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# A comprehensive management of cytostatics extravasation lesions: An overview

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## Abstract

**Introduction:** Cytostatics are antineoplastic drugs of vital importance and can be administered parenterally via a central or peripheral intravenous route. Despite advances in therapeutic techniques, the extravasation of chemotherapy drugs continues to be a fatal accident that leads to tissue necrosis, with a decrease in the quality of life of those affected and the need for early diagnosis and effective therapy, including surgery. With the aim of describing the state of the art of this complication, as well as the different therapeutic criteria, this review is carried out.

**Methods:** A systematic review of the medical literature on articles referring to cytostatic extravasation was carried out from January 2023 to August 2024. The databases used were: Pubmed, Infomed, Scielo, academic Google.

**Results:** 35 articles related to cytostatic extravasation were included.

**Discussion:** The inadvertent escape of cytostatic drugs from the blood vessels into the subcutaneous cellular tissue constitutes an unwanted and stressful complication, sometimes undiagnosed, and can cause irreversible damage to surrounding tissues, including necrosis and functional impotence of the affected limb.

**Conclusions:** Early detection and a comprehensive, standardized and interdisciplinary therapeutic approach must be implemented to reduce the negative consequences of lesions due to cytostatic extravasation.

**Keywords:** Cytostatics; Extravasation; Therapeutics; Necrosis.

## Introduction

Cytostatics are a group of drugs of vital importance for the treatment of cancer, because of its capacities of inhibit the growing of tumoral cells [1]. Generally they are administered intravenously, using central s or peripheral access [2]. In spite of the advances in therapeutics thecniques, they can cause adverses reactions, including the extravasation or escape of chemotherapics from a blood vessels during the infussion, damaging the surrounding tissues [3]. The severity of the accident depends on the quantity and quality of extravasated medication [2].

Peripheral veins are located in the subcutaneous celular tissue, a laxus fatty space, facilitating an easily collection of extravasated chemotherapics, so a damage of surrounding tissues occurs, involving skin, nerves, vessels, tendons and muscles [3,4].

The citotoxic properties of the drugs causing lesions of the tissues are the results of two main action mechanisms: (1) Absortion of the drugs by local cells, binding the microtubules and the celular DNA, and number, (2) Direct damage of tissues without affecting the DNA [4,5].

Citostatics extravasation lesions are considered a medical urgency, because of the severity of complications developed, including the temporary interruption of the specific oncological treatment, and affecting the quality of patient´s life [6].

Regarding the accidental nature of this complication, there are not specifics statisticals reports about the incidence of chemotherapy extravasation [7,8].

A proper knowledge of the pathophysiology of cytostatics extravasation lesions is important in order to determinate an early diagnosis and for an integral therapeutic approach, including a conservative treatment or a surgery, with the debridement of the necrotic tissues and a definitive coverage of the wound [9]. With the aim to describe the status of the art of cytostatics extravasation events, and the differents treatment criterias ,a review of the medical literature was carried out.

## Methods

A systematic review of the medical literature was carried out from January 2023 to August 2024. The searched databases included: Pubmed, Infomed, Scielo, academic Google. Medical Subject Headings (MeSH) were used for searching: Cytostatics Agents, extravasation, therapeutics, necrosis.

Medical articles related to chemotherapy extravasation lesions published from the year 2000 onwards, were searched.

**Inclusion and Exclusion Criteria**

- Inclusion criteria: Originals articles, Case presentations and review articles related to cytostatics extravasation.

– Exclusion Criteria:

Medical articles related to extravasation events, differentes to cytostatics medication

Articles published before the year 2000.

## Results

Of a total of 92 medical articles searched, 35th were included, distributed as follows: 21 reviews, 9 original articles and 5 case reports. Of them, 12 articles were published during the last 5 years (2019 to 2024).

**Figure 1:** Cytostatic extravasation of the forearm.

**Figure 2:** Cytostatic extravasation of the hand.

## Discussion

The inadvertent leakage of cytostatics drugs from a blood vessels to extravascular space during intravenous administration, is a stressfull and undesired complication, sometimes undiagnosed, and can results in severe and irreversibles tissue damages, including necrosis, and functional impairment of the affected extremity [12,13].

Several risks factors appears to be related to the development of this complication. García et al, [14] report local factors as venous fragility and sclerosis, previous irradiation of the injection site, presence of linfedemas, multiples venopunctures. Others general factors as: extremes ages (ancients or children), immunodepressions conditions, malnutrition. somnolence status [15,16].

Some predisposing factors depending on the technique are described: a proper selection of the size and type of intravenous cannula, selection of an optimal peripheral vein and site of injection, avoiding multiples punctions as well as the use of infussion pumps and butterflys [17,18]. A right competence and experience of the paramedical and medical team is required, to avoid an extravasation events. Prevention suposed to be the first line of attention [19,20].

An adequate education of patient for an early recognition of symptoms as: redness, pain, itching, burning, swelling, is essential for the instauration of an early treatment [21,22].

An inmediate intervention, interrupting the infussion of the medication, and remotion of the intravenous cannula is vital [22-24].

Vasoconstrictive properties of cold compresses applied to diminish the velocity of drug difussion in the subcutaneous space, and acute inflammation signs have been reported [24]. The usefullness of topic hot to increase the absortion of the extravasated cytostatic drug is based on its vasodilatation effects [24-26].

There is a lack of consensus regarding the Classification of antineoplastic agents [27]. According to their citotoxic capacities, cytostatics agents are classified in: Non agresives, Irritants, and Vesicants [22,25,27]. The vesicants ones are responsibles for necrotic and deep tissue injuries. Upper extremities are the most used anatomical areas for peripheral intravenous drug administration [28,29].

Antecubital fose have been signaled as the first site affected for extravasation events [30]. Alfaro Rubio [9] reports the dorsus of the hand as the main affected anatomic zone, (Figure 1) followed by the forearm (Figure 2). The dorsal zone of the foot results the most affected site injection in children [28,31].

Pluschnig [23] have preconized the usefullness of contrasted angiography with green indocianine for the evaluation of blood circulation in the extravasated area, it confirms the extensión of the damaged tissue, and helps to decide whether to apply a surgical or conservative treatment.

Pérez Fidalgo et al, [21] confirm the effectiveness of topic application of DMSO (dimetylsulfoxide 50%), inmediately after the extravasation, and twice a day for two weeks. Its a common solvent, that penetrates tissues, increasing the velocity of elimination of extravasated drug.

Enzymatic debridement of necrotic tissue with hialorunidasa have been described by several authors [31].

The effectiveness of topical steroids have not been confirmed [32]. Darmert et al, [33] inform that the topical use of antidotes as Dexrazoxane is considered controversial and its not an standard procedure.

The surgical debridement and the subsequent surgical coverage using local flaps or skin grafts have been demostrated to be the definitive treatment [34], that is why the early reference of affected patients to the Plastic Department for surgery, is advisible [35].

Jaime Fagundo et al [6] consider the amputation surgery as an exceptional approach, when the severity of the injury results in an impairment extremity viability [35].

The role of the early hyperbaric oxigenation therapy have been reported [33].

## Conclusions

An early diagnosis and an integral standarized therapeutic approach most be implemented to diminish the negative effcts of cytostatics extravasation lesions.

**Conflict of interest:** No conflicts of interests are declared between the authors.

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