



## REVISIONES

### Strategies for preventing obstruction in central catheters fully implanted in oncological patients

Estratégias de prevenção da obstrução em cateteres centrais totalmente implantados em pacientes oncológicos

Estrategias de prevención de la obstrucción en catéteres centrales totalmente implantados en pacientes oncológicos

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#### ABSTRACT:

**Objective:** To analyze scientific productions that address prevention and care strategies in the obstruction of central venous catheters that are fully implanted in cancer patients.

**Material and Method:** This is an integrative literature review, which took place on the MEDLINE, LILACS, CINAHL and EMBASE databases, from 20 July 2019 to 31 July 2019, using as descriptors: Central venous catheterization; Catheter obstruction and Oncology, in addition to the use of free terms: Catheter fully implanted and Neoplasia.

**Results:** In total, 10 studies were selected and included. After the analysis, the following analysis categories emerged: Strategies for preventing obstruction in CVC-TI and Care established in clearing the CVC-TI; having as main subjects approached: the comparison between the effectiveness in the use of heparin and saline solution for maintenance and time interval between them; unblocking methods and permeability assessment of CVC-TI.

**Conclusion:** Despite the emergence of new possible ways of preventing obstruction and care strategies for clearing CVC-TI, the literature does not have a consensus on the use of solutions with or without heparin and the time interval between maintenance for the effectiveness of the permeability of these devices in cancer patients.

**Keywords:** Central venous catheterization; Catheter obstruction; Oncology.

## RESUMO:

**Objetivo:** Analisar produções científicas que abordem a prevenção e estratégias de cuidado na obstrução de cateteres venosos centrais totalmente implantados em pacientes oncológicos.

**Material e Método:** Trata-se de uma revisão integrativa da literatura, que ocorreu nas bases de dados MEDLINE, LILACS, CINAHL e EMBASE, no período 20 de Julho de 2019 a 31 de Julho de 2019, utilizando-se como descritores: Cateterismo venoso central; Obstrução de cateter e Oncologia, além do uso dos termos livres: Cateter totalmente implantado e Neoplasia.

**Resultados:** Ao total, 10 estudos foram selecionados e incluídos. Após a análise, emergiram as seguintes categorias de análise: Estratégias de prevenção da obstrução em CVC-TI e Cuidados estabelecidos na desobstrução do CVC-TI; tendo então como principais assuntos abordados: a comparação entre a eficácia no uso da heparina e solução salina para manutenções e tempo de intervalo entre as mesmas; métodos de desobstrução e avaliação de permeabilidade dos CVC-TI.

**Conclusão:** Apesar do surgimento de novas formas possíveis de prevenção de obstrução e estratégias de cuidado na desobstrução dos CVC-TI, a literatura não apresenta consenso sobre o uso de soluções com ou sem heparina e o tempo de intervalo entre as manutenções para a efetividade da permeabilidade desses dispositivos em pacientes oncológicos.

**Palavras-chave:** Cateterismo venoso central; Obstrução de cateter; Oncologia.

## RESUMEN:

**Objetivo:** Analizar las producciones científicas que abordan las estrategias de prevención y atención en la obstrucción de los catéteres venosos centrales totalmente implantados en pacientes con cáncer.

**Material y método:** Esta es una revisión bibliográfica integradora, que se realizó en las bases de datos MEDLINE, LILACS, CINAHL y EMBASE, del 20 de julio de 2019 al 31 de julio de 2019, utilizando los siguientes descriptores: Cateterización venosa central; Obstrucción del catéter y oncología, más el uso de términos libres: catéter completamente implantado y neoplasia.

**Resultados:** En total, se seleccionaron e incluyeron 10 estudios. Después del análisis, surgieron las siguientes categorías de análisis: Estrategias para prevenir la obstrucción en CVC-TI y Atención establecidas en el despacho de CVC-TI; teniendo como principales temas abordados: la comparación entre la eficacia en el uso de heparina y solución salina para el mantenimiento y el intervalo de tiempo entre ellos; métodos de despacho y evaluación de permeabilidad CVC-TI.

**Conclusión:** A pesar de la aparición de nuevas formas posibles de prevención de obstrucciones y estrategias de atención en la eliminación de CVC-TI, la literatura no presenta consenso sobre el uso de soluciones con o sin heparina y el intervalo de tiempo entre el mantenimiento para la efectividad de permeabilidad de estos dispositivos en pacientes con cáncer.

**Palabras clave:** cateterismo venoso central; Obstrucción del catéter; Oncología.

## INTRODUCTION

Historically, the use of fully implanted central venous catheters (CVC-TI) emerged in the early 1970s as an innovation and evolution of vascular access in clinical practice. However, it was only in 1982 that the first results of the use of devices for the treatment of cancer patients were demonstrated <sup>(1)</sup>.

Currently, given its epidemiological, social and economic relevance, cancer is considered one of the main and complex public health problems in the world <sup>(2)</sup>. Its main treatment base is chemotherapy, which consists of the administration of chemical substances isolated or combined with the objective of destroying cancer cells or interrupting/minimizing their cell growth and division process. The most widely used and considered safest route of administration is intravenous because of its rapid absorption and maintenance of the serum level of the drug <sup>(3,4)</sup>. In the oncology area, CVC-TI is widely used, since they guarantee the long-term administration of intravenous antineoplastic drugs. In addition, they contribute to the increase in the quality of life of patients as they decrease the pain and anxiety commonly experienced by patients using the peripheral route due to the high number of punctures. Other advantages of CVC-TI include durability, mobility and comfort, in addition to greater

efficiency, since it minimizes complications resulting from other types of venous devices, such as infections <sup>(5)</sup>.

The CVC-TI or Portcath is implanted through a peripheral or central vein, and after passing through the subcutaneous path, it is connected to a reservoir (made of titanium or plastic with a single or double chamber), being usually housed on the muscular fascia of the chosen location. Thus, no segment of the set is exteriorized, thus having the lowest risk of infection and greater durability when compared to semi-implantable catheters. The access and activation of the device is done through a puncture through the skin over the Port with a non-cutting needle (Huber needle), and the fundamental cares for it include maintenance with flush with saline and heparinization <sup>(1)</sup>.

The use of CVC-TI offers several advantages; however complications may occur and require proper management, both for the preservation of the device and for the safety and comfort of the patient. Among the main complications mentioned in the literature, we highlight: obstruction, infection and leakage <sup>(6)</sup>.

Obstruction is a very common type of complication, which may occur due to the precipitation of drugs inside the lumen of the catheter, formation of thrombi or fibrin. In general, CVC-TI are more prone to thrombosis than the others due to their small caliber that favors obstruction, therefore, some literature does not indicate it for infusion of large volumes of fluids, or for blood transfusions and blood collections (except blood cultures) <sup>(7)</sup>.

Based on this, for the device to have greater durability and to avoid all the adversities that an obstruction may cause, it is the competence and responsibility of the nurse who handles it to have technical and scientific knowledge and training for its manipulation in an articulated and standardized way, since the prevention and early detection of possible risks and complications can minimize the damage and improve the quality of care for these patients.

In view of the above, the study aims to: analyze scientific productions that address prevention and care strategies in the obstruction of central venous catheters fully implanted in cancer patients.

This study is relevant because there are several protocols for CVC-TI maintenance, and therefore it is necessary to choose the most effective and safe techniques, based on scientific evidence. In this perspective, the study will contribute to new reflections on the proper handling of these catheters.

## **MATERIAL AND METHOD**

It is an integrative literature review, based on the authors Mendes; Silveira; Galvão for the construction of the six proposed stages <sup>(8)</sup>.

In the first stage, the theme was identified and the research question was formulated in the format of the acronym PICO (Population, Intervention, Control and Outcome): "What has been published currently regarding prevention and care strategies in the obstruction of central venous catheters fully implanted in cancer patients?".

In the second stage, the following inclusion criteria were established: original articles related to CVC-TI obstruction and clearance, published in Portuguese, English and Spanish, with full text and online. The exclusion criteria used were studies that addressed non-thrombotic obstruction of long-term central venous catheters.

The search took place on the databases MEDLINE, LILACS, CINAHL and EMBASE, in the period of July 2019, using the basic combination of the descriptors contained in the Health Sciences Descriptors (DECs) for the bases in Portuguese: Central venous catheterization; Catheter obstruction and Oncology; and Medical Subject Headings (MESH) for bases in English: Central venous catheterization; Catheter obstruction and oncology. In addition to the use of the main free terms related to the theme: Totally implantable catheter and Neoplasm (Neoplasm).

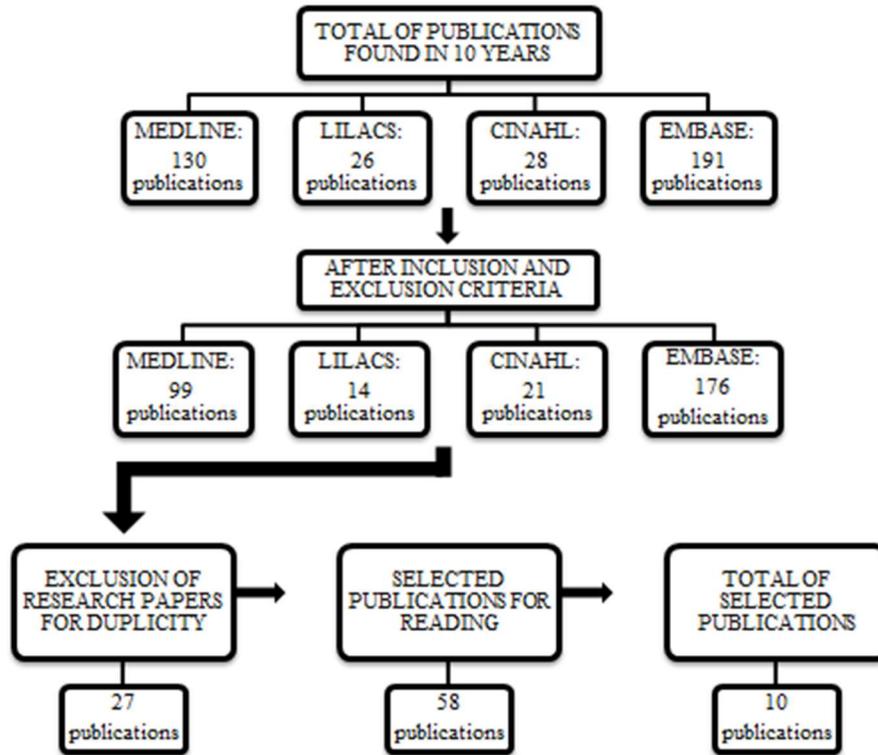
Initially, the 05-year period for data collection was considered due to the publication of the Clinical Protocols and Therapeutic Guidelines in Oncology, by the Ministry of Health in partnership with the National Cancer Institute (INCA), in accordance with Ordinance No. 140, of February 27, 2014, which reaffirms “the technical and scientific quality of the diagnostic, therapeutic and care procedures that are available in SUS”; however, the results obtained were not satisfactory, so it was necessary to extend the period to 10 years <sup>(9,10)</sup>.

In order to allow greater coverage in the selection of articles related to the theme, several search strategies were used in the different databases and portals. Thus, the strategy that resulted in a higher frequency of relevant publications within the established theme was selected.

Afterwards, in the third stage, the primary selection of publications was made by reading the title and abstract. Then, the selected studies were read in full, and the methodological evaluation was carried out according to the Oxford Center Evidence-Based Medicine, with the categorization of the studies using the instrument validated by Elizabeth Ursi <sup>(11,12)</sup>.

In this perspective, of the 58 studies selected for reading the full text, 48 were excluded, as they addressed other complications related to the catheter without emphasizing the proposed theme. At the end, 10 studies were included for analysis, as shown in Figure I:

**Figure I: Details of the selection of articles**



Thus, during the fourth and fifth stages, the studies were carefully evaluated and the results obtained were interpreted, so that the sixth stage was reached, where the discussion and synthesis of knowledge was formed.

## RESULTS

Each selected publication was evaluated separately, allowing the synthesis of studies. Thus, we have the following qualitative distribution according to Table I:

**Table I: Qualitative distribution representing the selected studies.**

Title	Author	Country / Year	Journal	Database	Type of study	Evidence
Diferença do Volume Presente e Requerido de Solução para Manutenção do Cateter Venoso Central Totalmente Implantado e Fatores Associados	GOMES, A. R.	Brazil 2013	Biblioteca Digital Brasileira de Teses e Dissertações	LILACS	Quantitative Observational Cross-sectional cohort	1B
Central Venous Access Devices: an investigation of oncology nurses' troubleshooting techniques	MASON, et al.	USA 2013	Clinical Journal of Oncology Nursing	CINAHL	Qualitative Exploratory Cross-sectional	2B

Incidence and Determinants of Port Occlusions in Cancer Outpatients	MILANI, et al.	Italy 2017	Cancer Nursing	CINAHL	Quantitative Observational Cohort Prospective	1B
Clearing Obstructed Totally Implantable Central Venous Access Ports	MUGUET et al.	France 2012	Support Care Cancer	CINAHL	Quantitative Observational Retrospective	2C
Diagnostic Accuracy of the Catheter Injection and Aspiration (CINAS) Classification for Assessing the Function of Totally Implantable Venous Access Devices	GOOSSE N et al.	Belgium 2015	Support Care Cancer	CINAHL	Quantitative Observational Cross-sectional	2B
Effects of Prolonged Flushing Interval in Totally Implantable Venous Access Devices (TIVADs)	RASERO et al.	Italy 2018	British Journal of Nursing	CINAHL	Quantitative Observational Cohort Retrospective	1B
Comparison Between Saline Solution Containing Heparin Versus Saline Solution in the Lock of Totally Implantable Catheters	BRITO, et al.	Brazil 2017	Annals of Vascular Surgery	CINAHL	Quantitative Observational Cohort Retrospective	1B
Maintaining Patency in Totally Implantable Venous Access Devices (TIVAD): a time-to-event analysis of different lock irrigation intervals	PALESE, et al.	Italy 2014	European Journal of Oncology Nursing	MEDLINE	Quantitative Control-case Exploratory Prospective	1B
Normal Saline Versus Heparin Solution to Lock Totally Implanted Venous Access Devices: results from a multicenter randomized trial	MOLIN, et al.	Italy 2015	European Journal of Oncology Nursing	MEDLINE	Quantitative Clinical trial Randomized Open-labelled	1B
Interventions to Obstructive Long-term Central Venous Catheter in Cancer Patients: a meta-analysis	COSTA, et al.	Brazil 2018	Supportive Care in Cancer	MEDLINE	Meta-analysis	1A

When analyzing the publications included in this study, there was a predominance of international publications with a quantitative approach, with level of evidence 1B. From the 10 selected articles, 06 were on CINAHL database, 04 on MEDLINE and 01 on LILACS. No study was selected from the EMBASE database.

After the critical analysis of the studies and categorization, the following categories of analysis emerged: Strategies for preventing obstruction in CVC-TI and Care established in clearing the CVC-TI.

## DISCUSSION

### Strategies for preventing obstruction in CVC-TI

It is unquestionable that the use of CVC-TI has several advantages for the treatment of cancer chemotherapy, mainly in relation to the reduction of infection rates when compared to other types of devices. However, thrombotic obstruction is still one of the most important complications and is associated with interruption and delay of treatment, in addition to prolonging the length of hospital stay, thereby increasing costs for the institution. For this, CVC-TI obstruction prevention strategies are studied for improving the quality of care.

Currently, the comparison between the use of heparinized solution and pure saline for the maintenance of catheters is still much discussed in the literature.

In order to compare the effectiveness of the solutions in question, Brito *et al.* observed two groups of patients, called the Hep group and the SS group, at different time periods. Each catheter received 1.5 ml of solution, which was replaced after the infusion of chemotherapy or at an interval of 4 weeks. The Hep group received heparinized solution (100 IU/ml), while the SS group used pure saline.

In total, 270 (31%) patients were in the Hep group, while 592 (69%) in the SS group. As a result, 8 cases of occlusion and 8 cases of reflux changes were reported in both groups (Hep: 2.96% and SS: 1.35%). However, 1 (0.37%) episode of altered flow was observed in the Hep group compared to 4 (0.68%) episodes observed in the SS group<sup>(13)</sup>.

At the end, despite the differences found in the cases of occlusion and dysfunction of the flow/reflux of the catheters, the analysis showed no significant difference when comparing the effectiveness of the solutions used in the study ( $p = 0.11$ )<sup>(13)</sup>.

In another experiment carried out in Italy in fourteen oncology clinics, it included 415 patients randomly divided into two distinct groups. One group would perform the maintenance of the CVC-TI with the saline solution, while the other would use the heparinized solution. At the end, it was noted that among the 24 total occlusions that occurred, 14 (6.90%) were using pure saline, while the rest (4.71%) occurred after using the heparinized solution. However, it was confirmed that there was no inferiority in the use of pure saline compared to heparinized solution ( $p = 0.05$ )<sup>(14)</sup>.

In this sense, in order to verify which are the main risk factors for partial obstruction when using saline solution, Milani *et al.* proposed a modification to the CVC-TI maintenance protocol, where the flush previously composed of heparinized solution was replaced by 20ml of pure saline. With a total of 4,111 observations, 54 partial obstructions (PO) were documented. As a main result, there was a significant increase in the PO rate ( $p < .0001$ ) in catheters that obtained at least one blood collection<sup>(15)</sup>.

However, when the group analyzed catheters that did not undergo a blood collection procedure in isolation, PO was more frequent ( $p < .0001$ ) in short treatment regimens (7-14 days) compared to longer regimens (21 -28 days) <sup>(15)</sup>.

The uncertainty related to the time interval between the maintenance required by this type of catheter is another constant investigation in the current literature.

Thus, a survey produced by nurses in a hospital in Florence with the objective of comparing the intervals between maintenance in CVC-TI, sought patients who had already reached the end of treatment, and distributed them in 2 groups. Group A where the maintenance occurred  $\leq 45$  days apart and Group B with  $> 45$  days. After the retrospective study, 7 patients who were in the  $\leq 45$ -day interval group had complications related to obstruction, while in the  $> 45$ -day interval group there were no complications, however, there was no significant difference during the analysis <sup>(16)</sup>.

An experiment developed in two "day hospitals" in Italy, all catheters were submitted to the same maintenance protocol, which, a flush of 20 ml of pure saline was followed by 3 ml of heparinized solution (250 IU/5 ml). The procedure was repeated every 4 or 8 weeks. In total, 6 occlusions have been documented. Of these, 4 cases were observed in the group with an interval of 8 weeks (20%) and 2 cases in the interval of 4 weeks (11.7%). However, no significant difference ( $p = 0.49$ ) was found between the groups, even after considering other variables that could directly affect the result, such as age ( $p = 0.651$ ) or catheter implantation time ( $p = 0.684$ ) <sup>(17)</sup>.

Therefore, no literature found statistical significance to prove safety and effectiveness related to the time interval between maintenance. However, it is known that increasing the interval time decreases access to this device, with a consequent reduction in the risk of infection and patient discomfort <sup>(16, 17)</sup>.

Still, during the present study, it was noted that there is a discrepancy between the required volumes and the amount of heparin used in the solutions for maintaining CVC-TI, and regardless of the manufacturer's recommendation, many units standardize a determined volume of the solution, such fact, which can cause changes in the expected result.

In view of this, an observational research was carried out with the objective of determining the ideal volume for an effective maintenance, since, the volume below the necessary considerably increases the risk of clot obstruction and thromboembolism, with consequent early removal of the device; therefore, it is always recommended to consider the user's biotype, device specificities and the final length after insertion, as catheters that have the same *prime* and *french* may nevertheless vary in volume according to the brand used. Therefore, with the use of the ideal volume for each catheter, it is possible to speculate the cost reduction for the health institution <sup>(18)</sup>.

As another way of preventing obstruction, a group of researchers suggested the use of a CVC-TI's permeability assessment tool, Catheter Injection and Aspiration (CINAS), which consists of 16 unique combinations of 4 different codes. Each combination reflects both the injection capacity of at least 1ml of fluid and the aspiration capacity of at least 3ml of blood, being classified on a scale of one to three (1: easy; 2: difficult; 3: impossible), the 4th combination refers to when the injection and/or aspiration is unknown. Taking into account the results presented, the accuracy of the CINAS

instrument is 98.7%, when comparing the classification made by nurses and the researcher. Thus, CINAS proved to be a simple, objective and low-cost instrument, which contains a uniform language to describe the functioning of CVC-TI <sup>(19)</sup>.

### **The care established in clearing the CVC-TI**

Several precautions are established as prevention; however, the obstruction may still occur. For this, techniques and drugs can be used in order to restore the permeability of CVC-TI, and thus maintain the treatment without interruption or prolongation.

In order to obtain a more in-depth knowledge about the methods used to unblock catheters in praxis, researchers sought through an electronic questionnaire to explore the techniques used by oncologist nurses to unblocking central venous access devices, and to describe their efficacy in clinical practice <sup>(20)</sup>.

As a result, the main techniques reported were: asking the patient to lift and/or move the catheter arm; ask the patient to lie down; so that it reproduces the cough reflex; and propose to take a deep breath. Among the techniques, nurses considered the most effective: the use of thrombolytic agents, followed by non-invasive techniques, such as asking the patient to lie down, using the "back-and-forth" technique and proposing that the patient take a deep breath. Some participants also replied that they used other techniques that were not described, such as: turning the head, chin and shoulder; or even laugh, sing and speak <sup>(20)</sup>.

Other protocols that are not usually used appeared in the questionnaire, such as: saline solution; corticosteroid; thrombolytic agents beyond the recommended time; and also, carry out a plan for future maintenance, which included increasing the heparinized solution to 1,000 IU, and using low-dose warfarin if the problem persisted. In addition, most of the participants would look for other ways to solve the obstruction, such as: looking for another nurse with more experience; refer the patient to the radiologist or surgeon who inserted the catheter <sup>(20)</sup>.

No association was established between the technique used and the years of professional experience with the device; specifics of work; academic certification or graduation. However, many participants reported techniques have been questioned, since the use of Heparin, for example, is indicated to inhibit coagulation and prevent the formation of fibrin and thrombi, and not to dissolve existing thrombotic occlusions. Still, 25% of nurses mentioned techniques considered to be "contraindicated", such as the use of fast flush against the resistance presented by the catheter <sup>(20)</sup>.

In another experiment carried out at Lyon Sud Hospital, in France, the authors describe a step-by-step protocol used to clear CVC-TI which, initially when noticing the signs of obstruction, changes the needle for another. If the obstruction still persists, the method validated by the University Hospital of Geneva is applied, in which a second needle is inserted through the Port, next to the first. A syringe with 0.9% saline is placed on one of the needles, and an empty syringe on the other. The plunger of the empty syringe is pulled, drawing the saline solution from the other syringe and, in turn, "washing" the reservoir (Port). The process can be repeated until the clear saline solution is aspirated <sup>(21)</sup>.

If the obstruction still remains, 2 syringes are used to fill the reservoir with 5,000 UU/ml diluted Urokinase, allowing it to act while the two needles are "closed". After 1 hour,

the clamp is removed and the permeability is checked. If this does not solve the obstruction, the clamp is placed again, and the permeability is checked every hour. At the end, if the proposed protocol does not provide the expected response, the nurse must communicate to the responsible physician to decide on new necessary interventions, including verification by X-ray or surgical removal of the device <sup>(21)</sup>.

In the same study, the protocol was tested, and 92% of the obstruction cases were resolved. The only case in which they were not successful, it was noted when referring the patient to the X-ray that the catheter was "clamped" <sup>(21)</sup>.

When taking into account the use of solutions, a meta-analysis with 15 studies identified the main drugs used to unblock and restore long-term CVC permeability. The drugs featured are: Urokinase (53.3%), Alteplase (20%), Tenecteplase (13.3%), Recombinant Urokinase (6.7%), Reteplase (6.7%) and Staphylokinase (6.7 %) <sup>(22)</sup>.

According to the results, Urokinase and Tenecteplase showed efficiency in clearing approximately 84%, while Alteplase showed success in 92% of reported cases <sup>(22)</sup>.

When evaluating the data of the qualitative analysis, a tendency of superiority in the effectiveness of the Tissue Plasminogen Activator (TPA) was observed in relation to the Urokinase. However, when the data from the meta-analysis were evaluated, the general frequency of restoration of the permeability found is similar among the drugs, with a slight superiority of Alteplase in relation to other interventions <sup>(22)</sup>.

However, most of the included studies had bias related mainly to the studied population, such as the absence of randomization, double-blind and control group; in addition to the high heterogeneity between the doses used and the infusion times.

Thus, the evidence found tends to confirm the success of thrombolytic therapy in general, however, there are not enough data to standardize the procedures and drugs mentioned <sup>(22)</sup>.

## CONCLUSIONS

It was observed that despite the differences found in the results obtained from this review, the replacement in the use of heparinized solution with pure saline for maintenance of CVC-TI is still not well defined. The use of heparin can bring risks to the health of those who use it, as it is an anticoagulant, it brings various reactions and undesirable effects such as thrombocytopenia, allergic reactions and iatrogenic hemorrhage, in addition to the higher cost for the health institution. However, in the current literature, no studies were found to prove the efficacy of saline solution for the prevention of obstruction in CVC-TI.

When dealing with the interval between the maintenance required by CVC-TI, no literature found a specific and effective period. However, the studies that made up this review reported in their results that the period between 4 and 8 weeks apart would at first be considered safe. In addition to this information, it was noted that the increase in the interval time decreased the access to this device, making it possible to reduce the risk of infection. Therefore, good nursing practices can help keep CVC-TI clear.

Another outstanding method that emerged in this research was the use of an instrument, CINAS, as an aid in assessing the permeability of CVC-TI, thus contributing to the prevention of thrombotic obstruction. The instrument proved to be effective, simple, objective and of low cost, which contains a uniform language to describe the functioning of the device.

When observing the care established for clearance, several techniques and drugs emerged in the study. The use of thrombolytic agents, followed by non-invasive techniques, such as asking the patient to lie down; using the “back-and-forth” technique and proposing that the patient take a deep breath, in practice, the most effective techniques for clearing deep venous catheters were considered, however many of them reported techniques were questioned and considered as “contraindicated”.

Through this research we can observe that, nowadays, more drugs and solutions are introduced in the market with the objective of restoring the permeability of CVC-TI and presenting significantly lower costs for the institution, besides reducing the time of treatment and the use of other services.

Thus, the evidence found tends to confirm the success of thrombolytic therapy in general, however, although several techniques and technologies appear daily for the prevention and management of obstruction, there is still no consensus in the current literature to standardize the procedures and drugs used. For this, the results of this study will serve as a basis for new research on the topic.

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