Address strategies to reduce care errors in intensive care	Review	ICU
10 <sup>20</sup> Spain	2013	Present incident with phenylephrine	Case report	ICU
11 <sup>21</sup> USA	2013	Report epinephrine dose/concentration ratio errors	Case report	Emergency
12 <sup>22</sup> Canada	2014	Present a case for the use of vasopressors	Case report	ICU
13 <sup>23</sup> USA	2015	Evaluate the safety of vasoactive drugs administered via peripheral intravenous access	Descriptive	ICU



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14 <sup>24</sup> USA	2015	Review the safety and efficacy of drugs that can be administered intranasally	Review	Emergency and Pre-hospital
15 <sup>25</sup> Spain	2016	Evaluate the impact of implementing vasoactive protocols on safety and efficacy in the treatment of critically ill patients	Intervention	ICU
16 <sup>26</sup> Sweden	2016	Describe the experiences of intensive care nurses learning to manage vasoactive drugs	Qualitative	ICU
17 <sup>27</sup> United Kingdom	2017	Discuss sedation in cardiology practice	Review	ICU
18 <sup>28</sup> Lebanon	2017	Determine the incidence of complications from the administration of vasopressors by peripheral venous catheter and to identify the associated factors	Prospective observational	Emergency
19 <sup>29</sup> USA	2017	Describe the vasopressors administered peripherally, the size and location of the peripheral venous route, the incidence and management of extravasation events	Descriptive	ICU
20 <sup>30</sup> USA	2017	Evaluate the safety of phenylephrine infusion through a peripheral intravenous catheter	Descriptive	ICU
21 <sup>31</sup> USA	2017	Review of the current literature on sedation for procedures outside the operating room	Review	ICU and emergency room
22 <sup>32</sup> United Kingdom	2018	Report nursing considerations on sedation and analgesia	Book chapter	Emergency
23 <sup>33</sup> USA and Canada	2018	Review the recommendations for the use of propofol in deep sedation for procedures	Review	Emergency
24 <sup>34</sup> Brazil	2019	Analyze dose errors in intravenous medication	Cross-sectional	Emergency
25 <sup>35</sup> England	2019	Explore the daily practices surrounding the coadministration of various intravenous drugs by nurses	Qualitative	ICU
26 <sup>36</sup> Australia	2019	Investigate how intensive care nurses prepare, initiate, administer, titrate and wean off vasoactive drugs	Systematic review	ICU
27 <sup>37</sup> Australia	2019	Evaluate the safety of vasopressor administration via peripheral intravenous catheters	Systematic review	ICU, pre-hospital, emergency
28 <sup>38</sup> USA	2020	Determine the safety and efficacy of long-term administration of vasopressors through a midline catheter.	Descriptive	ICU
29 <sup>39</sup> United Kingdom	2020	Present case of accidental overdose of norepinephrine	Case report	ICU

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30 <sup>40</sup> USA	2020	Describe the errors that can occur in the wrong dosage of ketamine sedation in a patient in response to a medical report	Comment	Emergency
31 <sup>41</sup> USA	2020	Evaluate in the literature the prevalence of complications of vasopressor infusion via peripheral venous catheter	Systematic review and meta-analysis	ICU and Emergency
32 <sup>42</sup> Italy	2021	Analyze the use of norepinephrine over a 2-year period	Descriptive	Emergency

Source: Prepared by the authors

\* ICU - Intensive Care Unit

Chart 2 presents the main topics on safety in nursing care when preparing and administering sedative, analgesic and vasoactive drugs to critically ill patients.

**Table 2.** Description of the main topics related to safe nursing care in the preparation and administration of sedative, analgesic and vasoactive drugs in critically ill patients.

Medications	Safety in nursing care
Sedatives, analgesics and vasoactive agents	Continuous monitoring of vital signs <sup>14,16,27,31-33,36,42</sup>
	Maintain or implement continuing education <sup>11,14,16,20,26,33,36</sup>
	Implementing care protocols <sup>14,23,29,31,38,40,41</sup>
	Communicate <sup>14,20-22,39</sup> in closed circuit format <sup>20,39</sup>
	Review and design compatibility charts for commonly used drugs and, when there is incompatibility, obtain new access and prioritize infusions <sup>14</sup>
	Use infusion pumps or syringe pumps <sup>19,39</sup>
	Prefer pumps with standardized drug libraries in integrated decision support systems <sup>17</sup>
Use pre-filled or pre-manipulated medicines <sup>18,19,25</sup>	

Source: Prepared by the authors

The nursing care involved in the preparation and administration of sedatives and analgesics to critically ill patients is delineated in Chart 3.

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**Table 3.** Description of the main topics related to safe nursing care in the preparation and administration of sedative and analgesic drugs in critically ill patients.

Medications	Safety in nursing care
Sedatives and painkillers	<p>Standardize drug infusions<sup>19</sup></p> <p>Check the prescription before administration and when the medication arrives from the pharmacy; avoid parallel conversations; respect the established timetables; prepare in a suitable place; identify the prepared medication and report the reason if it has not been administered; dispose of it properly; check that the infusion has been interrupted before it is finished<sup>34</sup></p> <p>Maintain a minimum number of concentrations and formulations in the unit<sup>40</sup></p> <p>Administration of intranasal medication: minimize protective barriers; the volume in each nostril should not exceed 1ml, divide the dose between the two nostrils; use appropriate device<sup>24</sup></p> <p>When performing invasive and painful procedures<sup>16,27,31-33,40</sup>: there are sedation models by nurses<sup>27</sup>; confirm pre-procedure information<sup>40</sup>; use supplementary oxygen<sup>27,33</sup>; establish venous access<sup>32</sup>; take a full history<sup>32</sup>; explain the procedure<sup>32</sup>; ensure availability of airway materials and resuscitation equipment/medicines<sup>27,32</sup>; check, prepare and administer prescribed medication<sup>32</sup>; ensure availability of appropriate reversal agents<sup>32</sup>; assess level of consciousness during procedure<sup>32,33</sup>; have a team for sedation<sup>16,31,33</sup></p>

Source: Prepared by the authors

The nursing care involved in the preparation and administration of vasoactive drugs to critically ill patients is enumerated in Chart 4.

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**Table 4.** Description of the main topics related to safe nursing care in the preparation and administration of vasoactive drugs in critically ill patients.

Medications	Safety in nursing care
Vasoactive	<p>Administer medication via midline catheter when possible<sup>38</sup> Administer medication preferably via central venous catheter<sup>14,39,42</sup></p> <p>Handle the infusion pump or syringe pump properly<sup>12,15,36</sup>, ensure uninterrupted medication administration<sup>11,13,26</sup></p> <p>Take care<sup>11,13,15,36</sup> and standardize<sup>13</sup> the syringe change technique on the syringe pump system.</p> <p>In hemodynamic instability, do not administer <i>boluses</i>, but increase the infusion rate,(except in situations of cardiorespiratory arrest)<sup>12,36</sup></p> <p>Provide clear instructions to the team regarding the target dosage of vasopressors and the defined hemodynamic goal<sup>14,22</sup>, concentrations, doses and routes<sup>21</sup></p> <p>Administer nitroglycerin with polyvinyl chloride-free materials and sodium nitroprusside with light-protective materials<sup>14</sup></p> <p>Implement systematic labeling of syringes<sup>20,39</sup></p> <p>Observe storage carefully<sup>21</sup></p> <p>Administer medication via peripheral venous catheter<sup>23,28–30,37,41,42</sup>: exclusive route<sup>29,42</sup>; presence of two accesses<sup>29</sup>; via infusion pump<sup>42</sup>; antecubital fossa<sup>30,37,42</sup> or above<sup>42</sup> or external jugular vein<sup>42</sup> or in the arm<sup>37</sup>; avoid antecubital fossa<sup>23,29</sup>; hand and wrist<sup>23</sup>; maximum duration 24 hours<sup>29</sup>, less than 12 hours<sup>42</sup>, up to 72 hours<sup>23</sup>, for a limited period<sup>30,37</sup>; test and maintain permeability of access<sup>11,23,28,29</sup> use well-fixed access<sup>28,30</sup>; access 20 gauge or larger<sup>23,29,41,42</sup>; in case of leakage, administer phentolamine<sup>23,42</sup> or terbutalin<sup>29,42</sup> and topical nitroglycerin<sup>23,29,42</sup></p>

Source: Prepared by the authors

## DISCUSSION

Studies on analgesia and sedation have shown that the main focus is on preparation and administration for procedures<sup>16,27,31–33,40</sup>. Continuous sedation is extensively utilized in critically ill patients; however, only one article<sup>35</sup> addresses the challenge of coadministering multiple drugs in the same lumen.

In regard to sedation and analgesia, three articles underscore the increasing significance of nurses in the sedation process<sup>27,38,40</sup>. The issue of anesthesiologist availability is a significant concern, prompting many institutions to train and qualify nurses to administer sedation<sup>38</sup>. Qualified nurses, under the direct supervision of a physician, can administer sedatives and

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analgesics, and should be aware of the adverse effects in case of complications, including airway management<sup>40</sup>. In Brazil, nursing technicians administer medicines under the supervision of nurses and in accordance with medical advice, which differs from the approach in other countries. Nurses must assess sedated patients by using scales that measure the level of sedation, monitoring sedation, or managing the daily break.

In the United Kingdom, nurses administer sedatives, and cardioversion services that require light sedation can be conducted by a nurse. In Brazil, a physician leads most services. Nurses play a vital role in these procedures, receiving comprehensive training in sedation administration, monitoring, understanding discharge criteria, and managing complications<sup>32</sup>.

Four articles analyzed the risk that these drugs can cause in the event of an adverse event and cited monitoring the continuous administration of sedatives and analgesics as a form of prevention. Monitoring parameters include heart rate, respiratory rate, axillary temperature, pulse oximetry, electrocardiogram, capnography (when available and in patients with specific comorbidities), and blood pressure, with the latter being checked every five minutes<sup>16,31-33</sup>. This practice is of paramount importance, as adverse reactions can be detected, avoiding complications related to the cardiovascular system and cerebral hypoxia<sup>43</sup>. The ideal level of sedation for procedures is moderate, but patients can quickly enter deep sedation, which can lead to hemodynamic and respiratory instability<sup>44</sup>. This instability would not be detected by the team if monitoring<sup>27</sup> was not in place. In addition, staff need to know how to administer these drugs and rescue patients from unintentional deep sedation<sup>45</sup>. Two studies<sup>27,40</sup> underscore the importance of care prior to the procedure, including patient confirmation, pre-assessment, medication dosage verification, recovery monitoring, and discharge planning. This practice should be encouraged in Brazil during the continuing and permanent education of the nursing team.

Another noteworthy practice from the study is the use of supplementary oxygen to prevent hypoxemia related to sedation and analgesia, facilitated by nasal catheter, nasal goggles, or mask<sup>43</sup>. The use of capnography is also considered important, although it is not considered standard. A study<sup>18</sup> revealed a high cost associated with capnography, with no reduction in adverse events during procedures<sup>31</sup>.

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Another effective and well-tolerated alternative to intramuscular and intravenous administration is the intranasal delivery of sedatives and analgesics, particularly in pre-hospital and emergency settings<sup>24</sup>. This approach is advantageous for patients who lack immediate venous access<sup>44</sup>, as it is a simple and efficient alternative. However, the application of this practice remains limited in Brazil due to the unavailability of intranasal sedatives and analgesics.

With regard to vasoactive drugs, some studies describe administration via peripheral venous access (PVA)<sup>23,28-30,37,41,42</sup>. This approach is of great importance for the clarification of the nursing team since there are usually controversies regarding the possibility of starting this type of medication by AVP. Studies indicate a low incidence of adverse events in the administration of vasoactive agents via AVP, with a rate of 2% to 7% of extravasation episodes with minor complications<sup>23,28-30,37,41,42</sup>. Furthermore, lower rates of adverse events considering serious complications<sup>41</sup> have been observed in some studies, with no reported cases of necrosis or ischemia of the limb<sup>23,28,30,37</sup>.

The majority of clinical reports on extravasation and skin necrosis after noradrenaline infusion in peripheral venous access date back 50 years<sup>42</sup> and case reports<sup>45</sup>. In line with this, the *Surviving Sepsis Campaign* (SSC) and the *Infusion Nurses Society* (INS) guidelines recommend administering vasopressors via peripheral venous access to restore mean arterial pressure, so as not to delay its onset until a central venous access is inserted<sup>46,47</sup>. Early initiation of vasopressors has been shown to promote restoration of target organ perfusion and reverse the state of systemic shock<sup>29</sup>. This approach is associated with reduced mortality<sup>42</sup>.

The administration of vasopressors via peripheral venous access is linked to specific precautions. There is no consensus on the caliber, but some studies suggest that the use of 20-gauge or larger would be associated with lower complication rates<sup>23,29,41</sup>. One study found that 20 gauge was the most common, but found no significant differences between gauge and infiltration rate<sup>30</sup>. However, another study showed that all three complications occurred in patients with 20-gauge catheters<sup>28</sup>. In clinical practice, unstable patients require larger-caliber peripheral access for the infusion of various medications, including those used for the initial administration of vasopressors.

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There is a lack of consensus on the optimal site for peripheral access insertion. One study suggested that the location of the catheter is not correlated with higher complication rates<sup>41</sup>. However, other studies suggest that the antecubital fossa<sup>23,30</sup>, hand<sup>23,28</sup>, wrist<sup>23</sup>, and veins close to joints, tendons, nerves or arteries should be avoided, as well as any sites that require more than one venipuncture<sup>29</sup>. It is recommended that access be inserted into the forearm or arm<sup>29</sup> only at the upper end and contralateral to the blood pressure cuff<sup>23</sup>. Another study recommends insertion into a vein in or above the antecubital fossa or into the external jugular vein<sup>42</sup>. The SSC guideline recommends inserting access into a vein in or near the antecubital fossa when using peripheral vasopressors<sup>46</sup>. This is a possible practice, as critically ill patients generally have reduced perfusion and hypotension, making it difficult to puncture the peripheral venous network. In such cases, the antecubital fossa or external jugular are the first choice.

There is no consensus on the optimal duration of vasopressor administration via peripheral routes. A meta-analysis suggested that infusion duration is not associated with an increase in complications<sup>41</sup>. However, another systematic review suggests that the administration of time-limited vasopressor infusions via peripheral access is associated with a low incidence of adverse events<sup>37</sup>. The duration of vasopressor infusion varies widely across studies, ranging from less than 12 hours for low-dose infusions<sup>42</sup> to up to 72 hours<sup>23</sup>, or a maximum of 24 hours (a longer duration must be approved, justified and documented in the patient's medical record)<sup>29</sup> or an average duration of 19 hours<sup>30</sup>. The INS suggests that peripheral vasopressor infusion until central catheter insertion should take place between 24 and 48 hours<sup>47</sup>. A systematic review comparing vasopressor use via central and peripheral venous access indicates that tissue damage is more likely to occur after 12 to 24 hours of infusion, and considered unlikely in less than 2 hours<sup>45</sup>. The SSC guideline recommends administering for a short period of time, less than 6 hours<sup>46</sup>.

In this line of care, a study establishing a protocol for the administration of vasopressors via the peripheral route suggests checking the position of the access using ultrasound, with the vein having a diameter greater than 4 mm<sup>23</sup>. However, this practice depends on trained staff

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and the availability of equipment, which is not the reality in most ICUs and emergency rooms in Brazil.

Another study suggests assessing access twice during the nursing shift<sup>29</sup> and then every two hours<sup>23</sup>. Before starting the infusion, the venous integrity and flow should be tested by aspirating a small amount of blood and observing its return<sup>23,29</sup>. The studies also describe other precautions, such as puncturing a second peripheral access if the primary one fails<sup>23,29</sup> clearly marking the access used for the medication at the connection site, and using only one vasopressor in a single access<sup>29</sup>. In addition, the insertion site should be monitored and evaluated every hour for signs and symptoms of extravasation, along with the degree of injury (if any), and documented accordingly<sup>29</sup>. These are feasible precautions.

If extravasation is suspected, the infusion should be stopped immediately, and the residual medication should be aspirated through the access port<sup>23,29</sup>. The literature describes the use of phentolamine, which is considered the standard for the management of vasopressor extravasation<sup>48-50</sup> and is the only pharmacological treatment approved by the *Food and Drug Administration* for this purpose<sup>49</sup>. However, there may be periods of shortage on the market, so the use of topical nitroglycerin and subcutaneous terbutaline is a potential alternative<sup>49</sup>. In addition, one study presented non-pharmacological management of the affected limb. The limb should be elevated to minimize edema and warm compresses should be applied for 20 minutes every 6 to 8 hours for the first 24 to 48 hours after extravasation<sup>29</sup>. These precautions are in line with the literature<sup>46</sup>. For this reason, it is essential to develop institutional protocols for the management of vasoactive drug extravasation.

Midline catheters are an alternative for administering vasoactive drugs. They last between two and four weeks and are less prone to decannulation than peripheral venous accesses. They should be inserted by trained nursing staff, guided by ultrasound, close to the antecubital region, with the tip ending in the axillary vein<sup>38,46</sup>. A midline venous catheter is a peripheral device that, due to the position of its tip, promotes greater hemodilution, which helps prevent phlebitis, infiltration, extravasation and discomfort during the administration of medication, and is an alternative to peripheral venous catheters and central venous catheters



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<sup>51,52</sup>. However, this practice is rare because it depends on trained personnel and materials that are rarely available in most emergency rooms and ICUs in Brazil.

The administration of vasopressors is typically associated with the use of an infusion pump or syringe pump, which offer advanced features such as dose calculations, programmable volume and time, and enhanced alarms, contributing to enhanced patient safety. These pumps are equipped with specialized drug libraries that allow for precise dosage determination, ensuring the safe and effective administration of medications<sup>17,19,39</sup>. It is important to note that there are different brands with their own infusion pump features, and each environment will need to train its staff to handle this equipment.

Studies have described hemodynamic instability during syringe exchange at the end of a vasopressor infusion<sup>11,13,15,36</sup> that can lead to cardiac arrest<sup>11</sup>. This event can occur because the syringe drivers do not have a drug reservoir in the intravenous line and the vasoactive drugs have a very short half-life<sup>36</sup>. It can be seen that there is no completely effective way of changing the syringe. However, it is suggested that the experience of the team, the knowledge of the nurse and the standardization in the institutions are the safest way to reduce adverse events<sup>11,13,15</sup>. Hemodynamic instability after syringe exchange is exacerbated when bolus doses of vasoactive agents are used to control severe blood pressure fluctuations, and it is recommended to increase the infusion rate until blood pressure stabilizes<sup>12,36</sup>.

Regarding physicochemical incompatibilities, one study emphasizes that sodium bicarbonate should not be administered by the same route as catecholamines (such as epinephrine, norepinephrine, dopamine and phenylephrine) because it causes precipitation and inactivation of both agents<sup>14</sup> a finding that supports the literature<sup>53,54</sup>. This incompatibility occurs because these are drugs that are frequently administered to critically ill patients, and it is important for the nursing team to be vigilant.

Strategies to manage the incompatibility include obtaining a new venous access, prioritizing, or changing the infusion line<sup>35</sup>. However, it should be noted that additional venous access is not always feasible, as it not only increases the risk of infection and thrombotic complications, but also increases costs and demands on the team<sup>55,56</sup>. Therefore, it is important

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to review and develop compatibility tables for commonly used medications using a multidisciplinary approach to create a comprehensive tool<sup>35</sup>.

Vasopressors should only be used only in facilities where vital signs are monitored<sup>14,36</sup>. Therefore, patients using these drugs should be in areas such as the ICU, emergency room, or surgical center. The literature indicates that blood pressure should be checked every 15 minutes during dose adjustment and every 30 minutes during the maintenance<sup>57</sup>; therefore, the alarm limits of the monitor should be set to request titration in response to changes in blood pressure or heart rate<sup>36</sup>. One aspect of care that should be reinforced with the team is the adjustment of the personalized monitor to each patient's needs, as this simple practice is often not performed.

It is important to provide the team with clear information about concentrations, doses, and routes of administration, as well as to signal the initial dose and a clearly defined hemodynamic target when starting vasopressors<sup>14,21</sup> so that all team members interpret it in a similar way (distinguishing between target range and minimum threshold)<sup>22</sup>. The rate and frequency of dose titration depends on the patient's hemodynamic parameters and clinical practice<sup>14</sup>. Vasoactive drug titration and weaning requires the ability to analyze and interpret technical data, adapt to clinical changes, and remain calm<sup>36</sup>. In a qualitative study, respondents indicated that the most common sources of ambiguity were the definition of acceptable blood pressure levels and the maximum tolerated dose of vasopressors<sup>22</sup>. Appropriate communication, concise and in a closed-loop format, can prevent loss of information and ensure continuity of care<sup>19,39</sup>. Daily multidisciplinary team rounds are a practice that should be encouraged so that information about the therapeutic plan is communicated to all professionals involved in the patient's care.

The studies also address the importance of communication<sup>14,20-22,39</sup> in a closed loop format<sup>20,39</sup>, which is a system that involves the transmission of concise information by the transmitter to the recipient, ideally using the recipient's name. The recipient confirms receipt by repeating the information, and the original transmitter acknowledges the correct understanding of the message. This format is designed to guarantee patient safety<sup>58,59</sup>, and it is evident in daily life that poor communication is one of the most significant problems encountered. Practices that encourage good communication are always welcome.

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Another key area of focus<sup>18,19,25</sup> is on the use of pre-filled medications by pharmacists or pharmaceutical companies, as these ready-made infusions are less prone to concentration errors and can reduce the time it takes to start medications. However, this approach may have financial implications for health service providers, especially in less developed countries<sup>18</sup>. In practice, few services can obtain ready-made medicines from the pharmaceutical industry due to financial constraints, and even fewer can prepare them in advance for nursing staff, often because of a shortage of pharmacists in hospitals.

The effective and safe preparation and administration of medicines is based on a team that knows the basic principles, which is why ongoing training is essential<sup>60</sup>. The use of digital resources in the qualification of nursing staff is a way of training these professionals and students in the face of an increasingly computerized world that can bring about immediate behavioral changes<sup>61</sup>.

One potential constraint of the study is the possibility of not including all the care related to these medications. However, we believe that this is mitigated by the extensive literature review and synthesis of care. The heterogeneity of the studies also underscores the complexity and range of care required with these medications.

The care outlined in this review is designed for students, nursing technicians, and nurses, with the objective of enhancing learning about nursing care in the preparation and administration of sedative, analgesic, and vasoactive drugs in critically ill patients, thereby promoting the safety of care for this vulnerable population. These materials can be utilized in hospitals and teaching institutions as a resource for ongoing education of nursing staff and the training of students. Additionally, the materials can be accessed for individual knowledge acquisition.

### **CONCLUSION**

This research reviewed the available evidence on the safety of nursing care in the preparation and administration of sedative, analgesic, and vasoactive drugs in critically ill patients. Regarding analgesia and sedation, the primary findings pertain to care during procedures, as only one study has addressed continuous sedation, highlighting the necessity for

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further research in this area. The articles related to vasoactive drugs indicate that they are safe to administer via peripheral routes, with the aim of not delaying the start of administration. However, there is no consensus on the caliber of access, puncture site, and duration. The findings underscore the significance of meticulous care in handling infusion pumps, effective team communication, checking for physical and chemical incompatibilities, the benefits of purchasing ready-made or manipulated medicines in the pharmacy, and the implementation of care protocols in institutions. The nursing team plays an essential role in maintaining safety in the preparation and administration of medicines, as it is considered the last barrier in preventing adverse events.

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**Author contributions:**

**Melissa Carleti:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

**Djulia Andrielle Wachter:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

**Juliana Neves Giordani:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

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**Rita Catalina Aquino Caregnato:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

**Carine Raquel Blatt:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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**Corresponding Author:**

Melissa Carleti

Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)

R. Sarmiento Leite, 245 - Centro Histórico, Porto Alegre/RS, Brazil. ZIP 90050-170

[mel.carleti@gmail.com](mailto:mel.carleti@gmail.com)

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