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MAINTENANCE OF TOTALLY IMPLANTABLE CENTRAL VENOUS CATHETER ACCESS PORT (PORT-A-CATH) IN ONCOLOGY: INTEGRATING LITERATURE REVIEW

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ABSTRACT

Introduction: The totally implantable central venous catheter access port (TICVAP), known as Port-a-cath, is the most suitable access to prolonged antineoplastic chemotherapy, whose handling and prevention of catheter occlusion are under the responsibility of the nurse. **Objective:** To analyze the available evidence on the maintenance TICVAP in oncology in the literature. **Methodology:** Integrative literature review with selection of works indexed in the databases: SciELO, Pubmed and ScienceDirect, using the keywords "Flushing and locking", "Totally Implantable Central Venous Catheters", "Oncology Patients" and "Protocols ". The research was carried out between January 2017 and August 2018, with publications from 2007-2018, 58 publications were selected relevant for the development of the study through the analysis of the abstracts and later with the evaluation of the texts in totally were selected 23 publications. **Results:** The use of 0.9% sodium chloride, ethanol, antimicrobials or heparin concentrate was identified for flushing and locking, but without standardization of the best solution to be used. **Conclusion:** There are few studies on the subject, without significant scientific evidence to support a standardization regarding the maintenance of TICVAP blockade, and it is necessary to carry out new researches with cancer patients to support the clinical practice based on evidence.

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INTRODUCTION

The totally implantable central venous catheter access port (TICVAP), also known as port-a-cath, is a device composed of a radiopaque flexible tube and a titanium chamber at one end with a silicone membrane in the central part. It is in this membrane that the punctures with Huber needles are realized (Gomes and Sá, 2014). In cancer patients, this catheter is indicated mainly for prolonged chemotherapy, with the advantage of reducing the risk of infection, not interfering with

the patient's quality of life and maintenance at longer time intervals compared to other devices (Gomes and Sá, 2014). Alternatively, its disadvantages include flow limitation for apheresis or photopheresis (hemodialysis requirements and bone marrow transplantation) (Albuquerque, 2015). Complications related to TICVAP may be early or late. The precocious occur in the perioperative period, being less frequent and being related to the surgical procedure such as pneumothorax, cardiac arrhythmia, arterial puncture and bleeding. The late complications are the main causes of early catheter removal such as infections, venous injury, thrombosis, pulmonary embolism, extravasation to the mediastinum or pleural space, fracture, catheter embolization, twisted catheter, Huber needle misalignment, reservoir exposure, hypertrophic scar and keloid, pyoderma gangrenosum and foreign body retention (Vieira, 2015; Goossens *et al*., 2015). Because it is a device of high cost and necessary to the chemotherapeutic treatment of the patient, its functionality is imperative. For this, strategies that avoid the venous return to the light of the catheter or the formation of thromb have been performed to optimize its viability. Thus, in order to prevent catheter obstruction, the TICVAP flush and lock is performed respectively. In the first, irrigation of the device with 0.9% sodium chloride for waste removal. In the latter, there is intraluminal injection of solution at predetermined time intervals when the catheter is not being used (Pittiruti *et al*, 2016). In flushing and locking substances are infused to fill the totally extent of the catheter, up to its tip (Keogh *et al*, 2015). Intrathoracic compression of the catheter increased intrathoracic pressure (cough, sneezing, crying, vomiting), abrupt arm movements, and withdrawal of the device's septal huber (Goossens *et al*., 2015). Non-standardization of protocols and catheter obstruction may result in increased risk of complications and early withdrawal of the catheter (Pittiruti *et al*, 2016). Thus, in view of the lack of consensus in the standardization of TICVAP flushing and locking and the nurse's responsibility to manipulate this catheter, this study aimed to analyze in the literature the available evidence on the maintenance of TICVAP in oncology.

MATERIAL AND METHODS

It is an integrative literature review (ILR) developed in the following stages: (I) formulation of the problem, (II) data collection, (III) data analysis and selection, and (IV) presentation of the results. Indexed productions were used in the electronic databases SciELO (Scientific Electronic Library Online), Pubmed (US National Library of Medicine National Center for Biotechnology Information) and ScienceDirect. The search for the selected articles resulted from the following combinations of keywords "Flushing and locking" and "Totally Implantable Central Venous Catheters", "Oncology Patients" and "Protocols". The data were collected from January 2017 to September 2018 through the application of the form validated by Ursi (Ursi, 2005). Inclusion criteria were defined as: a) literature review articles and experimental studies that had a totally version available online; b) texts written in Portuguese and English published between 2007-2018 c) publications containing elements on the use of TICVAP. The exclusion criteria were: a) studies that do not provide information in response to the research question; b) studies aimed at pediatric patients; c) studies that do not specifically address the maintenance of TICVAP in oncology.
After searching the databases, applying the inclusion and exclusion criteria, the texts that fit the study objective were selected by means of the title and abstract and, afterwards, evaluated by the careful reading of their contents to verify the suitability to the delimited criteria.

RESULTS

Using the combination of keywords, were observed the following results: oncological nursing and catheter obstruction 478 articles, oncological nursing and protocols 253 articles and oncological nursing and central venous catheters and protocols 272 articles. The researches of these combinations totaled 1009 articles, of which 58 studies potentially relevant to this review were selected through the analysis of the abstracts. After reviewing the texts in totally, 23 publications were selected, including 04 guidelines, 01 institutional protocol, 06 integrative literature reviews, 03 systematic reviews of the literature, 01 methodological validation study, 03 observational studies, 04 experimental studies and 01 retrospective study. The international publications were predominant, corresponding to 86.9% of the total studies and guidelines used in this research, as shown in Table 1, which presents the distribution and organization of the publications found as reference. Regarding the characterization of the studies, an article was published in each year of 2007, 2008 and 2018; two articles were published for each year of 2009, 2011 2013, 2014, 2016 and 2017, three articles published in the year 2012 and the highest scientific production was in the year 2015, with five articles published.

In this study, it was possible to identify (i) a small number of publications on the subject, (ii) a variety of solutions used as 0.9% sodium chloride, ethanol, antimicrobials or heparin concentrate for TICVAP washing and blocking in cancer patients and (iii) non-standardization regarding the choice of solution, concentration, volume, range of uses and choice of syringe applied to clinical practice. In addition, it was observed that (iv) some studies compared heparin to other flushing and locking, but with low results or with a reduced number of participants. The occurrence of central venous catheter occlusion is related to the type of catheter, puncture site, lavage, blockage and physical condition of the patient, as well as some still unclear factors that require additional testing (Zhong *et al*., 2017). Thus, the functionality of TICVAP in the cancer patient is imperative and the nurse is responsible for maintaining it, since the obstruction of the catheter can impact the therapeutic response.

According to Goossens *et al*., (2015) the flushing and locking prevents the formation of crusts, prevents the adhesion of microorganisms and formation of biofilms. In this study, a variety of blocking wash solutions, such as the use of ethanol, antimicrobials, heparin and 0.9% sodium chloride, were identified without standardization of choice, dose, concentration, volume, range of use and type of syringe used in the procedure. Among the solutions identified, ethanol showed to have a thrombolytic effect, bactericidal, fungicidal and biofilm degradation, being used in the blockade of catheters to prevent infections. The disadvantages of this solution were related to the potential degradation of the catheter (especially the polyurethane) and the occurrence of venous thromboembolism (VTE) (Mouw *et al*., 2008; Oliveira *et al*., 2011). Schilcher described that ethanol can precipitate plasma proteins in these catheters and suggests limitation in the maximum concentration of 28% in flushing and locking (Schilcher *et al*, 2013).

Table 1. Distribution and organization of the publications found as reference

Number	Title	Authors, Year e Country	Results
01	Heparin versus normal saline locking for prevention of occlusion in central venous catheters in adults	López-Briz *et al.*, 2018. Spain	There was no statistically significant difference between the heparin blocking and saline lavage groups over occlusion
02	Comparison between Saline Solution Containing Heparin versus Saline Solution in the Lock of Totally Implantable Catheters	Brito *et al.*, 2018. Brazil	
03	Normal saline versus heparin solution to lock totally implanted venous access devices: Results from a multicenter randomized trial.	Molin *et al*, 2015. Italy	
04	Flushing and locking of venous catheters: available evidence and evidence deficit	Goossens *et al*, 2015 Belgium	
05	Maintaining patency in totally implantable venous access devices (TIVAD): a time-to-event analysis of different lock irrigation intervals	Palese A *et al*, 2014 Italy	
06	Comparing normal saline versus diluted heparin to lock non-valved totally implantable venous access devices in cancer patients: a randomised, non-inferiority, open trial	Goossens, *et al.*, 2013. Belgium	
07	Efficacy of Normal Saline Versus Heparinized Saline Solution for Locking Catheters of Totally Implantable Long-Term Central Vascular Access Devices in Adult Cancer Patients	Bertoglio et *al.*, 2012. Italy	
08	Normal saline versus heparin for patency of central venous catheters in adult patients - a systematic review and meta-analysis	Zhong L *et al*, 2017 China	The heparinized solution is less than 0.9% sodium chloride in reducing occlusion of CVCs.
09	Heparin versus Saline Solution for Locking of Totally Implantable Venous Access Port (TIVAP): Cohort Study of the First Kurdistan Series of TIVAP.	Baram, *et al.,* 2014. Iraq	
10	Central venous access devices. Resource book.	Culverwell, 2015. New Zealand	The lavage of the catheter with saline should be considered together with heparinization
11	Standardizing Central Venous Catheter Care: Hospital to Home	Nailon*et al*, 2012. USA	
12	Management of the central venous catheter fully implanted in patients.	Vasques et al, 2009. Brazil	
13	BCSH guidelines on the insertion and management of central venous access devices	Bishop, *et al.*, 2007. USA	
14	Evidence-based criteria for the choice and the clinical use of the most appropriate lock solutions for central venous catheters (excluding dialysis catheters): a GAVeCeLT consensus	Pittirutiet *al.*, 2016. Italy	It is recommended to routinely wash with saline as the best way to prevent occlusion
15	Incidence and Determinants of Port Occlusions in Cancer Outpatients	Milani et *al.*, 2016. Italy	
16	Eficácia da heparina e soro fisiológico para manter a permeabilidade dos cateteres venosos centrais: revisão sistemática	Santos, *et al.,* 2015. Brazil	
17	Central venous catheter care for the patient with cancer: American Society of Clinical Oncology clinical practice guideline.	Schiffer, *et al.,* 2013. USA	
18	Totally implantable central venous access ports	Carrolliand Bennett, 2015. Australia	Blocking with heparin is recommended as the best way to prevent occlusion
19	Service for the use of long-term central venous catheters.	National Institute of cancer José Alencar Gomes da Silva (INCA), 2012. Brasil	
20	Validation of standard operating procedures in the nursing care of patients with a totally implanted catheter.	Honório *et al,* 2011. Brazil	
21	Prolonged interval in prophylactic heparin flushing for maintenance of subcutaneous implanted port care in patients with cancer	Kefeli U *et al*, 2009 Turkey	
22	Managing central venous access devices in cancer patients: A practice guideline	Green, *et al.*, 2008. Canada	
23	Anti-Infective Locks for Treatment of Central Line-Associated Bloodstream Infection: A Systematic Review and Meta-Analysis	O'Hara *et al.,* 2011 USA	The use of anti-infective blockade therapy in conjunction with systemic antibiotics is critical for catheter salvage.

Source: Elaborated by the authors with research data, 2018.

When prescribed, antimicrobials such as vancomycin, gentamicin, cefazolin, ticarcillin-clavulanic acid, ceftazidime or ciproflacin were used as flushing and locking in order to prevent or treat infection in catheters, but this practice is not routine. The disadvantages of using antibiotics are related to their association with heparin because they lack thrombolytic properties (O'Horo, Silva and Safdar, 2011) and the possibility of developing resistant microorganisms (Mouw *et al*, 2008). The sodium chloride (0.9%) was not present fibrinolytic action, its use was based on the combined physical action (mechanical action) between pulsatile flow (infusion) and positive pressure on the syringe plunger after infusion of the substance, when the flow cutter was closed and the needle withdrawn from the device (Lopez-Britz *et al* 2018; Araújo, 2015).

The use of positive pressure in addition to normal saline reduces the incidence rate of TICVAP partial occlusions (Milani *et al*., 2016), Goossens *et al*. (2015) adds that the type of flow is important in the swirling technique and the time interval between two boluses for efficient washing of residues and removal of fibrins deposited in their lumen. In addition, 0.9% sodium chloride was cited as cheaper and less harmful to health. Anticoagulant heparin was the most widely used solution in total catheter blockade to reduce catheter colonization and related infections (Chauhan *et al*, 2012), and unnecessary in valve devices (Goossens *et al*., 2015). It was observed that there was no compliance with the dosage, concentration, dilutions and frequency of blockade maintenance (Araújo, 2015, INCA, 2012; Kordzadeh, 2014). As disadvantages to the use of heparin, sensitivity, toxicity,

high cost, risk of bleeding, blood dyscrasias, risk of contamination of the heparin flask and its inhibition by gentamicin have been described (Garajová *et al*, 2012). Larger studies, which did not focus on oncology, compared the heparin and sodium chloride solution 0.9% for reduction of catheter occlusion, and no statistically significant differences were observed in occlusion between groups (Mitchell *et al*., 2009). Schallom *et al.* (2012) found a 0.9% sodium chloride blockade rate similar to the heparin solution (3 ml, 10 IU / ml), and the sodium chloride solution may favor short-term maintenance and reduction the risk of thrombocytopenia. In a retrospective cohort study, lavage with 10 IU / ml (low molecular weight) heparin reduced thrombotic occlusions of central catheters when compared to 0.9% sodium chloride (Jonker *et al*, 2010). Among the experimental studies, all presented the same comparative method of analysis, through the randomization of the subjects in two groups, the blockade group with heparin and the group with sodium chloride 0.9%.

Goosens (2013) stated that 0.9% sodium chloride should have a rigorous protocol, such as that presented in the study, with education and training of all staff who work in the management of TICVAP (Goossens *et al*, 2013). Baram (2014) reinforced the use of 0.9% sodium chloride in catheter maintenance, presenting as results the non-functionality of heparin in the prevention of early or late complications, including TICVAP occlusion (Garajová *et al*, 2012). However, Molin (2015) did not find significant differences in the risk of catheter occlusion in the use of any of the two solutions tested, which was also concluded in Bertoglio's observational study (Molin *et al*, 2015; Bertoglio *et al*, 2012). In a study comparing washes with ethanol-isopropanol-heparin showed to be effective in relation to heparin, since it presented lower rates of occlusion, fungal and bacterial growth, whereas ethanol-heparin resulted in the formation of precipitate capable of causing obstruction of the device (Restrepo *et al*, 2015). In a study Santos *et al* (2015) identified saline as a sufficient substance to maintain the permeability of TICVAP, preventing the risks associated with the administration of heparin. In contrast, Brito *et al* (2018) affirm that there is no statistically significant difference between the heparin and saline groups in relation to occlusion, reflux dysfunction and flow dysfunction in TICVAP. Regarding the volume of blocking solution, there was variability in the studies, indicating 20 mL of 0.9% sodium chloride followed by heparin flushing and locking (100 IU / mL) as the best maintenance strategy (Vasques *et al*, 2009, Honório *et al*, 2011). While Green *et al*,(2008) suggested the use of a volume of 5 ml of heparin solution at a concentration of 100 IU / ml after each use of the catheter or monthly when not in use. Goossens *et al* (2015) emphasized that the volume of the solution should be according to the prescription by the patient's weight, length and diameter of the catheter, and the excess volume could cause serious effects upon reaching the systemic circulation.

As for heparin concentrations, fluctuations in the standardization of 250 IU / ml (Baram *et al*, 2014), 100 IU / ml (Nailon *et al*, 2012, Vasques *et al*., 2009) (Molin *et al*, 2015, Bishop *et al*, 2007), and 10 IU / ml (Bishop *et al*, 2007, Carroll and Bennett, 2015). However, most of the volume used was 5ml (Nailon *et al*, 2012, Molin *et al*, 2015, Bishop *et al*, 2007, Green *et al*., 2008, Carroll and Bennett, 2015). It is worth noting that some authors do not bring standardization and even in studies that do, it was emphasized the necessity of patient evaluation and individualization of the prescription and even the follow-up of recommendations of the manufacturers for use in TICVAP (Nailon*et al*., 2012; Vasques *et al*., 2009; Carroll and Bennett, 2015). It is noting that the studies presented, with the exception of the institutional protocol of the National Cancer Institute in Brazil (INCA), did not mention the dilution of the heparin solution for the blockade. INCA instructed that 1 ml of sodium heparin 25,000 IU (5,000 IU / ml) was aspirated and 9 ml of 0.9% sodium chloride was added and 2 ml of this solution was introduced into the reservoir (INCA.2012).

The volume of the syringe used was highlighted, since the volume-pressure ratio is inversely proportional, or be, the smaller the volume, the greater the pressure exerted inside the catheter, thus increasing the risk of impairment of quality and decrease of the useful time (Araújo, 2015). Among the publications analyzed, only two referred to the use of a syringe less than 10 ml (Goossens *et al*., 2015; Nailon *et al*, 2012). As for the interval between heparin maintenance, there was a tendency to prolong it for every 6 to 8 weeks instead of monthly maintenance with 0.9% sodium chloride (Goossens *et al*., 2015; Kefeli *et al*., 2009; Palese *et al*, 2014). Goossens *et al*. (2015) reported that it was unnecessary to aspirate low-weight (100UI) heparin infused prior to performing a new block maintenance, provided a wash was performed between them. However, additional research is needed to provide scientifically reasoned answers about the best time to renew a block. It is important to point out that the manipulation of this catheter must be exclusive to the nurse given its complexity, provided that they are qualified to do so, and there is no requirement of specialization in specific areas for this procedure (Culverwell, 2011; Palese *et al*., 2016; Ignatov *et al*, 2010).

Conclusion

Currently, the standardization of flushing and locking constitutes an important gap in the performance of health professionals, since there is no standardization of the best substance used and no parameters to be followed. The analysis of the scientific publications of the last ten years on lock solution showed that there was no consensus on the standardization of maintenance in TICVAP regarding the choice of solution, volume, concentration, dilution, maintenance interval and syringe choice. It was also observed that there is a reduced number of scientific publications on the subject, and it is necessary to carry out further experimental studies with cancer patients, in order to create clinical practice based on evidence. Meanwhile, more standardized Flushing and locking preparations should be used, avoiding early withdrawal of the device due to occlusion or other complications. The most applied solutions were 0.9% sodium chloride and heparin with similar results in relation to the incidence of obstruction, but with particular emphasis on their respective advantages. Heparin presented a reduction in infection and thromboembolic events, while sodium chloride was noted for the reduction of expenditures, toxicities and systemic events since it was performed by pulsatile and positive pressure and monthly maintenance techniques. In view of the scarcity of scientific evidence and the lack of standardization of nursing actions in the use of flushing and locking, our results suggest new studies addressing clinical benefits, economic evaluations, cost-effectiveness, patient safety, implementation of a new guideline systematizing this care.

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