A Case Series of Patients Developing Thrombophlebitis after Administration of Flucloxacillin via a Peripheral Intravenous Catheter

Kathleen O'Connor, RN, BN, Grad Cert in Emergency Nursing
Vascular Access Team, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia
Andie Lee, MBBS, DTM&H, MSc
Department of Infectious Diseases, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia
Central Clinical School, Sydney Medical School, Camperdown, New South Wales, Australia
Gloria Fong, MBBS, PhD, BMLSc
Department of Dermatology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia
Central Clinical School, Sydney Medical School, Camperdown, New South Wales, Australia

Introduction

Flucloxacillin is a narrow spectrum beta-lactam antibiotic of the penicillin class. Flucloxacillin exerts antibacterial activity by binding to and inactivating penicillin-binding proteins present on the inner membrane of the bacterial cell wall.[1] Inactivation of penicillin-binding proteins interferes with cross-linkage of peptidoglycan chains to cause interruption of the bacterial cell wall resulting in cell lysis.[1] Flucloxacillin is used to treat a range of infections caused by gram-positive bacteria, including skin and soft tissue infections, osteomyelitis, and endocarditis.[1] The prescribed dose of intravenous flucloxacillin can range from 250 mg to 2 g delivered every 4-6 hours.

To deliver medications intravenously, peripheral intravenous catheters (PIVCs) are commonly used in the acute setting. The complications of using PIVCs to deliver intravenous medications include phlebitis, local infection, bloodstream infection, infiltration occlusion, extravasation, and inadvertent removal.[2] The use of intravenous antibiotics in particular is a risk factor for the development of infusion phlebitis and the risk varies by antibiotic type.[3] Flucloxacillin is particularly phlebitogenic and it is not uncommon for patients to develop phlebitis following treatment beyond 2 days.[4] In 1 prospective study,[5] phlebitis was significantly associated with intravenous flucloxacillin with a hazard ratio of 2.01 (95% confidence interval 1.26-3.21).

Correspondence concerning this article should be addressed to gloria.fong@sydney.edu.au
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Phlebitis is a condition in which the inner lining of the vein, the tunica intima, becomes inflamed. Phlebitis may be present at the site of insertion or may extend along the length of the vein.[6] It is diagnosed by examining the PIVC site or the area where the PIVC was removed. If the area is erythematous, tender, warm, and swelling is present along the course of the vein, this is highly suggestive of phlebitis.[7] Phlebitis has the potential to evolve into thrombophlebitis where sustained irritation of the veins leads to clot formation within the veins.[7] Clinically, thrombophlebitis presents as pain along the PIVC site and is associated with erythema, induration (ie, skin hardening), a palpable venous cord, and pyrexia. A commonly used modality for diagnosing thrombi in veins is venous ultrasonography.[8]

A previous audit conducted at our institution by the vascular access team (VAT) found that besides routine change of PIVCs within 72 hours, there was a lack of further monitoring and reporting of PIVC sites. In addition, nursing staff often reported that PIVCs had "tissued," and it was not until the site was reviewed by medical officers or by the VAT that thrombophlebitis was recognized. This alerted us to the need to increase education and assessment of PIVC sites.

This case series describes a number of patients who developed thrombophlebitis after administration of high-dose flucloxacillin (2 g every 4-6 hours) via a PIVC.

Case Description

Methods

These case studies were collected from patients admitted to a 911-bed tertiary referral center in Sydney, Australia. At this facility, PIVCs are inserted by both medical and nursing staff and the condition of the insertion site is monitored and

documented by nursing staff on a daily basis. There is a VAT at the hospital that has 2 main roles: insertion of peripherally inserted central catheters (PICCs) and assisting with ultrasound-guided peripheral cannulation in patients with poor venous access.

Retrospective Chart Review of Thrombophlebitis

A retrospective review of the medical records of patients who developed thrombophlebitis after flucloxacillin administration was performed by two of the authors (KO and GF). Thrombophlebitis was defined as inflammation of the vein in conjunction with formation of a blood clot (thrombus). Patients with thrombophlebitis were identified by medical officers and the VAT when repeated cannulation was required and/or a PICC was requested due to thrombophlebitis and difficult venous access.

Patient Interviews

Patients referred to the VAT were also questioned regarding their experience with their PIVCs and any symptoms they developed as the medication was being administered. The aim of the questions was to obtain a general overview of patients' experiences to improve on vascular access requirements and limit the number of PIVCs patients received.

This quality improvement initiative was approved by the Research Ethics and Governance Office at the hospital.

Results

A total of 16 patients were identified and included in this case series (Table), spanning across all specialties, including cardiology, geriatrics, and surgical subspecialties. There were 6 male and 10 female patients with an average age of 56 years. The cases were identified over a 9-month period from July 2016 to March 2017. The gauge of PIVCs inserted ranged from 20 to 22 and were placed in the hand, wrist, forearm, or cubital fossa. Out of 16 patients included in this case series, 7 patients had formal ultrasound investigation performed in the vascular laboratory confirming thrombophlebitis. Of the 9 remaining patients, 7 had a bedside ultrasound conducted by the VAT confirming thrombosis and 2 patients were diagnosed on clinical assessment by the medical officer (Table).

Of the 16 patients included, 15 were prescribed 2 g flucloxacillin delivered every 4-6 hours, although 1 patient was charted as receiving 1 g 4 times daily. Of particular note among the cases was a young male patient who had 3 PIVCs sited in the right arm who developed a thrombus extending from his wrist to his shoulder. The patient's left arm could not be used because he had an axillary clearance. This unacceptable adverse outcome triggered investigation for further cases. Two of 16 patients developed bilateral upper limb thrombophlebitis from PIVCs sited in the forearm and cubital fossa region confirmed by formal ultrasound studies. Flucloxacillin was administered via all 4 sites in these patients.

All staff members reported that 2 g flucloxacillin was administered in 0.9% sodium chloride over a period of 1 hour. Staff did not bolus the medication for any of the patients.

Patient Perspective

When patients were questioned regarding their general experience of their PIVC and flucloxacillin administration, pain from the cannula when the drug was being administered was commonly reported. Many patients complained of a "burning sensation" during the infusion, some asked for the infusion to be slowed but "that made no difference." A patient with cubital fossa thrombophlebitis complained of extreme pain and was unable to bend her arm for 2 days. Some patients were concerned about the frequent PIVC changes when infusions became painful. A number of patients who warranted insertion of PICCs later expressed dissatisfaction at the pain that was inflicted on them before the PICC being inserted. It is worth noting that following the diagnosis of thrombophlebitis, 1 patient required anticoagulation therapy. Some patients with more extensive thrombophlebitis required progress venous ultrasonography to monitor for resolution of the thrombophlebitis after discharge from the hospital.

Discussion

Thrombophlebitis was found to be a common complication of intravenous flucloxacillin administration and was associated with substantial patient discomfort.

At our institution, we advocate for and encourage the use of the visual infusion phlebitis (VIP) score, adapted from Jackson et al,[9] to monitor and document PIVC sites. This score was introduced to identify and reduce the complications associated with peripheral cannulas. The VIP score is a validated scoring system used to assess thrombophlebitis. It grades the presence and severity of cannula site reactions from 0 to 5.[9] The VIP score also provides guidelines as to when to observe, resite, or consider treatment of phlebitis.[9] A VIP score of 1 corresponds to slight pain or erythema at the intravenous access site, and would warrant close monitoring of the PIVC because these features are possible first signs of thrombophlebitis. VIP scores of 2 or above may indicate signs of phlebitis characterized by a combination of erythema, swelling, or pain near the PIVC site. In this situation, it is recommended that the PIVC be resited to prevent further complications.

In our institution, as part of quality assurance for patient safety, a VIP score of 4 (corresponding to severe thrombophlebitis) mandates official reporting to the Incident Information Management System, an internal notification system where all staff members can report any complications patients encounter during their admission. This system assists the VAT in monitoring the number of patients influenced by thrombophlebitis. Currently, we suspect that the numbers of cases are underreported. This may be attributed to poor documentation of PIVCs, including the rationale for PIVC removal. This is supported by a retrospective chart audit conducted by Carr et al[10] in an Australian hospital where more than half of the most common medical invasive devices were not documented. In addition, as highlighted in a systematic review by Ray-Barruel et al,[6] the lack of validated and consensus phlebitis assessment measures in the clinical setting further contribute to the disparities in the reported incidence of phlebitis.

To minimize the risk of thrombophlebitis, the prescribed medication and duration of therapy should guide clinicians in choosing the most suitable vascular access device for the individual patient.[11] With intravenous flucloxacillin, the risk of