ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803-5253

REGULAR ARTICLE

Younger age and *in situ* duration of peripheral intravenous catheters were risk factors for extravasation in a retrospective paediatric study

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Keywords
Extravasation, Neonatal intensive care unit, Neonates, Paediatric intensive care unit, Peripheral intravenous catheters

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Received
25 August 2017; revised 11 December 2017; accepted 14 February 2018.

DOI:10.1111/apa.14280

Some of this research was presented during poster sessions at the 2nd Congress of the Swiss Hospital Pharmacists, Interlaken, Switzerland (November 2014) and at the 20th Congress of the European Association of Hospital Pharmacists, Hamburg, Germany (March 2015).

ABSTRACT

Aim: Epidemiological data on the incidence and risk factors of extravasation of peripheral intravenous catheters (PIVC) in neonates and children are scarce and that is what this study explored.

Methods: This was a one-year retrospective study of all neonates and paediatric intensive care patients with at least one recorded PIVC at the Geneva University Hospitals, Switzerland, in 2013. The extravasation rate was determined for all patients, including neonates below 28 days, and for all PIVCs. Multivariate analysis of the associated risk factors was performed.

Results: We analysed 1300 PIVC in 695 paediatric patients with a median age of 1.5 years. The overall extravasation incidence was 17.6% for all patients and 11.7% for PIVC. The overall incidence rate of PIVC extravasation was 4.5 per 100 catheters days, and the risk was highest in the 201 neonates, at 28.4%. The incidence rate four days after insertion of the PIVC was around three times higher than on day one. Neonates and the *in situ* duration of PIVCs were associated risk factors ($p < 0.001$).

Conclusion: Extravasation was frequent and neonates were particularly at risk. Younger age and longer *in situ* PIVC duration were independent risk factors for extravasation.

INTRODUCTION

Extravasation is defined as the accidental injection or leakage of a solution such as a fluid, drug or parenteral nutrition into the subcutaneous or perivascular tissues (1). Extravasations are iatrogenic injuries that can have severe consequences for patients, including skin necrosis or compartment syndrome, and they may induce long-term injuries that need surgical procedures and grafts (2–6). The soft-tissue injuries resulting from extravasation are related to the solution's osmolarity, its inherent cytotoxicity or vasoconstrictive properties and the infusion pressure (7). Infiltration, which is seen as benign, is the term used in the literature when the leakage concerns nonvesicant solutions. However, tissue necrosis has even been observed with isotonic solutions, probably due to compression from the infiltrated volume (3,8). Extravasations contribute to extra patient morbidity and treatment costs and length of stay (9).

Parenteral infusion for neonates and children is particularly challenging due to the limited number of venous access sites, the small-bore of catheters and the small drug volumes (10,11). Small veins are difficult to cannulate and may predispose neonates and infants to extravasation.

Epidemiological data on extravasation in neonates and children are scarce and mainly based on case reports (2,4–6) or retrospective studies (8,12,13). An extravasation incidence of 16% has been reported for children from birth to 18 years of age who have been fitted with a peripheral intravenous catheter (PIVC) and hospitalised in a paediatric surgical ward (12). An extravasation incidence rate of 0.04 per patient day was calculated in another study of paediatric patients between birth and 18 years of age and

Abbreviation
PIVC, Peripheral intravenous catheter.

Key notes

- Epidemiological data on incidence and risk factors of extravasation of peripheral intravenous catheters (PIVC) in neonates and children are scarce.
- Our analysis of 1300 PIVCs in 695 paediatric intensive care patients showed that extravasation occurred in 17.6% of subjects at least once and in 11.7% of PIVCs or 4.5 per 100 catheters days.
- Younger age and longer *in situ* PIVC duration were independent risk factors that predisposed paediatric patients to extravasation.

93% of these cases involved a PIVC (8). Severe extravasation has been reported with an incidence of 2.4% in neonates, causing skin necrosis in 0.4% of cases (6). In another study, 38 per 1000 neonates experienced extravasation with skin necrosis (13). These patients had a mean postmenstrual age of 26.1 weeks and 93% of the injuries involved a PIVC. Different risk factors have been highlighted, such as low birthweight (6), continuous administration of hyperosmolar drugs (8) and intravenous therapy for more than five days or the presence of phlebitis (12). To our knowledge, only one study has evaluated the risk factors in a large sample of children with and without extravasation (14). Different drugs, for example phenytoin or 10% dextrose, and inserting a PIVC on a lower limb were independently associated risk factors for extravasation.

In our combined neonatal and paediatric intensive care unit, continuous infusions of highly concentrated drugs are administered through central venous catheters and less aggressive solutions can be given through PIVCs. However, in the last five years, several cases of extravasation of peripheral infusions in neonates and small children have been documented in our incident reporting system, some leading to skin necrosis and grafts. As extravasation contributes to patient morbidity, treatment costs and length of stay, it may be considered as a hospital indicator of quality of care. This study aimed to determine the extravasation rate of peripheral infusions in neonates and older paediatric patients and to evaluate the associated risk factors in order to better understand what can be carried out to prevent these iatrogenic injuries.

PATIENTS AND METHODS

This was a one-year retrospective cohort study of all neonates and paediatric patients hospitalised in 2013 in the neonatal and paediatric intensive care unit of the Geneva University Hospitals in Switzerland with at least one PIVC. The study was approved by the hospital's institutional ethics committee. No parental consent was required for this retrospective study.

Setting

The Geneva University Hospitals is a single institution. The neonatal and paediatric intensive care unit is a combined unit and is part of the Department of Paediatrics. It is a tertiary care centre with 35 beds consisting of 12 paediatric intensive care beds and 23 neonatal beds. About 1000 patients per year are hospitalised in the unit and these include 200 patients who mainly receive cardiac surgery and 500 patients who are admitted at birth because they are premature or otherwise need neonatal care. Other patients are hospitalised for different kind of surgical or traumatic pathologies, including about 10 patients per year for liver transplantation and other for infections such as bronchiolitis or sepsis. The patients included in this study ranged from birth to 18 years of age and were hospitalised between January and December 2013.

Vascular access is systematically documented on our electronic patient record system by nurses. Cardiac patients are hospitalised after surgery with one, two or three lumen central venous catheters and two PIVCs. Other paediatric intensive care patients have PIVCs. Preterm patients requiring parenteral nutrition or antibiotics are given an umbilical venous catheter for the first days of life and this is changed to a single lumen peripherally inserted central catheter if the treatment needs to be continued. Only a percentage of the preterm patients have a PIVC inserted and this depends on the number of drugs that need to be infused. Neonates with conditions such as hypoglycaemia or an infection risk have a PIVC. Late preterm and term neonates hospitalised for clinical surveillance often have no intravenous catheters and only a nasogastric tube if necessary. PIVCs may be placed by physicians or nurses. The PIVCs used in our unit are the BD Neoflon (Becton Dickinson Infusion Therapy, Helsingborg, Sweden), BD Insyte-N and BD Insyte-W (Becton Dickinson Infusion Therapy, Sandy, Utah, USA) and Vasofix Safety PUR (B Braun, Melsungen, Germany). Their sizes range from 14G to 26G. The *in situ* duration of PIVCs is not limited by our policies. An institutional document provides recommendations about which drugs can be delivered by a PIVC, based on drug concentrations and osmolarity.

The reasons for PIVC removals in the neonatal and paediatric intensive care unit are documented daily by nurses from the choices in the drop-down menu in our electronic patient record system. The items included in the menu are extravasation, blockage, accidental dislodgment, suspected infection, no longer needed and others. Drugs administered via the PIVC at the time of removal are not documented. In our unit, extravasation is used to describe any vesicant or nonvesicant inadvertent deposition of intended intravenous fluids or infusion, such as total parenteral nutrition or drugs, into local tissues. This terminology may differ from the ones used in other studies or guidelines that differentiate between infiltration injuries, defined as inadvertent leakage of a nonvesicant solution into the surrounding tissue, and extravasation injuries, defined as inadvertent leakage of a vesicant solution into the surrounding tissue (15).

Main outcome measurements

Entries described in the drop-down menu of the electronic patient record system as extravasation were defined as extravasation. Patients with at least one documented extravasated PIVC were compared to patients with a PIVC without extravasation. A subgroup analysis of neonates with a postnatal age of less than 28 days was performed.

The rate of extravasations linked to peripheral infusions was determined for all patients and PIVCs and for the subgroup of neonates. Associations between extravasation and risk factors, such as sex, gestational age, weight at admission, age at PIVC removal, *in situ* PIVC duration and the anatomical site of the PIVC insertion, were tested.

Data collection

Data were collected from the electronic patient record system, namely Centricity Critical Care 8.0 (General Electric

Healthcare, Barrington, IL, USA) according to an extraction model with specific search criteria. Demographic data, such as the patient's sex, age at admission, gestational age, weight at admission and age at PIVC removal, were extracted. The anatomical site of the PIVC insertion, recorded as the dorsum of the hand, forearm, antecubital fossa, the dorsum of the foot or ankle or others, was also collected.

The *in situ* PIVC duration in days was calculated from the date of PIVC insertion to the date of removal. Data were anonymised for each patient using a patient identification number.

Statistical analysis

An overall analysis of occurrences of extravasation for all PIVCs and patients was performed, followed by a subgroup analysis of the neonates. Demographic parameters and *in situ* PIVC duration were expressed as median values, with 25–75% interquartile ranges, and the minimum and maximum values. Patients with at least one documented extravasated PIVC were compared to patients with none using Fisher's exact test for categorical data and the Mann-Whitney test for continuous data. To assess the risk of PIVC extravasation, exposure time related to *in situ* PIVC duration was measured by assessing the incidence rate of PIVC extravasation using a Poisson regression model. To account for repeated measurements, as one patient could have several PIVCs, we used mixed-effects regression models with a random intercept. Univariate analyses were carried out to assess associations between the incidence of PIVC extravasation and different covariates, including sex and, gestational age, categorised as extremely preterm for less than 28 weeks, very preterm for less than 32 weeks, late preterm from 32 weeks to less than 37 weeks and full-term for 37 weeks of more. Postnatal age at the time of the PIVC removal was categorised as neonates, infants under the age of two, children aged two to 11 and children aged 12 or more. We also looked at the anatomical site of the PIVC insertion. We suspected that the risk of extravasation would vary with regard to the exposure time from the placement of a PIVC, and a time-dependent variable was added to the regression model to test this variation. Multivariate analyses were conducted to adjust for confounding factors. Weight and age at admission were not introduced in the multivariate models because of their strong correlation with age at PIVC removal, as determined by the Spearman correlation coefficient ($R = 0.96$, $p < 0.0001$ respective $R = 0.99$, $p < 0.0001$). Statistical significance was considered as a p value of <0.05. Two different software programmes were used for data handling and analysis: R version 3.3.1 (R Core Team, Vienna, Austria) and Stata software version 14.0 (Stata Corp, College Station, TX, USA).

RESULTS

We analysed 695 patients with a median age of 1.5 years who received 1300 PIVCs. More than half of the patients had several PIVCs simultaneously. The demographic characteristics of the patients and the PIVCs are described in Table 1.

The reasons for the PIVC removal were only documented in 30.8% of the cases extravasation was the main reason (11.7%), followed by no longer needed (9.3%), a blockage (5.7%) and accidental dislodgment (3.4%).

At least one extravasation occurred in 17.6% of patients and their age and weight at admission were significantly lower than in patients without extravasation. Patients with extravasation also had a higher number of PIVCs inserted, with 16.4% of patients having more than three PIVCs compared to 2.8% of the patients without extravasation. About half of the extravasated PIVCs had been placed in neonates. Extravasated PIVCs also had a longer *in situ* duration (Table 1).

The overall incidence rate of extravasation was 4.5 per 100 PIVC days, with a 95% confidence interval (95% CI) of 3.4–5.8. Although the patient's sex and the anatomical site of the PIVC showed no statistically significant association with the risk of extravasation, the incidence rate increased with the duration of the PIVC insertion and decreased as patients got older (Table 2). The incidence rate of extravasation in infants was one-third of the rate seen in neonates and was the lowest in children aged 12 or more. The incidence rate on day four after PIVC insertion was three times the incidence rate during the first day of PIVC insertion (Fig. 1).

A subgroup of 201 neonates with 272 inserted PIVCs was analysed. At least one extravasation occurred in 28.4% of patients and in 24.3% of the PIVCs. The median gestational age of the neonates with extravasation was 33.4 weeks (IQR 32.0–37.2, range 24.3–41.3 weeks) and was significantly lower than the median gestational age of those without extravasation, which was 36.3 weeks (IQR 33.6–39.4, range 24.1–42.0 weeks).

The overall incidence rate of extravasation in the subgroup of neonates was 12.6 per 100 PIVC days (95% CI: 9.9–16.0). The incidence rate was 5.9 per 100 PIVC days in the first day following PIVC insertion (95% CI: 9.9–16.0), 16.1 per 100 PIVC days between the first day and until the third day (95% CI: 11.2–23.1) and 17.7 per 100 PIVC days from the fourth day following insertion (95% CI: 6.7–23.1). In the multivariate analysis, *in situ* PIVC duration was an independent significant risk factor for extravasation. The incidence rate after the first day of PIVC insertion was around three times the incidence rate on the first day (Table 3).

DISCUSSION

Extravasation of a PIVC can lead to severe injuries in neonates and children. In the present study, 17.6% of a large sample of neonates and paediatric intensive care patients experienced extravasation, which was 11.7% of all the PIVCs inserted. Neonates were particularly at risk, with 28.4% experiencing extravasation. This was consistent with the literature, which reported that 22% of cases in a

Table 1 Overall data for patients and peripheral intravenous catheters

	All	Extravasation	No extravasation	p Value
Patients (n)	695	122	573	
Sex, n (%)				
Female	298 (42.9%)	51 (41.8%)	247 (43.1%)	0.87
Male	397 (57.1%)	71 (58.2%)	326 (56.9%)	
Age at admission (years)*	1.5 [0.0; 7.7] [0.00; 25.9]	0.3 [0.0; 2.5] [0.0; 18.2]	1.7 [0.1; 9.2] [0.0; 25.9]	<0.0001
Age at admission categorised, n (%)				
Neonates <28 days old (postnatal)	206 (29.6%)	60 (49.2%)	146 (25.5%)	<0.0001
Infants ≥28 days and <2 years	189 (27.2%)	29 (23.8%)	160 (27.9%)	
Children 2–11 years	189 (27.2%)	24 (19.7%)	165 (28.8%)	
Children ≥12 years	111 (16.0%)	9 (7.4%)	102 (17.8%)	
Weight at admission (kg)*	8.9 [3.4; 21.0] [0.6; 95.0]	4.2 [1.9; 11.6] [0.7; 80.0]	9.7 [3.7; 24.8] [0.6; 95.0]	<0.0001
PIVCs per patient, n (%)				
1	302 (43.5%)	38 (31.1%)	264 (46.1%)	<0.0001
2	271 (39.0%)	40 (32.8%)	231 (40.3%)	
3	86 (12.4%)	24 (19.7%)	62 (10.8%)1	
≥4	36 (5.2%)	20 (16.4%)	16 (2.8%)	
PIVC (n)	1300	152	1148	
Age of patient at PIVC removal (days)*	821 [83; 3892] [0; 9453]	132 [4; 966] [1; 6647]	984 [154; 4146] [0; 9453]	<0.0001
Age of patient at PIVC removal categorised, n (%)				
Neonates <28 days old (postnatal)	292 (22.5%)	71 (46.7%)	221 (19.3%)	<0.0001
Infants ≥28 days and <2 years	337 (25.9%)	37 (24.3%)	300 (26.1%)	
Children 2–11 years	406 (31.2%)	29 (19.1%)	377 (32.8%)	
Children ≥12 years	265 (20.4%)	15 (9.9%)	250 (20.4%)	
In situ duration of PIVC (days)*	1.6 [0.8; 2.7] [0.1; 19.4]	1.8 [1.1; 3.0] [0.1; 12.7]	1.5 [0.8; 2.7] [0.1; 19.4]	0.01
In situ duration categorised, n (%)				
<1 day	483 (37.2%)	33 (21.7%)	450 (39.2%)	0.0001
≥1 and <4 days	657 (50.5%)	94 (61.8%)	563 (49.0%)	
≥4 days	160 (12.3%)	25 (16.4%)	135 (11.8%)	
Anatomical site, n (%)				
Dorsum of hand	501 (48.4%)	53 (42.7%)	448 (49.1%)	0.31
Forearm	190 (18.3%)	20 (16.1%)	170 (18.6%)	
Antecubital fossa	78 (7.5%)	11 (8.9%)	67 (7.3%)	
Dorsum of foot or ankle	253 (24.4%)	39 (31.5%)	214 (23.5%)	
Others	14 (1.4%)	1 (0.8%)	13 (1.4%)	
MD**	264	28	236	

PIVC = Peripheral intravenous catheter.
*Expressed as median [interquartile range] [minimum and maximum values]. Patients with several PIVC are counted several times in the calculation of the median since the age of patients at each PIVC removal is accounted.
**Missing data.

neonatal unit involved PIVCs (8) and the rates were 12% in a paediatric intensive care unit (8) and 16% in a paediatric surgical ward (12). Severe extravasation has been reported in 2.4% (6) to 3.8% (13) of neonates, causing skin necrosis in 0.4% of the cases (6). The present study did not determine the severity of extravasation, as no grading scale was available in the electronic patient record system. It is probable that the majority of cases were benign, but this could not be definitively assessed.

The median *in situ* duration of PIVCs was 1.6 days and ranged from 2 hours to 19 days, which is similar to a study by Malyon et al. (16). Multivariate analysis revealed that age and the *in situ* duration of the PIVC were independent risk factors. The risk was highest in neonates. Gestational age was not a significant risk factor, even though a trend was noted. Similar results were found in a study of neonates where gestational age was not identified as a risk factor but was correlated with the incidence of skin necrosis (6). In our study, an *in situ* PIVC duration of more than three days was associated with a risk that was about 3.8 times greater than on day one. A PIVC retention time of more than 120 hours was reportedly associated with the occurrence of infiltration in children in paediatric medicine and surgery, but was not significant in the multivariate analysis (14). Our patients were younger, and most of them were critically ill, which may explain the observed difference.

The present study had several limitations, and the results should be interpreted with caution. First, as it was a retrospective study, its results may have been biased by under-reporting of extravasated PIVCs in the electronic patient records. For extravasated PIVCs, the quality of documentation on the circumstances was low and the reason for the PIVC removal in general was only documented in 30.8% of the cases. Device failure due to

Table 2 Associations between potential risk factors and the incidence of PIVC extravasation (n = 695 patients and 1300 PIVCs)

	Unadjusted IRR (95% CI)*	p Value	Adjusted IRR (95% CI)*,†	p Value
Sex				
Female	1 (Reference)	0.77	1 (Reference)	0.68
Male	1.06 (0.73–1.53)		1.09 (0.74–1.60)	
Age at PIVC removal, categorised				
Neonates <28 days old	1 (Reference)	Overall p < 0.001‡	1 (Reference)	Overall p < 0.001‡
Infants ≥28 days and <2 years	0.37 (0.25–0.57)	<0.001	0.33 (0.21–0.54)	<0.001
Children 2–11 years	0.24 (0.16–0.38)	<0.001	0.22 (0.13–0.36)	<0.001
Children ≥12 years	0.19 (0.11–0.35)	<0.001	0.16 (0.08–0.31)	<0.001
In situ duration of PIVC				
<1 day	1 (Reference)	Overall p < 0.001‡	1 (Reference)	Overall p < 0.001‡
≥1 and <4 days	3.22 (2.10–4.94)	<0.001	2.90 (1.91–4.40)	<0.001
≥4 days	4.03 (2.06–7.88)	<0.001	3.82 (2.02–7.24)	<0.001
Anatomical site				
Forearm	1 (Reference)	Overall p = 0.49‡		
Dorsum of hand	0.98 (0.57–1.69)	0.95		
Antecubital fossa	1.56 (0.72–3.38)	0.26		
Dorsum of foot-ankle	1.36 (0.77–2.39)	0.30		
Others	0.98 (0.12–7.80)	0.99		

PIVC = peripheral intravenous catheter, IRR: incidence rate ratio.

*Associations are expressed as incidence rate ratios which represent the ratio of incidence between a category and its reference category (for instance between male and female). An IRR > 1 indicates that the incidence is higher than in the reference category.

†The anatomical site was not introduced in the multivariable model because of the amount of missing data (MD see Table 1).

‡The overall p value is for the test on an overall difference of incidence rate across all categories.

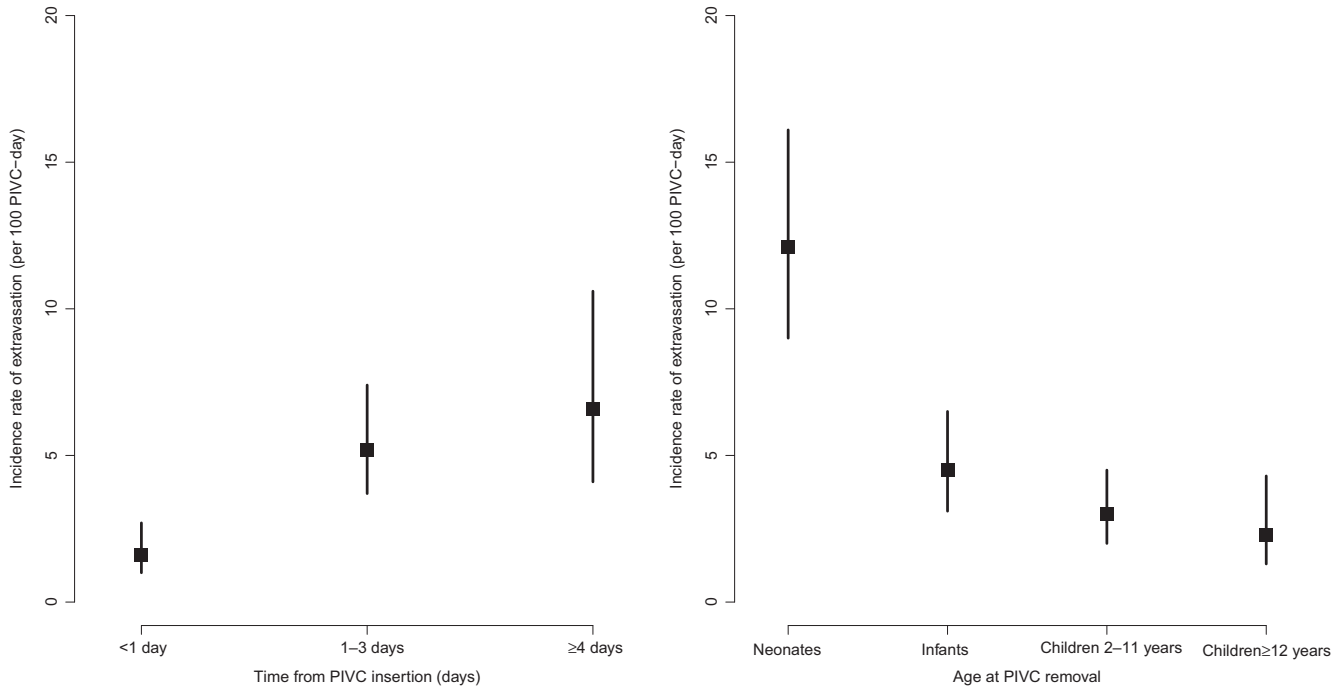

Figure 1 Incidence rate of PIVC extravasation according to time from PIVC insertion and age at PIVC removal. The incidence rates are represented by squares and 95% confidence intervals by vertical lines.

extravasation was documented in 11.7% in our study, and this rate was consistent with another study that reported that the devices were removed due to infiltration in 14.3% of the cases (16). Despite this similarity, we cannot exclude the possibility that we underestimated the incidence of extravasation in the present study. Second, the data came from one single hospital and practices may differ in other institutions. Finally, our study could not identify the drugs

Table 3 Associations between potential risk factors and the incidence rate of PIVC extravasation in neonates less than 28 days old (postnatal) (n = 201 patients and 272 PIVC)

Variable	Unadjusted IRR (95% CI)*	p Value	Adjusted IRR (95% CI)*	p Value
Sex				
Female	1 (Ref)	0.16	1 (Ref)	0.63
Male	0.70 (0.43–1.14)		0.87 (0.50–1.51)	
Gestational age				
Extreme or very preterm (<32 week)	1 (Ref)	Overall p = 0.0509†	1 (Ref)	Overall p = 0.09†
Late preterm (≥32 week to < 37 week)	0.87 (0.46–1.66)	0.68	0.77 (0.40–1.50)	0.45
Full-term (≥37 week)	0.43 (0.20–0.92)	0.03	0.44 (0.21–0.94)	0.03
In situ duration of PIVC < 1 day	1 (Ref)	Overall p = 0.005†	1 (Ref)	Overall p = 0.01†
≥1 and <4 days	2.71 (1.49–4.93)	0.001	2.65 (1.40–5.00)	0.003
≥4 days	2.98 (0.88–10.13)	0.08	3.54 (0.97–12.83)	0.055

PIVC = peripheral intravenous catheter; IRR = incidence rate ratio.
*Associations are expressed as incidence rate ratios which represent the ratio of incidence between a category and its reference category (for instance between male and female). An IRR > 1 indicates that the incidence is higher than in the reference category. Multivariate analysis was adjusted for subunit.
†The overall p value is for a test of an overall difference in incidence across all categories.

that were infused through each individual PIVC and involved in the extravasation, because this was not documented in the records. We cannot exclude the possibility that including those drugs in the analysis could have led to other results. A prospective study needs to be performed to increase knowledge of this pertinent issue. Moreover, to improve follow-up, a grading scale of extravasation severity and a free-text option to document extravasated drugs and infusions should be integrated in the electronic patient record system.

Implementing strategies to prevent extravasation injuries is gaining popularity in hospitals as it is an intervention with the potential to improve quality of care. Methods of reducing peripheral intravenous extravasation can include staff training and guidelines for its prevention and management (17–19). However, compliance with guidelines may fail, or be an unsustainable strategy, without the creation of a true clinical culture for preventing extravasation injuries (19,20). In the 1990s, attempts to predict or detect extravasation resulting from PIVCs used in-line pressure measurements or resistance monitoring of fluid infusions in infants. Although these early systems, which were based on isolated in-line pressure failed (21), systems monitoring flow resistance have shown some potential (22).

Based on the present study's results, we believe that greater efforts should be put into developing a clinical culture that prevents extravasation. Extravasation should be considered as an indicator that can be used to monitor quality of care. In future, multidisciplinary efforts, involving nurses, physicians and other healthcare professionals, should be planned in order to increase catheter surveillance and information on drug infusion risks, improve the recording and analysis of cases of extravasation and develop infusion monitoring technologies.

CONCLUSION

In this large retrospective study in a single neonatal and paediatric intensive care unit, extravasation was frequent and 17.6% of patients with a PIVC experienced at least one event. Neonates were particularly at risk, with an extravasation rate of 28.4%. Younger age and longer *in situ* PIVC duration were independent risk factors that predisposed paediatric patients to extravasation. Multidisciplinary efforts, involving nurses, physicians and other healthcare professionals, should be planned in future to improve documentation and develop a clinical culture that prevents extravasation.

ACKNOWLEDGEMENTS

The authors wish to thank Y Levy-Jamet for extracting the data from the electronic patient data files and N Bochaton for her support in interpreting the data.

FINANCE

This study did not receive any specific funding.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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