Patterns of care in prevention and treatment of clinical evidence-based antineoplastic extravasation

Padrões de cuidados em prevenção e tratamento de extravasamento de antineoplásicos baseado em evidências clínicas

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RESUMO

Objetivo: descrever padrões de cuidados em prevenção e tratamento de extravasamento de antineoplásicos baseado em evidências clínicas. Métodos: revisão integrativa da literatura realizada nas bases de dados Medline/PuBMed, CINAHL, LILACS e Science Direct. Resultados: foram localizados 30 estudos em inglês e espanhol, entre 2005 a 2015. Os temas predominantes quanto ao extravasamento são fatores de risco, medidas de prevenção e tratamento, como o uso de compressas e antídotos, estes foram organizados em quadros e classificados quanto ao nível de evidência e grau de recomendação. Conclusão: a prevenção é a principal estratégia. Ressalta-se a importância de implementação de protocolo assistencial.

Descritores: Antineoplásicos; Extravasamento de Materiais Terapêuticos e Diagnósticos; Enfermagem.

ABSTRACT

Objective: to describe patterns of care in the prevention and treatment of clinical evidence based antineoplastic extravasation. Methods: integrative literature review carried out in Medline/PuBMed, CINAHL, LILACS and Science Direct databases. Results: 30 studies were conducted in english and spanish between 2005 and 2015. The predominant themes regarding extravasation are risk factors, prevention and treatment measures, such as the use of compresses and antidotes, these were organized in tables and classified as level of evidence and degree of recommendation. Conclusion: prevention is the main strategy. It is important to emphasize the importance of implementing a care protocol.

Descriptors: Antineoplastic Agents; Extravasation of Diagnostic and Therapeutic Materials; Nursing.

NOTA

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INTRODUCTION

Cancer is considered a global public health problem. In 2012, there were 14.1 million new cases of cancer, 8.2 million deaths from cancer and 32.6 million people living with cancer (within 5 years after diagnosis was given). Of these, 57% of new cases, 65% of deaths and 48% of prevalent 5-year cases of cancer occurred in less developed regions[1].

Regarding treatment, the three most used therapeutic modalities are surgery, radiotherapy and chemotherapy. These are used together, since currently, few malignancies are treated with only one therapeutic modality. The choice depends on the type of cancer, the recurrence, the staging and the age of the patient [2].

Chemotherapy treatment acts directly in the process of cell division by means of isolated or combined chemicals from drugs called antineoplastic drugs. It can be used palliatively, curatively, as well as adjuvant and neoadjuvant forms[3].

One of the concerns arising from the chemotherapy treatment is extravasation. Considered a tissue damage that results from the accidental escape of the antineoplastic to the surrounding tissue[4]. Extravasation can be classified into three broad categories based on its potential to cause damage: non-vesicants, irritants and vesicants. The former can cause ulceration but does not progress to necrosis. Irritants can cause pain at the site and along the vein, in addition to the possibility of inflammation and ulceration in some cases. Vesicants, on the other hand, form vesicles and ulcerations that, when left untreated, can evolve into necrosis[5].

It is estimated that extravasation accounts for 0.5% to 6.0% of adverse events associated with treatment. When considering the number of adverse events associated with cancer treatment, the absolute number of extravasation is quite significant[6-7].

In this context, the nurse's role in relation to antineoplastic agents is ensured in Brazil by the Federal Nursing Council Resolutions 210 of 1998 and 257 of 2011, which emphasize that it is the nurse's job to elaborate nursing therapeutic protocols in the prevention, treatment and minimization of side effects, in addition to preparing and administering the antineoplastic chemotherapy [8-9].

Nursing care requires theoretical references that can guide the care provided. In this way, the Evidence Based Practice (EBP) allows the nurse to apply the best clinical evidence to the situation found. It is configured as a coherent, secure and organized way of establishing professional practices. It enables the best results and optimizes the available resources, according to the active participation of a multidisciplinary team[10].

Considering that nursing plays an essential role in the delivery of cancer care, being responsible for the administration of antineoplastics and related care, this study made possible recommendations to guide clinical practice in order to reduce or minimize risks and damages that an extravasation can bring to the patients, besides promoting a uniform care by different professionals. The objective of this study was to describe patterns of care in the prevention and treatment of clinical evidence of antineoplastic extravasation.

METHOD

This is an integrative review of the literature on antineoplastic extravasation. For the construction were followed the steps proposed by Mendes; Silveira; Galvão[11]: identification of the theme, establishment of inclusion and inclusion criteria, categorization of studies, evaluation of studies, interpretation of results and presentation of the review.

The search was performed in the databases: *Medical Literature Analysis and Retrieval System Online* (Medline / PuBMed), *Cummulative Index to Nursing and Allied Health Literature* (CINAHL), *Latin American and Caribbean Literature in Health Sciences* (LILACS) and *Science Direct*. It was guided by the following research question: What are the scientific evidence and recommendations regarding the extravasation of antineoplastics?

In the identification, key terms / descriptors and specific search methods were used for each base, according to Table 1.

The following studies were included in the research: applied in humans; which address extravasation of vesicant, irritant and non-irritating antineoplastic agents; related to the prevention and treatment of extravasation of chemotherapy; published national and international; published in English, Portuguese or Spanish; between the years 2005 and 2015; and studies that serve clients above 18 years.

RESULTS

With the key terms were found 639 articles. After applying the inclusion and exclusion criteria, 30 articles were selected, characterized by periodical, year of publication, type of study and objectives (according to table 1). Of these 11 (36.67%) articles are of the case study type, 8 (26.67%) are literature reviews and 18 (60%) have been published in the last five years.

The analysis of the articles was done through an adapted instrument that allowed the formulation of the evidence. Therefore, they were classified according to the level of evidence according to the Melnyk reference; Fineout-Overholt[12] and National Pressure Ulcer Advisory Panel[13] recommendation grade. The evidence was described in Tables 2 and 3, for more prevalent themes, the first describes the prevention measures and the second treatment.

TABLE 1 – Bases, descriptors and search schemes. Teresina-PI, 2016.

Base	Medline	Cinahl	Science direct	Lilacs
Keywords / key terms	MeshTerms*	Cinahl Titles	Uncontrolled descriptors	Decs**
	1 Antineoplastic 2 Agents 3 Extravasation of Diagnostic and Therapeutic Materials 4 Therapeutics 5 Nursing Care	*1 Antineoplastic 2 Agents 3 Extravasation of Diagnostic and Therapeutic Materials*	*1 Antineoplastic 2 Extravasation*	1 Antineoplastic 2 Extravasation
Search Schemes	*((“Antineoplastic Agents”[Mesh]) AND “Extravasation of Diagnostic and Therapeutic Materials”[Mesh]) AND “Nursing Care”[Mesh]*	*Antineoplastic Agents AND Extravasation of Diagnostic and Therapeutic Materials*	*Antineoplastic AND Extravasation*	Antineoplastic AND Extravasation
	Antineoplastic Agents AND Extravasation of Diagnostic and Therapeutic Materials			Antineoplastics

Subtitle: * *Medical Subject Headings*. ** Descritores em Ciências da Saúde.

TABLE 1 – Characterization of the articles found. Teresina-PI, 2016.

Article	Periodics	Year	Study Type	Goals
A1	Seminars in Oncology Nursing	2011	Expert Opinion	To present a clinical update on prevention, detection and treatment of extravasation of evidence-based bladder chemotherapy.
A2	The Journal of Medicine	2011	Case study	Report treatment of extravasation of vinorelbine.
A3	Japanese Journal of Clinical Oncology	2014	Quantitative study	Describe clinical features of extravasation.
A4	BMJ Case Reports	2013	Case study	Describe anthracycline extravasation treatment.
A5	BMJ Case Reports	2013	Case study	Describe ducts in anthracycline leakage.
A6	The Journal Medicine	2012	Case study	Report extravasation treatment after chemotherapy cycle.
A7	European Journal of Oncology Nursing	2015	Group control	Validate instrument for evaluation of intravenous insertion difficulty.
A8	Surgical Oncology	2012	Quantitative study	To evaluate the rate of complications in fully implanted catheter patients.
A9	EJSO The Journal of Cancer Surgery	2015	Case series	To propose a structured procedure for extravasation management.
A10	Annals Dermatology Venereol	2007	Case study	To describe treatment of extravasation of cisplatin in a fully implanted catheter.
A11	Journal of Plastic, Reconstructive & Aesthetic Surgery	2011	Case study	Describe the SWOP * technique for extravasation.
A12	Chinese Journal of Traumatology	2009	Case study	To present the use of vacuum therapy in the extravasation of vinorelbine.
A13	Cancer Nursing Practice	2011	Descriptive study	To describe the lavage technique with extravasation saline solution.
A14	Journal of The National Cancer Institute	2007	Case study	It presents treatment for extravasation of antineoplastic.
A15	Journal of Clinical Oncology	2009	Case study	Report Trabectedin extravasation treatment.
A16	Cancer Nursing	2005	Quantitative study	To verify the incidence of extravasation of cytotoxic patients in a hospital in São Paulo.
A17	European Journal of Cancer Care	2013	Case series	To present a series of cases of extravasation of cytotoxic agents treated with saline solution.
A18	Annals of Oncology	2012	Expert Opinion	To present management of extravasation of chemotherapy based on the clinical guidelines of the European Oncology Nursing Society.

A19	Farmacia Hospitalaria	2012	Integrative review	To present updates of treatments of extravasation by cytostatic agents.
A20	European Journal of Oncology Nursing	2008	Expert Opinion	Provide guidance on extravasation based on the guideline of the European Oncology Nursing Society.
A21	Seminars in Oncology Nursing	2007	Expert Opinion	To describe injury mechanisms associated to DNA-binding and non-DNA binding vesicants. To evaluate procedures used in clinical practice to manage extravasations of vesicants.
A22	Online Brazilian Journal of Nursing	2008	Integrative review	To identify in the literature evidence related to the prevention of extravasation of vesicant chemotherapy in patients with peripheral intravenous infusion.
A23	Clinical Journal of Oncology Nursing	2013	Expert Opinion	Provide nurses with evidence-based information useful to eliminate or reduce the severity of an injury by extravasation chemotherapy.
A24	The Oncologist	2008	Literature review	Present approval of Dexrazoxane (Totect) for treatment of extravasation of chemotherapy by anthracycline.
A25	The International Journal of Clinical Practice	2013	Literature review	Demonstrate efficacy of Dexrazoxane (Savene) for extravasation of anthracyclines.
A26	Emergency Medicine	2012	Literature review	To review in the literature the effect of dexrazoxane in reducing the risk of necrosis after anthracycline extravasation.
A27	European Journal of Cancer Care	2015	Systematic review	Analyze the quality of the evidence that supports contemporary practice and to determine if the patient's experience is taken into account.
A27	Clinical Journal of Oncology Nursing	2009	Expert Opinion	Describe manufacturer recommendations, list antidotes and FDA approved treatments, and published recommendations.
A28	Cancer Nursing Practice	2009	Expert Opinion	To describe evidence-based treatments for tissue necrosis caused by vesicants.
A29	Oncology Nursing Forum	2006	Literature review	To review the literature on the incidence, practice, recommendations, nursing management and knowledge gaps relevant to extravasation of vesicants.
A30	Oncology Nursing Forum	2006	Literature review	Sintetizar recomendações atuais, e discutir contradições a respeito do tratamento de extravasamento de vesicantes.

Subtitle: **Subcutaneous wash-out procedure.*

As there are several therapeutic techniques for treatment of extravasation, Table 4 was constructed, which describes the antidotes with dosages and application of the others of each type.

DISCUSSION

Clinical Evidence

Epidemiology

The occurrence of extravasation is rare, but it causes damage. A study conducted at a chemotherapy outpatient clinic in Chiba University Hospital, Japan, showed an incidence of 0.08% extravasation in a sample of 43,557 patients. The low value is due to the application of a chemotherapy protocol used in the outpatient clinic, together with a multidisciplinary and specialized team[14].

This protocol establishes the flow of care that begins with the approval of the prescription by a committee, later the same was arrived at by the pharmacist. In addition, at the outpatient clinic the nurse explained about the procedure, extravasation and adverse events. The preparation of the agents occurred in security cameras by pharmacists[14].

Studies indicate that extravasations occur mainly in the peripheral vein in the ulnar fossa, forearm, and back of the hand[14-15]. These two sites provide more damage when extravasation occurs, as they have less adipose and muscular tissue, thus, cause greater impairment of nerves and tendons, as pointed out by a North American expert[16].

RISK FACTORS

There are several factors that can lead to extravasation. These may relate to the condition of the client in use of antineoplastic, to the equipment used in the administration, as well as the properties of the infused antineoplastic agents.

Thus, the patient is more prone to endothelial dysfunction (due to age, diabetes mellitus, hypertension, dyslipidemia, atherosclerosis, chronic renal insufficiency), in cases of previous radiotherapies, compromised blood flow, high pressure infusion (pediatrician or altered sensory perception), patients unable to describe pain (pediatrics, sensory perception compromised), and due to the inexperience of the team[17].

TABLE 2 – Evidence on the prevention of extravasation of antineoplastic agents. Teresina-PI, 2016.

Temas	Recomendations	Evidence	GR*
Peripheral venous network	Evaluate the peripheral venous network for the availability of veins.	IV	B
	Avoid small caliber veins.	IV	B
	Do not infuse into tortuous and sclerotic veins.	IV	B
	Check venous return before resuming a leisurely infusion.	IV	B
	Puncture large caliber veins in the forearm.	VI	C
	Do not palpate the vein at the time of puncture.	VII	C
Punching devices	Do not use a needle catheter.	IV	B
	Make use of fully implanted catheter.	VI	C
	Infusions and vesicants with duration between 12 and 24h indicated central venous catheter.	VII	C
	Use small-caliber catheters in infusions.	VI	C
	Administer vesicants in infusion pump drop by drop.	VI	C
Location of peripheral puncture	Give preference to the forearm, back of the hand, wrist and antecubital fossa, respectively.	VI	C
	Do not use in lower extremities.	VII	C
	Do not use in the presence of edema.	VII	C
	Check the location of the central venous catheter	VII	C
Nursing Care	Nurse monitor the infusion every 30 min.	VI	C
	Stop the infusion if the patient needs to move.	VI	C
	Record actions in follow-up form.	VI	C
	Wash the access with 10 to 20 ml of 0.9% SF between different drug infusions.	VII	C
	Infusions of bolus vesicants should be administered concomitantly with the compatible fluid.	VII	C
	Evaluate the appearance of symptoms: edema, pain, flushing and slow infusion.	VII	C
	Standardize venipuncture technique	VII	C
Protocols	Make use of protocol for management of extravasation of chemotherapy.	VI	C

TABLE 3 – Evidence for treatment of extravasation of antineoplastic agents. Teresina-PI, 2016.

Themes	Antineoplastics	Recomendationd	Evidence	GR*
Immediate actions	Vesicants, irritants and non-vesicants	Immediate suspension of infusion when suspicion or confirmation of extravasation	VI	C
		Estimate the amount extravasated	VI	C
		Measure the extravasation area	VI	C
		Record photo extravasation area	VI	C
	Non-vesicant	Perform X-ray for fully implanted catheter location analysis (CTI)	VI	C
	Cisplatin	Surgical removal of CTI	VI	C
Physical treatment	Anthracyclines	Application of cold packs	VI	B
	Mitoxantrone		VI	B
	Dacabarmazine		VI	C
	Vinblastine	Applying hot compresses	VI	C
	Vesicants and irritants	*Subcutaneous wash-out procedure* (SWOP)	VI	C
	Vinorelbine	Utilização terapia à vácuo após desbridamento cirúrgico	VI	C
Topicals	Vinorelbine	Use of gauze impregnated with acetate for three weeks	VI	C
	Flourouracil, Epirubicin, Cyclophosphamide docetaxel **	Use of gauze impregnated with antibiotics for one week	VI	C
		Subcutaneous wash-out procedure (SWOP)	VI	C
	Epirubicin, paclitaxel and trabectin **		VI	C
	Doxorubicin	Topical Dimethylsufoxide 99%	VI	C
Antidotes	Antraciclinas	Dexrazoxane (up to 6 h after extravasation)	VI	C
		Systemic use of dexrazoxane	VI	C
Surgical approach	Anthracyclines	Surgical debridement followed by grafting in case of late detection with evolution for tissue necrosis	VI	C
	Vinorelbine		VI	C

Caption: *Degree of recommendation. ** Chemotherapy Cycle.

TABLE 4 –Treatments for extravasation of antineoplastics. Teresina-PI, 2016.

Antineoplastic	Antidote/ Technique	Dose / Therapy	Evidence – GR***	
Vesicants and irritants	*Subcutaneous wash-out procedure* (SWOP)*	Back of the hand: 200 ml of 0.9% physiological solution (SF).	VI	C
		Thorax: 2000ml of SF at 0.9%.	VI	C
Vinorelbine	Vacuum Therapy**	Pressão de 125 mmHg contínuo durante uma semana.	VI	C
Vinca alkaloids	Hyaluronidase	Administer subcutaneously 1 ml of the solution into five 0.2 ml injections (change the needle at each injection).	VII	C
	Hot compress	Moderate dry local heat for 30 min after hyalurodinase. Alternative: 15 min every 6 hours for 2 days.	VII	C
Anthracyclines: Doxorubicin Daunorubicin Epirubicina Idarubicina	Topical Dimethylsufoxide 99%	4 drops / 10cm2 of cutaneous surface every 8h. And twice the affected area for 7-14 days.	VII	C
	Cold compress	Local cold for 1 h every 8 h after application of DSMO for 3 days.	VII	C
	Dexrazoxane Confirmed: > 5 ml or Suspected:> 10 ml	Infuse within six hours of overflow. For 1-2 hours for three days in a different area than the overflow site. The recommended dose is based on body surface area: • Day 1: 1000 mg / m^2 • Day 2: 1000 mg / m^2 • Day 3: 500 mg / m^2	VII	C
Mechlorethamine	10% sodium thiosulfate	Inject 2 ml to each ml of extravasated, subcutaneous mechlorethamine around the affected area. Change needle with each injection.	VII	C
Taxanes Etoposide	Hialuronidase	Administer 250U in 6 ml of saline given in 6 subcutaneous punctures around the affected area.	VII	C

* The amount of SF at 0.9 will depend on the location of the extravasation. ** After surgical debridement. *** Degree of recommendation.

In this context, North American and European protocols describe other features of the venous network that favor greater risk, such as decreased elasticity, fragility and in small caliber veins, obesity, multiple previous punctures, presence of disseminated skin disease and during the infusion[16-18].

As for the equipment used, the risk is inherent to the peripheral catheter, mainly because of the possibility of deppositioning related to inadvertent palpation at the time of puncture, which may cause perforation of the vein, use of a needle catheter and inadequate fixation[19-16].

Case studies performed in the Netherlands, India and Italy, showed extravasation in the peripheral venous network of vinorelbine, anthracyclines, vinorelbine, respectively. The treatment varied according to the extravasated agent. These studies evidenced the need for prevention and early detection, if it occurs, for the immediate implementation of therapeutic measures[20-21-22].

Central venous accesses, although safer, also pose risks of extravasation. For infusion in the fully implanted catheter it is necessary to use a needle of adequate size and shape, since very short or oscillating needles may cause extravasation by deppositioning. As well, when they are inserted in places of difficult stabilization, as in the abdomen. The central venous catheter is risky because it is possible that its extension and tip curl or rupture, as well as thrombus formation at the tip[16].

In this sense, in Germany, a case study of a patient who suffered anthracycline leakage, diagnosed late, progressed to necrosis with immediate withdrawal of the catheter and, subsequently, restorative surgery with a cutaneous graft23. A similar situation occurred in the United States, an 81-year-old woman suffered extravasation of trabectin in the central venous catheter, requiring surgical debridement[24].

Another relevant factor is that the drugs administered cause risks according to their physical-chemical properties or solution infused. In this sense, the ability to bind directly to deoxyribonucleic acid (DNA), the ability to kill replicating cells, to cause vascular dilatation, existence of pH outside the range of 5.5-8.5, plasma osmolarity greater than 290 mmol / l, vasoconstricting agents, infusion of more than one vesicant, DNA binding vesicants and antineoplastics composed of alcohol and polyethylene glycol[25-16].

Prevention of extravasation

The most efficient prevention is the application of an institutional protocol that makes it possible to unify actions, through a standardized and systematic language, based on evidence[18].

As there is no consensus as to the most appropriate choice of catheter, oncology specialists[19-16-18] indicate a multifactorial analysis as to: unrestricted limb choice and

a preferably non-tortuous vein; peripheral device compatible with the selected vein; evaluation of infusion time; and age and peculiarity of each client; recommended do not palpate the vein at the time of puncture; central venous access.

In this context, a study carried out in Italy sought to validate an instrument for the evaluation of intravenous insertion difficulty, the validated items described as non-puncture prevention in non-visible or nonpalpable, thin caliber, sclerotic, tortuous, mobile veins that suffered multiple anterior punctures[15].

Other recommendations mentioned in a chemotherapy outpatient study in Japan underscore the importance of nursing care, in which care should be given for the administration of dribbling vesicles in an infusion pump, evaluation every 30 minutes and filling in the side dish. It also discusses which nurse should pause administration each time the patient goes to the bathroom, and check the venous return before restarting the infusion[14].

Experts on the subject recommend, as a prevention, washing access with 10 to 20 ml of 0.9% physiological solution between different drug infusions. As well as, that infusion of bolus vesicants should be administered concomitantly to a compatible fluid. They clarify that the nurse should evaluate the appearance of symptoms such as edema, pain, flushing and slow infusion and emphasize the importance of standardizing techniques in institutions[18].

Treatment of extravasation

There are several therapies to minimize the damage caused by an extravasation. These depend on the extravasated drug, the time elapsed between the event and the detection, the location of the event, the amount of extravasated antineoplastic, the infusion route, among others.

In this way, this review listed therapeutic methods, among them: the application of immediate actions to the diagnosis of extravasation, physical treatment by means of heat and cold application, topical, antidotes, surgical approach and SWOT technique. subcutaneous lavage).

Case studies (21-26), retrospective work[14], specialist[16] and literature review[27] agree that immediate actions may delay complications in the event of extravasation. If it is necessary to stop the infusion immediately the suspicion or confirmation, identify the antineoplastic, estimate the extravasated amount, measure and register the area with photo. These actions make it possible both to make a decision regarding the treatment to be implemented and to promote adequate follow-up.

The application of heat and cold depends on the extravasated drug, literature review published in 2012[28] and the specialist Schulmeister[29] agree with applications of hot compresses for vinca alkaloids and oxaliplatin, and cold packs for anthracyclines, mitomycin, mitoxantrone, fluorouracil and cisplatin. Schulmeister[29] adds the use of cold compress for mechlorethamine and taxanes.

O mecanismo de ação do calor é induzir vasodilatação e, consequentemente, facilitar o aumento da absorção e distribuição sistêmica do agente, causando menos danos locais. A ação das compressas frias baseia-se na indução de vasoconstricção com consequente diminuição da velocidade de difusão da droga no interior dos tecidos, de modo a reduzir a potencial área de dano tecidual[30-31-16].

A retrospective study performed at a High Complexity in Oncology Center in the state of São Paulo, Brazil, showed that of the 216 extravasations that occurred in a five year period in 35,475 patients submitted to chemotherapy, there were absences of records when the prescription of hot compresses or cold. He emphasized that of the eight registries found, three patients were submitted to treatments with inadequate compresses to the extravasated drug[30].

These facts reflect on the performance of nursing, which is responsible for drug administration and care implementation. Whereas, inadequate application of compresses can potentiate the tissue damage, depending on the extravasated drug. Influence the need for a specialized and updated team and standardized service flows.

Another treatment technique evidenced in this review was the Subcutaneous wash-out procedure (SWOP) or subcutaneous lavage procedure. This was used for vesicant and irritants in different situations, as described in the case studies[26-6-32-10], presented positive results regarding the prevention of tissue necrosis.

A series of cases analyzed at the Cancer Center in South East England, with 89 patients who had suffered leakage in peripheral veins in 10 years, pointed out that local lavage with saline was efficient in all cases, only one patient presented local infection that was properly treated with antibiotics. No patient required surgical debridement or had subsequent complications[6].

However, when it comes to central venous catheter, as a fully implanted catheter, complications after extravasation are more recurrent due to the location and larger amount of drug. A study carried out in Austria with eight patients showed that the immediate withdrawal of the catheter followed by the application of SWOP were efficient in cases with early detection of extravasation in three patients, in which it prevented tissue necrosis causing only side effects. The remaining cases, with late detection, required surgical debridement[32].

This technique was developed by plastic surgeons in the UK so that nurses could act promptly on the occurrence of extravasation, offering interventions in a more timely and less inconvenient way for patients. It consists of the subcutaneous administration of saline solution in order to wash the place and remove the extravasated

antineoplastic. It is a minimally invasive technique, however, it requires team training[27].

The other therapeutics implemented are called antidotes, whose administration depends on extravasated drug. 99% dimethylsulfoxide (DMSO) is indicated as an antidote for extravasation of anthracyclines and mitomycin C, according to the European Oncology Nursing Society[18], its application is topical and the mechanism of action is based on increased skin permeability, promoting absorption of drugs and elimination of free radicals. In contrast, specialist Schulmeister 16 says that its topical application is not recommended as an antidote because it needs high concentration to guarantee efficacy and it is not released for medical treatment in the United States.

Another antidote used is sodium thiosulfate. Although it has a mechanism of action yet to be clarified, experts believe that it can chemically neutralize reactive alkylating species and reduce the production of radicals that cause tissue damage. It is indicated for mechlorethamine and should be immediately after extravasation by the subcutaneous route[16-18]. Its use for extravasation of cisplatin is indicated by a specialist[33].

Hyaluronidase is an enzyme that modifies the permeability of connective tissue through the hydrolysis of hyaluronic acid. It promotes the diffusion and absorption of the drug. It is effective for prevention of tissue necrosis by vinca alkaloids[33-34-31]. It should be pointed out that these drugs make up a group of cytostatics with greater vesicant power. In this sense, hyaluronidase is used in the application of dry heat. In theory, they potentiate the absorption power of the drug and do not present toxicity to the treatment[28].

As already mentioned, there is a group of cytostatics that present greater vesicant power. This group includes anthracyclines. Extravasation by these drugs causes severe tissue necrosis, thus presenting great risk to patients[35]. The European Oncology Nursing Society indicates, as the only effective antidote against anthracyclines, dexrazoxane, called Savene in Europe and Totec in the United States [36].

The efficacy of dexrazoxane was tested in a study conducted in Portsmouth, England, of the 12 patients who suffered extravasation, none required a surgical approach, and only 25% of them had secondary symptoms[37].

CONCLUSION

Extravasation can cause significant tissue damage. Therefore, prevention is the best strategy to be adopted by the multidisciplinary team. This review infers on the importance of individual assessment of the patient regarding risk factors, and the implementation of a care protocol that standardizes actions and language.

As well as, evidenced several treatments to be used in clinical practice, with due training of the team and according to the indications of each institution. The studies found do not provide high levels of recommendations, but they have gathered the most current information on the subject. It is hoped that this evidence may guide the praxis of nurses in order to improve care for patients with cancer.

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