

Safe and successful treatment of intravenous drug users with a peripherally inserted central catheter in an outpatient parenteral antibiotic treatment service

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Received 26 June 2010; returned 9 August 2010; revised 16 August 2010; accepted 25 August 2010

Background: The enrolment of intravenous drug users (IVDUs) into an outpatient parenteral antibiotic treatment (OPAT) service using a peripherally inserted central catheter (PICC) is controversial and often avoided. The National University Hospital in Singapore has a policy of permitting OPAT-based treatment of IVDU patients with appropriate medical indications. We report on our experiences.

Methods: A prospective observational study was conducted on IVDU patients requiring parenteral antibiotics via an OPAT service from January 2005 to December 2009. Clinically appropriate patients were screened using pre-defined criteria and enrolled into our service, where standardized measures were enforced to prevent and detect PICC abuse and optimize treatment. Outcomes measured included mortality, completion of therapy, PICC abuse, and readmission for infective or treatment-related complications during OPAT and a 30 day follow-up period.

Results: Twenty-nine IVDU patients received treatment in our OPAT service (total 675 patient-days). The median duration of therapy was 18 days (range 1–85). Infective endocarditis was the primary diagnosis in 42% of cases. Two patients (7%) had recrudescence infection after absconding during their inpatient stay. These two patients subsequently completed treatment in OPAT. There were no deaths or cases of PICC abuse. Five patients (17%) during OPAT and one patient (3%) during the 30-day follow-up period required readmission for infective or treatment-related complications.

Conclusions: Appropriately selected, counselled and monitored patients with a history of being an IVDU can be treated safely and successfully via OPAT centres. It is likely that some will respond better to treatment in an outpatient setting.

Keywords: endocarditis, *Staphylococcus aureus*, addiction

Introduction

Infections are the leading cause of hospital admissions in injecting drug users and are often serious and require lengthy intravenous antimicrobial therapy.¹ Since its inception in 1974 in the USA, outpatient parenteral antibiotic treatment (OPAT) has grown to become a standard modality worldwide in treating patients with serious infections² and has been in place in Singapore since 2002.³ Various guidelines have been developed to aid healthcare practitioners who treat patients in OPAT,^{4–6} and healthcare centres have described their safety and efficacy outcomes using OPAT to treat a range of infections.^{7–9} There is, however, remarkably little published on the OPAT treatment of intravenous drug users (IVDUs). It is unclear to what degree this patient population is being routinely excluded from this

form of therapy. The approaches and outcomes of centres that do accept IVDU patients are generally unknown. It is not possible to generate guidelines or recommendations for treating IVDU patients without such efficacy and safety data. At the National University Hospital Singapore, our OPAT centre enrolls up to 300 patients per year, including selected IVDU patients, and this report outlines our approaches and outcomes in this subgroup.

Methods

A prospective observational study was conducted assessing the care of IVDU patients requiring outpatient intravenous antibiotic therapy, admitted to the National University Hospital Singapore (NUH)—a 900 bed acute care tertiary academic hospital, between January 2005 and December 2009. The study protocol was granted ethics approval by the

research and development review board at this institution. IVDU patients were defined as those currently using or those with a history of intravenous drug use in the preceding 12 months. Clinically stable patients requiring intravenous antibiotic therapy were referred to the OPAT service from specialty teams within the hospital. In those patients who received antibiotics via a peripherally inserted central catheter (PICC), these were inserted during the patient's hospital stay by radiologists under ultrasound guidance. Patients were required to meet pre-defined criteria before being accepted into OPAT. These included adequate housing, a reliable guardian and the signing of a contract stating that they would be compliant with daily OPAT clinic visits for treatment and review, they would not access the PICC line for intravenous drug use and that they would not take any other drugs that were not prescribed by the hospital. Patients and families were educated regarding the appropriate care of the PICC line. A zero tolerance policy to any perceived PICC abuse was reinforced. Formal drug counselling was provided to each patient at the start of the treatment and subsequently on an as-needed basis. Patients presented to the OPAT clinic daily for antibiotic

administration (including inspection of the PICC exit site and PICC dressing change). On completion of the intermittent antibiotic infusions, security seals in the form of hospital-specific, semi-perforated stickers (usually used to seal confidential envelopes) were applied over the PICC exit port and infuser (Figure 1) to detect and deter tampering. For continuous (24 h) infusions the stickers sealed all line junctions. Patient-consented urine drug screens were performed on patients suspected of ongoing intravenous drug use. Patients were encouraged to declare any ongoing intravenous drug use, or inclinations to do this, to the OPAT staff so that appropriate drug counselling could be arranged. Intermittent intravenous drug use, however, was not a definite dismissal criterion from OPAT as long as the patient did not use the PICC for this purpose and all other criteria were adhered to, including daily reviews and compliance in all respects relating to the treatment of their infection. Outcome measures were: mortality, completion of planned duration of antibiotic therapy, rates of PICC line abuse, and rates of readmission for infection or treatment-related complications during OPAT and a 30 day follow-up period after completion of OPAT.

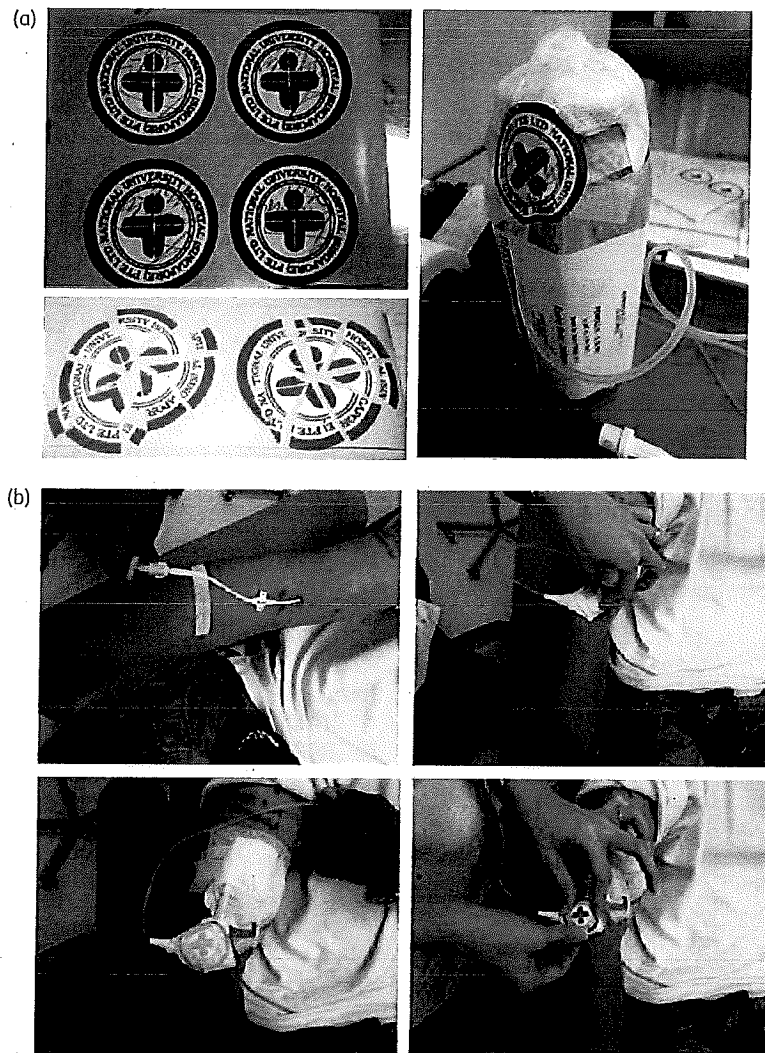


Figure 1. (a) Security seals over PICCs and infusers; intact security seals (top left), perforated seals (bottom left); seals over infuser (right). (b) Security seals over PICC (order of dressing application: clockwise from top left). This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

Results

Between January 2005 and December 2009, 906 patients were enrolled in OPAT at NUH. Of these, 29 (3.2%) fulfilled the study criteria for enrolment. The median length of hospital stay prior to OPAT was 15 days (range 2–48), whereas the median length of OPAT treatment was 18 days (range 1–85) equating to 675 patient-days of OPAT. The median age of patients was 41 years (range 26–53). The majority were male (89.7%), and Malays were an overrepresented ethnic group at 48.3%, compared with 13.4% of the Singapore population. Chinese (27.6%) and Indian (10.3%) ethnic groups were also in our IVDU OPAT cohort (comprising 74.2% and 9.2%, respectively, of the total Singapore residents).¹⁰ Ten patients (34.5%) had a known history of hepatitis C on admission and another three were diagnosed during the admission. Two new cases of HIV were also diagnosed. Other co-morbidities included stable psychiatric illness in three patients (10.3%) and diabetes mellitus in one (3.4%). Of the intravenous agents reported to be abused, buprenorphine (13.8%) and buprenorphine combined with midazolam (13.8%) were the most common, followed by midazolam alone (7%) and heroin (7%). In the majority of patients (58.6%), however, the type of intravenous drug abused was not known. The injecting of buprenorphine, a drug initially introduced into Singapore to be administered sublingually to address opiate dependence, has been reported previously to be associated with significant infective complications, in particular infective endocarditis.¹¹

Similarly in this study, infective endocarditis was the most frequently treated infection (12 cases, 41.4%), with most cases complicated by septic emboli or disseminated infection (66.7% of all infective endocarditis cases). All 12 cases involved right-sided heart valves, including one which involved both sides. Other infections included bone/joint infections (27.6%), bacteraemia with no focus (10.3%) and soft tissue infections (6.9%). Methicillin-sensitive *Staphylococcus aureus* (MSSA) accounted for most infections (70.0%). All cases of infective endocarditis were due to MSSA. *Neisseria gonorrhoeae* was the next most common organism treated (6.7%). Correspondingly, flucloxacillin (51.4%), cefazolin (17.1%) and ceftriaxone (9%) were the most commonly used antibiotics. Our cohort included six patients (20.7%) who required intensive care support. Two patients left hospital against medical advice and were subsequently readmitted with recurrent sepsis. Encouragingly, both of these patients proceeded to be successfully treated via OPAT after hospital discharge.

Of the 29 patients, all but one (96.6%) completed the intended duration of OPAT antibiotic therapy. This patient defaulted 30 days into the OPAT treatment. There were no instances of PICC or infuser security seal breaches and there were no deaths or significant misadventures. This is an encouraging result, given that in previous studies *S. aureus* bacteraemia has been associated with significant mortality,^{11,12} especially when complicated by infective endocarditis.¹³ Our low mortality rate was likely influenced by the stringent selection criteria used, in that only clinically stable patients, in the recovery phase of their illness, were considered appropriate for OPAT. This has been shown to be an important selection criterion in infective endocarditis patients with respect to treatment outcomes in OPAT.⁸ Urine drug screens were performed on two patients

who were suspected of ongoing intravenous drug use. One revealed trace opiates and the other was negative.

Six patients (20.7%) required hospital readmissions: five during OPAT and one during the 30 day follow-up period. Two of the cases were for PICC infections (involving *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*). A further two cases were for complications relating to infective endocarditis (worsening septic lung emboli and worsening valvular dysfunction). One patient during OPAT and another during the follow-up period were readmitted with bacteraemia (*Haemophilus influenzae* and *Streptococcus* sp., respectively) due to an organism different from the initial infection. Overall, the incidence of readmissions and PICC infections in our IVDU patients was similar to that found in non-IVDU infective endocarditis patients treated in OPAT.^{7,9} Reports of OPAT patients with lower rates of readmission^{3,5} had much lower proportions of patients with serious infections, such as infective endocarditis. Of the six patients who were readmitted to hospital, five resumed therapy with OPAT and successfully completed the remainder of their treatment in the service.

Discussion

While there are many publications outlining experiences in OPAT, we know little of the outcomes of the subgroup of IVDU patients and it is known that some centres completely exclude them due to safety concerns. Our study revealed no deaths, serious misadventures or line tampering. Furthermore there was no excess of hospital readmissions or PICC infections. Thus, in our setting, selected patients can be safely and successfully treated for serious infections with the use of a PICC. It is likely that some IVDU patients actually have better outcomes when managed as an outpatient compared with a prolonged inpatient stay. This is evidenced by the two patients in our study who defaulted inpatient hospital management but were subsequently successfully treated in OPAT. In addition, the vast majority (96.6%) of our IVDU OPAT patients were compliant with attendance for the entire duration of therapy with OPAT.

Our 'package intervention' to facilitate treatment of IVDU patients in OPAT involved appropriate patient selection, prevention strategies such as tamper-proof security seals over PICCs and infusers, counselling and careful monitoring. Although the recurrent bacteraemia seen in two of our patients may have suggested ongoing intravenous drug use, we were confident that the PICCs were not used for this purpose, given the intact security seals. This simple but novel idea of applying security seals over the PICCs appears to be an effective deterrent.

There are a number of limitations to this study. It would have been useful to establish the number of IVDU patients that would benefit from OPAT compared with the number actually enrolled in our centre. The degree to which a primary physician screens and excludes particular IVDU patients prior to referral to OPAT for assessment varies however, and we could not track this information to enable this comparison to be made. Other limitations were that it was an observational study, and subjects were selected, not randomized. It was conducted in a single centre in Singapore, and hence the results may not be generalizable to other regions with different drug cultures, healthcare resources and legal implications. There is currently a conspicuous

absence of information concerning the approaches to and outcomes of treating IVDU patients in OPAT centres. Further studies are urgently needed to allow the establishment of protocols, guidelines and benchmarks for the management of serious infections in these often challenging patients.

Acknowledgements

We thank our wonderful, dedicated and hardworking OPAT team, without whose help this service would not be available: Cassandra Lim, Rosmawati, Tricia Loke and Kleopatra Ng.

Funding

This study was undertaken as part of our routine clinical activity and did not receive any additional funding.

Transparency declarations

None to declare.

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