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Soft tissue infections related to peripheral intravenous catheters in hospitalised patients: a case–control study

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SUMMARY

Peripheral intravenous (i.v.) catheter-related soft tissue infections begin with local skin and soft tissue inflammation, which can progress to cellulitis or even tissue necrosis requiring aggressive surgical treatment. We conducted a matched case–control study to investigate risk factors for peripheral i.v. catheter-related soft tissue infections in hospitalised patients. We retrospectively identified 46 cases that occurred during 2006–2008 in two teaching hospitals. Each case was randomly matched with four control subjects from the same ward and on the same day that the soft tissue infections arose. Risk factors were analysed using conditional logistic regression. Multiple regression analysis identified the following independent risk factors: >24 h of continuous i.v. fluid infusion (odds ratio: 5.2, $P = 0.001$), insertion site in lower extremity (8.5, $P = 0.003$), use of an infusion pump (4.6, $P = 0.023$), and hospitalisation due to a neurological or neurosurgical condition (3.6, $P = 0.018$). The population-attributable fractions (the percentage of cases in the study population that could be prevented if the exposure were removed) were 40%, 19%, 24% and 25%, respectively. Minimising unnecessarily prolonged i.v. fluid infusion and avoidance of insertion in the lower extremity may significantly reduce the incidence of peripheral i.v. catheter-related soft tissue infection in the study hospitals.

Introduction

Peripheral intravenous (i.v.) catheter-related soft tissue infections begin with local skin and soft tissue inflammation, which can progress to cellulitis or even tissue necrosis requiring aggressive surgical treatment.[1] Infection may spread to the bloodstream with resulting morbidity and increase in the duration of hospitalisation.[2–4] Despite implementation of hand hygiene measures, aseptic technique, skin antisepsis and scheduled replacement,[5] more than 40 cases of peripheral i.v. catheter-related soft tissue infections occurred in our hospitals during 2006–2008 (incidence rate: 0.06 cases per 1000 bed-days). In several cases, debridement, reconstruction and skin grafting were required. To investigate risk factors for this complication we conducted a matched case–control study.

Methods

Setting

This study was conducted at two teaching hospitals: (i) Cathay General Hospital (Taipei, Taiwan), an 800 bed medical centre admitting patients from Taipei city and nearby areas that provides acute inpatient and intensive care for all medical, surgical, obstetric and paediatric subspecialties except psychiatry; and (ii) Hsinchu Cathay General Hospital (Hsinchu, Taiwan), a 300 bed community teaching hospital that provides acute inpatient and intensive care for all medical, surgical, obstetric and paediatric specialties except psychiatry and cardiac surgery. The institutional ethics review boards of Cathay General Hospital approved this study.

Standard procedures were applied to peripheral i.v. catheter insertion and maintenance. Alcoholic chlorhexidine preparations were not commercially available in Taiwan before 2010, so during the study period the skin was disinfected with 75% alcohol followed by 10% povidone-iodine, which remained on the skin for 2 min

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before insertion.[5] Cannulae were inserted by nurses trained in antiseptic technique. After insertion, exit sites were dressed with non-transparent sterile elastic bandages.[6] Patency was maintained by either continuous or intermittent infusion (in which case an extension tube or plastic cap was used to seal the catheter). Catheters not continuously infused were flushed with normal saline at least daily, as well as before and after drug injections. Before flush or injection the caps were disinfected with 75% alcohol. For patients without complications, catheters and sets were changed within 72 h.

Study design

We used a retrospective density case–control design. Cases of peripheral i.v. catheter-related soft tissue infection were compared with controls that received peripheral i.v. catheters but did not develop catheter-related infection. Cases and controls were matched based on the hospital ward and onset date.

Nosocomial infection surveillance

In both hospitals, infection control nurses routinely survey healthcare-associated infections using the Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network surveillance definitions.[7] Cases of peripheral i.v. catheter-related soft tissue infection were retrospectively identified from nosocomial infection surveillance databases.

Case definition

To be included as a case at least one of the following had to be fulfilled:

1. Purulent drainage, pustules, vesicles or boils documented at the insertion site.
2. Cellulitis or abscess diagnosed by a physician or surgeon either by routine observation, during a surgical operation, by histopathological examination, or other laboratory-confirmed evidence of infection.
3. The insertion site had at least two of the following signs or symptoms in the absence of another known cause: local pain or tenderness, localised swelling, redness or heat, and at least one of the following:
   (a) Organisms cultured from the aspirate or drainage from the affected site. If the organisms were skin commensals (i.e. *Corynebacterium* spp., *Bacillus* spp. other than *Bacillus anthracis*, *Propionibacterium* spp., coagulase-negative staphylococci, viridans streptococci, *Aerococcus* spp. or *Micrococcus* spp.) they must have been isolated in pure culture.
   (b) Organisms cultured from the blood that were considered to have arisen from the i.v. catheter, including the above-listed normal skin flora.
4. The insertion site had at least two of the signs or symptoms described above without any other known cause, and the symptoms/signs persisted for more than three days after the removal of the catheter.

Selection of controls

Controls were selected from hospitalised patients who had received peripheral i.v. catheters but did not develop peripheral i.v. catheter-related infective complications during the same period. We used random sampling without replacement from a computerised hospital administration registry, aiming to select four control subjects for each case.

Data collection

The medical records of all cases and controls were retrospectively examined. Information on the following data were systematically collected: (i) patient-related data (age, gender, service, medical comorbidities, surgical procedures); (ii) catheter-related data (inserter, insertion site, continuity of infusion, use of infusion pump); (iii) drug and infusate administration data (use of hypertonic fluid, blood components, lipid emulsion, peripheral parenteral nutrition, immunosuppressive agents, antibiotics, antiarrhythmics or cerebral vascular drugs; amount of fluid per day); and (iv) microbiological data.

Statistical analyses

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All analyses were conducted using SPSS version 15.0 (SPSS, Chicago, IL USA). Risk factors were analysed using conditional logistic regression. In multiple regression analysis, a backward elimination procedure was used to select a minimally adequate model for calculating adjusted odds ratios (ORs). To estimate the potential impact of control measures, population-attributable fractions (PAFs) were calculated for independent risk factors.[8,9] PAF is the proportion of cases that could be prevented if the exposure is removed.[9] $P < 0.05$ was considered statistically significant.

Results

Cases

From 1 January 2006 to 31 December 2008 we identified 46 cases (in 46 patients) of peripheral i.v. catheter-related soft tissue infection: 18 cases in 2006, 13 cases in 2007 and 15 cases in 2008. Twenty-eight cases were from Cathay General Hospital (0.05 cases per 1000 bed-days), 18 were from Hsinchu Cathay General Hospital (0.1 cases per 1000 bed-days). The mean age was 64 years (range: 20–94) and 57% of cases were male.

Of these 46 cases, eight (17%) had purulent discharge or cellulitis at the insertion site and were treated with antibiotics; one of these also developed a bloodstream infection caused by the same pathogen as isolated from the peripheral i.v. catheter insertion site. Six cases (13%) had abscesses and received surgical drainage/debridement. Six cases (13%) had bacteraemia and local inflammation at the insertion site. The remaining 26 cases (57%) had signs of local inflammation that persisted more than three days after catheter removal, without any other known causes.

Cultures from the insertion site or blood were performed for 20 of the 46 cases. Microbiological results were as follows: *Staphylococcus aureus* (seven patients, one in blood, six in purulent discharge), *Escherichia coli* (two patients, one in blood, one in purulent discharge), coagulase-negative staphylococci (two patients, one in blood as well as in purulent discharge, one in purulent discharge), *Flavobacterium indologenes* (one in blood), *Klebsiella pneumoniae* (one in blood) and *Streptococcus mitis* (one in blood). Six cultures yielded no growth (six patients with purulent discharges).

Controls

A total of 188 control patients were selected with a mean of four controls per case (range three to five). The mean age was 63 years (range: 20–96) and 48% were male.

Table I
Risk factors for soft tissue infections related to peripheral intravenous (i.v.) catheters

Characteristics	Cases ($N = 46$)	Controls ($N = 188$)	Crude OR (95% CI)	Adjusted OR (95% CI)	PAF, % (95% CI)
Hospital					
Cathay General Hospital	28	112	0.9 (0.5–1.8)		
Hsinchu Cathay General Hospital	18	76	1		
Age (years)					
≥65	33	108	2.0 (1.0–4.4)		
<65	13	80	1		
Sex					
Female	26	98	0.7 (0.3–1.3)		
Male	20	90	1		
Service					
Internal medicine[a]	34	151	0.5 (0.1–1.6)		
Surgery[b]	12	37	1		
Neurology/neurosurgery service					
Yes	16	37	3.4 (1.4–8.3)*	3.6 (1.2–10.2)*	25 (6–38)
No	30	151	1	1	
Surgical procedure[c]					
Yes	12	40	1.6 (0.6–4.6)		
No	34	148	1		
Diabetes mellitus[d]					
Yes	13	63	0.8 (0.4–1.7)		
No	33	125	1		
Renal disease[e]					
Yes	5	20	1.0 (0.4–2.9)		
No	41	168	1		
Liver cirrhosis[f]					
Yes	3	15	0.8 (0.2–2.9)		
No	43	173	1		
Pre-existing infection[g]					
Yes	21	85	1.1 (0.5–2.1)		
No	25	103	1		
Inserter					
I.v. therapist team	26	112	0.9 (0.3–2.3)		
Regular nurses	20	76	1		
Insertion site					
Lower extremity	10	15	5.9 (1.9–18.1)*	8.5 (2.1–34.4)*	19 (8–30)
Upper extremity	36	173	1	1	
>24 h continuous infusion[h]					
Yes	23	30	6.7 (3.0–14.9)*	5.2 (1.9–14.2)*	40 (22–54)
No	23	158	1	1	
Hypertonic fluid[i]					
Yes	11	50	0.9 (0.4–1.9)		
No	35	138	1		
Use of an infusion pump[j]					
Yes	14	19	6.3 (2.3–17.1)*	4.6 (1.2–17.0)*	24 (5–37)
No	32	169	1	1	
Amount of i.v. fluid/day					
>1000 mL	14	71	0.7 (0.4–1.5)		
<1000 mL	32	117			
Drug administration[k]					
Yes	41	170	1.0 (0.3–3.0)		
No	5	18	1		
Blood components[l]					
Yes	7	17	1.8 (0.7–4.5)		
No	39	171	1		

Lipid emulsion[m]			
Yes	5	1	20.8 (2.4–178.3)*
No	41	187	1
Immunosuppressives[n]			
Yes	0	3	0.0 (0.0–9327.7)
No	46	185	1
Antibiotics			
Yes	26	110	1.0 (0.5–1.9)
No	20	78	1
PPN[o]			
Yes	4	1	15.0 (1.7–135.9)*
No	42	187	1
Drugs for arrhythmia or ischaemic heart disease[p]			
Yes	3	8	2.4 (0.7–8.1)
No	43	180	
Cerebral vascular drugs[q]			
Yes	11	15	0.5 (0.1–1.7)
No	35	173	

OR, odds ratio; CI, confidence interval; PAF, population attributable fraction = P(E/D){[OR − 1]/OR}, while P(E/D) is the proportion of cases exposed to the factor.[8]

*Statistically significant, $P < 0.05$.

[a] Including rehabilitation service.

[b] Including obstetrics and gynaecology services.

[c] Patients who received operation in this hospitalisation before the removal of the studied peripheral i.v. catheters.

[d] Symptoms of diabetes plus a casual plasma glucose concentration ≥200 mg/dL, or fasting plasma glucose concentration ≥126 mg/dL. For patients already receiving antidiabetic agents or insulin, a previous diagnosis was considered sufficient.

[e] Including both end-stage renal disease and chronic renal failure.

[f] As the patient's discharge diagnosis.

[g] Patient who had an active bacterial infection at admission (e.g. urinary tract infection, pneumonia, bacteraemia, wound infection, cholecystitis, infectious endocarditis, liver abscess, arthritis, peritonitis etc.).

[h] The peripheral i.v. catheter in case subjects (or the peripheral i.v. catheter in matched control subjects) had been continuously used for infusion for >24 h when soft tissue infections arose.

[i] 10% dextrose, 500 mL; 50% dextrose, 20 mL; Taita electrolytes solution®, 500 mL (solution containing multiple electrolytes for injection that contains 10% glucose and 0.082% NaCl); Glycerol®, 500 mL (osmotic diuretic, contains glycerin 10%, fructose 5% and NaCl 0.9%). These hypertonic fluids were infused/injected via the studied peripheral i.v. catheter.

[j] Abbott Plum XL Infusion Pump, Abbott Laboratories, USA.

[k] Patient who received parenteral medication via the studied peripheral i.v. catheter.

[l] Whole blood, packed RBCs, platelet, fresh frozen plasma or frozen plasma were infused via the studied peripheral i.v. catheter.

[m] Lipofundin® medium chain triglycerides/long chain triglycerides (MCT/LCT) 10%, 500 mL (solution containing soya bean oil 50 g/L, medium chain triglycerides 50 g/L, egg lecithin 12 g/L, glycerol 25 g/L, essential fatty acids 24–29 g/L) was infused via the studied peripheral i.v. catheter.

[n] Chemotherapy agents or steroids (oral and parenteral medications) were infused/injected via the studied peripheral i.v. catheter.

[o] Peripheral parenteral nutrition combined with an amino acid and glucose admixture or parenteral nutrition products with an osmolarity <850 mOsm/L were infused via the studied peripheral i.v. catheter.

[p] Agents used to suppress rhythms and angina of the heart, such as nitroglycerin, amiodarone, phenytoin, were infused/injected via the studied peripheral i.v. catheter.

[q] Cerebral-circulatory and metabolic drugs, such as piracetam and midazolam, were infused/injected via the studied peripheral i.v. catheter.

Risk factors for peripheral i.v. catheter-related soft tissue infections

By univariate analysis, the following factors predicted the development of peripheral i.v. catheter-related soft tissue infections: >24 h of continuous i.v. fluid infusion (OR: 6.7, $P < 0.001$), use of infusion pumps (6.3, $P < 0.001$), insertion site in the lower extremity (5.9, $P = 0.002$), hospitalisation due to a neurological or neurosurgical condition (3.4, $P = 0.007$), lipid emulsion infusion (20.8, $P = 0.006$) and peripheral parenteral nutrition (15.0, $P = 0.016$) (Table I). By multivariate analysis the following factors remained independent predictors for peripheral i.v. catheter-related soft tissue infection: >24 h of continuous i.v. fluid infusion (OR: 5.2, $P = 0.001$), insertion site in the lower extremity (OR: 8.5, $P = 0.003$), use of infusion pumps (4.6, $P = 0.023$) and hospitalisation due to a neurological or neurosurgical condition (3.6, $P = 0.018$) (Table I). The PAFs were 40%, 19%, 24% and 25% respectively (Table I).

We examined the variables in multiple regression modelling but identified no statistically significant interactions.

Discussion

The infections in this study were caused by a variety of microorganisms. Our analysis shows that >24 h of continuous i.v. fluid infusion, insertion in the lower extremity, use of infusion pumps, and hospitalisation due to a neurological or neurosurgical condition were independent risk factors. The higher risk associated with these factors was unlikely to be explained by differences in adherence to the skin disinfection protocol because cases and controls were matched by ward and onset date.

We were unable to study the effects of chlorhexidine-based skin disinfection nor of the i.v. therapist team. Trials have demonstrated that 2% alcoholic chlorhexidine is more effective than 10% providone-iodine in the prevention of vascular catheter-associated infections and surgical site infections.[10,11] However, these preparations were unavailable in Taiwan during the study period, so the regime used for skin disinfection was 75% alcohol followed by 10% povidone-iodine. i.v. Therapist teams specialising in the insertion and maintenance of peripheral i.v. catheters can result in lower rates of phlebitis and overall infection rates.[5,12–14] In this study, cases and controls were matched by ward and therefore had the same access to i.v. therapist teams.

Continuous infusion systems can be contaminated during changing infusate bottles or infusion sets. Even with good nursing practice, studies have shown an infusate contamination rate of 0.6–0.9%.[15,16] Even though the initial inoculum may be small, since the infusate is hung for long periods, organisms can proliferate to concentrations high enough to cause infections.[15,17–19] It has been observed previously that continuous infusion is associated with a higher risk than intermittent infusion of catheter colonisation.[14] The present study shows that this is translated to an increased risk of catheter-related soft tissue infection.

It is known that i.v. fluids are often prescribed unnecessarily.[20] Thirty of 188 control subjects (16%: a random sample of patients hospitalised in the study hospitals) received >24 h of continuous i.v. infusion. We were often unable to tell retrospectively whether continuous infusion was used to maintain i.v. patency or was prescribed as part of ongoing medical care. In any case it is imperative for physicians to evaluate patients carefully and to ensure that i.v. fluids are clinically indicated and not prescribed simply to keep a peripheral i.v. catheter patent.

Catheters inserted in the lower limbs have been shown previously to suffer a greater risk of thrombophlebitis and thrombosis than those inserted in the upper limbs.[21,22] Guidelines on the prevention of intravascular device-related infection recommended that the upper extremities are the preferred site of catheter insertion.[5] When there is no alternative but to use the lower limb, peripheral i.v. catheters should be removed as early as possible to minimise the risk of catheter-related soft tissue infections.

When potent i.v. medications need to be given in accurate dose, infusion pumps can ensure delivery at a controlled rate. However, if the infusate is contaminated or the catheter tip is colonised, the positive pressure applied by the infusion pump can facilitate spread of bacteria into the tissue around the insertion site.[1] Known complications of infusion pumps include tissue necrosis, wound infection, and cellulitis.[23] If used, pump infusion systems should be prepared under sterile conditions by trained personnel.[24]

The final independent risk factor revealed in this study was hospitalisation due to a neurological or neurosurgical condition. We hypothesise that immobilisation and the poor general condition of many of these patients may predispose them to i.v. catheter-related soft tissue infections. Furthermore, patients with impaired consciousness and cognitive dysfunction may be less able to report discomfort, so delayed recognition may be important. Frequent inspection of catheter sites and prompt response to patients' complaints remain an essential aspect of nursing care.

In conclusion, this study identified that >24 h of continuous i.v. fluid infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation due to a neurological or neurosurgical condition were independent risk factors for peripheral i.v. catheter-related soft tissue infections. Minimising unnecessary continuous infusion and avoiding insertion in the lower extremity may significantly reduce the incidence of peripheral i.v. catheter-related soft tissue infections in the study hospitals.

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Conflict of interest statement
None declared.

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