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REVIEW ARTICLE

CENTRAL VENOUS CATHETER CLEARANCE IN NEWBORNS AND INFANTS: SCOPING REVIEW

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ABSTRACT

Objective: to map the scientific evidence related to the solutions used for the clearance of central venous catheter in newborns and infants. **Methods:** scoping review, conducted as recommended by the Joanna Briggs Institute. The search was conducted in November 2023 using the PCC strategy (Population, Concept and Context), and in this review, the population are newborns and infants; the concept is the substances for clearance of central venous catheter; and the context is the use of central venous catheter. It was performed in the databases of the Online Search System and Analysis of Medical Literature, Cochrane Library, Scopus, Web of Science, and the Portal of the Virtual Health Library. Studies without language and time restriction were included. **Results:** seven studies were selected from the 10,044 found, most of them published in the United States. To clear clots, urokinase and alteplase stand out and, in relation to the precipitates, there is sodium bicarbonate (alkaline), hydrochloric acid 0.1% (acids and minerals) and ethanol 70% (lipids). It is observed that there is a predominance of the use of the drug infusion technique over the use of negative pressure. In the case of mechanical occlusion, bends and twists must be corrected. **Conclusion:** the evidence found on the clearance of central venous catheter in newborns and infants points to the need to know the cause of obstruction, since one is directly related to another. Thus, there are divergences in the type of medications and/or solutions used for the clearance of central venous catheter

Keywords: Central venous catheterization. Catheter obstruction. Newborn. Infant.

INTRODUCTION

The central venous catheter (CVC) is a device used in severely ill patients who require prolonged intravenous therapy. The insertion of this device comprises a highly complex procedure at risk of complications[1]. The indication for its insertion is the infusion of blood products, hemodynamic monitoring, parenteral nutrition, administration of drugs for a period of six days or more and/or infusion of vesicant or irritants and/or hypertonic substances (greater than 600 mOsmol/L), such as vasoactive drugs, glycoside solution with concentrations above 12.5% and chemotherapy[1-3]. However, for its insertion and manipulation, it is necessary that there is training of the health team, because its use can lead to complications such as thrombosis, infection, occlusion, displacement of the distal end and extravasation. In newborns (NB) and infants these complications often lead to catheter removal, reducing the length of stay of the device[4].

Among the most common complications in the child population, obstruction of the CVC stands out, which often leads to non-elective removal before the end of treatment[5,6]. The occlusion of the catheter compromises its permeability and may occur in whole or in part, leading to resistance or impossibility of infusion of medicines and/or solutions. CVC obstruction may occur by fibrin or clots that are related to the presence of blood within your lumen, a possible consequence of inadequate saline flush or retrograde flow of the infusion pathway. Another cause that can lead to the occurrence of

[1] Extracted from doctoral thesis entitled: "Soluções para desobstrução do cateter do cateter central de inserção periférica neonatal: estudo in vitro"

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occlusion of this venous access is the mixture of incompatible medications provoking precipitations. In addition, interruptions of adequate flow in the lumen of the catheter may occur due to mechanical causes such as bends and twists[7].

Obstruction of the central catheters may result in the unplanned removal of 11 to 50%[6], causing pain and discomfort to the NB and infant, when the objective is to perform a new access, often without success. In practice, it is observed that in an attempt to avoid the removal of the device before the end of treatment, many services use empirical techniques, unaware of the risks and effectiveness of the solutions used[8]. Therefore, it is of fundamental relevance the mapping of studies that indicate the knowledge about the solutions that can be used for the clearance of central venous catheter in the production of evidence that can allow the professional to know the solutions used and already studied.

Thus, this research aims to map the scientific evidence related to the solutions used for the clearance of central venous catheter in newborns and infants.

METHOD

This is a scoping review study, which aims to map knowledge about a particular topic in question, relating the year and place of publication, type of study and area belonging (clinical or academic). It aims to elucidate a certain scientific knowledge, identify gaps and the type of research developed[9,10]. Thus, we chose to conduct a scope review in order to map the existing knowledge due to the absence of random tests that address the solutions used for the clearance of CVC of NB and infants and to direct the occurrence of eventual systematic reviews.

For the accomplishment of this research, the following recommendations Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews PRISMA-ScR[11], with registration in the Open Science Framework (OSF) platform available in https://osf.io/muep3/?view_only=6431c3a918e846a2843a805bffe64164, under the number DOI 10.17605/OSF.IO/MUEP3, conducted with methodological rigor as recommended by the Joanna Briggs Institute (JBI)[12]. The steps followed were: 1- Elaboration of the research question; 2- Search of articles in the databases with the descriptors; 3- Selection of studies, according to the inclusion and exclusion criteria; 4- Collection of results and 5- Synthesis, grouping and exposure of data[13,14].

Therefore, the research question was elaborated according to the mnemonic strategy PCC (Population, Concept and Context), being: population (P) newborns and infants; concept (C) substances for clearing CVC and context (C) the use of CVC. The following research question was elaborated: "What scientific evidence addresses the solutions used to unclog the central venous catheter in newborns and infants?"

For the search of the studies, the descriptors searched in the Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH) in English: "Catheter Obstruction" "Catheterization, Central Venous" "Vascular Patency" "Permeability", "Infant, Newborn" and "Infant". Combinations were performed using the Boolean operators OR and AND, in addition to the use of parentheses to establish order in the process, separation of term sets with quotation marks, used in cases of compound term, thus forming a search strategy (Chart 1). The search strategy was used for the research in the following databases: Online Search System and Analysis of Medical Literature (PUBMED), Cochrane Library (Cochrane), Scopus, Web of Science and the Portal of the Virtual Health Library (VHL). The search was conducted in November 2023.

The eligibility criteria were original scientific articles from qualitative, quantitative studies, mixed method, reviews, descriptive or analytical, guidelines, event annals, theses, dissertations, monographs, theoretical articles, without time restriction and that agreed with the objective of this research. Therefore, we considered studies that addressed NB and infants (zero to two years). Studies with all types of central venous devices were included, among them, the central venous catheter of peripheral insertion, because, despite being inserted peripherally, its distal end has a central location.

There was no language restriction. All studies used were available in full and were accessed through the CAPES CAFe portal via the university login to which this research is linked. The exclusion criterion was studies that approached the cancer patient because there is a specificity in the type of treatment received. Duplicate articles were computed only once.

Chart 1. Search strategies used in databases and on the Virtual Health Library Portal. Paraná, Brazil, 2023.

Databases and VHL Portal	Search strategy	Studies found
VHL Scopus	*#1* (Catheter Obstruction) OR (Vascular Patency)) OR (Permeability)) AND (Catheterization, Central Venous)) AND (Infant, Newborn)	7
	#2(Obstrução do Cateter) OR (permeabilidade) AND (cateterismo venoso central) AND (recém-nascido)	18
	("Catheter Obstruction" OR "Catheterization Central Venous") AND (newborn OR infant)	2402 - open access 534
Web of Science	Catheter Obstruction AND Catheterization Central Venous AND Infant	15
PUBMED	Catheter Obstruction OR Permeability OR Catheterization Central Venous AND Infant	6365- age cut 5737
Cochrane	Catheter Obstruction OR Permeability AND Catheterization, Central Venous AND Infant	1237 - not duplicated 734

To ensure the reliability of this research, the search and selection of studies was performed by two reviewers separately (both authors of this work); in case of disagreement, the tiebreaker occurred by a third reviewer. The readings of the titles and abstracts of the pre-selected articles were made and, subsequently, their reading in full for the inclusion or exclusion of the research, based on the objective of this study.

The studies selected for the research were synthesized and organized by analyzing the differences, similarities, identification of gaps and type of study. It was used a data collection instrument prepared by the authors for the registration of the selected studies with information about title, authors, year and country of publication, objective, type of study, population, type of obstruction, clearance technique, solutions used for clearance and outcome.

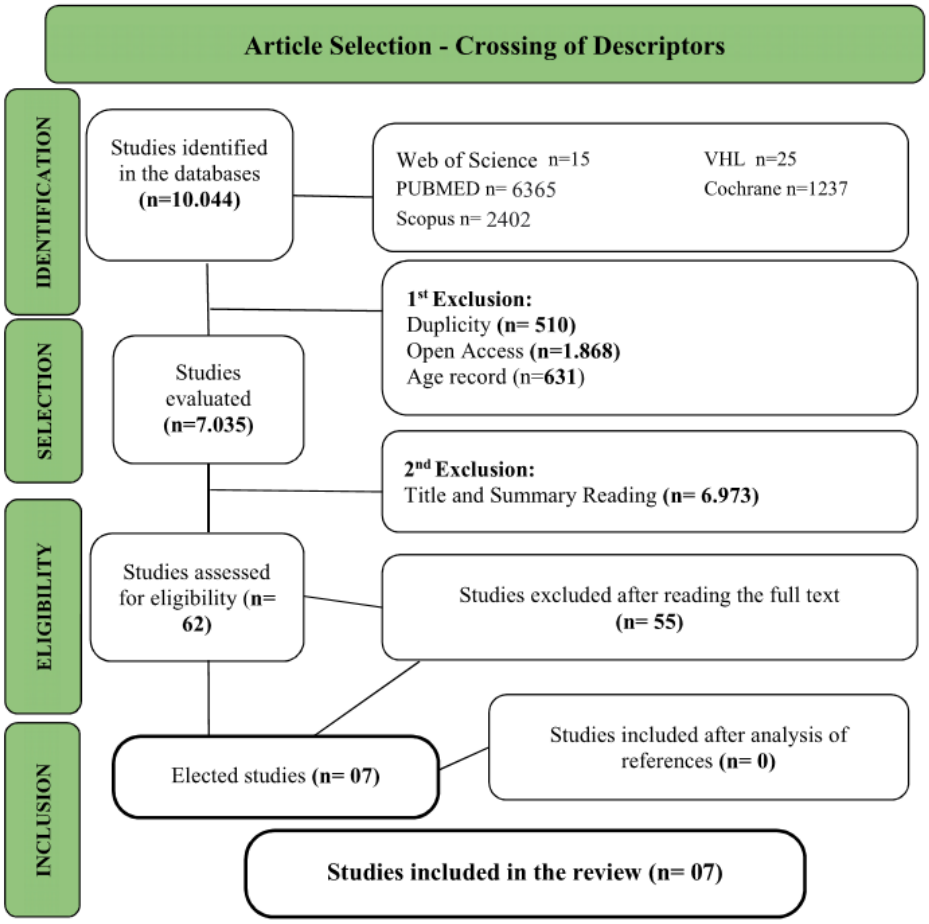
In the chosen studies, the articles used in their references were searched manually and those that met the inclusion criteria were also included in this review.

For the presentation of the results were synthesized the main findings of each research and presented the evidence found. Thus, two tables with the data collected were elaborated by the authors of this study, based on the requirements of JBI[12] and adapted for this review. The first table consists of a characterization of the selected studies (title, authors, year and country of publication, objective, type of study and population) and the second table is a synthesis of the type of obstruction, the solutions used for clearance and outcome. The synthesis of the data was performed in a descriptive way with the critical analysis of the findings, in which the theoretical foundation and the comparison of the main results were performed.

RESULTS

The search in the databases mapped 10,044 studies. After evaluation through the eligibility criteria, a total of seven studies selected for this scope review was obtained. A flowchart illustrating the path taken for article selection was developed, based on the Preferred Reporting Items for Systematic Review and Meta-Analyses PRISMA-ScR[11] (Figure 1).

Figure 1. Flowchart of the selection of articles included in the scope review. Paraná, Brazil, 2023.



It is noteworthy that the period of publication occurred between the years 1989 to 2017. Of the seven studies selected for the research, it is observed that there is a predominance of publication in the United States of America (N=5). It is noteworthy that the existing scientific evidence consists of experimental research (N = 3), review (N = 2) and retrospective (N = 2) (Chart 2).

Chart 2. Characterization of the articles included in the review. Paraná, Brazil, 2023

ID	Title, authors, year and country of publication	Type of study, objective and population studied
0	Treatment of central venous catheter occlusions with hydrochloric acid [15] Duffy LF et al - 1989 – USA	Experimental study To evaluate the use of hydrochloric acid for clearing precipitates from central venous catheters. 19 CVC obstructions in 51 infants
0	Die Behandlung von Obstruktionen und Thrombosen bei zentralvenösen Kathetern [16] Leititis JU - 1991 – Germany	Review article Discuss the unblocking of central venous access due to clots and precipitates. 117 CVC of premature babies
3	Treatment of central venous catheter occlusions with ethanol and hydrochloric acid [17] Werlin S et al - 1995 - USA	Experimental research Develop a protocol for unblocking a central venous catheter using hydrochloric acid and ethanol. Determine which pharmaceutical agents most obstruct catheters at the researched institution. 39 obstructed CVCs of neonates weighing between 1 and 3 kg that were not unblocked by urokinase

4	Efficacy of local instillation of recombinant tissue plasminogen activator for restorting occluded central venous catheters in neonates [18] Soylu H et al - 2010 – USA	Retrospective cohort study To evaluate the efficacy of local instillation of tissue plasminogen activator to restore the function of occluded central venous catheters in the neonatal population. CVC of 18 neonates
5	Prevention, assessment, and treatment of central venous catheter occlusions in neonatal and young pediatric patients [19] Doellman D - 2011 - USA	Review article Describe the best solutions for unblocking central catheters according to the type of obstruction. CVC in newborns and infants
6	Heparin for unblocking peripherally inserted central venous catheters in newborns: in vitro study [20] Balaminut T et al - 2015 - Brazil	In vitro experimental study To compare the effectiveness of two concentrations of heparin for clot clearance of neonatal peripherally inserted central venous catheter (PICC) in vitro.
7	Recombinant tissue plasminogen activator to restore catheter patency: efficacy and safety analysis from a multihospital NICU system [21] Scott DM et al - 2017 – USA	Retrospective study To carry out a retrospective analysis of alteplase in unblocking central venous catheters in a neonatal ICU III 169 CVC for neonates

Regarding the type of occlusion addressed in the studies, obstruction is observed only by clots (N=3), followed by obstruction by clots and precipitates (N=2), obstruction by clots, precipitates, and mechanics (N=1) and obstruction only by precipitates (N=1). There is prevalence of medication infusion (N=4) compared to infusion and negative pressure (N=2) and only negative pressure (N=1) (Chart 3).

It should be noted that the substance used for clearing depends on the cause of the obstruction. Urokinase/streptokinase was found in 3 studies, alteplase in 4, low molecular weight heparin in 1. In the clearance by precipitates was used 0.1% hydrochloric acid in 4 articles, 70% ethanol in 2, sodium bicarbonate in 1 publication. In the clearance by mechanical causes has been repositioning/correction of twists and folds in 1 study.

Chart 3, Characterization of the type of obstruction, solutions used to unclog it and main outcomes of the included articles. Paraná, Brazil, 2023

ID	Type of obstruction, solution, technique, outcome and side effects
01 [15]	**Obstruction type:** precipitates **Solution:** 0.1% hydrochloric acid **Technique:** infusion **Outcome:** all 11 CVC, in which calcium and phosphorus precipitation was observed, were unobstructed, with 2 receiving two instillations and 1 receiving three, 5 partially unobstructed, 3 not unobstructed
02 [16]	**Type of obstruction:** clots and precipitates **Solution:** clots: urokinase (500 U/ml) or streptokinase. or alteplase (1 mg/ ml). Precipitates (long-term use of NPP): 0.1% hydrochloric acid with heparin 10 U/ml every hour **Technique:** Infusion **Outcome:** 114 CVC unblocked; 3 CVC did not unblock
03 [17]	**Type of obstruction:** clots and precipitates **Solution:** clot: urokinase infusion. Precipitates: a) lipids: 70% ethanol; b) minerals: negative pressure technique with 0.1% hydrochloric acid **Technique:** infusion and negative pressure **Outcome:** 15 CVC cleared by urokinase; of the remaining 24, 19 were unblocked by ethanol or hydrochloric acid (9 ethanol and 10 hydrochloric acid); 6 CVC remained obstructed
04 [18]	**Type of obstruction:** clots **Solution:** alteplase 1 mg diluted in 2 ml and 0.5 mg with 2 ml of saline **Technique:** infusion

	Outcome: 55% of CVCs had their patency reestablished (10 of 18); This percentage of clearance was lower in neonates than in older patients.
05 (19)	**Type of obstruction:** clots, precipitates and mechanics **Solution:** mechanics - correct the cause (folds, positioning and twists); precipitates - a) minerals: hydrochloric acid from 0.2 to 0.5 ml; b) lipids - 70% ethanol (0.55 ml/kg); c) alkaline pH - sodium bicarbonate; d) acidic pH - hydrochloric acid; clots - alteplase (1 mg/ml) **Technique:** infusion and negative pressure **Outcome:** 55% to 95% of CVC clearance after alteplase infusion; 54 of 73 CVCs cleared by alteplase infusion in neonatal patients. 30 of 43 children's CVCs were unobstructed after infusion of 0.1 HCl
06 (20)	**Type of obstruction:** clots **Solution:** low molecular weight heparin in two concentrations 25 IU/ml and 50 IU/ml **Technique:** negative pressure **Outcome:** low molecular weight heparin at a concentration of 50 IU/ml proved to be more effective.
07 (21)	**Type of obstruction:** clots **Solution:** alteplase (one to four doses) **Technique:** infusion **Outcome:** 58% CVC clearance with the use of alteplase

DISCUSSION

When mapping the scientific evidence, experimental[15,17,20], review[16,19] and retrospective[18,21] research were found. Regarding the causes of obstruction found in the studies chosen were clots[16-21], precipitates of drug interactions (acids and alkalis), lipids and minerals[15-17,19], and mechanical[19].

One of the main causes of CVC obstruction is clots occurring about 20 to 40% in the pediatric population. This type of occlusion is caused by intraluminal, extraluminal thrombi or fibrin sheaths. It is important to highlight that there are particularities in the fibrinolytic system of children and adults, therefore, it should be considered that there are differences according to the age of the pediatric patient[16-22].

The mechanism of formation of fibrin sheath and thrombus resulting from CVC is the creation of biofilm, which corresponds to intraluminal or extraluminal bacterial fixation. Some factors may favor this obstruction: low levels of antithrombin III, protein C, platelet activation, high levels of fibrinogen and homocysteine[16-21,23].

Thrombolytic medications act by activating plasminogen, which acts by activating plasmin, the proteolytic enzyme responsible for destroying the cross-links of fibrin structures that are insoluble - these are the bonds that form clots. Recombinant tissue plasminogen activator dissolves thrombi, mainly fibrin[16-19,21,24].

The classification of thrombolytic drugs is according to the specificity of fibrin. Urokinase and streptokinase are classified as non-specific, the tissue plasminogen activator is of the specific type and reteplase is of next generations[13,16,19,33].

Streptokinase is a polypeptide enzyme of bacteria in the Strepthococcus β-hemolytic group. It acts by converting plasminogen into plasmin, which is responsible for hydrolyzing clots. Urokinase is a type of plasminogen activator composed of a fibrinolytic polypeptide chain; it has high activity converting plasminogen into plasmin[18,19,21,25].

Alteplase, classified as a recombinant human tissue plasminogen activator, promotes thrombolysis and destruction of fibrin. Reteplase is a type of non-glycosylated modified recombinant tissue plasminogen that acts on the dissolution of thrombi[23,28,30,33,35].

In this research, we found older studies (until the 1990s) that used streptokinase and/or urokinase[16,17] and in the most recent (from the 2000s) there is the use of alteplase in the literature[18, 19, 21]. Therefore, it is important to highlight that, until 1999, the medication used for the clearance of CVC in children was urokinase. However, in January of the same year, the Food and Drug Administration (FDA) banned the use and commercialization of urokinase derived from human cells due to the possibility of contamination by infectious agents. It was replaced by recombinant urokinase (non-human cells) for use in the USA[16,17,22].

In the only national study found in this study,

heparin was used as a substance for the clearance of central venous catheters[20]. Heparin is a polysaccharide compound with anticoagulant action through interaction with antithrombin III, inhibiting coagulation factors Xa and IIa. It is available in non-fractionated and low molecular weight forms[27].

Another cause of CVC obstruction is by precipitates of drug interactions. In the incompatibility between intravenous infused drugs, there is a chemical and/or physical reaction due to the contact of two or more medications. Precipitates are formed when there is physical incompatibility, and changes in consistency and/or color may also occur; in chemical incompatibility there are changes in the molecules of the compounds. These reactions can alter the effectiveness of treatment, provoke inflammatory reactions, embolism and obstruction of CVC - the compatibility between medications for simultaneous infusion should be ensured[16,17,19,28].

Blockages caused by precipitates of drug interactions may occur due to lipid compounds, drugs, and minerals. In the occlusion caused by lipids stands out the use of sodium hydroxide followed by ethanol. For deposits of medicines and minerals it is recommended the use of L-cysteine and, later, by hydrochloric acid[15,18,38].

In this research we found the predominance of the use of the infusion technique[15-19,21] in relation to the negative pressure[17,19,20]. In 2016 the Infusion Therapy standards of Practice was launched, which indicates the use of the drug infusion technique for clearance when there is partial occlusion of the CVC and, in the case of total occlusion clearance, recommends the use of the negative pressure technique to reduce the damage that can be caused in the CVC[17,19,20,29].

Another cause of obstruction of central venous catheters found in this study is the mechanical etiology[19], caused by folds and twists. For this event, although there is no use of drug solutions, the importance of correcting the positioning and correctly performing CVC fixation during dressing execution is highlighted[26,27].

There was a predominance of international research in relation to national ones. However, even with the lack of scientific evidence on the clearance of central venous catheters in newborns and infants, in Brazil there is no restriction regarding the use of medications and only heparin has been tested[20]. Brazilian studies only address the use of solutions in the maintenance of permeability[30,31].

This research presents some limitations that are related to the nature of the review itself, mainly in the indication of subsidies for the use of medicines and/or solutions for clearance of central venous catheters in newborns and infants. It is believed that the present study may support the planning of future studies, systematic review or randomized clinical trial, in order to enable the comparison of solutions or the efficacy/safety of a specific solution.

CONCLUSION

The evidence found points to the need to discover the cause of obstruction, because the clearance of central venous catheter in newborns and infants is directly related to the cause of obstruction. Thus, there are divergences in the type of medications and/ or solutions used for the clearance of central venous catheter in this population, and in events related to clots there is reference in the literature on the use of urokinase/streptokinase, low molecular weight alteplase and heparin. In the central venous catheter clearance, related to precipitates of drug interactions, the use of 0.1% hydrochloric acid in minerals and acid solutions, 70% ethanol in lipids, sodium bicarbonate in alkaline compounds were found.

There was a predominance of the use of the technique of infusion of drug solutions compared to the use of negative pressure both in the clearance by clots and by precipitates of drug interactions. In the case of mechanical occlusions, the correction of positioning, folds and twists was found.

The occurrence of new studies, specific to the neonatal population and infants, with more robust methods, such as randomized clinical trial, is necessary because there is a lack of scientific evidence produced only with this population.

DESOBSTRUÇÃO DE CATETER VENOSO CENTRAL EM RECÉM-NASCIDOS E LACTENTES: SCOPING REVIEW

RESUMO

Objetivo: mapear as evidências científicas relacionadas às soluções utilizadas para a desobstrução de cateter venoso central em recém-nascidos e lactentes. **Métodos:** scoping review conduzida conforme recomendado pelo

Instituto Joanna Briggs. A busca foi realizada no mês de novembro de 2023 utilizando a estratégia PCC (População, Conceito e Contexto), sendo que, nesta revisão, a população são os recém-nascidos e lactentes; o conceito são as substâncias para desobstrução de cateter venoso central; e o contexto é a utilização de cateter venoso central. Foi realizada nas bases de dados do Sistema Online de Busca e Análise de Literatura Médica, Cochrane Library, Scopus, Web of Science e no Portal da Biblioteca Virtual em Saúde. Foram incluídos estudos sem restrição de idioma e tempo. **Resultados:** foram selecionados sete estudos dos 10.044 encontrados, sendo a maioria publicada nos Estados Unidos. Para desobstrução de coágulos destaca-se a uroquinase e a alteplase e, em relação aos precipitados, tem-se o bicarbonato de sódio (alcalinos), ácido clorídrico 0,1% (ácidos e minerais) e etanol 70% (lipídicos). Observa-se que há predomínio do uso da técnica de infusão de medicamentos em detrimento do uso da pressão negativa. No caso de oclusão mecânica, deve-se corrigir dobras e torções. **Conclusão:** as evidências encontradas sobre a desobstrução de cateter venoso central em recém-nascidos e lactentes apontam para a necessidade de saber a causa da obstrução, pois uma está diretamente relacionada a outra. Assim há divergências no tipo de medicações e/ou soluções utilizadas para a desobstrução de cateter venoso central na população estudada.

Palavras-chave: Cateterismo venoso central. Obstrução do Cateter. Recém-Nascido. Lactente.

DESOBSTRUCCIÓN DE CATÉTER VENOSO CENTRAL EN RECIÉN NACIDOS Y LACTANTES: *SCOPING REVIEW*

RESUMEN

Objetivo: mapear las evidencias científicas relacionadas con las soluciones utilizadas para la desobstrucción del catéter venoso central en recién nacidos y lactantes. **Métodos**: *scoping review*, conducido conforme recomendado por el Instituto Joanna Briggs. La búsqueda fue realizada en el mes de noviembre de 2023 utilizando la estrategia PCC: recién nacidos y lactantes son la Población; sustancias para desobstrucción de catéter venoso central son el Concepto; y el uso de catéter venoso central es el Contexto. Se realizó en las bases de datos del Sistema *Online* de Búsqueda y Análisis de Literatura Médica, *Cochrane Library*, *Scopus*, *Web of Science* y en el *Portal da Biblioteca Virtual em Saúde*. Se incluyeron estudios sin restricción de idioma y tiempo. **Resultados**: fueron seleccionados siete estudios de los 10.044 encontrados, siendo la mayoría publicada en los Estados Unidos. Para desobstrucción de coágulos se destaca la uroquinasa y la alteplasa y, con relación a los precipitados, se tiene bicarbonato de sodio (alcalinos), ácido clorhídrico 0,1% (ácidos y minerales) y etanol 70% (lipídicos). Se observa que hay predominio del uso de la técnica de infusión de medicamentos en vez del uso de la presión negativa. En caso de oclusión mecánica, se deben corregir dobleces y torsiones. **Conclusión**: las evidencias encontradas sobre la desobstrucción del catéter venoso central en recién nacidos y lactantes señalan la necesidad de saber la causa de la obstrucción, pues una está directamente relacionada con otra. Así hay divergencias en el tipo de medicaciones y/o soluciones utilizadas para la desobstrucción de catéter venoso central.

Palabras clave: Cateterismo venoso central. Obstrucción del Catéter. Recién Nacido. Lactante.

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