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Supervised self-administration of outpatient parenteral antibiotic therapy: a report from a large tertiary hospital in Australia

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SUMMARY

Introduction: Outpatient parenteral antibiotic therapy (OPAT) has become established as a standard of care in most Australian hospitals to treat a variety of infections. Since 1998, the Alternate Site Infusion Service (ASIS) has provided an OPAT service to five hospitals in southern Brisbane, Queensland, using predominantly a patient or carer administration model (self-administered, S-OPAT). The aim of this study was to evaluate outcomes of our S-OPAT programme.

Methods: Consecutive patients treated by ASIS at the Princess Alexandra Hospital from January 1, 2011 to December 31, 2011 were reviewed. Data on patient demographics, diagnoses, microbiology, antimicrobial therapy, duration, outcome, and complications were sourced from a prospectively collected database and from patient medical records.

Results: There were 150 episodes involving 144 patients resulting in 3520 days of OPAT; the median duration on the programme was 22 days (range 4–106 days). Patient or carer administration occurred in the majority of episodes. The most common indication by far was bone or joint infection (47% of patients), followed by infective endocarditis (9%). *Staphylococcus aureus* was the most frequently treated organism. The overall cure rate was 93%. On multivariate analysis, patients with two or more comorbidities had an increased risk of failure. Line-related complications occurred in 1.4/1000 catheter-days. Rash was the most common drug-related event. Despite the extensive use of broad-spectrum antibiotics there were no cases of *Clostridium difficile* infection during therapy and for up to 28 days post cessation of intravenous antibiotics. The cost of OPAT per patient excluding drug administration and home visits was approximately A$ 150.00/day, significantly lower than the cost of an inpatient bed, which is estimated to be A$ 500–800/day.[5]

Conclusion: OPAT using a patient or carer administration model is an effective and safe option for the management of selected patients with infection requiring intravenous antibiotics.

1. Introduction

The first reports of outpatient parenteral antibiotic therapy (OPAT) came from the USA in the 1970s. Since then, OPAT has been adopted worldwide and in Australia[1–5] in various healthcare settings.[6–10] With appropriate patient selection, it has been shown to be safe, efficacious, and cost-effective.[9–14] The ability to manage patients in the community setting provides the freedom for patients to return to work or educational facilities, reduces pressure on hospital bed utilization, and reduces the risk of developing nosocomial infections.[9–13]

There are various models of care for OPAT, which include hospital-based infusion centres, nursing outreach services to patient homes for the administration of antibiotics, and administration by self or family members.[15] In Australia, most hospitals provide hospital-centred nursing outreach programmes to patient homes for the administration of antibiotics,[1,2] which allows daily direct supervision of the patient. However, the nursing costs in this model can be significant.[15] Self-administration of intravenous antibiotic therapy involves training the patient or their carer to administer parenteral antibiotics that are pre-packaged ready for use with ambulatory devices. The reduction in nursing costs and increased patient autonomy are advantages of this model, although adequate patient or carer training is essential to facilitate drug administration in a safe and effective manner with minimal complications.[15–17] A peripherally inserted central catheter (PICC),

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or less commonly, a peripheral cannula, is used as an access device. Antibiotics can be administered as intermittent or continuous infusions via an electronic pump or elastometric device.[18,19]

This is the first report from an Australian hospital on outcomes of a successful self-administered OPAT (S-OPAT) programme. The results of this study will provide assistance to clinicians and administrators who are involved in making decisions regarding the development of future hospital services.

2. Methods

We reviewed patients treated by the Princess Alexandra Hospital Alternate Site Infusion Service (ASIS) from January 1, 2011 to December 31, 2011. Information on patient demographics, diagnoses, microbiology, antimicrobial therapy, duration, complications, and outcome were obtained from a prospectively collected database and by reviewing the patient medical records. The Metro South Health Services District Human Research Ethics Committee granted ethics approval for the study (HREC/12/QPAH/38). The statistical analysis was performed using Stata v. 11 (StataCorp LP, College Station, TX, USA). A multivariate logistic regression model was developed to identify potential risk factors for treatment failure. Odds ratios (OR) with 95% confidence intervals (95% CI) were reported. A p-value of <0.05 was considered statistically significant.

2.1. Definitions

Success was defined as cure or a major improvement as shown by clinical progress, a significant decrease in C-reactive protein, and the absence of relapse within 28 days of cessation of intravenous antibiotics. Although the majority of patients were continued on oral antibiotics at the end of OPAT, monitoring of this was not included in the present study. Failure occurred when the prescribed course of OPAT did not result in cure or a major improvement as defined by criteria used in a previous study:[2] (1) there was a need to continue intravenous therapy beyond the original prescribed course; (2) there was a need for unanticipated surgery for source control within 4 weeks of completion of the originally prescribed intravenous course; (3) hospital re-admission related to OPAT complications; or (4) any evidence of relapse or recurrence of infection within 4 weeks of completion of the originally prescribed course. Drug-related complications included rash, hepatitis, gastrointestinal symptoms, *Clostridium difficile* infection, and acute kidney injury requiring either cessation or a change of parenteral antibiotics. Line-related complications included line infection, thrombosis, inadvertent removal of the intravenous access by the patient, and lymphatic leakage. Administration was categorized as either a 24-h continuous infusion or intermittent boluses.

2.2. Setting

Princess Alexandra Hospital is one of three tertiary hospitals in Brisbane, Queensland and provides care in all major adult specialties excluding obstetrics. The hospital has 780 beds and provides an extensive range of acute medical, surgical, trauma, mental health, cancer, and rehabilitation services, as well as a state-wide transplantation service for livers, kidneys, bone, cartilage, and corneas. ASIS is an OPAT service that was established at the Princess Alexandra Hospital in 1998. ASIS is integrated within the Infectious Diseases Department at the Princess Alexandra Hospital and consists of a multidisciplinary team that includes medical, nursing, and pharmacy personnel. Since then, the service has expanded to provide services to Ipswich, Logan, Queen Elizabeth II, and Redland hospitals. A visiting consultation service is provided to the other hospitals by infectious diseases physicians from Princess Alexandra Hospital.

2.3. Patient selection

An infectious diseases physician or a registrar assessed the suitability and medical stability of patients for enrolment into ASIS. Further in-hospital assessment of suitability was performed by dedicated ASIS nursing staff, and the patient was provided with training on self-administration of antibiotics prior to discharge. Training took place on the day before discharge and usually required 1–2 h of nursing time at the bedside. A visit to the home was usually scheduled for the day of discharge and whenever required thereafter. Training the patient to administer the antibiotics safely was the main focus of ASIS. However, in situations where patients were unable to self-administer antibiotics, training was provided to the carer. The majority of patients were able to return to work or studies whilst on ASIS, provided their infection did not pose functional limitations. Only four of the 144 patients were unable to self-administer and did not have carers who could be trained to administer antibiotics. Nursing staff visited those patients' homes daily to administer intravenous antibiotics. The inability to self-administer was not a criterion for exclusion from OPAT care. Patients treated by ASIS were under the care of an infectious diseases team and were required to attend a weekly clinic where they were reviewed by an infectious diseases specialist or a registrar.

3. Results

In 2011, 150 OPAT episodes were treated by ASIS in 144 patients. One hundred and six patients (74%) were male. The median age was 55 years (range 16–90 years). Hypertension was the most common comorbidity, occurring in 59 patients (40%), followed by diabetes mellitus (37 patients, 25%), ischaemic or valvular heart disease (30 patients, 21%), and chronic kidney disease (25 patients, 17%). Forty-two percent of patients had at least two or more comorbidities. All patients had a PICC line inserted for the administration of intravenous antibiotics.

The patient self-administration model was used in 140 patients and the nursing administration model in the remaining four patients. During the 12-month period, 466 home visits were made for 84 patients. Sixty-six patients did not require home visits during their OPAT care. The median duration of time spent on patient/carer training was 105 min.

3.1. Diagnoses and microbiology

Bone and joint infections (BJI) were the most common primary diagnoses, occurring in 71 patients (47%). Osteomyelitis accounted for 85% of BJI and septic arthritis for 15%. Other diagnoses were infective endocarditis (13 patients, 9%), infected intravascular catheters (12 patients, 8%), skin and soft tissue infection (10 patients, 7%), surgical site infection (10 patients, 7%), blood stream infection (nine patients, 6%), central nervous system infection (six patients, 4%), and intra-abdominal infection (six patients, 4%). Table 1 summarizes patient demographics and diagnoses.

Causative organisms were identified from blood cultures, surgical specimens, or wound swabs. A confirmatory microbiological diagnosis was made in 130 patients (87%). Twenty (13%) patients were recorded as having 'no growth' from cultures. Polymicrobial infection was present in 27 patients (18%). The most frequent microorganism isolated was *Staphylococcus aureus*, found in 72 patients (48%). Methicillin-resistant *S. aureus* (MRSA) was isolated in nine patients (6%). Of the nine MRSA isolates, seven

Table 1
Patient demographics and diagnoses of all patients treated by ASIS

	Receiving ASIS, *n* (%)
Episodes (*n*)	150
Median age in years (range)	55 (16-90)
Males	106 (74)
Comorbidities	
Hypertension	59 (40)
Diabetes mellitus	37 (25)
Ischaemic or valvular heart disease	30 (21)
Chronic kidney disease	25 (17)
Chronic lung disease	21 (14)
Other chronic illness	47 (31)
Number of comorbidities	
0	44 (29)
1	43 (29)
2	26 (17)
3 or more	37 (25)
Diagnosis	
Bone and joint infections	71 (47)
Infective endocarditis	13 (9)
Infected intravascular catheter	12 (8)
Skin and soft tissue infection	10 (7)
Surgical site infection	10 (7)
Blood stream infection	9 (6)
Central nervous system infection	6 (4)
Intra-abdominal infection	6 (4)
Lung/renal/liver abscess	5 (4)
Empyema	3 (2)
Other	5 (3)

ASIS, Alternate Site Infusion Service.

were non-multi-resistant MRSA. The second most common group were the *Enterobacteriaceae*, identified in 15 patients (10%), including *Enterobacter spp* in six (4%), *Klebsiella spp* in four (3%), *Escherichia coli* in two (1%), and *Serratia marcescens* in two (1%). *Pseudomonas aeruginosa* was isolated in 14 patients (9%), *Streptococcus spp* in nine (6%), anaerobes in nine (6%), *Enterococcus spp* in eight (5%), other *Staphylococcus spp* in eight (5%), and mixed enteric bacteria in five (3%). Figure 1 illustrates the causative organisms in graphical format.

3.2. Antimicrobial therapy and duration

One hundred and sixty-two antimicrobials were prescribed for the 150 episodes of care. One hundred and ten (76%) patients were continued on oral antibiotics upon completion of the intravenous course. Twelve (8%) patients were treated with more than one antimicrobial at the same time. Continuous intravenous infusions were used in 119 (74%) episodes and intermittent bolus administration in 43 (36%). As a class, beta-lactam antibiotics were the most frequently prescribed. Flucloxacillin was the most common antibiotic used and was prescribed in 57 patients (35%), followed by ticarcillin–clavulanic acid in 31 patients (19%). Vancomycin was used to treat 17 patients (10%), benzylpenicillin for 12 (7%), ceftriaxone for 11 (7%), ertapenem for nine (6%), meropenem for eight (5%), cefazolin for six (4%), ceftazidime for four (2%), lincomycin for three (2%), and teicoplanin for one (1%). Vancomycin was administered as a continuous infusion in four patients and as intermittent boluses in 13 patients. Trough levels were assessed weekly and the median trough level was 16 mg/L (range 9–35). Figure 2 demonstrates the antibiotics prescribed in graphical format.

The total number of inpatient bed-days saved by administration of intravenous antibiotics outside the hospital was 3520. The median duration on ASIS was 22 days (range 4–106 days). Blood stream infections were on the programme for a median of 25 days, BJI for 23 days, surgical site infections for 22 days, complicated soft tissue infections for 16 days, and infective endocarditis for 15 days. There were 10.7 patients on average on the ASIS programme at any one time, being cared for by four full-time equivalent ASIS nurses who were on-call 7 days a week. Figure 3 illustrates the duration of treatment for the different infections in graphical format and the split between inpatient and OPAT.

3.3. Adverse events

There were 11 (7%) drug-related adverse events, one of which resulted in patient re-admission to hospital. The rest were managed with symptomatic treatment, earlier cessation, or a change of antibiotic. The most common drug-related adverse event was rash, accounting for six out of the 11 drug-related adverse events. Flucloxacillin (three patients) was the most common culprit, followed by vancomycin (two patients) and cefoxitin (one patient). A switch to a different antibiotic was necessary for four patients who developed a rash whilst on OPAT; two patients who developed a rash had their antibiotics ceased earlier than intended (Table 2).

One patient developed biliary lithiasis secondary to ceftriaxone, which resolved after ceftriaxone was ceased earlier than intended. Drug fever occurred in one patient treated with ticarcillin–clavulanic acid. The patient was admitted to hospital for further investigations and antibiotics were ceased in hospital. Acute kidney injury due to gentamicin occurred in one patient treated for enterococcal endocarditis. The other case of acute kidney injury was presumed flucloxacillin-induced interstitial nephritis, which resolved after the antibiotic was switched to cefazolin.

Line-related adverse events occurred in five (3%) patients or 1.4/1000 catheter-days. There were two PICC line infections, which resulted in cessation of antibiotics earlier than planned. In both cases, the diagnosis of line infection was made on clinical suspicion and neither of them resulted in detectable bacteraemia. This line-related

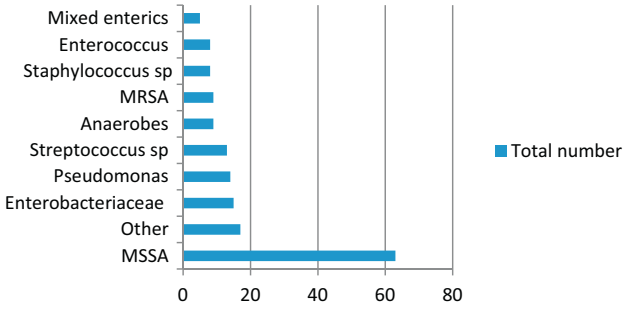

Figure 1. Principle organisms treated in 2011 by ASIS (MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*).

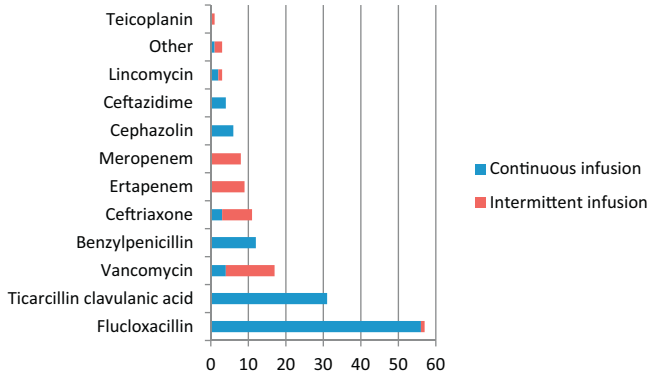

Figure 2. Antibiotics prescribed in 2011 by ASIS.

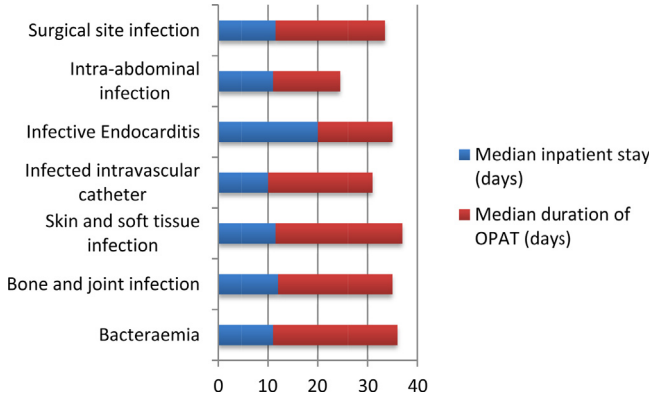

Figure 3. Duration of treatment for various infections treated by ASIS in 2011.

infection rate is lower than those reported from other S-OPAT programmes described in the literature.[21,25] Two patients had problems with lymphatic leakage from their PICC line, which was managed with additional dressings. Intravenous antibiotics were continued for the planned duration in both cases. One patient was re-admitted to hospital for re-insertion of the PICC line as it fell out inadvertently. The line-related sepsis rate in our study is similar to other published results.[18,24]

3.4. Outcome

The overall cure rate in our study was 93%. ASIS-related re-admissions occurred in nine patients within 28 days of cessation of intravenous antimicrobials. Six of those re-admissions were due to clinical deterioration requiring source control or surgical debridement and one re-admission was due to clinical failure on current antibiotics requiring a change of antimicrobial therapy. There was one drug-related re-admission and one line-related re-admission. On multivariate analysis, patients with two or more comorbidities had an increased risk of failure (OR 2.15, 95% CI 1.28–3.65; $p = 0.004$).

4. Discussion

We describe a patient- or carer-administered OPAT model run by a multidisciplinary team through the Infection Management Service at the Princess Alexandra Hospital. To our knowledge, this is the first study from Australia that has specifically evaluated the outcomes of S-OPAT. In line with other international published data, our study shows that patient- or carer-administered OPAT is a safe and effective option for the management of selected patients with serious infection.[17,20,21]

The median age of the patient cohort in our study is similar to previous studies; however the male to female ratio is higher.[10,21–23] In accordance with other published data, BJI were the most commonly treated infections.[10,17,21,24] *S. aureus* was the most commonly isolated organism, but the proportion of MRSA in our study was lower than those reported in similar published studies.[10,23]

Antibiotic prescribing in our programme was concordant with our hospital prescribing guidelines and the choice of antibiotic was not made solely on the basis of dosing convenience. Narrow-spectrum beta-lactam antibiotics were used where possible to match the culture-proven microbiological diagnoses. Flucloxacillin was the most frequently used antibiotic and was prescribed in 57 patients (35%). Cefazolin and ceftriaxone were only prescribed in six (4%) and 11 (7%), respectively. In the majority of published studies, vancomycin, ceftriaxone, and cefazolin were most frequently prescribed due to the convenience of a once- or twice-daily dosing regimen. All patients in our cohort had a PICC line for the administration of antibiotics. Line-related complications were uncommon, similar to previously reported studies, which have shown that these adverse events are not necessarily increased in S-OPAT.[24]

The overall median duration of OPAT was 22 days (range 4–106 days). The median duration of OPAT was highest for bacteraemia and BJI, and lowest for infective endocarditis. Princess Alexandra Hospital is a referral centre for cardiac surgery and most patients with infective endocarditis had completed a significant proportion of their prescribed antibiotic therapy in hospital whilst undergoing surgical therapy. Patients who did not have cardiac surgery usually required medical and surgical assessment and stabilization for a period of time as inpatients prior to commencing OPAT.

The clinical outcome in our study was excellent, with cure achieved in 93% of patients despite complicated baseline diagnoses. Most treatment failures occurred in complex surgical patients who required repeated surgical treatment for better source control; hence the treatment of these patients in an outpatient setting did not necessarily result in clinical failure. In our study, outcomes were only measured for 28 days post cessation of OPAT. A longer duration of follow-up would detect clinically significant late relapses following the cessation of OPAT.

The nursing staff spent significant time in our OPAT on patient or carer training. Most patients in our cohort had complicated infections, unlike those recruited in other studies in which cellulitis was the most frequently treated infection through OPAT.[20,23,25] As most patients require at least a day or two to become proficient in self-administering parenteral therapy, our OPAT programme is not likely to shorten the length of stay for patients with cellulitis. Most patients in our programme had complicated infections that required some days in hospital for the initial management; hence the time spent in training patients to self-administer antibiotics did not necessarily lengthen their overall hospital stay.

The OPAT model of care is important in developed countries like Australia where healthcare costs and the demand for inpatient care are rising in the context of limited hospital bed supply. The possibility of reducing healthcare-acquired infections and reducing the costs of inpatient care whilst maintaining patient autonomy has led to increasing interest in OPAT services, with many organizations now being set targets to achieve.[5,26]

The total costs incurred by our OPAT service were reduced by the low number of home visits our nursing staff made over the 12 months. The cost of our OPAT, excluding drug administration and home visits, is estimated to be approximately A$ 150.00 per day, significantly lower than the cost of an inpatient bed, which is estimated to be A$ 500–800 per day depending on the Diagnosis Related Groups (DRG).[25] Patients enrolled in our OPAT lived on average 20 km (range 1–58.2 km) away from the hospital. If all patients were managed with the nursing administered model of care, there would have been approximately 3300 home visits during the year, as opposed to the 466 home visits made during the year through our OPAT.

Table 2
Outcome of patients treated by ASIS

Outcome	No. of patients (%)
Clinical cure	140 (93)
Failure	10 (7)
Re-admission	9 (6)
Inadequate source control	6 (4)
Inappropriate antibiotic	1 (0.6)
Drug-related adverse event	1 (0.6)
Line-related adverse event	1 (0.6)

ASIS, Alternate Site Infusion Service.

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Conflict of interest: None.

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