UPDATE IN RADIOLOGY

Extravasation of contrast media at the puncture site: Strategies for management

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Abstract The incidence of contrast medium extravasation at the venipuncture site has increased with the generalized use of automatic injectors. Most extravasations only cause slight edema and erythema. Nevertheless, in some cases extravasation can result in severe skin lesions or even in compartment syndrome. Lesions caused by extravasation usually resolve spontaneously with conservative treatment. Although the complications of extravasation are well known, institutional protocols are normally lacking and the criteria for taking action and the type of treatment, whether based on the literature or personal preferences, tend to vary. In this article, we review the incidence, risk factors, clinical manifestations, and options for preventing and treating contrast medium extravasation in soft tissues. Finally, we present the protocol we use to manage extravasation at our hospital.

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Extravasación de medios de contraste intravenosos en el sitio de la punción: Protocolo de actuación

Resumen La incidencia de extravasación de medios de contraste en el sitio de la punción venosa ha aumentado con el uso generalizado de los inyectores automáticos. La mayoría de las extravasaciones sólo ocasionan edema y eritema leves. Sin embargo, en algunos casos pueden originar lesiones cutáneas graves e incluso llegar a provocar un síndrome compartimental. Las lesiones por extravasación suelen resolverse espontáneamente y con tratamiento conservador. A pesar de que las complicaciones de las extravasaciones son bien conocidas, es común que los criterios de actuación y el tratamiento, basados en la bibliografía o en preferencias

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Introduction

IV contrast media extravasation into the soft tissues is an uncommon yet well-known complication that can happen even when the injection technique is appropriate. Today its incidence has grown due to the widespread use of automatic injectors in both computed tomography and magnetic resonance studies.\textsuperscript{1-4} The consequences of extravasations vary from mild skin reactions to more serious lesions including necrosis, skin ulcers, and compartmental syndrome.\textsuperscript{1,5} Prevention, early diagnosis and the optimal therapy are the keys to avoid serious lesions.

Yet despite the existence of numerous publications and guidelines from the European Society of Genitourinary Radiology (ESUR) and the American College of Cardiology (ACC) on IV contrast media extravasation into soft tissues the information on how to proceed is some times fuzzy and controversial.\textsuperscript{1,2,5-8}

The goal of this study is to do an update on the incidence, risk factors, toxic effects, diagnosis, prevention and management of IV contrast media extravasations into soft tissues and to put forward a protocol to proceed in these situations.

Incidence

IV contrast media extravasations into soft tissues surrounding one vein is one of the most common complications of IV injection.\textsuperscript{3} It can occur both when it is injected manually or through automatic injectors. The generalization of CT automatic injectors has increased the incidence both of extravasations from 0.1\% to 1.2\%, and the extravasated volume.\textsuperscript{4,5,9-12} The incidence of extravasations of gadolinium chelates in magnetic resonances is not as big (0.05\%) as that of the iodinated contrast media.\textsuperscript{13}

Risk factors

The risk factors of IV contrast media extravasations are associated both with the injection technique used and with the patient’s conditions (Table 1).

Associated with the injection technique

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with the injection technique</td>
<td>Vein access with needles or metallic catheters</td>
</tr>
<tr>
<td>Puncture in suboptimal sites or small peripheral veins</td>
<td>Injection through catheters beyond 24 h</td>
</tr>
<tr>
<td>Repeated punctures in the same vein</td>
<td>Use of an automatic injector</td>
</tr>
<tr>
<td>Hyperosmolar contrast media</td>
<td></td>
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</tbody>
</table>

Associated with the patient

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired ability to communicate</td>
<td>Fragile or damaged veins (elderly, repeated venous punctures or prior radiotherapy in the puncture site, chemotherapy)</td>
</tr>
<tr>
<td>History of peripheral vascular diseases (atherosclerosis, diabetes, Raynaud’s syndrome)</td>
<td>Lymphatic or venous drainage involved (thrombosis or venous failure, lymphedema due to former surgical intervention)</td>
</tr>
<tr>
<td>Weakened patients (little muscular mass, atrophy of the subcutaneous cellular tissue)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 Risk factors associated with IV contrast media extravasation.

caliber of the canocalized vein are more important than the velocity of injection. The veins of hands, wrists, feet, and ankles are more prone to extravasation injury and they should be avoid as much as possible.\textsuperscript{5,8,11} Risk is also greater when injecting peripheral venous catheters implanted for over 24 h and when performing multiple punctures in the same vein.\textsuperscript{7,8,12}

Other important factor is automatic injectors since volumes are larger, the pressure selected can be greater than the resistance of the vessel and it is not always possible to monitor the puncture site.\textsuperscript{1,4,11}

Extravasations are more frequent with ionic and hyperosmolar contrast media than with non-ionic or low-osmolality contrast media. Iodinated contrast media (ICM) do not usually cause pain and early extravasation can be unnoticed to the patient.\textsuperscript{4,14}

Associated with the patient

Extravasations are more common in children, elderly and patients with a low level of consciousness due to their difficulties when it comes to verbalizing the pain caused by extravasation.\textsuperscript{15,6} Precautionary measures are also necessary in patients with fragile veins (elderly, repeated vein punctures, former radiotherapy in the same area, chemotherapy) or in patients with little muscle mass and atrophy of the subcutaneous cellular tissue. Other
factors like the history of peripheral vascular conditions (atherosclerosis, diabetes, Raynaud’s syndrome) or patients with venous/lymphatic return disorders (thrombosis or venous failure, lymphedema due to previous surgery) even they probably do not increase the risk of extravasation they are related to a greater possibility of serious injuries.\textsuperscript{1,5,6}

**Mechanisms and toxicity**

**Iodinated contrast media**

ICM are iodinated saline solutions and the enhancement they achieve in tissues depends on the concentration of iodine atoms they contain.\textsuperscript{1,5} The benzene ring is the basic substrate that these iodine atoms attach to. They can be categorized according to their osmolality, ionic trend and molecular structure – all of which is associated with adverse reactions.\textsuperscript{15}

Most non-ionic ICM extravasations (97%) do not have side effects or if they do there are minimal, usually cause little early pain and the initial extravasation be unnoticed to the patient.\textsuperscript{1,5,14} Serious side effects are relatively rare.\textsuperscript{4}

In the pathogenesis of ICM extravasation lesions contrast osmolality, cytotoxicity and the volume of extravasated contrast play a part.

**Osmolality**

Determined by the number of particles generated in solution osmolality can be high (from 1200 to 2400 mOsm/kg H$_2$O) or low (from 290 to 860 mOsm/kg H$_2$O). Among the low osmolality ones isomolars show a similar osmolality to that of plasma (290 mOsm/kg H$_2$O).\textsuperscript{1,5,15}

Osmolality is the most important factor associated with the toxicity of the skin extravasation and the subcutaneous cellular tissue. It is directly associated with cellular lysis and is greater the bigger contrast osmolality is.\textsuperscript{1} Even though low osmolality-contrasts are better tolerated than the most osmolar ones they can also cause necrosis.\textsuperscript{1,4}

**Cytotoxicity**

Contrast cytotoxicity has been associated with the ionic trend (ionic or non-ionic) depending on the radicals in positions 1, 3, and 5 of benzene nucleus\textsuperscript{1} yet there are publications with contradictory results when it comes to the cytotoxicity of ionic and non-ionic contrast media.\textsuperscript{5,14}

Ionic-ICM dissociate from aqueous solutions into a negatively charged anion responsible for contrast and into a positively charged cation that gives them osmolality. Electrolytically charged particles resulting from dissociation can influence the electrophysiological events of the organism.\textsuperscript{5,14}

Non-ionic-ICM are obtained combining a contrast media acid with a sugar or polyvalent alcohol that produce links that do not dissociate but remain in solution formation as an electrically neutral particle. Thus osmolality is lower. Hydrophilicity and the absence of electrical charges can be traduced into a less strong union with proteins, fewer enzyme inhibition and not that much effect on the function of biological membranes.\textsuperscript{1,3}

The most widely used ICM today are the non-ionic-ICM since it has been observed a lower incidence of necrosis, edema, and hemorrhages than with low osmolality-ions\textsuperscript{15} probably due to its lower osmolality.\textsuperscript{1,3,5}

**Volume of extravasated contrast**

Most extravasations are small and symptoms resolve in 24–48h.\textsuperscript{1,2,4}

Non-ionic ICM extravasation into soft tissues is not very painful and this is why it can be unnoticed when it is relatively big. Big extravasation is more common in the upper limb\textsuperscript{8} when the injection has been performed in a deep area\textsuperscript{6} or through automatic injectors and puncture site is not monitored during the time of injection.\textsuperscript{5,14} It can cause serious injuries and the mechanical compression of tissues that can lead to compartmental syndrome.\textsuperscript{1,4,11} Nevertheless the extravasated volume per se is not correlated with the probability or seriousness of a secondary injury. 150 ml-non-ionic-ICM extravasations have been reported to reabsorb without sequelae\textsuperscript{17,16} so if the patient remains asymptomatic a thorough appropriate evaluation and monitoring of patient might do.\textsuperscript{6} However ulcers and cutaneous necrosis have been reported with volumes as little as 10 ml.\textsuperscript{6,11}

**Gadolinium compounds**

Free gadolinium is a toxic metal that turns into non-toxic when combined with a chelate agent. These agents distinguish themselves between one another based on their linear or cyclic structure, osmolality, ionic trend, viscosity, and stability. Cyclic chelating agents have a greater thermodynamic stability than linear ones so they are not as prone to releasing gadolinium (transmetallation) when injected.

Toxicity from the extravasation of doses equivalent to gadolinium chelates is greater than that of ICM mainly due to its greater osmolality.\textsuperscript{17} However the extravasation of these chelates in the puncture site is less common and is usually better tolerated than that of ICM. This is due both to the fact that the velocity of injection is lower and that with the doses of gadolinium chelates normally used the osmolar loading is very low (0.5–2 mOsm).\textsuperscript{5,17}

Yet despite some studies carried out in animals have proved that the incidence of edema, necrosis, and hemorrhage is greater with nonionic gadolinium compounds rather than with non-ionic ones the likelihood of having a serious injury due to extravasation of gadolinium chelates in the puncture site is lower than that of ICMs.\textsuperscript{5,17}

**Diagnosis**

The diagnosis of contrast media extravasation is clinical. With automatic injectors with which the injection can only be monitored at the beginning usually the 1st sign of extravasation is the absence of contrast media in images.\textsuperscript{18} We do not need to perform image tests to confirm this since therapy depends exclusively on the patient’s symptoms.
Mild extravasations

Symptoms are varied. Most patients present with pain or itch at the puncture site, local edema, and erythema while other remain asymptomatic and can only be diagnosed by the absence of contrast media in images. Symptoms usually resolve in 24–48 h.1,2,4

Extravasation injuries need to be distinguished from local reactions both by the hypersensibility of the fluid injected and the local irritant effects of contrast media in the wall of venous cannulation.

In these reactions both the edema and the erythema are usually absent and if the IV is maintained the catheter will be in the correct position inside the vein.

It is important to bear in mind that it is not possible to predict what the evolution of injuries will be and this is why local symptoms both in asymptomatic and patients with mild injuries need to be monitored 2–4 h after extravasation to detect new injuries, confirm the resolution, or detect the progression of more serious injuries.5,7,8,10 After this time it is also important to tell the patient that he should go to the hospital if he is not feeling well.

Serious extravasations

After the first 2–4 h from the moment of extravasation and if pain is still persistent, the edema has enlarged or there are blisters, ulcers or skin necrosis the patient will need to be assessed by the plastic surgeon.7,8

The least but most feared common complication of all is the acute compartmental syndrome secondary to mechanical compression exerted by the extravasated contrast media. It usually happens when the volume is large even it has also been reported with relatively small extravasations – especially in the dorsal and volar wrist surfaces.6

The main symptom is the intense pain that increases when the affected muscles are passively stretched. The pain is accompanied by paleness, ulcers and skin blisters, reduced mobility, distal cyanosis, reduction or absence of pulse of the main compartment artery, and distal paresthesias.19 It is not unusual that the early symptoms are limited to local paresthesias.8 Long term-sequelae include hypoesthesia, pain, significant weakness, and flexion contractures. They depend on the volume and type of extravasated contrast as well as on the affected anatomical region.5

Therapy

Mild extravasations

The first measure is to stop immediately the injection and remove the extravasated IV. Yet despite there is no consensus in literature when it comes to the course of action to follow with extravasations the members of the ESUR security committee of contrast media and the ACR committee on drugs and contrast media of the quality and security commission recommend that the management of mild extravasations should consist of elevating the affected limb, topical application of ice and monitoring the patient.7,8

Elevation of the affected limb

It is recommended to elevate the affected limb beyond the level of the heart.7,8 Even though its efficiency has not been proven yet18 this easy maneuver reduces capillary hydrostatic pressure promoting the reabsorption of the extravasated fluid and reducing the edema. The elevation of the limb needs to be done without compromising its artery supply or venous return.1,5,6,10

Topical application of ice or heat

The topical application of ice or heat is not supported by scientific evidence.8 ESUR recommends the topical application of ice through ice bags wrapped up in gauzes or cloths in the area of extravasation—3 times a day for 15–60 min to cause vasoconstriction and thus limit inflammation, alleviate the pain6–7 and is associated to fewer skin ulcers.4,5

Bandages, towels or wet dressings should not be used since humidity can macerate the skin. Even if it causes vasodilation the topical application of heat improves the reabsorption of the extravasated contrast material and is more beneficial than the topical application of ice.5

Monitoring of patient

Seriousness and prognosis of extravasation is hard to determine in an early evaluation. It is very important to monitor the patient and reevaluate him for the next 2–4 h to discard more serious injuries.7,8 When there is serious sign or symptom of serious extravasation like inflammation or progressive pain, perfusion disorders, sensitive alterations, ulcers or skin necrosis the patient needs to go to the plastic surgeon immediately.8

Other therapies

The utility of other measures like the aspiration of extravasated contrast media through an inserted needle, the injection of saline serum in the site of extravasation or the use of local antidotes like hyaluronidase, dimethyl-sulfoxide, corticosteroids and vasodilators has not been proven.1,5,9 Contrast aspiration from the site of extravasation before removing the needle or in the operating room through liposuction cannulas is controversial.21 The local injection of saline serum in the site of extravasation reduces the concentration of extravasated contrast in the subcutaneous cellular tissue. However for this measure to be effective half the extravasated volume needs to be injected causing a major mechanical damage to the tissues.1 Hyaluronidase is an enzyme that provisionally reduces the viscosity of hyaluronic acid—the major component of connective tissue. Injected subcutaneously it increases tissue patency enabling the absorption of extravasated contrast media through both the vascular and lymphatic systems.6 The doses recommended vary from 15 U to 250 U diluted in 1.5–6 mL of saline serum1 during the 1st hour since the extravasation in order to achieve the greater reduction of skin edema.1,5,21 They can be administered right through the catheter through which the contrast media was extravasated or injected around the area of extravasation. Most clinical studies and studies with animals show that there is benefit in this but although the only side effect reported is rash certain authors question its efficiency.1,5,8
Serious extravasations

Over-infection prevention
To prevent the over-infection of injury when in presence of skin blisters most plastic surgeons recommend the application of argentic sulfadiazine and coverage with a local band-aid twice a day. But no series have specifically focused on radiologic contrast extravasations.\textsuperscript{5,16,20} It is important to eliminate necrotic tissue and clean the lesion before each application of argentic sulfadiazine.\textsuperscript{1,5}

Surgery
In most serious extravasations surgical intervention is not necessary since the signs and symptoms disappear a few days later after the administration of conservative therapy.\textsuperscript{4-8,20} Most articles published recommend surgical drainage when the volume is >100 ml.\textsuperscript{1,5,16,21} However the extravasated volume is not the only variable when taking surgical intervention into consideration since serious lesions with volumes >10 ml have been reported too.\textsuperscript{6,8,20}

In the most recent publications surgical drainage is recommended during the first 6 h in the presence of signs or symptoms of serious lesion regardless of the extravasated volume or urgent fasciotomy if there is suspicion of acute compartmental syndrome.\textsuperscript{4,5,8}

Prevention
The patient’s easiness plays an important role in the prevention of contrast media extravasations. Explaining each step of the proceeding with possible foreseeable changes—blush, mild sensation of heat in the puncture site spreading throughout the body that can be especially intense in the perineum and metallic taste that goes away rapidly can help the patient.\textsuperscript{22} If the patient shows pain or sensation of swelling in the puncture site the injection needs to be interrupted.

Whenever possible low osmolality non ionic-ICM are recommended because if extravasation occurs tissue reaction is lower than with hyperosmolar ionic-ICM.\textsuperscript{1,2,4}

When using automatic injectors the vein needs to be cannulated with a flexible plastic needle. Before connecting the catheter to the injector the IV always needs to be tested with a saline solution to test that there is no resistance to the injection.\textsuperscript{7,8,18} Flow velocity needs to be appropriate for the caliber of needle used.

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**Figure 1** Action protocol in a IV contrast media extravasation into soft tissues.

*Progressive inflammation or pain, perfusion disorders, sensitive alterations and ulcers or skin necrosis.

*It is convenient to tell the patient that he needs to go to the hospital if symptoms grow worse or if he has got some other issues.
3 ml/s or more-flows are needed and they must be used with a ≥20 caliber-needle and the most appropriate puncture site is the forearm antecubital vein. In peripheral veins—hand, wrist, ankle flow velocity is not recommended beyond 1.5 ml/s.5

Peripheral vein catheters cannulated over 24 h should not be used since they are usually associated with flebitis which in turn increases vascular resistance and consequently the risk of extravasation.1,7,8,12 We rather cannulate a new vein when the patient comes to radiology.

The direct monitoring of puncture site through palpation during the early stage of puncture is one of the most important preventive measures to detect extravasation and stop the injection. A constant communication between operator and patient through an inter-communicator needs to be on during the whole examination process.

The automatic injection through central vein catheters can be done safely as long as certain precautionary measures are taken. First of all the correct location of the catheter tip needs to be confirmed and before connecting the injector a saline solution needs to be injected through the catheter to confirm that there is no resistance to the injection. We cannot assume that all vascular catheters including a central catheter of peripheral insertion will tolerate mechanical injections. It is important to read the instructions from the central vein catheter manufacturer to see if automatic injectors can really be used due to the risk of tear in some catheters.23

**Action protocol**

Figs. 1 and 2 include both the action protocol and data collected by our hospital when contrast media extravasation in soft tissues occurs.

**Management of extravasation**

When contrast media extravasation is suspected the 1st thing to do is to stop the injection and then initiate the action protocol (Fig. 1). The 1st step is to remove the IV through which the contrast media was extravasated and then apply the antiedema measures by elevating the affected limb beyond the level of the heart. Then ice bags in the site of extravasation need to be applied 3 times a day for 15–60 min. The ice bags cannot be in direct contact with the skin and they need to be wrapped up in gauzes or cloths. The next step is to analyze how serious the extravasation is and
Extravasation of contrast media at the puncture site

what the repercussions are. If the patient’s signs and symptoms suggest serious extravasation assistance from a plastic surgeon will be required. When extravasation is mild the patient needs to be monitored at the radiology unit for 4 h to assess the evolution of findings and detect progression to more serious lesions.

Data collection

In the collected data sheet (Fig. 2) the name of the patient, his number of clinical history, age, and risk factors will be written down. It is important to register the generic name and commercial name of the contrast media used in the injection, the type of catheter caliber used, the site of extravasation, and the patient’s symptoms and signs. If possible the volume of extravasated contrast media needs to be quantified or estimated always bearing in mind the volume injected until the moment when extravasation happened.

In the radiological report the site of extravasation, its consequences, and the therapeutic measures need to be written down too.

Conclusions

In radiology the extravasation of contrast media is an uncommon yet serious complication due to the potential damage it can unleash in the extravasated tissues. It is important to know the risk factors, the manifestations of extravasation, precautionary measures and the right therapy to avoid having serious complications. Most contrast media extravasations resolve without sequelae with conservative therapy.

Ethical responsibilities

Protection of people and animals. Authors confirm that no experiments have been performed on human beings or animals.

Confidentiality of data. Authors confirm that in this report there are no personal data from patients.

Right to privacy and informed consent. Authors confirm that in this report there are no personal data from patients.

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References