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REVIEW

Overview of the Pathophysiology of Extravasation of Anesthetic Drugs

Sevinç Açışlı Ersan, Ahmet Şen

Department of Anesthesiology and Reanimation, Health Sciense University Trabzon Faculty of Medicine, Trabzon, Türkiye

ABSTRACT

Intravenous administration of drugs is frequently employed to achieve rapid and effective systemic effects. However, it is undesirable to administer drugs into the tissue as a result of extravasation of the intravenous cannula. Both the closed extremities to which the IV route is applied due to the surgical method to be applied make it difficult to access the vascular access during surgery and the use of pressurised instruments in the administration of drugs through the IV route makes the work of the anaesthetist difficult. In addition, patients cannot report their pain due to unconsciousness. In the operating theater and intensive care unit for anesthesia practice, induction, fluid therapy, nutrition, etc., although rare, difficulty in vascular access maintenance and drug extravasation cause serious complications in many procedures. This study aimed to emphasize the importance of perioperative anesthetic drug extravasation and its physiopathology by presenting current information.

Keywords: Anesthesia, anesthetic drugs, drug extravasation, extravasation.

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Introduction

Intravenous (IV) administration of drugs is frequently employed to achieve rapid and effective systemic effects. However, it is undesirable to administer the drug into the tissue as a result of extravasation of the IV cannula. To prevent extravasation, trainings are continuously provided by health authorities worldwide through postgraduate education or inservice training in clinics. With the widespread use of quality management systems, extravasation events are recorded with adverse event feedback records. Guidelines for preventing and managing extravasation have also been published by health authorities. The main reason for constantly keeping extravasation on the agenda and trying to prevent it is the severity of tissue damage that it may cause. Extravasation is of particular importance for medical anesthetists. The closed extremities to which the IV route is applied due to the surgical method to be applied make it difficult to access the vascular access during surgery, the use of pressurised instruments in IV drug administration and the inability of patients to report their pain due to unconsciousness make the work of the anaesthetist difficult. Due to these difficulties, large volumes of drugs and solutions may be administered extravenously. Thus, it is extremely important for healthcare professionals and patients to predict the degree of damage that may occur in the extravasation of anesthetic drugs.

Extravasation and Infiltration

Extravasation and infiltration are the conditions in which the drug is injected into the subepidermal or perivascular area as a result of the cannula being outside the vein while the drug is intended to be injected intravenously. If the drug is in the vesicant group, it is called extravasation; if the drug is not in the vesicant group, it is called infiltration. In both conditions, serious damage may occur at the tissue level.[1]

The clinical conditions that occur due to extravasation range from mild local irritation to tissue necrosis, tissue and limb loss, as well as nerve, tendon, and joint contractures and deformities. Severe tissue injuries due to extravasation may require extensive surgical treatment.[2]

Address for correspondence: Ahmet Şen, MD. Sağlık Bilimleri Üniversitesi Trabzon Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Trabzon, Türkiye

Phone: +90 462 341 56 41 **E-mail:** ahmetsenau@gmail.com

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The incidence of extravasation in adults has been reported to be between 0.1% and 6%,[3] whereas in pediatric patients, it is approximately 11%.[4] There is no comprehensive statistical information about extravasation of anesthetic substances in the literature.[5]

Risk Factors

In the literature and extravasation management guidelines, the risk factors related to the development of extravasation are categorized into patient-, procedure-, and product-related factors.

Patient-related factors include thin and fragile vasculature of infants, children, and elderly patients, hard and thick vasculature (particularly in patients receiving chemotherapy), obesity, excessive movement during venipuncture, prolonged drug infusions, Raynaud's syndrome, uncontrolled diabetes mellitus, severe peripheral vascular disease, and circulatory disorders such as lymphoedema and vena cava superior syndrome.[6]

Procedure-related factors include inexperienced or untrained personnel and multiple cannulation attempts.[3] Additional procedural factors for anesthetic drugs include unconsciousness of the patient and the use of automatic syringe pumps and pressurized bags for the infusion of drugs. If the intravascular cannula is incorrectly placed, these devices will continue to deliver the drug pressurized into the perivascular space. Furthermore, large volumes of fluid may pass into the perivascular space intraoperatively because the extremities are covered with sterile drapes.[7]

Extravasation may also occur in central venous catheters, which is even more dangerous because it is difficult to detect.[5] In all three cases, the amount of extravasated drug and the area where the drug is distributed will significantly increase, which will worsen tissue damage.

Finally, product-related factors include the use of poor or inappropriate materials.[3,6] Intravascular administration of drugs and solutions is considered to be a risk factor for the development of tissue damage in extravasation.[5] The physicochemical properties of drugs and solutions affect the degree of tissue damage. However, these properties vary depending on the adjuvant substance used in drug production. Some substances used as adjuvants (e.g., polyethylene glycol, benzyl alcohol, and propylene glycol) may contribute to tissue damage by changing the physicochemical properties of drugs and by triggering inflammation.[8] For this reason, many countries attempt to establish lists of noncytotoxic drugs according to their potential to cause tissue damage according to the information obtained from drug manufacturers through working groups.[9,10]

Clinical Features of Extravasation

Extravasation and infiltration-induced extravasation may cause limited local tissue inflammation and lead to severe pain, tissue necrosis, or compartment syndrome and even limb loss if not appropriately managed. Therefore, clinical staging of extravasation has been performed to manage it (Table 1).[11]

Symptoms of extravasation injury can be analyzed in two separate windows: early and late symptoms.[5,12] Dougherty divided the symptoms into postextravasation symptoms and symptoms after 24 h.[12] In the early period of extravasation damage, the findings are usually mild. These findings occur immediately after leakage but may persist for days or weeks. Initially, local stinging and burning pain, edema, and itching develop in the infusion area. The intensity of the pain may increase or decrease over time. Within 2 or 3 days, erythema, hardening of the tissue, shedding of the skin, or formation of blisters at the infusion site may develop. These findings may disappear or become more severe in a few days.[13] If tissue damage is severe, ulcer, necrosis, and eschar formation may occur within a few days. No granulation tissue is present in these ulceration areas. If the patient is not treated, permanent damage of the tissue, including in the joints, nerves, and tendons, may occur.[14,15]

Classification of Drugs and Solutions According to Their Potential to Damage Tissues in Case of Extravasation

Drugs can be divided into three classes according to their potential to develop tissue damage after extravasation: vesicants, irritants, and nonvesicant drugs.

1. Vesicant agents are substances that cause pain, inflammation, and consequently tissue necrosis and tissue death in tissues after extravasation. Drugs classified as vesicants are divided into two groups: those that bind to DNA and those that do not bind to DNA. Vesicant agents mainly include chemotherapeutics, hyperosmolar solutions, parenteral nutrition solutions, drugs and solutions with high acid or alkaline properties with pH outside the range of 5.0–9.0, and vasoconstrictive agents.[16] An evidence-based list of noncytotoxic vesicant drugs was published by the Global Scale Infusion Nurses Association in 2017.[9]
2. Irritant agents cause local irritation, burning, and pain sensation. The tissue damage is limited to localized inflammation and rarely progresses to tissue damage.[17]
3. Nonvesicant agents are a group of drugs that can rarely cause localized tissue damage and generally do not have effects similar to those of irritant or vesicant drugs.[18,19]

Clark et al.[20] published a table in which drugs are classified according to their potential to cause tissue damage in case

Table 1. Clinical staging of extravasation[11]

Grade	Symptoms
1	Painful infusion site
	No redness
	Local edema (1%–10% of the extremity)
	Pulse is taken
2	Painful infusion site
	Local edema (up to 25% of the extremity)
	Mild erythema localized in the central area of extravasation
	Rapid capillary refill at the leak site (1–2 s)
	Pulse is taken
3	Painful infusion site
	Moderate edema in the infusion area (25%–50% of the extremity)
	Marked erythema (extending beyond the center of extravasation)
	Rapid capillary refill at the leak site (1–2 s)
	Balancing (only in vasopressor agent extravasation)
	Cold skin
	Pulse can be taken
4	Painful infusion site
	Significant edema in the infusion area (more than 50% of the extremity)
	Extremely marked erythema
	Disruption of skin integrity, including necrosis
	Capillary filling time prolonged for >4 s
	Balancing (in the extravasation of a nonvasopressor agent)
	Cold skin
	No or decreased pulse in the extremity

of extravasation (Table 2). According to this classification, drugs are divided into three types according to their potential risk status. Drugs with red code are classified as high risk, drugs with yellow code as medium risk, and drugs classified with green code as low risk. While creating these classifications, the properties of the drugs in terms of pH, osmolality, vasoactivity, and cytotoxicity were examined, and lists were created considering these properties. In the lists, the red code corresponds to vesicant drugs, the yellow code to irritant drugs, and the green code to nonvesicant drugs. Again, in the study by Clark et al.[20] it was emphasized that peripheral IV infusion was not safe. Even saline in the nonvesicant group may cause compartment syndrome if extravasated in large volumes.[20]

Shibata et al.[16] grouped noncytotoxic agents according to their physicochemical properties and their potential to develop pathophysiological damage based on case reports and the results of animal experiments. The agents were divided into seven groups: vasoconstrictive agents, direct cytotoxic agents, concentrated electrolyte solutions, hyperosmolar solutions, acidic agents, basic agents, and agents causing mechanical compression. The drugs in these seven groups were classified as vesicant agents, irritant agents, and agents that do not damage the tissue (Table 2). The main reason for classifying the drugs in this way is that extravasation injury mechanisms are closely related with the physicochemical properties of the drugs. Shibata et al.[16] The summary table of drugs used in anesthesia induction and intensive care, which was created from the tables of drugs made by Shibata et al.[16] and Clark et al.,[20] is given in Table 2.

Pathophysiological Mechanisms of Tissue Damage Due to Extravasation

The osmolarity, pH values, and cytotoxicity potentials of extravasated drugs and solutions, degree of vasoconstriction or vasodilatation caused by the drug on the vessel wall, mechanical compression effect that develops in direct proportion to the amount of fluid leaking into the perivascular area, concentration of the drug in the solution, and duration of leakage are highly effective in the severity of tissue damage that will develop. The patient's age, comorbidities, and anatomical structures in the area where fluid leakage occurred are effective in the severity of the damage that may occur. Therefore, the pathological mechanisms of extravasation can be explained not only by a single pathway but also by the combination of many mechanisms. The

Table 2. Classification of some specific drugs used in anesthesia induction and intensive care according to their potential to cause tissue damage in extravasation

	According to SHIBATA		According to CLARK
Vasoconstrictive agents	Vesicants	Adrenaline 1 mg/mL Noradrenaline 0.05–0.3 µg/kg/min Dopamine hydrochloride > 5 µg/kg/min Dobutamine hydrochloride ≥ 10 µg/kg/min	High Risk (Red)
	Irritants		
	Nonvesicant agents		
Hyperosmolar agents	Vesicants	25%–50% Glucose	High Risk (Red)
	Irritants	10%–20% Glucose, 10%–20% Mannitol	High Risk (Red)
	Nonvesicant agents	5% Glucose, 5% Mannitol	Low Risk (Green)
Concentrated electrolyte solutions	Vesicants	10% Sodium chloride	High Risk (Red)
	Irritants		
	Nonvesicant agents		
Direct cytotoxicity	Vesicants	Diazepam 5 mg/mL, Digoxin 0.25 mg/mL	Medium Risk (Yellow)
	Irritants		
	Nonvesicant agents		
Basic Drugs	Vesicants	Thiopental sodium 25 mg/mL	Medium Risk (Yellow)
	Irritants	Dantrolene sodium hydrate 0.33 mg/mL	
	Nonvesicant agents		
Acidic Drugs	Vesicants	Vancomycin hydrochloride > 10 mg/mL	Medium Risk (Yellow)
	Irritants	Vancomycin hydrochloride < 10 mg/mL	Medium Risk (Yellow)
	Nonvesicant agents		
Mechanical compression	Vesicants	Propofol 10 mg/mL	
	Irritants		
	Nonvesicant agents		

pathophysiology of extravasation has not yet been fully explained due to the combination of many factors.[2,21]

The six possible mechanisms used to explain the tissue damage occurring in extravasation have been defined as follows:[16]

1. Direct damage due to cytotoxic agents
2. Damage formation due to vasoconstriction
3. Damage due to the formation of osmotic pressure gradient across the cell membrane with hyperosmolar/hypoosmolar substances
4. Damage due to mechanical compression
5. Damage caused by substances that do not have a physiological pH (acidic and basic)
6. Damage formation due to absorption resistance mechanism.

Direct Cytotoxicity Mechanism

The direct cytotoxic mechanism explains the tissue damage caused by the infusion of chemotherapeutic drugs.[11] Anesthetic drugs do not exert a direct cytotoxic effect on cells.[5] Therefore, this item was not mentioned in the section of explanation of pathophysiological mechanisms in our article.

Damage Formation due to Vasoconstriction

Tissues exposed to vesicants are at risk due to vasoconstriction caused by vasopressors and nonvasopressors. Vasoconstriction is induced chemically and mechanically. Vasopressors and electrolyte solutions induce vasoconstriction chemically. Mechanical induction of vasoconstriction with large volumes of extravasated fluids and drugs or with small amounts of fluids because of anatomical regional stenosis may cause circulatory disruption and develop ischemia.[11]

Extravasated vasopressors are thought to cause vasoconstriction in the vessels, capillaries, and vasa vasorum in the area of leakage, leading to local ischemia and consequently skin damage. The main cause of vasoconstriction is α-adrenergic stimulation caused by high doses of vasopressors in the infiltration area. Vasospasm developing as a result of α-adrenergic stimulation decreases the distal blood flow in the infusion area. The hydrostatic pressure in venous structures increases, which significantly causes vasopressors to pass into the tissues. As the distribution area of vasopressors in the tissue expands, ischemia expands in the same region in parallel. The α-adrenergic stimulation pathway is used by noradrenaline, adrenaline, dopamine, ephedrine,

dobutamine, and phenylephrine among vasoconstrictor agents. Vasopressin exerts its vasoconstriction effect by using the inositol 1,4,5-trisphosphate-mediated signaling pathway via the V1 receptor.[4]

Dopamine, noradrenaline, and adrenaline were compared in an experimental rat model by Shibata et al.[21] It was reported that local skin lesions caused by all three agents in the first 24 h were similar. In subsequent follow-ups, it was observed that there were differences in the severity and healing times of the lesions. Using the experimental extravasation method with dopamine, ulcer development was not observed, and tissue healing occurred within 5–7 days. Conversely, using the experimental model with noradrenaline and adrenaline, ulcer development was observed in the lesion area, and the tissue healing time was 18–23 days, which was significantly longer than that with dopamine. This suggested that the damage caused by dopamine was milder than that caused by noradrenaline and adrenaline.

While extravasation injury has been reported with high doses of dopamine and dobutamine, tissue necrosis has rarely been reported with low doses of these drugs. Extravasation of low doses of dopamine and dobutamine frequently causes localized inflammation and edema.[16] IV infusion of phenylephrine and noradrenaline, which are short-acting vasopressors, is frequently employed in operating theaters because hypotension is observed at rates ranging from 5% to 99% during general anesthesia.[22] In intensive care units, the use of noradrenaline IV infusion and other vasopressor agents is recommended, particularly in the treatment of sepsis and vasogenic shocks.[23] There are many case reports on intraoperative vasopressor extravasation and tissue damage in intensive care units and operating theaters.[24,25]

The potential of noradrenaline extravasation to cause permanent skin damage is a source of concern among anesthetists; thus, noradrenaline is not widely used in anesthesia practice in the USA.[26] Based on this concern, a retrospective cohort analysis was conducted by Pancaro et al.[26] to determine the major risks after perioperative noradrenaline infusion. In the study, 14,385 patients who received noradrenaline infusion between 2012 and 2016 were analyzed. It was reported that extravasation occurred in five patients. In the same study, the estimated risk rate of extravasation was 1–8 events per 10,000 patients.

The physicochemical properties of vasopressor drugs commonly used by anesthetists are given in Table 3.

Damage due to Osmotic Pressure Gradient Across the Cell Membrane with Hyperosmolar/Hypoosmolar Substances

Hyperosmolar solutions cause tissue damage by applying osmotic pressure when extravasated. Drugs with osmolality ≥500 mOsm/L and ≤200 mOsm/L are classified as vesicant drugs. The higher the osmolarity of hyperosmolar solutions, the higher their potential to cause tissue damage.[39] Table 4 presents the osmolarity and pH of some drugs used in anesthesia induction and intensive care.

When hyperosmolar solutions pass through the perivascular space, they create an osmotic gradient on the cells in the perivascular space, causing the fluid inside the cell to move out of the cell, whereas hypoosmolar solutions direct the water into the cell, causing cell disintegration and hemolysis. Both mechanisms may cause tissue damage in case of extravasation. Cell damage is more pronounced, particularly in hyperosmolar solutions. The effects of hyperosmolar solution in the extravasated area continue until the high osmolarity of the solution reaches isotonic osmolarity levels. Therefore, even in small amounts, tissue damage caused by hyperosmolar fluids may be serious. There are very few reports of tissue damage due to extravasation of hypoosmolar agents in the literature. Hyperosmolar cation-containing solutions, develop another damage mechanism with protein denaturation by collapsing with proteins in addition to osmotic damage at the cellular level.[16,39,40]

Osmotic stress caused by extravasation of hyperosmolar solutions causes the formation of reactive oxygen radicals in cells, DNA and protein damage, changes in cell membrane permeability, and finally induction of apoptosis. As a result of apoptosis, cellular death and tissue destruction occur in parallel.[4]

Calcium salts are among the noncytotoxic agents for which tissue damage due to extravasation has been reported the most.[41] Calcium salts increase the amount of fluid in the extravasation area by increasing the osmotic gradient and triggering the inflammatory response, causing vasodilatation and increase in the permeability of capillaries.[42] Furthermore, calcium salts may cause protein denaturation and soft-tissue calcification in the extravasated area.[40]

Mannitol, a hyperosmolar solution, is frequently used in neurosurgical operations and nephrectomy to control increased intracranial pressure after brain damage and also in intensive care units as part of antiedema treatment.[43] Mannitol extravasation is important because of its frequent use in anaesthesia and the severity of the damage it can cause. Mannitol has strong osmotic properties. When infused into the perivascular tissue, 1 L of fluid is expected to pass from the intracellular and intravascular spaces to the extracellular space for every 50 g of mannitol. When this fluid passes through the intravascular space, it can be easily tolerated. However, one of the main problems in extravasation is the anatomical narrowness of the area, which poses a major problem in mannitol extravasation. Compartment syndrome develops when interstitial pressure exceeds the capillary perfusion pressure in muscle sections in the infusion area.

Table 3. Summary table of physicochemical properties, vesicant status, extravasation injury mechanism, and case reports of some agents commonly used in anesthesia practice

Drug name	Physicochemical properties	Vesicant	Reports on extravasation and tissue damage mechanisms
Atropine	pH: 3.5–6.0		No case reports
Adrenaline	pH: 2.5–5 273–348 mOsm	Yes	Mechanism of tissue damage due to vasoconstriction Tissue necrosis[9,20]
Noradrenaline	pH: 3–4.5 278–300 mOsm	Yes	Mechanism of tissue damage due to vasoconstriction Tissue necrosis[9,26]
Vasopressin	pH: 2.5–4.5	Yes	Mechanism of tissue damage due to vasoconstriction Tissue necrosis[9,20]
Ephedrine	pH: 4.5–6.5	Yes	Mechanism of tissue damage due to vasoconstriction Tissue necrosis
Dopamine	pH: 2.5–5 261–619 mOsm	Yes	Mechanism of tissue damage due to vasoconstriction Tissue necrosis[27–29]
Dobutamine	pH: 2.5–5.5 273–361 mOSm	Yes	Mechanism of tissue damage due to vasoconstriction Phlebitis, local inflammation, tissue necrosis[9]
Propofol	pH: 6.0–8.5 307–335 mOsm	No	Mechanism of resistance to mechanical compression and absorption Tissue necrosis[30–32]
Thiopental	pH: 10.7–11.1 392–400 mOsm	Yes	Alkali drug-induced tissue damage mechanism Tissue necrosis, ischemia
Midazolam	pH: 3.5–3.8 261–280 mOsm	No	No case reports
Etomidate	pH: 4.0–7.0	No	No case reports
Ketamine	pH: 3.5–5.5 280–307	No	Local erythema, edema[33]
Dexmedetomidine	pH: 4,1–5.6 277–306mOsm	No	No case reports
Remifentanil	pH: 3.4–3.7 287–293 mOsm	No	Tissue damage mechanism unknown Local erythema, edema, and bullae development[34]
Fentanyl	pH: 4.2–5.1 280–299 mOsm	No	No case reports
Morphine	pH: 2.5–6.5 275–287 mOsm	No	No case reports
Pethidine hydrochloride	pH: 3.5–6.0	No	No case reports
Tramadol hydrochloride	pH: 1.9–7.0	No	No case reports
Succinylcholine	pH: 3.5–4.0 338 mOsm	No	No case reports
Atracurium	pH: 3.0–3.65	No	Ischemia–Necrosis
Vecuronium	pH: 3.8–4.2	No	Report of prolonged curarization[35]
Rocuronium	pH: 3.9–4.0 279–300 mOsm	No	Report of recurrence,[36,37] local irritation[2]
Pancuronium	pH: 3.8–4.2	No	Report of prolonged curarization[38]
Neostigmine	pH: 3.0–5,0	No	No case reports
Sugammadex	pH: 7.0–8.0 300–500 mOsm	No	No case reports
Flumazenil	pH: 4.0–4.1 297–300 mOsm	No	No case reports

Table 4. Osmolarity and pH values of vesicant drugs and solutions frequently used in anesthesia practice and intensive care[5]

Classification	Medicines	Osmolarity	pH
Vasoconstrictive agents	Epinephrine (1 mg/mL)	295–350 mOsm /L	2.2–4.0
	Norepinephrine (1 mg/mL)	310–350 mOsm /L	2.0–4.5
	Vasopressin	Unknown	2.5–4.5
	Dopamine infusion (5 mg/mL)	270 mOsm /L	2.5–5
Concentrated electrolyte solutions	Calcium chloride (5.5%)	1.500 mOsm /L	5–7
	Calcium gluconate (10%)	658 mOsm /L	5.7–7.7
	Potassium chloride (7.45%)	2.000 mOsm /L	5.0–7.0
	Sodium chloride (10%)	3.400 mOsm /L	5.0-7.0
	Sodium bicarbonate (4.2%/8.4%)	1000/2000 mOsm /L	7.0–8.5
Hyperosmolar solutions	Glucose 20%	1.118 mOsm /L	3.5–5.5
	Mannitol 15%	825 mOsm /L	3.6–6.6

Tissue perfusion is impaired and tissue hypoxia develops. If not properly managed, ischemic necrosis may develop as a result of tissue hypoxia.[44]

Damage due to Acidic and Basic Drugs

Physiological pH:7,4. The pH range accepted as physiological is 5.0–9.0. Drugs and solutions with pH values outside this range (≤5.0 and ≥9.0) are considered to be vesicant. Drugs and solutions with pH values <2 and >11 are thought to cause significant tissue damage in extravasations. Those with pH values close to the physiological pH range are considered to cause the least damage.[39]

The main reason for tissue damage caused by extravasation of acidic drugs and solutions is that acidic substances cause coagulation necrosis and form scar tissue.[4,16]

The main reason for tissue damage in the extravasation of alkaline substances is that this substance releases hydroxyl ion. Hydroxyl ion causes protein denaturation, collagen damage in the extracellular matrix, and apoptosis. At the end of this process, tissue necrosis develops. Tissue damage caused by alkaline substances is more severe and deeper than damage caused by acidic substances. This is because the hydroxyl ions produced by alkaline substances continue to cause tissue damage until they are completely neutralized.[4,16]

Sodium thiopental, which is widely used in anesthesia practice, belongs to the vesicant drug group. In a study conducted by Shibata et al.[45] on rats, it was demonstrated that thiopental caused skin necrosis. Skin lesions developed immediately after thiopental injection, and these lesions reached the maximum intensity within 24 h. Edema, degeneration, inflammatory cell migration, and necrosis were observed in epidermal, dermal, and subcutaneous tissues 24 h after injection. Regeneration of the epidermis, excoriation of granulation and necrotic areas, and development of eschar were reported 2–3 days after injection. The lesions are reportedly hard, erythematous, and oval in shape. Furthermore, ulceration was observed on the lesion ground, and epidermal integrity was completely restored within 18–27 days after treatment. According to the result, it was concluded that extravasation of thiopental is serious and that this drug should be classified as vesicant.

Mechanism of Damage Formation due to Mechanical Compression

Large amounts of extravasated drugs may cause a decrease in tissue perfusion due to the high hydrostatic pressure they place in the tissue space. As a result of decreased tissue perfusion, compartment syndrome and permanent tissue damage may occur. This damage mechanism is frequently observed in cases of fluid administration using automatic syringe pumps or pressurized bags. The mechanism of damage due to mechanical compression is independent of the physicochemical properties of the drugs infused into the lesion area.[16]

Propofol is a commonly used drug in anesthesia, has physiological pH and osmolarity, and is not expected to cause tissue necrosis or compartment syndrome. However, Kalraiya et al.[30] reported a case of compartment syndrome due to the extravasation of propofol. According to the case report, 3,410 mg of propofol was administered to the patient using an infusion pump during the perioperative period. However, propofol extravasated and compartment syndrome developed afterward.[16] The most probable cause of the damage was the mechanical compression mechanism generated by the drug in the tissue. Although rare, cases of tissue necrosis with propofol have been reported.[16,30–32]

Mechanism of Damage Formation by Absorption Resistance Mechanism

Absorption resistance mechanism was proposed as the 6th pathophysiological mechanism of extravasation injury by Ong et al.[11]. If drugs that are not well absorbed by the tissues (e.g., lipophilic drugs) are extravasated, they may remain in the infusion area for a long time and cause necrosis in the tissue and compartment syndrome.[11]

The fact that propofol, an anesthetic drug, is resistant to absorption owing to its presence in lipid solvent is a factor facilitating the formation of compartment syndrome.[45]

Conclusion

Although few drugs are mentioned about extravasation of anesthetic drugs, these drugs are widely used and the damage they cause may cause serious complications. In addition to anesthetic drugs, adjuvant and inotropic drugs are frequently used, and follow-up of patients administered with these drugs is important because of complications due to extravasation. While there are few studies in the literature about extravasation of drugs, there are almost no studies mentioning extravasation with anesthetic drugs. In the operating theater and intensive care unit for anesthesia practice, induction, fluid therapy, nutrition, etc., although rare, difficulty in vascular access maintenance and drug extravasation in many procedures cause serious complications. We aimed to emphasize the importance of perioperative anesthetic drug extravasation and its physiopathology by presenting current information. We also believe that awareness of this issue should be increased.

Disclosures

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