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Title:

Nurse management of vasoactive medications in intensive care: A systematic review

Date:

2020-02-01

Citation:

Hunter, S., Considine, J. & Manias, E. (2020). Nurse management of vasoactive medications in intensive care: A systematic review. *Journal of Clinical Nursing*, 29 (3-4), pp.381-392. <https://doi.org/10.1111/jocn.15093>.

Persistent Link:

<https://hdl.handle.net/11343/286674>

Nurse management of vasoactive medications in intensive care: A systematic review

Running title

Nurse management of vasoactive medications

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/JOCN.15093](https://doi.org/10.1111/JOCN.15093)

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Acknowledgements

Conflict of Interest Statement

There are no conflicts of interest to report

Funding

PhD Scholarship, Faculty of Health, Deakin University, Burwood, Victoria

Eastern Health Foundation, PhD Scholarship, Eastern Health, Box Hill, Victoria

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Article type : Review

Nurse management of vasoactive medications in intensive care: A systematic review

Introduction

The management of vasoactive medications is core business for intensive care nurses, but little is known on how nurses manage these ubiquitous and potentially harmful medications.

Aim

To investigate how intensive care nurses prepare, initiate, administer, titrate, and wean vasoactive medications.

Methods

The databases CINAHL Complete, Medline Complete and EMBASE were searched from 1965 to January 2019 with keywords under five concept headings and in a variety of configurations. This systematic review was conducted according to the PRISMA guidelines. Studies were assessed for quality and bias, and a modified narrative synthesis was used to analyse data, investigate findings and explore relationships within and between studies.

Results

The review identified 13 studies: two observational studies, two pre and post intervention studies, four survey studies, two quasi-experimental studies, one longitudinal time series, one prospective controlled trial, and one interview incorporating content analysis.

Discussion

Four studies on preparing and initiating vasoactive medications described a lack of standardisation in infusion preparation and inconsistencies in dosing units and patient weights. Five of six studies on vasoactive medication administration examined nurses' use of syringe changeovers to reduce patient haemodynamic compromise and there were three studies on titration and weaning.

Conclusion

Further research on nurse management of vasoactive medications is needed to develop an evidence base for specialist education and standardised practices aimed at reducing risk for patient harm.

Relevance to Clinical Practice

Nurses working in intensive care units in many parts of the world are responsible for the management of vasoactive medications. There is great variation in practices that include preparation, initiation, administration, titration and weaning of vasoactive medications, which increases the risk for medication errors and adverse events in a vulnerable population of critically ill patients.

Keywords

Nursing intervention, Intensive care, Medication management, Vasoactive medication, Systematic review

Introduction

Intensive care nurses prepare, initiate, administer, titrate and wean prescribed vasoactive medications for patients who are haemodynamically unstable. Despite management of vasoactive medications being a key intervention undertaken by intensive care nurses, little is known about how they make decisions in managing these potent medications.

Due to their short half-life, vasoactive medications are generally administered as continuous infusions to patients who are haemodynamically compromised, and unable to maintain an adequate blood pressure or cardiac function, due to sepsis, trauma, cardiac failure or other autonomic dysfunction (Nogueira et al., 2015). While vasoactive medications are an essential tool in maintaining perfusion to the brain, heart and other vital organs, they have been implicated in patient complications including cardiac arrest, stroke, limb ischaemia and necrosis and long-term peripheral neuropathies (Hazardous Substances Database, 2010). The potential for risk associated with the use of vasoactive medications highlights that nursing practice is fundamental to their safe management.

Vasoactive medication is a broad term describing inotropes and vasopressors employed to manage cardiovascular instability resulting from a variety of aetiologies and pathologies. Vasoactive medications increase systemic vascular resistance or cardiac output depending on their site of action, either directly at one or more autonomic receptors, or reflexively via second messenger systems (Holmes, 2005; Jentzer, Coons, Link, & Schmidhofer, 2015).

In intensive care units (ICU) doctors generally prescribe vasoactive medications and nurses are responsible for managing the preparation, timing of initiation, administration, titration and weaning of vasoactive infusions. Infusion preparation involves mixing a concentrated active drug with a compatible admixture to achieve a desired concentration, and often using patient weight and complex calculations to determine the required dose (Adapa et al., 2012; Valentin et al., 2009). Once infusions of vasoactive medications are prepared, the time for actually commencing or initiating the infusion depends upon nursing prioritisation of care and organisational factors, such as workforce limitations, suitability of

the intravenous access and availability of equipment.

The preparation and initiation of vasoactive medication infusions can be time-critical for patients who need them to maintain circulating blood volume and organ perfusion (Brindley, O'Dochartaigh, Volney, Ryan, & Douma, 2017). Administration of vasoactive medications is the process of delivering the active ingredient to the patient, usually as a continuous infusion. Infusion administration requires calculating flow rates to determine the dose or using a syringe driver or volumetric pump to deliver a preset or titratable rate (Adapa et al., 2012; Carter et al., 2014; Garrigue et al., 2016; Jung, Couldry, Wilkinson, & Grauer, 2014).

Variable-dose vasoactive infusions are described as being titrated when the flow rate, and therefore the medication dose, are increased or decreased to achieve and maintain desired, predetermined goals of therapy. These goals are based on haemodynamic measures for blood pressure, heart rate and cardiac output that are monitored by nurses using a range of assessments including invasive and non-invasive haemodynamic monitoring and electrocardiography (Fadale, Tucker, Dungan, & Sabol, 2014).

Weaning of vasoactive infusions is the reduction in flow and dose of the medication until it can be eventually ceased. The weaning process occurs in response to improvements in patient haemodynamic status, indicating that cardiovascular supports are no longer required. Weaning is an intervention that determines the time and total dose of drug infusion delivered, and can impact patient length of stay in the intensive care unit (Anstey et al., 2017).

Aims and Methods

Aim

The aim of this systematic review was to explore the research literature on how intensive care nurses prepare, initiate, administer, titrate and wean vasoactive medications. No previous systematic reviews have been undertaken on this topic and identification of gaps in the literature will inform future research and clinical practice in the intensive care environment.

Methods

The Participant, Intervention, Comparator, Outcome and Study design (PICOS) statement identified participants as nurses working in ICUs, managing vasoactive medications.

This systematic review was conducted according to PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses (See Supplementary File 1)) (Moher, Liberati, Tetzlaff, & Altman, 2009) and the protocol was registered on the PROSPERO website <https://www.crd.york.ac.uk/prospero> (registration CRD42018087144) (Booth et al., 2011).

Search strategy

Keyword, MeSH terms, phrase and concept searches were conducted from 1965 to January 2019 using the electronic sources: CINAHL Complete, Medline Complete and EMBASE. A keyword search was undertaken in Cochrane CENTRAL, the World Health Organisation International Clinical Trials Registry Program, on ClinicalTrials.gov, Science Citation Index and Australian Clinical Trials. Manual searching was also conducted of bibliographies of review articles and systematic reviews, the grey literature, guidelines and reference lists of eligible papers. Keywords, MeSH terms and phrases included noradrenaline OR norepinephrine OR adrenaline OR epinephrine OR (MH "catecholamine") AND nurs* OR (MH "Critical Care Nursing") (Appendix 1).

Inclusion and exclusion criteria

Inclusion criteria were any study that focused on the population of intensive care nurses managing vasoactive medications, and that reported on the preparation, initiation, administration, titration or weaning of vasoactive medications, regardless of outcome measures. The vasoactive medications chosen were noradrenaline (norepinephrine), adrenaline (epinephrine), vasopressin, dobutamine, dopamine, milrinone, metaraminol, levosimendan and isoprenaline (isoproterenol) as these medications are commonly used by intensive care practitioners (Levkovich et al., 2016). Exclusion criteria were study methodologies of basic research, research using animal models, simulation studies, and research focusing on prescribing vasoactive medications or comparing the effectiveness of different vasoactive medications. Review articles, editorials, abstracts of conference papers, case studies, and papers not available in English were also excluded.

Papers identified in the keyword MeSH terms and phrase searches were uploaded from the search databases onto the Rayyan platform (Ouzzani, Hammady, Fedorowicz, &

Elmagarmid, 2016) and an independent title and abstract screening process was undertaken by three investigators to identify papers for potential full-text inclusion. Disagreement on inclusion of papers was resolved once the screening was un-blinded through discussion between the three investigators. Independent screening of full-text papers from all sources was then undertaken. Any disagreement identified at the full-text level was again resolved by discussion between the three investigators after the screening was un-blinded.

Data extraction

Included studies were tabulated into groups based on key interventions. Quality and bias assessments were completed using the checklist for assessment of methodological quality (Table 1) (Downs & Black, 1998). Additional information extracted included the type and size of study, participant groups, outcomes, and the bias score expressed as a percentage. For the one included qualitative study, the Critical Appraisal Skills Program (CASP) Appraisal Tool for Qualitative Research was used to assess quality (Critical Appraisal Skills Program. CASP Qualitative Research Checklist., 2017). The quality and bias assessment was undertaken by one investigator and subsequently critiqued and evaluated independently by the other investigators. Any discrepancies were resolved through collaborative discussion.

Data synthesis

There was marked heterogeneity in identified papers and as a result, narrative synthesis was chosen as the most appropriate method to analyse and explain findings. For instance, three studies evaluated different methods of syringe changeovers for continuous vasoactive infusions (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015) and the outcome measures of mean arterial pressure, systolic blood pressure or heart rate indicating a haemodynamic incident were sufficiently disparate that results could not be pooled for meta-analysis. Narrative synthesis involved a modified version of the framework developed by Popay (2006) to investigate findings, and to explore relationships within and between the data. This process involved tabulating study data under headings that included participants, intervention, comparisons, outcomes and themes (Popay et al., 2006). Tabulation allowed for consideration of themes related to key interventions, the development of textual

descriptions, and exploration of relationships within and between studies for an overall assessment of the strength of evidence (Popay et al., 2006).

Results

The systematic search found 2028 non-duplicate citations with 13 full text English language papers remaining after the title, abstract and full-text screening (Figure 1). A range of methodologies were represented including two prospective observational studies (Hernandez et al., 2005; Herout & Erstad, 2004), two pre and post intervention studies (Argaud et al., 2007; Tan, Said, Rahman, & Taha, 2017), a quasi-experimental interrupted time series (Haniffa et al., 2017), four survey studies (Crisp, 2002; Jung et al., 2014; Melo et al., 2016; Morrice, Jackson, & Farnell, 2004), two quasi-experimental studies (Cour et al., 2013; Esfahani, Varzaneh, & Changiz, 2016), a prospective controlled trial (Greau et al., 2015), and one qualitative interview study using content analysis (Häggström, Bergsman, Månsson, & Holmström, 2017). The studies were geographically diverse with three conducted in France, one from Iran and two from the United Kingdom. There were two studies from the United States and one study each conducted in Malaysia, Iran, Brazil, Chile, Sweden and the Indian sub-continent.

Investigators focused on examining three specific areas of nursing management of vasoactive medications under the headings of preparation and initiation, administration, and titration and weaning. Some of the studies merged across more than one area, for example Tan et al. (2017) included elements of preparation and administration of parenteral infusions in their education bundle (Table 1) (Tan et al., 2017). When assessed for quality, the studies scored between 16% and 59% using the quality and bias assessment tool from Downs and Black (1998) with only four studies scoring over 50% (Table 1) (Downs & Black, 1998). The interview study with content analysis performed well when assessed for quality using the CASP Appraisal Tool (Critical Appraisal Skills Program. CASP Qualitative Research Checklist., 2017). Results are presented here in narrative format with figures reported in Table 1.

Preparation and initiation

Four of the reviewed studies involved an examination of nursing preparation and initiation of vasoactive medications (Herout & Erstad, 2004; Jung et al., 2014; Melo et al., 2016; Tan et al., 2017). A pre and post implementation study (Tan et al., 2017) and a self-

administered survey (Melo et al., 2016) identified nursing practices that included the use of incompatible diluents as admixtures and incorrect volumes to dilute medications into a usable concentration (Melo et al., 2016; Tan et al., 2017).

Tan et al. (2017) introduced an education bundle coupled with pre and post implementation measurements observing nurses preparing and administering parenteral infusions in a Malaysian ICU. The education bundle included a Power-point presentation, video describing reconstitution guidelines, medication compatibilities and administration rates for parenteral medications, a memory aid containing calculations and a preparation guide for commonly used infusions (Tan et al., 2017).

A convenience sample of Brazilian ICU and emergency room nurses by Melo et al (2016) was surveyed on clinical practice when managing vasoactive medications. The authors reported that 86% (69/80) of the surveyed nurses had completed their undergraduate nursing course, but it was not reported if nurses had completed any specialist critical care training (Melo et al., 2016).

Investigators of a prospective observational study documenting the incidence of medication errors of parenteral infusions in critically ill patients, proposed the need for consistency in patient body weight measurements used for weight-based infusion dosing (Herout & Erstad, 2004). Nurses were reported indiscriminately using ideal, dry or actual body weights to calculate infusion doses and rates for the same patient, leading to wide variations in infusion concentration, infusion rates and inconsistent documentation (Herout & Erstad, 2004).

A survey on variability in recording of dose units conducted before implementation of a standardised guideline, identified potential sources of medication error in nursing practice (Jung et al., 2014). Dosing units were described as micrograms per kilogram per minute, milligrams per kilogram per hour or milligrams per hour (Jung et al., 2014).

Administration

Of the six reviewed studies focusing on the administration of vasoactive medications, three compared methods of infusion syringe changeovers (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015) and three focused on guideline development and education implementation (Crisp, 2002; Esfahani et al., 2016; Morrice et al., 2004). Crisp (2002) first

reported problems with the use of syringe drivers for delivery of vasoactive medications and their contribution to patient haemodynamic instability in 2002, and this practice continued to be associated with haemodynamic compromise more than a decade later (Crisp, 2002).

The three studies comparing different methods of changeovers including the quick-change method, double pumping and automated relays using smart pump technology, all reported significant reductions in haemodynamic incidents (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015). Examples of changeovers include the quick change method, when a near empty syringe of medication is replaced with a full one, or double pumping, when a new syringe is run concurrently with a near empty syringe to maintain flow (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015).

Argaud et al. (2007) examined the quick change method of syringe changeover before and after the implementation of a quality improvement program that consisted of a one-day nurse training program introduced to streamline syringe changeovers (Argaud et al., 2007). The primary outcomes of a prospective controlled study comparing the quick change method with smart pump technology was the proportion of syringe changeovers followed by a drop in mean arterial pressure greater than or equal to 20% of baseline within 15 minutes after the changeover (Greau et al., 2015). A quasi-experimental study by Cour et al (2013) measured changes in mean arterial pressures within 30 minutes of a syringe changeover and recorded the amount of time nurses spent managing continuous vasoactive infusion pumping, including related haemodynamic incidents (Cour et al., 2013).

At a time when there were few guidelines on the nursing management of vasoactive medications, Crisp (2002) conducted a single site survey with intensive care nurses to identify patterns of practice and decision making around the administration of vasoactive infusions. A second survey explored double pumping practices at a number of teaching hospitals in the United Kingdom and the resulting guidelines introduced nursing strategies to reduce patient haemodynamic compromise (Crisp, 2002; Morrice et al., 2004). Morrice et al (2004) used three consecutive audits to evaluate nursing practice when managing vasoactive medications, to assess practice after guideline implementation and then compare safety of syringe changeover methods (Morrice et al., 2004).

Esfahani et al. (2016) conducted a quasi-experimental study using checklists administered before and after an education session on mortality events attributed to

medication errors for high risk drugs, nurse responsibilities, expected goals of practice and a safety action plan (Esfahani et al., 2016). The clinical observation sessions used a validated checklist of safe practices to evaluate the efficacy of the education sessions on medication administration practices of 32 ICU nurses. The nursing sample was chosen through random stratification from four ICUs located at one hospital in Isfahan, Iran (Esfahani et al., 2016).

Titration and weaning

Three reviewed studies focused on titration and weaning of vasoactive medications, comprising a qualitative content analysis (Häggström et al., 2017), evaluation of the implementation of an education program (Haniffa et al., 2017) and a prospective interventional study introducing a titration algorithm into practice (Hernandez et al., 2005). Participants identified specialist education and collegial support during titration episodes as essential to the development of decision-making and affective skills, while describing clinical experience and integrating technology as instrumental to developing psychomotor skills (Häggström et al., 2017). An interrupted time series study compared the impact of a modular training program for ICU doctors and nurses at three sites in India, Nepal and Bangladesh (Haniffa et al., 2017).

In a prospective interventional study, an algorithm using noradrenaline as first line treatment for vasoplegia prescribed a starting dose of 0.05mcg/kg/min with dose increases until a mean arterial pressure goal of 70-80mmHg was achieved (Hernandez et al., 2005). Titrations of dose increments were not prescribed, however, nurses were required to adjust noradrenaline doses at least hourly in response to continuous monitoring, to achieve minimum mean arterial pressure goals (Hernandez et al., 2005). One hundred patients were managed using the study algorithm with 67 patients receiving noradrenaline doses up to 0.3mcg/kg/min and 33 needing higher doses that prompted the nurse to consider introducing either adrenaline or dobutamine (Hernandez et al., 2005) .

Discussion

The literature on intensive care nurses' management of vasoactive medications highlighted the variability that nurses experienced in accessing specialist education and evidence based guidelines to inform their practice. Nursing practice was also influenced by the ICU culture, access to resources, and health service locations described in the literature.

Preparation and Initiation

Four studies focused on preparation and initiation of vasoactive infusions (Herout & Erstad, 2004; Jung et al., 2014; Melo et al., 2016; Tan et al., 2017). Tan et al (2017) reported that their education intervention was successful in reducing observed preparation and administration errors in parenteral medications (Tan et al., 2017). However concentration errors in noradrenaline infusions actually increased post-intervention when infusions were assayed against standard curves of known dilution using isocratic liquid chromatography. These results may reflect the complexity of local protocols that comprised six different concentrations for noradrenaline infusion preparation (Tan et al., 2017).

Weight based dose calculations rely on accurate measurement of patient weights, with variable weight measures potentially contributing to sentinel and adverse events in critically ill patients (Herout & Erstad, 2004). Intensive care nurses working in a mixed medical/surgical ICU were reported to align their choice of dose units with the preferences of the patient's parent team, with surgical teams favoring weight-based doses and medical teams preferring non weight-based units (Herout & Erstad, 2004).

These four studies indicated that providing education and standardisation of practices could support nursing practice on the preparation of vasoactive infusions and reduce risk for medication errors (Herout & Erstad, 2004; Jung et al., 2014; Melo et al., 2016; Tan et al., 2017).

Administration

All methods of syringe changeovers examined had associated issues with patient haemodynamic instability, sometimes to the point of cardiac arrest. Patient haemodynamic instability was often compounded by the use of bolus doses of vasoactive medications to control severe blood pressure fluctuations (Cour et al., 2013; Morrice et al., 2004). In the three studies comparing syringe changeovers, participating nurses attended education programs about the study intervention, comprising pump management and standardisation of practice; however, there was no discussion on how changes in nursing practice contributed to a reduction in haemodynamic incidents (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015).

In adult patients, the use of syringe drivers to deliver vasoactive medications with very short half-lives was fraught with unnecessary risk for patient haemodynamic instability due to lack of drug reservoir in the intravenous line. This practice also increased nursing workload due to small infusion volumes necessitating increased frequency of changeovers (Argaud et al., 2007; Cour et al., 2013; Greau et al., 2015). There were no follow-up evaluations reported on the efficacy and sustainability for the clinical guidelines developed by Crisp (2000) or Morrice et al., (2003) or the education sessions developed to improve nurse administration of vasoactive medications (Crisp, 2002; Esfahani et al., 2016; Morrice et al., 2004).

Titration and Weaning

The concept analysis by Häggström et al (2017) on how nurses learn to manage vasoactive medications, identified skills specific to the titration of vasoactive infusions that included the ability to analyse and evaluate technological data, adapting to changing clinical situations and staying calm. Both theoretical and practical education that encouraged the development of critical thinking skills was identified as necessary to the development of safe clinical practice when learning to manage vasoactive medications (Häggström et al., 2017).

A structured training bundle implemented into three ICUs in Nepal, India and Bangladesh emphasised the importance of monitoring vital signs and setting monitor alarm limits to prompt appropriate titration in response to blood pressure or heart rate changes (Haniffa et al., 2017). At the Indian study site, earlier discontinuation of vasoactive medications was reported after the training bundle was implemented, however, it was not clear if this practice change resulted from nursing or medical decision making. The study results highlighted difficulties in resource allocation for standardisation of practice and the provision of specialist training in low resource countries and ICUs (Haniffa et al., 2017).

While it is now accepted practice that noradrenaline is first line therapy for treatment in patients with sepsis (Hamzaoui, Scheeren, & Teboul, 2017), there are no known algorithms in current use to support nursing titration practices. This lack of guidance may be due to the unpredictable nature of patient responses to noradrenaline dosing secondary to pharmacokinetics, confounding actions of other medications and the nature of the critical illness. The mean arterial pressure goals of 70-80mmHg used in the study would be considered much higher than current mean arterial pressure recommendations of 65mmHg (Hamzaoui et al., 2017). High mean arterial pressure goals might have increased the number

of patients (33%) receiving high vasoactive doses, increased their exposure to adrenaline or dobutamine and contributed to subsequent high mortality (Hernandez et al., 2005).

The systematic review described great variations in how nurses in ICUs managed vasoactive medications and highlighted that practice variation contributes to medication errors, patient harm and nurse anxiety. There was no apparent evidence base on which to establish standardisation of practice to support nurses and not all nurses working in ICU had access to specialist education, mentoring or technology. In the spirit of developing a practice culture of patient safety, historical practices such as using syringe drivers and bolusing vasoactive infusions that contribute to patient harm, should be challenged.

This systematic review has identified gaps in the literature on intensive care nurse management of vasoactive medication that warrant further research. While all the studies were peer reviewed and contributed to expanding the knowledge base on the topic, some methodological issues were evident. With the exception of studies conducted by Crisp (2002), Häggström et al. (2017) and Haniffa et al. (2017), all studies were conducted at single centres and only Esfahani et al. (2016) and Cour et al. (2013) used randomisation in sample selection. Reported limitations included small sample sizes (Morrice et al., 2004) and failure to establish knowledge baselines or monitoring for sustainability in the education programs (Haniffa et al., 2017; Tan et al., 2017).

Many studies did not address issues of systematic bias and while eight of 12 quantitative studies reported p values in their analysis (Argaud et al., 2007; Cour et al., 2013; Esfahani et al., 2016; Greau et al., 2015; Haniffa et al., 2017; Hernandez et al., 2005; Herout & Erstad, 2004; Tan et al., 2017) only three reported confidence intervals (Cour et al., 2013; Greau et al., 2015; Haniffa et al., 2017). Conducting this systematic review has helped to define the focus and boundaries for future research and will inform a study design that aims to generate an empirical and contextualised understanding of nurse decision making on the topic in order to provide an evidence base for safer, patient centered clinical practice.

Two non-English papers were identified as meeting the inclusion criteria for the systematic review, however, we were unable to find English language translations for these studies. Inclusion of these papers may have provided additional perspectives on the topic (Paim et al., 2017; Rocha, Rocha, Andrade, & Mota, 2010).

Conclusion

The studies evaluated in this systematic review provided examples of how nurses prepare, initiate, administer, titrate and wean vasoactive medications in intensive care settings and reported great variability of clinical practice. Nursing practices were positively influenced by access to specialist education and expert mentoring, but were often affected by the prevailing workplace culture and grounded in personal preference, history and habitual practices. Identified practice variation increased risk for preparation and administration errors and increased the risk of patients receiving vasoactive boluses and experiencing haemodynamic instability. The practice of delivering vasoactive medications using syringe drivers is a known risk for haemodynamic instability. Yet, research on how to minimise this risk has not considered the use of volumetric pumps for drug delivery that would eliminate the risk entirely. Future research should focus on developing an evidence base to provide standardisation of care and support nurse decision making in managing vasoactive medications.

Relevance to Clinical Practice

Intensive care nurses manage vasoactive medications that support critically ill patients and are potentially dangerous. There is inadequate investigation of how nurses prepare, initiate, administer, titrate and wean vasoactive medications and there is little information about the impact of these nursing practices on patients. Great variability in practice is reported between ICUs, within hospitals and between healthcare providers and there is no recognised and accepted evidence based best practice on this topic.

What does this paper contribute to the wider global clinical community?

- This is the first systematic review appraising the literature on how intensive care nurses prepare, initiate, administer, titrate and wean vasoactive medications that support critically ill patients.
- Management of vasoactive medications is core business for nurses in many parts of the world and often undertaken without adequate clinical support, specialist education or equipment.
- There is great variability in practice between health services, intensive care units and

between nurses when managing vasoactive medications and the evidence-base for best practice on this topic is inadequate.

Funding

Deakin University and Eastern Health Foundation have provided funding to support this systematic review in the form of PhD Scholarships.

References

- Adapa, M., Mani, V., Murray, L., Degnan, B., Ercole, A., Cadman, B., . . . Wheeler, D. (2012). Errors during the preparation of drug infusions: a randomized controlled trial. *British Journal of Anaesthesia*, *109*(5), 729-734.
- Anstey, M., Wibrow, B., Thevathasan, T., Roberts, B., Chhangani, K., Yeung Ng, P., . . . Eikermann, M. (2017). Midodrine as adjunctive support for treatment of refractory hypotension in the intensive care unit: a multicenter, randomized, placebo controlled trial (the MIDAS trial). *BMC Anesthesiology*, *17*(47). doi:10.1186/s12871-017-0339-x
- Argaud, L., Cour, M., Martin, O., Saint-Denis, M., Ferry, T., Goyatton, A., & Robert, D. (2007). Changeovers of vasoactive drug infusion pumps: impact of a quality improvement program. *Critical Care*, *11*.
- Booth, A., Clarke, M., Gherzi, D., Moher, D., Petticrew, M., & Stewart, L. (2011). PROSPERO - Establishing a Minimum Dataset for Prospective Registration of Systematic Reviews: An International Consultation. *PloS One*, *6*(11), e27319.
- Brindley, P., O'Dochartaigh, D., Volney, C., Ryan, S., & Douma, M. (2017). Time delays associated with vasoactive medication preparation and delivery in simulated patients at risk of cardiac arrest. *Journal of Critical Care*, *40*, 149-153.
- Carter, A., Kazemi, A., Grealy, B., Schell, D., Bhonagiri, D., Seppelt, I., . . . Holmes, J. (2014). *Noradrenaline Survey Results and Discussion*. Retrieved from ANZICS
- Cour, M., Hernu, R., Bénet, T., Robert, J., Regad, D., Chabert, B., . . . Argaud, L. (2013). Benefits of smart pumps for automated changeovers of vasoactive drug infusion pumps: a quasi-experimental study. *British Journal of Anaesthesia*, *111*, 818-824.

Crisp, H. (2002). Minimising the risks: Safe administration of inotropic drug infusions in intensive care. *Nursing in Critical Care*, 7.

Critical Appraisal Skills Program. CASP Qualitative Research Checklist. (2017).

Downs, S., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology in Community Health*, 52, 377–384.

Esfahani, A., Varzaneh, F., & Changiz, T. (2016). The effect of clinical supervision model on high alert medication safety in intensive care units nurses. *Iranian Journal of Nursing and Midwifery Research*, 21, 482-486.

Fadale, K., Tucker, D., Dungan, J., & Sabol, V. (2014). Improving Nurses' Vasopressor Titration Skills and Self-Efficacy via Simulation-Based Learning. *Clinical Simulation in Nursing*, 10, e291-e299.

Garrigue, B., Dehu, Y., Girault, F., Figadère, B., Leblanc, K., Briole, N., . . . Laborne, F.-X. (2016). Preparing Drugs for Infusion Via Syringe Pump: A Key Step to Ensure Homogeneous Concentration. *Critical Care Nurse*, 36(4).

Greau, E., Lascarrou, J.-B., Le Thuaut, A., Maquigneau, N., Alcourt, Y., Coutolleau, A., . . . Reignier, J. (2015). Automatic versus manual changeovers of norepinephrine infusion pumps in critically ill adults: a prospective controlled study. *Annals of Intensive Care*, 5. doi:10.1186/s13613-015-0083-7

Häggström, M., Bergsman, A., Månsson, U., & Holmström, M. (2017). Learning to manage vasoactive drugs—A qualitative interview study with critical care nurses. *Intensive and Critical Care Nursing*, 39, 1-8.

Hamzaoui, O., Scheeren, T., & Teboul, J.-L. (2017). Norepinephrine in septic shock: when and how much? *Current Opinion in Critical Care*, 23(4), 342-347. doi:10.1097/MCC.0000000000000418

Haniffa, R., Lubell, Y., Cooper, B., Mohanty, S., Alam, S., Karki, A., . . . Dondorp, A. (2017). Impact of a structured ICU training programme in resource-limited settings in Asia. *PloS One*, 12.

Hazardous Substances Database. (2010). Retrieved 20/09/2018, from U.S National Library of Medicine <https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+51-41-2>

- Hernandez, G., Bruhn, A., Romeroa, C., Larrondo, F., De La Fuente, R., Castillo, L., & Bugedoa, G. (2005). Management of septic shock with a norepinephrine-based haemodynamic algorithm. *Resuscitation*, *66*, 63-69.
- Herout, P., & Erstad, B. (2004). Medication errors involving continuously infused medications in a surgical intensive care unit. *Critical Care Medicine*, *32*.
doi:10.1097/01.CCM.0000108876.12846.B7
- Holmes, C. (2005). Vasoactive drugs in the intensive care unit. *Current Opinion in Critical Care*, *11*, 413-417.
- Jentzer, J., Coons, J., Link, C., & Schmidhofer, M. (2015). Pharmacotherapy Update on the Use of Vasopressors and Inotropes in the Intensive Care Unit. *Journal of Cardiovascular Pharmacology and Therapeutics*, *20*(3), 249-260. doi:10.1177/1074248414559838
- Jung, B., Couldry, R., Wilkinson, S., & Grauer, D. (2014). Implementation of standardized dosing units for i.v. medications. *American Journal of Health-System Pharmacy*, *71*, 2153-2158.
- Levkovich, B., Bui, T., Bovell, A., Watterson, J., Egan, A., Poole, S., & Dooley, M. (2016). Variability of intravenous medication preparation in Australian and New Zealand intensive care units. *Journal of Evaluation in Clinical Practice*, *22*, 969-974.
- Melo, E., Cavalcante, H., Marques, A., Ferreira, A., Ferreira de Abreu, M., Lima, V., & Garces, T. (2016). Nurses On Knowledge Vasoactive Drugs Used In Critical Patients. *Journal of Nursing UFPE on-line*, *10*, 2948-2955.
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine (OPEN ACCESS)*, *151*(4).
- Morrice, A., Jackson, E., & Farnell, S. (2004). Practical considerations in the administration of intravenous vasoactive drugs in the critical care setting. Part II—How safe is our practice? *Intensive and Critical Care Nursing*, *20*, 183-189.
- Nogueira, L., Padilha, K., Silva, D., Lança, E., de Olivera, E., & de Sousa, R. (2015). Pattern of nursing interventions performed on trauma victims according to the Nursing Activities Score. *Revista Da Escola De Enfermagem Da USP*, *49*(Esp), 28-34.
- Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan — a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(210). doi:10.1186/s13643-016-0384-4

Paim, A., Nascimento, E., Bertoncello, K., Sifron, K., Salum, N., & Nascimento, K. (2017).

Validation of an instrument regarding nursing intervention in patients in vasoactive therapy. *Revista Brasileira de Enfermagem*, 70(3), 453-460.

doi:<http://dx.doi.org/10.1590/0034-7167-2016-0254>

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., . . . Duffy, S. (2006).

Guidance on the Conduct of Narrative Synthesis in Systematic Reviews: A Product from the ESRC Methods Programme.

Rocha, P., Rocha, M., Andrade, I., & Mota, M. (2010). Assessment of nurses' knowledge about the importance of continuous infusion of catecholamines in intensive care unit. *Revista Mineira de Enfermagem*, 14(4), 459-464.

Tan, S., Said, M., Rahman, R., & Taha, N. (2017). The effect of education intervention on parenteral medication preparation and administration among nurses in a general intensive care unit. *Journal of Pharmacy Practice and Research*, 47, 8-15.

doi:10.1002/jppr.1203

Valentin, A., Capuzzo, M., Guidet, B., Moreno, R., Metnitz, B., Bauer, P., & Metnitz, P. (2009).

Errors in administration of parenteral drugs in intensive care units: multinational prospective study. *British Medical Journal*, 338. doi:10.1136/bmj.b814

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Table 1. Summary of included studies and quality and bias assessment score

| | | Key interventions Preparation (P), Initiation (I), Administration (A), Titration (T), Weaning (W) | | | | | | Results (If p value not included then no p values reported) | Quality score | |
|--------------------------------|--|--|---|---|---|---|---|--|---|-----------------------|
| Author, Date,Country | Study design | Sample size and characteristics | P | I | A | T | W | | | |
| Argaud et al., 2007. France | Prospective pre and post intervention study of continuous vasoactive infusion pump (CVIP) changeover improvement program using standardisation of the quick change (QC) method | 43 ICU patients with septic shock 913 total CVIP events 435 Pre-intervention CVIP episodes 478 Post- intervention CVIP episodes | | | ✓ | | | <p>Number of patients who experienced haemodynamic (HD) incident of increased or decreased SBP or HR >20mmHg or 20BPM</p> <p>Total HD incidents</p> | <p>Pre-intervention 92% (23/25) Post-intervention 61% (11/18) (p=0.02)</p> <p>Pre-intervention 18% (78/435) Post-intervention 5.9% (28/478) (p<0.0001)</p> | 56.25% (18/32) |

| | | | | | | | | | | |
|--------------------------------|---|--|--|--|---|--|--|---|--|-----------------------|
| Cour et al., 2013. France | Quasi-experimental study comparing the quick change method with automatic relays using automated smart pumps | 133 ICU patients with septic shock 1329 CVIP events 681 QC episodes 648 Automated Smart Pump episodes | | | ✓ | | | Primary outcome = change in MAP>15mmHg or HR 15 BPM within 30 minutes of CVIP | QC - 22.17% (151/681) Automated Smart Pumps - 13% (83/648) (p<0.01) | 59.37% (19/32) |
| | | | | | | | | Reduced nurse and doctor time spent on vasoactive activities | QC - 21.73% (148/681) Automated Smart Pumps - 3.85% (25/648) (p<0.001) | |
| Crisp 2002. United Kingdom | Pre & post survey for education & guideline implementation for quick-change continuous vasoactive infusion pump changeovers | Not reported | | | ✓ | | | Guidelines prompted nurses to <ul style="list-style-type: none"> • Chose a dedicated central line • Group infusion pumps on the same side of the bed and at the same height • Avoid giving bolus doses | 37.50% (12/32) | |
| Esfahani et al., 2016. Iran | Quasi-experimental prospective study comprising one group before and after implementation of an | 32 Nurses Patient population not reported | | | ✓ | | | Scores for preventing medication errors in noradrenaline. Out of a possible score of 13 | Pre- education - 76% 9.90/13 (SD+/-1.21) Post-education - 95% 12.29/13 (SD+/-0.93) (p<0.001) | 34.37% (11/32) |

| | | | | | | | | | | |
|--------------------------------|---|---|--|--|---|---|--|--|---|-------------------|
| | education program | | | | | | | Scores for the prevention of adverse drug events for noradrenaline. Out of a possible score of 12 | Pre-education - 39% 4.7/12 (SD+/-1.03) Post-education - 61% 7.42/12 (SD+/-0.82) (p<0.001) | |
| Greau et al., 2015. France | Prospective controlled trial comparing quick change (QC) to smart pump changeovers | 50 ICU patients with septic shock | | | ✓ | | | Primary outcome = proportion of syringe changeovers followed by drop in MAP >20% from baseline. | QC - 12.4% Smart Pump - 5.5% (p=0.01) | 56.25% (18/32) |
| | | | | | | | | Severe hypotension of MAP<50mmHg | QC - 4.7% Smart Pump - 4.1% (p=0.79) | |
| Häggström et al., 2017. Sweden | Qualitative content analysis on how critical care nurses learn to manage vasoactive drugs | 12 critical care nurses from three Swedish ICUs | | | | ✓ | | Themes that emerged <ul style="list-style-type: none"> Practice and collegial support needed while developing psychomotor, cognitive and affective skills Development of critical thinking skills in a safe environment. | | |

| | | | | | | | | | | |
|--------------------------------------|--|--|--|--|---|---|---|--|---|----------------|
| Haniffa et al., 2017. South Asia | Quasi-experimental Interrupted time series study comparing the impact of a modular training program for ICU doctors and nurses at three sites in India, Nepal and Bangladesh | 3868 Adult ICU patients | | | ✓ | ✓ | ✓ | Mortality at Indian site Mortality at Nepalese site Mortality at Bangladesh site | Increased 28% to 30%, with an adjusted sub-distribution hazard ratio (AHR) of 1.17 (p=0.49) Reduced from 41% to 18% AHR 0.16 (p<0.001) Reduced from 62% to 51% AHR 0.62 (p=0.03). | 56.25% (18/32) |
| Hernandez et al., 2005. Chile | Prospective observational study on the introduction of an algorithm using noradrenaline as the first line agent for vasoplegia | 100 Adult surgical patients with septic shock. | | | | ✓ | ✓ | Use of pulmonary artery catheters | 31% (31/100) patients | 46.87% (15/32) |
| Mortality for noradrenaline doses of | | | | | | | | | | |
| <0.3mcg/kg/min | | | | | | | | | 13% (9/67) | |
| >0.3mcg/kg/min | | | | | | | | | 73% (24/33)(p<0.05) | |

| | | | | | | | | | | |
|-----------------------------|--|--|---|---|---|--|--|--|--|-------------------|
| | | | | | | | | Total mortality pre and post algorithm introduction | 33% (33/100) | |
| Herout and Erstad 2004. USA | Observational study documenting incidence of medication errors of continuous infusions due to variation in patients weights used | 42 Adult surgical patients | ✓ | | ✓ | | | The overall medication error rate | 105.9 per 1000 patient days | 37.50% (12/32) |
| | | | | | | | | No body weight recorded | Male patients - 30% (15/50) Female patients - 47% (10/21) | |
| Jung et al., 2014. USA | Pre and post education implementation survey | 1830 nurses in pre-survey 864 nurses in post-survey | ✓ | ✓ | | | | Nurse reported confidence when undertaking weight based calculations | | 15.62% (5/32) |
| | | | | | | | | Pre-implementation survey | 21% (181/864) | |
| | | | | | | | | Post implementation survey | 40% (732 /1830) | |

| | | | | | | | | | | |
|--|---|---------------------|---|---|---|--|--|---|--|-------------------|
| Melo et al., 2016. Brazil | Descriptive exploratory survey | 80 ICU Nurses | ✓ | ✓ | ✓ | | | Unable to identify compatible diluents, admixture volumes/doses | 18% (15/80) | 37.50% (12/32) |
| | | | | | | | | Unable to identify clinical indication for vasoactive medication | 26% (34/80) | |
| | | | | | | | | Unable to identify when to initiate vasoactive medication | 43% (34/80) | |
| Morrice et al., 2004. United Kingdom | Mixed method study incorporating three consecutive audits, interviews & observation of nurse practice after the implementation of a continuous vasoactive infusion pump (CVIP) changeover guideline | 83 CVIP changeovers | | | ✓ | | | Method 1. Quick change (QC) method | Decrease in SBP of greater than 30mmHg in 66.7% (2/3) of episodes. | 37.50% (12/32) |
| | | | | | | | | Method 2. Two infusion syringes running together and turning off the first infusion once the target blood pressure had been reached | Increase in SBP of greater than 30mmHg of 11% (1/9) and 11% (1/9) had a decrease greater than 30mmHg | |

| | | | | | | | | | | |
|-------------------------------|---|---|---|--|---|--|--|--|--|-----------------------|
| | | | | | | | | Method 3. Two syringes running together and titrating the first infusion down slowly once the target blood pressure had been reached | 16.7% (2/12) increase in SBP of greater than 30mmHg and a 25% (3/12) decrease of greater than 30mmHg | |
| Tan et al., 2017. Malaysia | Prospective pre & post education implementation study | 39 nurses pre-education intervention 35 nurses post-education intervention | ✓ | | ✓ | | | Noradrenaline infusion concentrations errors Pre-education Post-education | 48% (19/40) 53% (8/15) (p=0.70) | 46.87% (15/32) |
| | | | | | | | Incorrect preparation Pre-education Post-education | 69% (57/122) 32% (30/105) (p<0.001) | | |
| | | | | | | | Incompatible diluents Pre-education Post-education | 13% (11/122) 3% (3/105) (p<0.001) | | |

Figure Legend

AHR = Adjusted Sub-Distribution Hazard Ratio

BPM = Beats Per Minute

CVIP = Continuous Vasoactive Infusion Pump

ICU = Intensive Care Unit

HD = Haemodynamic

HR = Heart Rate

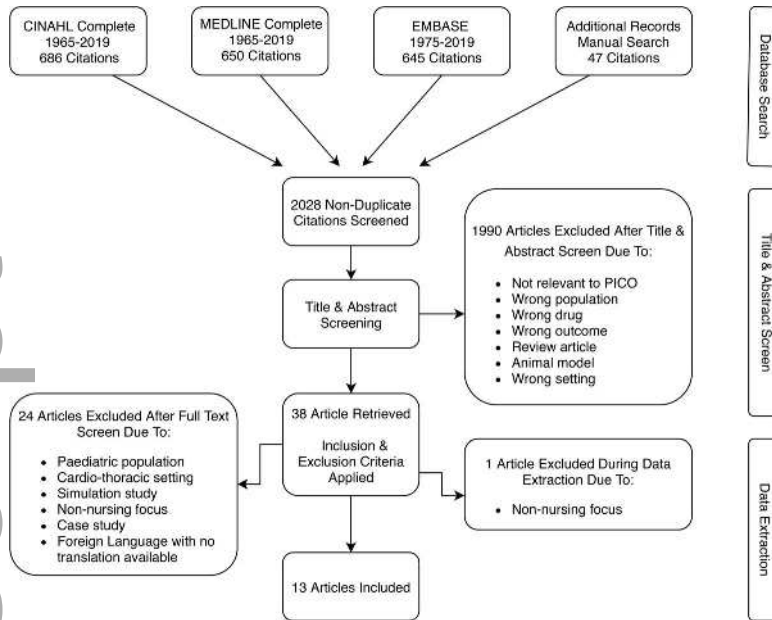
MAP= Mean Arterial Pressure

mmHg = millimeters of mercury

QC = Quick Change

SBP = Systolic Blood Pressure

SD = Standard Deviation



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