Describing Intravenous Extravasation Injuries in Children (DIVE2 Study)

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ABSTRACT

Background: Extravasation is the erroneous delivery of IV medication or fluid into the extravascular space. Complications ranging from mild injury to amputation can result, depending on the physical and pharmacologic properties of the infusate. Children are at increased risk for extravasation injuries. There is a paucity of data on the treatment and outcomes of extravasation injuries, particularly in terms of the role of pharmacologic antidotes.

Objectives: To describe the incidence of extravasation at a tertiary pediatric care centre (as an update to a previous study), to identify the agents most commonly involved in extravasation injuries, to describe the antidotes used for management of injuries and their related adverse drug effects, and to describe complications related to injuries.

Methods: The medical records of pediatric patients who experienced an extravasation injury at the BC Children's and BC Women's Hospitals, between September 1, 2008, and September 30, 2020, were reviewed. Data regarding management (adherence with institutional protocol) and outcomes of injuries were collected.

Results: The 242 charts included in the analysis noted a total of 245 extravasation injuries, for an extravasation incidence of 0.04% per patient-day. Of the 242 patients, 110 were excluded from secondary outcome analysis due to lack of data detailing the extravasation event. Of the remaining 132 patients, the majority were neonates (n = 54, 40.9%), infants (n = 33, 25.0%), and children (n = 34, 25.8%), and more than a third were treated on general pediatric wards (n = 50, 37.9%). The medications most frequently involved were total parenteral nutrition with lipids (36/132, 27.3%), vancomycin (36/132, 27.3%), and IV fluids (35/132, 26.5%). Most of the patients had mild outcomes and recovered without complications. No adverse drug events from antidotes were reported.

Conclusions: The incidence of extravasation at the study institution remained low, with the medications involved being similar to those reported in the literature and the majority of patients having mild outcomes. Additional prospective studies are needed to assess the efficacy and safety of antidotes administered for extravasation injuries.

Keywords: extravasation, IV medications, pediatrics, hyaluronidase, phentolamine, infiltration

RÉSUMÉ

Contexte : L'extravasation est l'administration erronée de médicaments ou de liquides IV dans l'espace extravasculaire. Des complications allant d'une blessure légère à l'amputation peuvent en résulter, en fonction des propriétés physiques et pharmacologiques de la perfusion. Les enfants courent un risque accru de blessures par extravasation. Il existe peu de données sur le traitement et les conséquences des blessures par extravasation, notamment en ce qui concerne le rôle des antidotes pharmacologiques.

Objectifs : Décrire l'incidence des extravasations dans un centre de soins pédiatriques tertiaires (en tant que mise à jour d'une étude précédente), recenser les agents les plus couramment impliqués dans les blessures par extravasation, décrire les antidotes utilisés pour la gestion des blessures et leurs effets indésirables liés aux médicaments et décrire les complications liées aux blessures.

Méthodologie : Les dossiers médicaux des patients pédiatriques ayant subi une blessure par extravasation entre le 1er septembre 2008 et le 30 septembre 2020 aux hôpitaux BC Children's Hospital et BC Women's Hospital ont été examinés. Des données concernant la prise en charge (c'est-à-dire le respect du protocole de l'établissement) et les conséquences des blessures ont été recueillies.

Résultats : Les 242 dossiers inclus dans l'analyse indiquaient un total de 245 blessures par extravasation, pour une incidence d'extravasation de 0,04 % par jour-patient. Parmi les 242 patients, 110 ont été exclus de l'analyse secondaire des conséquences en raison d'un manque de données concernant les détails de l'extravasation. Sur les 132 patients restants, la majorité était des nouveau-nés (n = 54, 40,9 %), des nourrissons (n = 33, 25,0 %) et des enfants (n = 34, 25,8 %) et plus du tiers ont reçu des soins dans un service de pédiatrie générale (n = 50, 37,9 %). Les médicaments les plus fréquemment impliqués étaient la nutrition parentérale totale avec des lipides (36/132, 27,3 %), la vancomycine (36/132, 27,3 %) et des liquides IV (35/132, 26,5 %). Les conséquences sur la plupart des patients étaient bénignes et ils se sont rétablis sans complications. Aucun effet indésirable lié aux antidotes n'a été signalé.

Conclusions : L'incidence des extravasations dans l'établissement à l'étude est restée faible, les médicaments impliqués étant similaires à ceux rapportés dans la littérature et les conséquences pour la majorité des patients étaient bénignes. Des études prospectives supplémentaires sont nécessaires pour évaluer l'efficacité et la sécurité des antidotes administrés pour les blessures par extravasation.

Mots-clés : extravasation, médicaments IV, pédiatrie, hyaluronidase, phentolamine, infiltration

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INTRODUCTION

Extravasation is the erroneous delivery of medications to extravascular tissue, as a result of poor placement or displacement of a cannula or leakage of medication from the venous vasculature.[1,2] Neonates, infants, and children are at increased risk of extravasation because of their small blood vessels with weaker endothelia, immature skin, lack of subdermal fat, and limbs that are constantly in motion.[3-6] Furthermore, an inability to verbalize symptoms may put younger pediatric patients at increased risk of injury from extravasation, because they must rely on others to check the IV site to identify an injury.[3,7] A retrospective cohort study conducted at a Canadian tertiary care pediatric hospital (for patients who experienced injury between 2006 and 2008) reported an incidence of 0.04% per patient-day.[1] A study conducted at a pediatric hospital in Turkey reported a prevalence of 5.5 per 1000 patient-days for infiltration and 4.4 per 1000 patient-days for extravasation.[2]

Severe complications can result from extravasation injuries, including blistering, skin breakdown, severe swelling, diminished peripheral pulses and perfusion beyond the injury site, necrosis, and significant tissue injury requiring skin grafts and fasciotomy.[3,4] Amputation is an extreme consequence of extravasation.[8,9] Pharmacologic factors contributing to the risk of extravasation injury include pH (< 5 or > 9), osmolarity (< 281 mOsm/L or > 350 mOsm/L), vasoconstrictive potential, and cytotoxicity.[8] Most IV medications have one or more of these properties, putting patients at increased risk of extravasation injury. Some examples are antimicrobials, IV fluids and electrolytes, antineoplastic agents, parenteral nutrition fluids, and vasoconstrictors.[1,8]

Prevention of extravasation injuries is a priority when providing IV-based care. Strategies for prevention include training health care providers in cannula insertion, using standard guidelines for prevention and management of extravasation, performing frequent routine checks of the IV site and line (including overnight checks), reducing opportunities for patients or others to pull on the line, actively monitoring for pain and numbness, ensuring dryness of the IV site, ensuring visibility of the line, and using saline flushes before administration of substances known to carry a higher risk of injury.[7,10,11] Early identification and quick management of extravasation are critical to minimizing tissue damage, especially in pediatric patients, who are not always able to verbalize symptoms.[8] Supportive care, manual extraction of extravasated fluids with or without the use of surgical techniques, use of dispersal agents to dilute extravasated fluid, and use of pharmacologic antidotes are all potential options in the management of these injuries.[7]

The pharmacologic antidotes used to treat extravasation injuries include hyaluronidase, sodium thiosulfate, dimethyl sulfoxide, phentolamine, and dexrazoxane. Hyaluronidase is not on the market in Canada but can be obtained through the Health Canada Special Access Programme for use in the management of extravasation injury. Sodium thiosulfate, dimethyl sulfoxide, phentolamine, and dexrazoxane have been approved by Health Canada for other indications and have been used off-label for the management of extravasation injury.[12-15] Data concerning the use of antidotes in children is scarce, so information has been extrapolated from animal and adult studies.[1] The 2006–2008 study reported improper management for about half of patients with a documented extravasation injury, in that the relevant institutional guidelines were not followed.[1] As a result, the study institution created protocols with key practice changes to prevent and improve the management of extravasation and related injuries. Further investigation is required to determine how these changes have affected the incidence of extravasation, its management, and its complications at this institution.

The primary objective of this study was to describe the incidence of extravasation injuries at our institution (where the 2006–2008 investigation[1] also took place). The secondary objectives were to identify the agents most commonly involved in extravasation injuries, to describe the circumstances surrounding extravasation injuries, to describe the antidotes used for management of extravasation injuries and any related adverse drug effects, to determine the time to extravasation after the line was placed in situ and the time to treatment after extravasation, and to describe the complications and outcomes related to these injuries.

METHODS

This retrospective cohort study, based on the medical records of patients with documented extravasation injuries resulting from IV administration of medication or fluids, was undertaken at the British Columbia Children's Hospital, a tertiary care pediatric institution, and the British Columbia Women's Hospital neonatal intensive care unit, in Vancouver, British Columbia, after receipt of approval from the University of British Columbia / Children's and Women's Health Centre of British Columbia research ethics board. Patients were identified using British Columbia's Patient Safety Learning System (PSLS), a computerized system used by health care providers across the province to report adverse events, and the institutional pharmacy's dispensing records for antidotes used to treat extravasation injuries. Incidents appearing in both lists were counted only once.

Patients who were 19 years of age or younger at the time of a documented extravasation injury between September 1, 2008, and September 30, 2020, were included. The start date was chosen to capture events that occurred after the timeframe of the previous study. Documented extravasation injuries were considered to have been appropriately managed if the criteria outlined in Appendix 1 were met for the

extravasated drug. Data were extracted from the records by one investigator (J.A.D.), who used a standardized data collection form within the Research Electronic Data Capture (REDCap) web application. The Naranjo tool was used to determine the association between any adverse drug effects and the antidote administered.[16]

The outcomes of extravasation were categorized as follows: mild—recovery without complication, requiring no further consults or follow-up; moderate—resulting in superficial injury/scar or requiring consult with or management by the institutional plastic surgery service; severe—requiring any postdischarge follow-up solely for the purpose of managing the extravasation injury; critical—resulting in loss of limb or life because of the extravasation; or unknown—outcome not reported or patient transferred to another institution before the outcome was known.

The appropriateness of management following an extravasation injury was determined by the same investigator, using the criteria described in the institution's extravasation treatment protocol (Appendix 1). Information about the extravasated medications was obtained from the medical record or the incident report. In the event that the incident report did not specify the extravasated medication, data were obtained from the patient's medication administration records. If more than one medication was being co-infused through an IV access when an extravasation occurred, all medications were recorded as being involved in the incident.

Statistical Analysis

Descriptive statistics were used to report patient demographic data, characterize medications involved in extravasation injuries (causative agents and antidotes), and report adverse events of antidotes administered. Data are presented as medians with ranges (from lowest to highest value) for continuous variables and as numbers and percentages for categorical variables. The incidence of extravasation was calculated per number of inpatient days for all patients admitted to the study institution during the study period.

RESULTS

After removal of duplicate reports, a total of 121 reports from the PSLS and 141 antidote prescriptions from pharmacy dispensing records were identified, for a total of 262 charts. Twenty records were excluded (Figure 1) because of use of an antidote not related to management of an extravasation injury, resulting in 242 charts detailing 245 extravasation events (Figure 1). Of the extravasation injuries for which an antidote was prescribed, only 21.3% (30/141 records) had a corresponding incident report completed in the PSLS. All identified eligible events were included for calculating the primary outcome. Due to missing or incomplete data, 113 events (110 patients) were excluded, such that 132 events (involving 132 patients) were included for the secondary outcome analysis.

As noted above, the 242 charts included in the primary outcome analysis detailed a total of 245 extravasation injuries, for an extravasation incidence of 0.04% per patient-day. Table 1 describes patient and IV line characteristics for the 132 events (in 132 patients) used in the analysis of secondary outcomes. Extravasation injury treatment parameters and circumstances are described in Table 2. The most common medications involved in IV extravasations were total parenteral nutrition (TPN) with lipids, vancomycin, and IV fluids, although in some instances multiple medications were being infused through the same line (Table 3). Hyaluronidase was the most commonly used antidote (n = 92), followed by no antidote being administered (n = 38). Phentolamine was administered in only 2 cases. There were no indications for or use of dimethyl sulfoxide or dexrazoxane.

Extravasation management was appropriate (i.e., in accordance with the institutional protocol) in 78.0% (103/132) of the extravasation injuries. In all cases where an antidote was used to manage an extravasation injury, the

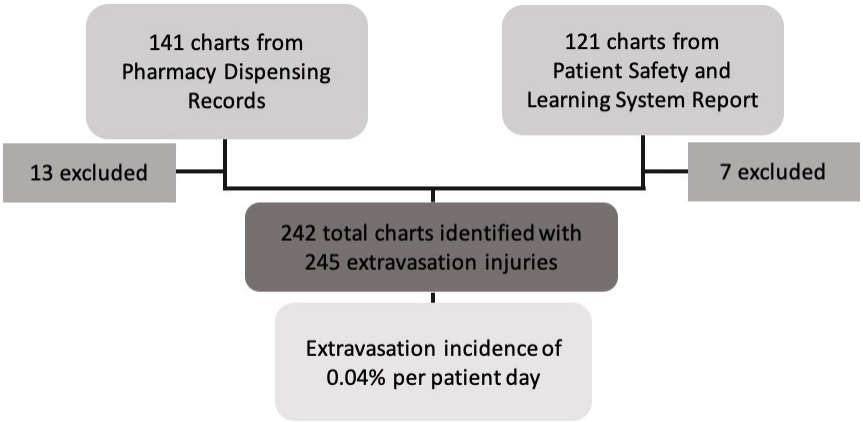

FIGURE 1. Study flow diagram. Calculation of extravasation incidence was based on a total of 609 006 patient-days.

antidote was selected correctly. Reasons for not following the institutional protocol included physician choice, recommendation against the protocol by the institutional plastic surgery service, and patient or family refusal. No adverse drug effects were reported from the antidotes administered.

TABLE 1. Patient Characteristics

Characteristic	No. (%) of Patients[a] (*n* = 132)
Age (years) (median and range)	0.15 (0.00–17.92)
Age group	
Premature neonate (< 37 weeks GA)	26 (19.7)
Term neonate (37 to 44 weeks GA)	28 (21.2)
Infant (1 to 12 months)	33 (25.0)
Child (12 months + 1 day to 12 years)	34 (25.8)
Adolescent (12 years + 1 day to 19 years)	11 (8.3)
Sex, male	73 (55.3)
Weight (kg) (median and range)	4.6 (0.83–100)
Admission diagnosis	
Prematurity	26 (19.7)
Respiratory distress	7 (5.3)
Congenital heart disease	7 (5.3)
Infectious disease	45 (34.1)
Seizure	16 (12.1)
Gastrointestinal disorder	17 (12.9)
Metabolic disease	2 (1.5)
Oncologic condition	2 (1.5)
Surgical condition	6 (4.5)
Other	4 (3.0)
Program area	
General medicine (CTU)	50 (37.9)
Neonatal intensive care unit	37 (28.0)
Pediatric intensive care unit	36 (27.3)
Emergency department	4 (3.0)
Surgery	3 (2.3)
Oncology	2 (1.5)
Type of line	
Peripheral IV	127 (96.2)
Implanted port	2 (1.5)
Central venous catheter	2 (1.5)
Intraosseous access	1 (0.8)
Location of IV access	
Right hand	22 (16.7)
Left hand	31 (23.5)
Right foot	23 (17.4)
Left foot	22 (16.7)
Right arm	13 (9.8)
Left arm	10 (7.6)
Scalp	8 (6.1)
Implanted port	2 (1.5)
Femoral vein	1 (0.8)

CTU = clinical teaching unit, GA = gestational age.
[a]Except where indicated otherwise.

The majority of patients experienced a mild outcome and recovered without any complications (Figure 2). Moderate, severe, and critical outcomes were experienced by smaller proportions of patients, with all patients in these outcome categories receiving treatment as per institutional protocol (Figure 2). Extravasated medications that were associated with severe outcomes were TPN (*n* = 3) and magnesium sulfate (*n* = 1). The single case of a critical outcome was associated with TPN; amputation of 2.5 toes was required. The outcome was unknown in 4.5% (*n* = 6) of the cases because of missing data or transfer of the patient to another institution before the outcome could be determined.

DISCUSSION

Extravasation of IV medications or fluids in pediatric patients is an uncommon event, and there is a paucity of published data on the management of extravasation injuries.[3,17] In this study, we found an extravasation incidence of 0.04% per patient-day, which is identical with the finding in the previous study at the same institution[1] and lower than that reported elsewhere.[18] Although no change in the incidence of extravasation was expected since the previous study,[1] given there had been little change in clinical practices and procedures for insertion of peripheral IV catheters, we observed an increase in the rate of management of extravasation injuries as per institutional protocol (78% in this study vs 50% in the 2006–2008 study[1]), which may reflect education and awareness of the extravasation protocol that occurred in the interim. However, there is still a

TABLE 2. Extravasation Injury Treatment Parameters and Circumstances[a]

Variable	Median (Range) or No. (%)
Time to extravasation after line in situ (hours) (*n* = 66 cases of extravasation)	27 (0.5–134)
Time to treatment after extravasation (minutes) (*n* = 75 cases of extravasation)	84 (15–435)
Acute circumstance	*n* = 14
Seizure	3 (21.4)
Accidental line displacement	4 (28.6)
Moving/repositioning patient	4 (28.6)
During imaging (CT or MRI)	3 (21.4)
Routine circumstance	*n* = 116
Fluid replacement	23 (19.8)
Bedside medication administration	59 (50.9)
Total parenteral nutrition	34 (29.3)

CT = computed tomography, MRI = magnetic resonance imaging.
[a]For each variable, the *n* value represents the number of cases of extravasation for which the relevant data were available (e.g., median time to treatment after extravasation was based on data from 75 patients who experienced extravasation).

TABLE 3. Medications Involved in 132 Extravasation Injuries (in 132 Patients)

Medication	No. (%) of Extravasations[a] (*n* = 132)
Vancomycin	36 (27.3)
Parenteral nutrition + lipids	36 (27.3)
D10W	18 (13.6)
D5W	10 (7.6)
Acyclovir	5 (3.8)
Cloxacillin	5 (3.8)
Phenytoin	5 (3.8)
Sodium bicarbonate	5 (3.8)
Dexmedetomidine	4 (3.0)
D12.5W/D25W	4 (3.0)
CT contrast	3 (2.3)
Normal saline	3 (2.3)
Cefotaxime	2 (1.3)
Ampicillin	1 (0.8)
Dopamine	1 (0.8)
Epinephrine	1 (0.8)
Furosemide	1 (0.8)
Ketamine	1 (0.8)
Magnesium sulfate	1 (0.8)
Mannitol	1 (0.8)
Methotrexate	1 (0.8)
Metronidazole	1 (0.8)
Midazolam	1 (0.8)
Morphine	1 (0.8)
Norepinephrine	1 (0.8)
Rocuronium	1 (0.8)

CT = computed tomography, D5W = dextrose 5% in water, D10W = dextrose 10% in water, D12.5W = dextrose 12.5% in water, D25W = dextrose 25% in water.

[a]Percentages sum to more than 100 because a patient with an extravasation injury might have been receiving more than one IV medication.

gap in terms of documentation in the PSLS of extravasation injuries managed with antidotes. Given the rarity of occurrence of these injuries, documentation in an adverse event or patient safety system is important to allow review, tracking, and trending of these types of safety events, as well as to drive improvements in patient safety through institutional practice changes. Thomas and Petersen[19] suggested that active clinical surveillance could be the most effective means of measuring adverse events. This strategy would integrate reporting of extravasation injuries in the PSLS with adherence to standardized management guidelines and outcome measures.[19] For example, the institution could make incident reporting mandatory every time an extravasation injury is identified or an antidote ordered and could emphasize protocol-based management/documentation so that information about such events could be collected in a standardized way for later review and analysis.

The properties of medications, including pH, osmolarity, vasoconstrictive potential, and cytotoxicity, are important risk factors for injuries from extravasation.[8] The most common infusates involved in extravasation injuries were vancomycin and TPN with lipids, both of which have many of the properties conducive to extravasation injury, as outlined in the Introduction. For example, vancomycin, a commonly prescribed antibiotic in the pediatric population, has a pH of 3.9,[20] below the threshold of 5 associated with risk of injury. As such, the risk of extravasation injury should be another consideration for discontinuation of vancomycin in patients with infections not requiring this particular antibiotic. The largest proportion of injuries by age group occurred in neonates, which may have been associated with the common use of TPN with lipids for the NICU population. Furthermore, TPN with lipids was the most common extravasated infusate reported for patients with severe and critical outcomes of extravasation injuries. These findings underscore the importance of preventive and timely management of extravasation, especially in neonates. The properties of TPN that increase the risk of extravasation injury include higher osmolarity (often > 900 mOsm/L to meet nutritional requirements) and the presence of other electrolytes, including calcium and potassium, that can cause cell death and injury.[21,22]

For all cases in which an antidote was used, the patient received the correct antidote for the medication/fluid extravasation. This is an improvement over the previous study, in which one patient received an incorrect antidote.[1] Based on the most commonly extravasated infusates and the institutional protocol, it was not surprising that hyaluronidase was the most commonly used antidote. No adverse drug effects were reported from the antidotes administered. However, the lack of reported adverse effects from antidotes could be due to a lack of recognition or documentation; for example, patient discomfort (pain or anxiety) during administration of an antidote may not have been recognized, or there might have been an inability to differentiate between this type of pain and the discomfort of the extravasation injury itself.

As expected and as described in the literature, the majority of extravasation injuries were associated with peripheral IV therapy in neonates and younger children.[7,23] More than one-third of the injuries occurred during routine administration of medications or IV fluids on general pediatrics wards, as opposed to acute situations or in critical care

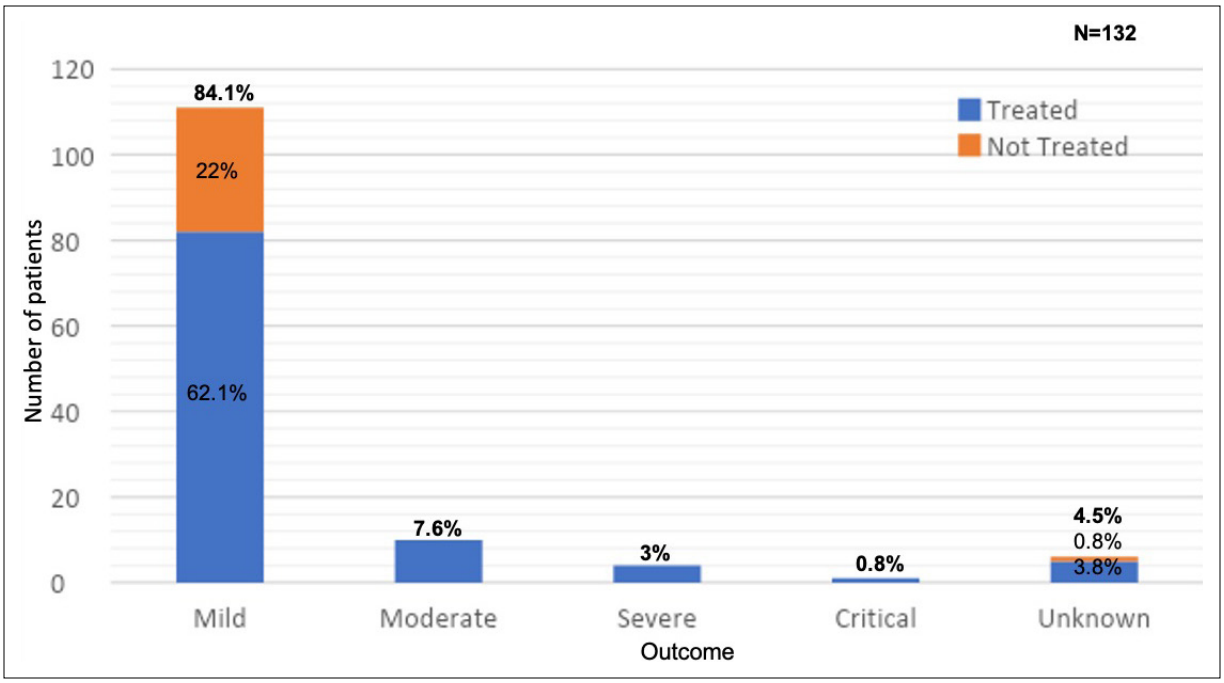

FIGURE 2. Outcome of extravasation injury, by presence or absence of treatment, for 132 events in 132 patients. Mild = recovery without complication (no follow-up required); moderate = plastics consult and management required, patient was left with scar or superficial injury; severe = long-term postdischarge follow-up required for extravasation injury; critical = extravasation resulted in loss of limb or loss of life; unknown = outcome not reported in chart or patient transferred before outcome was known.

areas. This finding may reflect less frequent "site to source" checks (which involve nursing staff tracing the tubing from site of the source syringe or bag to the site where the IV line crosses the patient's skin), protocolized management strategies for upkeep of IV lines, or more peripheral (vs central) lines in these units. Less commonly, extravasation occurred with other IV access types (implanted port, peripherally inserted central catheter, intraosseous vascular access, central venous catheter). These findings highlight the importance of proper monitoring and maintenance care strategies, regardless of setting or IV access type.

Given that extravasation injuries can threaten life or limb, they are considered medical emergencies requiring quick intervention. The primary goal of managing IV extravasation is to prevent progression of tissue necrosis and ulceration.[23] Timely administration of antidotes is expected to reduce tissue damage.[23] In this study, the median time to intervention with an antidote, when one was indicated, was 84 minutes (range 15–435 minutes), longer than the time reported in a study of extravasation in adult patients (mean 18.6 minutes).[24] Timely identification of extravasation and timely intervention may need to be considered in future quality improvement initiatives. Hanrahan[23] observed a significant reduction in the mean time to administration of hyaluronidase after implementation of an IV extravasation management guideline (125 minutes before implementation vs 76 minutes after implementation).[23] No data of this type are available from before implementation of our institution's extravasation protocol; however, data from the current study show a post-implementation time to administration of antidote similar to that reported by Hanrahan[23] (84 minutes vs 76 minutes).

Overall, the majority of patients who experienced extravasation injuries recovered, with only mild outcomes not requiring follow-up. Nonpharmacologic management alone has been reported as inadequate in the literature[2]; however, some patients in the current study experienced moderate to critical outcomes despite receiving an appropriately selected pharmacologic antidote. Given the severity of the injuries and the retrospective nature of this study, it is difficult to know whether management with antidotes improved injury outcomes.

This study had some limitations. The retrospective nature of the study might have led to bias due to underreporting or inconsistent reporting in the medical records. There is a risk of selection bias, because patients were identified through documentation of antidote medications and incident reports of extravasation; as such, minor injuries may not have been captured. Extravasation injuries that were neither managed with an antidote nor documented in the PSLS could not be identified, and the calculated incidence may therefore be low. Confounding bias may have been present, as there may have been other factors relating to the prescription of antidotes and the identification and documentation of extravasation injuries that might have influenced the results of the study. Even though

documentation of extravasation injuries was found to be quite robust, there may still be a risk of information bias, because there was a level of interpretation and subjectivity when extracting data from retrospective records. Lastly, limitations in access to complete charts for analysis of the secondary outcomes could have biased the results reported.

CONCLUSION

The incidence of extravasation remained low and unchanged from a previous study at the same pediatric tertiary care institution. The medications involved in extravasation injuries were similar to those previously reported in the literature. There was an improvement in management of extravasation injuries relative to the earlier study; however, documentation of extravasation injuries in the adverse events reporting system still requires improvement. The majority of extravasation injuries resolved without complications, and antidotes were well tolerated by patients. Further research should investigate the efficacy and safety of antidotes used to manage extravasation injuries and their place in therapy.

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APPENDIX 1 (part 1 of 2): British Columbia's Children's Hospital protocol for management of extravasation and infiltration. © 2021 BC Children's Hospital and BC Women's Hospital. Reproduced with permission.

PREVENTION AND MANAGEMENT OF INFILTRATION AND EXTRAVASATION – GUIDELINES FOR ANTIDOTE ADMINISTRATION

DOCUMENT TYPE: PROCEDURE

GUIDELINES FOR ANTIDOTE ADMINISTRATION

It is difficult to be certain that injection of antidotes into the area of extravasation is of benefit and reports are conflicting. Most small extravasations do not result in serious problems without injection of antidotes, so that injection of specific antidotes should likely be restricted to larger extravasations (>1-2 mL). The use of an antidote requires a physician's order. Antidotes, other than dimethylsufoxide (DMSO) and dexrazoxane are to be administered by a physician.

Extravasated Drug	Suggested Antidote	Method of Administration
daunorubicin doxorubicin epirubicin mitomycin	dimethylsulfoxide (DMSO) 99.9% **topical** solution (4 drops per 10 cm^2 area)	Apply to an area twice that affected by the extravasation, allow to air dry, do not cover, repeat 4 times per day for at least 7 days. **Do not use DMSO in conjunction with dexrazoxane. This combination may increase tissue damage.**
	dexrazoxane **intravenous (IV)** daily for 3 days	1. Dilute reconstituted dexrazoxane with Dextrose 5% or 0.9% sodium chloride to a final concentration of 1.3 to 5 mg/mL. 2. Administer daily over 1-2 hours 24 hours apart for 3 consecutive days: Days 1 & 2: 1000 mg/m^2/day (max 2000 mg) Day 3: 500 mg/m^2 (max 1000 mg) 3. Administer as soon as possible and within 6 hours of extravasation. 4. Remove cooling packs (if used) at least 15 minutes prior to start of dexrazoxane infusion. **5. Do not use DMSO in conjunction with dexrazoxane. This combination may increase tissue damage.** 6. Monitor for neutropenia, thrombocytopenia.
vinblastine vincristine vindesine vinorelbine aminophylline calcium chloride (> 10%) cloxacillin dextrose (≥ 10%) magnesium sulfate (>20%) mannitol	hyaluronidase 150 units/mL -2 mL vial **subcutaneous (SC) or intradermal** **DO NOT ADMINISTER INTRAVENOUSLY.** hyaluronidase (Amphadase ®) is available through Health Canada Special Access Program.	**Administration by physician only.** 1. Use four or five 1 mL syringes and draw up hyaluronidase 0.2 mL into each syringe. 2. Using a 27-30 gauge needle, inject 0.1-0.2 mL subcutaneously or intradermally in 4 to 5 sites around the circumference of infiltrate, using a new needle with each injection. 6. Wait 10-15 minutes and inject 3-5 mL 0.9% sodium chloride into each injection site. 7. Most benefit if injected within 1 hour of extravasation.
Parenteral Nutrition (PN) phenytoin potassium chloride (> 2meq/mL) radio contrast media sodium bicarbonate (8.4%) vancomycin		

APPENDIX 1 (part 2 of 2): British Columbia's Children's Hospital protocol for management of extravasation and infiltration. © 2021 BC Children's Hospital and BC Women's Hospital. Reproduced with permission.

dobutamine dopamine epinephrine norepinephrine phenylephrine	phentolamine (1mg/mL) **subcutaneous** (SC) **DO NOT ADMINISTER INTRAVENOUSLY.**	**Administration by physician only.** 1. Reconstitute 5 mg phentolamine vial with 5 mL normal saline (NS) to achieve a 1 mg/mL dilution 2. Use four or five 1 mL syringes and draw up 0.2 mL into each syringe 3. Using a 27-30 gauge needle, inject 0.1-0.2 mL subcutaneously in 4 to 5 sites around the circumference of infiltrate, using a new needle with each injection. Neonates:Do not exceed 0.1 mg/kg or 2.5 mg total Infants & Children: Do not exceed 0.2 mg/kg or 5 mg total 4. Wait 10-15 minutes and inject 3-5 mL normal saline into each injection site. 5. Blanching should reverse within 1 hour. Monitor site: If blanching recurs, additional phentolamine may be needed. 6. Most benefit if injected within 1 hour of extravasation but can be used up to 12 hours after extravasation.