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Setting up an outpatient parenteral antimicrobial therapy (OPAT) unit in Switzerland: review of the first 18 months of activity

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Abstract

Objectives

Outpatient parenteral antimicrobial therapy (OPAT) has been recognised as a useful, cost-effective and safe alternative to inpatient treatment, but no formal OPAT unit existed in Switzerland until recently. In December 2013 an OPAT unit was established at Lausanne University Hospital. We review here the experience of this new OPAT unit after 18 months of activity.

Methods

Patient characteristics, clinical activities and outcomes were recorded prospectively. Need and acceptance was evaluated as number of OPAT courses administered and number of patients refusing OPAT. Safety and efficacy were evaluated as: 1) adverse events linked to antimicrobials and catheters, 2) re-admission to hospital, 3) rate of treatment failures and 4) mortality.

Results

Over 18 months, 179 courses of OPAT were administered. Acceptance was high with only 4 patients refusing OPAT. Urinary tract infections with resistant bacteria and musculoskeletal infections were the most common diagnoses. Self-administration of antibiotics using elastomeric pumps became rapidly the most frequently used approach. 16 patients presented with adverse events linked to antimicrobials and catheters. OPAT- related readmissions occurred in 9 patients. The overall cure rate was 94%.

Conclusion

This study shows that OPAT is very well accepted by patients and medical staff, even in a setting which has not used this type of treatment approach until now. Self-administration using elastomeric pumps proved to be particularly useful, safe and efficient. OPAT offers a good alternative to hospitalisation for patients presenting with infections due to resistant bacteria that cannot be treated orally anymore and for difficult to treat infections.

Keywords

OPAT, drug delivery, antibiotic resistance, difficult-to-treat infections

Introduction

Some patients require parenteral antibiotic therapy, but are well enough to return home. Outpatient parenteral antimicrobial therapy (OPAT) was first developed in the USA in the 1970s for patients with cystic fibrosis, before being adopted by many countries [1-4]. It has been recognised as a useful, cost-effective and safe alternative to inpatient treatment. It is now a standard care in several countries and different national guidelines have been established [5-7]. There are various models of care for OPAT and most OPAT centres provide hospital-centred nursing programmes or services based on nurses visiting the patient's home. A few centres have also shown that self-administration of intravenous antibiotic therapy is an effective and safe option for selected patients [8, 4]. Furthermore, use of continuous infusion of antibiotics increases the number of feasible treatments. Continuous infusion by pumps of antibiotics with a time-dependent killing mechanism is a practical option which has been described for treatment of

methicillin-susceptible *Staphylococcus aureus* (MSSA) infections and exacerbations of cystic fibrosis [9,10,11]. In Europe, even if many specialists feel that OPAT is required in their country, it is still underdeveloped because of lack of funding, lack of leadership and lack of coordination between hospitals and community care [12].

In the last decades, programmes to enhance care delivery on an outpatient basis in order to contain health costs have been developed in Switzerland. Administration of outpatient intravenous antibiotic therapy for patients who require parenteral therapy, but are otherwise fit enough to go home, hasn't been used widely until recently and, to our knowledge, no official OPAT programme has been implemented in our country. In December 2013, an outpatient parenteral antibiotic treatment (OPAT) unit was initiated at Lausanne University Hospital with the goal of offering an alternative treatment programme that is equally effective and as safe as inpatient treatment.

The purpose of this study was to review the experience after implementation of a new OPAT unit in the context of the Swiss Health System. Data were prospectively recorded in an OPAT registry in order to evaluate the need and acceptance, as well as the efficacy and security of the programme.

Methods

The OPAT service

The University Hospital of Lausanne is a 1462-bed teaching hospital providing care in all major specialties. The OPAT service is led by infectious diseases physicians and a team of nurse practitioners. Patients are referred to the OPAT service by the physicians from the inpatient hospital wards, emergency

department, outpatient clinics and private hospitals. The Infectious Diseases Society of America (IDSA) guidelines are used as a basis for the organisational aspects of the unit [5, 13]. Antimicrobials are administered via peripheral catheters or peripherally inserted central catheters (PICC lines), the latter being inserted by specialist radiologists. The route of therapy (peripheral catheter vs PICC line) depends on the length of treatment and the type of administration (intermittent vs continuous drug administration), PICC lines being usually used for treatment longer than 7 days and for continuous infusions. Antibiotic administration is ensured using one of three options: 1) an OPAT nurse at the infusion centre (hospital OPAT); 2) at home with a visiting nurse (homecare OPAT); 3) the patient himself or a relative using elastomeric infusers (Easypump, B. Braun, Germany and Autofuser, Teleflex, Germany) (self OPAT). Elastomeric pumps are non-electronic pumps which deliver medication by deflation of an elastomeric membrane. They are prepared by a commercial compounder and are delivered to the infusion centre or directly to the patient's home. In addition to being used for self-administration of intermittent infusions, elastomeric infusers are employed for continuous infusions of all antibiotics showing good stability for at least 24 hours [14, 15].

If self OPAT is considered feasible, the patient is provided with training in self-administration of antibiotics prior to discharge. Training takes place at the bedside and requires 1-2 hours of nursing time. If necessary, the patient is seen once or twice more at the OPAT clinic for additional training.

Patients needing short courses of antibiotics (less than 4 days) are usually proposed to be treated at the OPAT clinic and those with limited mobility are treated at home by homecare OPAT.

Patients are reviewed by a physician and a nurse at least once a week at the OPAT clinic for symptom review, inspection and care of the intravascular device and blood monitoring. Follow-up imaging studies are done if considered necessary.

Data collection

Demographic data, site and nature of infection, antibiotic used, mode of administration, duration of therapy, and outcome of infection were prospectively recorded for all patients treated at the OPAT unit between December 2013 and May 2015 (18 months). Patient readmissions, adverse events related to antibiotics requiring stopping therapy, vascular access complications and death were also recorded. If a patient was, for any reason, re-hospitalized during an OPAT course and then re-enrolled without any change in diagnosis or treatment, he was included as the same OPAT episode and was not regarded as failure.

Failure was defined as any evidence of relapse during antibiotic treatment, need for unanticipated surgery to control the infection or recurrence of infection within 90 days of cessation of intravenous antibiotics.

The study was approved by the Ethics Committee of Vaud Canton. Patients were informed about the data collection and gave informed consent.

Results

Patients

Over the study period of 18 months, 237 patients were referred to the OPAT unit. The OPAT unit refused to take care of 73 patients (30%). 20 presented health conditions not suitable for ambulatory care. 16 were living too far away (> 20km). 20 were switched to oral therapy or didn't need antibiotics anymore. 17 were refused for other reasons. Only 4 patients refused OPAT.

179 courses of OPAT (= OPAT episodes) were administered to 160 patients, resulting in a total of 2533 days of patient care (median per patient: 9 days, range 1-78). The majority of patients were male (101/160; 63%) and the median age was 58 years (range 18-92). Over those 179 OPAT episodes, 86 patients (48%) had a PICC line, 84 patients (47%) a peripheral catheter and 9 patients (5%) a portacath. The majority of patients (36%) were referred from surgical departments, followed by ambulatory care (33%) and internal medicine (31%).

Diagnosis and microbiology

The infectious diseases diagnoses are summarised in Figure 1. The most common primary diagnoses were urinary tract infections (58 episodes, 32%) and bone and joint infections (40 episodes, 22%).

Microbiological data were available for 159 patients (88%). The most frequent microorganisms isolated were *Enterobacteriaceae* (59 cases, 33%). *Escherichia coli* was by far the most common pathogen and was found in 50 episodes (28%). Extended-spectrum β-lactamase (ESBL) producing and

fluoroquinolones-resistant *E. coli* were predominant (27/50 and 14/50 respectively). The second most common microorganism was *Staphylococcus aureus*, identified in 21 patients (12%). Methicillin-resistant *S. aureus* was isolated in only 3 patients. *Streptococcus spp* were isolated in 18 patients (10%), *Staphylococcus epidermidis* in 15 patients (8%) and *Pseudomonas aeruginosa* in 9 patients (5%).

We took charge of 11 patients more than once for different infectious episodes. 8 patients presented with recurrent urinary tract infection and were colonised with resistant Enterobacteriaceae (fluoroquinolones-resistant *E. coli* or ESBL-producing Enterobacteriaceae) or *P. aeruginosa*. 4 of those patients were solid organ transplant recipients. Those episodes were not related one to another and were not regarded as failure (too much time between episodes, different sites of infection, different types of bacteria).

Antimicrobial therapies

Antimicrobials used are shown in Figure 2. β-Lactams and glycopeptides were the most commonly used antibiotics. The most frequently prescribed agents were ceftriaxone which was used in 64 OPAT episodes for 825 days of treatment (33%), followed by ertapenem in 38 OPAT episodes (469 days of treatment, 17%) and flucloxacillin in 19 OPAT episodes (308 days of treatment, 12%). Vancomycin was used in 11 OPAT episodes (213 days of treatment, 9%) and teicoplanin in 6 (189 days of treatment, 8%). The hospital OPAT model was used for 82 patients (46%), self-administered OPAT for 55 patients (31%) and the homecare OPAT model for 42 patients (23%). As illustrated in Figure 3, self-administration was the preferred service model (1109 days, median per patient: 9; range 3-66) in terms of treatment-days and a significant increase of this approach was noticed during the 18 months of follow-up with 75% of patients treated this way during the last 6 months. Elastomeric pumps were used for 66 OPAT episodes (37%).

Continuous intravenous infusion was used for all antibiotics showing sufficient stability for 24 hours infusion. 42 patients were administered continuous infusions (24%) of flucloxacillin (19 episodes), cefepime (6), piperacillin-tazobactam (6), vancomycin (5), cefazolin (3), amoxicillin (2), and ceftazidime (1).

Adverse events and outcome

Drug-related and line-related adverse events were recorded. 16 of 179 OPAT episodes (9%) had some complication recorded. Drug-related adverse events accounted for the majority of complications and occurred in 10 patients (5.5%): drug rash *n*=3, thrombocytopenia *n*=2, acute hepatitis *n*=2, neutropenia *n*=1, acute renal insufficiency *n*=1, fever *n*=1.

Three patients were readmitted to hospital for these drug-related adverse events. There were 6 line-related adverse events (3.5%), all related to PICC lines. Two were PICC line related thrombosis of the upper arm, which were treated by anticoagulation for 6 weeks. Neither of these patients had clinical evidence of pulmonary embolism. Three patients had PICC line infections. One patient presented with two distinct episodes of catheter-related bacteraemia with two different bacteria (*Enterobacter aerogenes* and *Klebsiella pneumonia*). He was readmitted to hospital for change of the PICC line for both episodes. A second patient also presented with bacteraemia and secondary infection of his knee's spacer. He was readmitted for surgery. In both cases, antibiotics were administered at home by a nurse. The last patient was self-administering antibiotics for a *Staphylococcus aureus* bacteraemia. He was asymptomatic, but had control blood cultures which were positive for *Enterobacter cloacae.*

We did not observe any episode of *Staphylococcus aureus* PICC line infection or *Clostridium difficile* colitis during treatment or during the 3 months of follow-up after completion of treatment.

Re-admission to hospital occurred in 24 OPAT episodes (12%), of which 7 were planned re-admissions and 8 unrelated to OPAT. OPAT-related re-admissions occurred in nine patients (5%) of whom two were self-administering antibiotics. Two patients were readmitted for PICC line infections, one of whom was readmitted twice. Three patients (1.6%) were readmitted because of drug-toxicity. Only three patients (1.6%) were readmitted because of treatment failure during OPAT. No patient died during OPAT.

The overall cure rate was 94% with 11 patients presenting as clinical failure. Five patients needed surgical intervention for source control: three for abscess incision and two for removal of osteosynthesis material. Six patients relapsed after treatment completion. All of them had a urinary tract infection and were successfully retreated in an ambulatory setting. Outcomes are summarised in Table 1.

Discussion

There is a continuous pressure on hospital beds in Switzerland and the health authorities encourage a more community-based model of care in order to reduce hospital stay, reduce costs and increase availability of beds. In December 2013, an OPAT service was established at the University Hospital of Lausanne to improve ambulatory care of patients needing intravenous antimicrobials, but whose general condition allows them to go back home. This study shows that there is a real need and a high acceptance for an OPAT structure. During the first 18 months following the implementation of the service, 179 patients were treated by OPAT, a number that concords with what has already been described and shows

that there is a real demand from the inpatient structure [16-18]. Furthermore, 2533 bed-days of inpatient admission have been avoided, which meets the demands of the hospital and the National Health System. These figures are a strong argument for the development of other OPAT programmes in our country.

Musculoskeletal infections predominated in terms of treatment-days administered. This is not surprising considering that prosthetic surgery is increasing in an aging population as in Switzerland, and that prosthetic infections do invariably occur in a small percentage of these cases. It is to be expected that patient need for OPAT will increase in the future. Most of the patients with urinary tract infection treated by our OPAT unit had infections with ESBL producing and fluoroquinolones-resistant gram-negative bacilli. Switzerland is currently facing a strongly increasing burden of infections with resistant gram-negative bacilli, which will in the future increase the need for parenteral treatment [19]. These data suggest that OPAT structures will be increasingly needed for “difficult to treat” - such as prosthetic infections, as well as for new situations like the current epidemic of resistant gram-negative bacillary infection.

A characteristic of the OPAT model in Lausanne is its adaptability to a wide range of clinical situations and lengths of treatment. The fact that the OPAT service proposes three different types of administration means that any intravenous antibiotic can be administered in an ambulatory setting. Patients can be taken care of promptly by hospital OPAT if they present with a diagnosis which doesn’t need hospitalisation, like urinary tract or skin and soft tissue infections. Collaboration with home care providers has also made it possible to treat patients with limited mobility at home. The home care providers have been particularly flexible in the sense that they can ensure up to 4 antibiotic injections per day. Finally, self-administered

OPAT has been shown in our setting to be particularly useful, well accepted and safe. Patients receiving both, long and short antibiotic courses, tend to appreciate the advantages of treatment with elastomeric pumps and demonstrate good abilities for managing those treatments themselves. In addition, the organisation of the hospital discharge is facilitated when self-administration is chosen. Beside the instruction of the technique of self-administration with the pumps, this approach does not require the availability of OPAT nurses or infrastructure, except for the occasional follow-up visits. During the last six months of the study period, an important increase of self-administration was observed and currently 75% of patients are treated by self-administered OPAT. This is probably explained by a concordance of different factors, such as development of clear guidelines, more confidence about the use of pumps by the team and high satisfaction of the patients.

Self-administration using elastomeric pumps is likely to be interesting from an economic point of view. Elastomeric pumps cost about US$ 50 per piece and the cost to prepare them is about US$ 50 per pump excluding the drug cost [20]. One treatment day with an elastomeric pump costs therefore US$ 100, which is less than the cost of 2 hours of nursing time (US$ 80 per hour) for a home visit, or the nursing time and the cost of the treatment room to administer the antibiotics at the hospital [21]. This cost difference between self OPAT and nurse-administered OPAT is particularly important if the antibiotics have to be administered several times a day. A complete economic analysis is currently being conducted to clarify this point.

Antibiotics being traditionally given in hospital, it was not known how patients and medical staff would accept this new way of treatment. Acceptance was better than expected and only 4 patients refused to be

taken care of by the OPAT unit. We noticed however that some habits are difficult to change. For instance, patients are traditionally kept at hospital until the end of fever even if their clinical situation has been stabilised. Many practitioners also don't know that some antibiotics that require multiple doses per day, for example flucloxacillin, can be prescribed by continuous infusion, which facilitates treatment at home.

Cure was achieved in 94% of patients, which is in line with the results from other published cohorts. In addition, the re-admission rate of 12% is comparable to what has already been described and only 9 of those were related to OPAT care [2, 18, 22, 23]. These figures are reassuring, considering that a relatively large proportion of the patients have been self-administering their treatment with elastomeric pumps. It can in particular be highlighted that line-related complications were rare and infections were not related to self-administration in three cases out of four.

The use of elastomeric infusers for self-administration is well described and antibiotic stability tables have been published [15, 24-26]. Most antibiotic stability data have been produced by manufacturers of elastomeric pumps under standardised laboratory conditions and there can be a concern about drug-stability depending on the infuser temperature under real-life conditions. Preliminary data measuring drug concentrations in the elastomeric pumps and in the plasma of patients (data not shown) seem to be reassuring, but additional such data will be collected in the future at our OPAT unit.

Conclusion

In conclusion, this study demonstrates that there is a real need and acceptance for an OPAT unit even in a setting that has traditionally been favouring hospital-based treatment of patients requiring intravenous

antibiotics. The data collected also prove that it is safe and efficient with low levels of failures and complications, even if a large proportion of patients were treated by self-administered OPAT using elastomeric pumps. Considering that infections due to multi-drug resistant bacteria, and difficult-to-treat such as prosthetic infection were the most frequent infections treated by the OPAT unit, and that these types of infection are likely to increase, it is probable that the need for an OPAT unit will even be more important in the future.

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Conflicts of interest:

None to declare

Transparency declarations

None to declare

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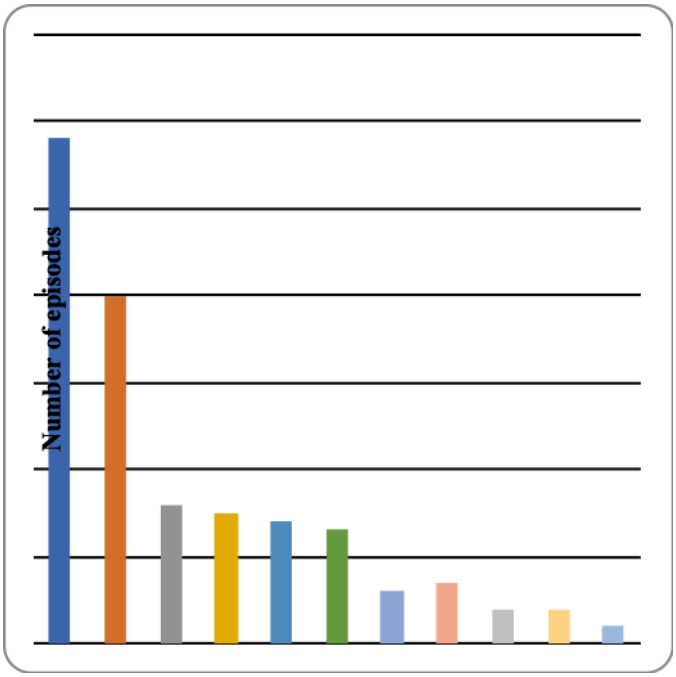

Fig. 1A Infections treated in terms of number of episodes (total number of episodes n = 179)

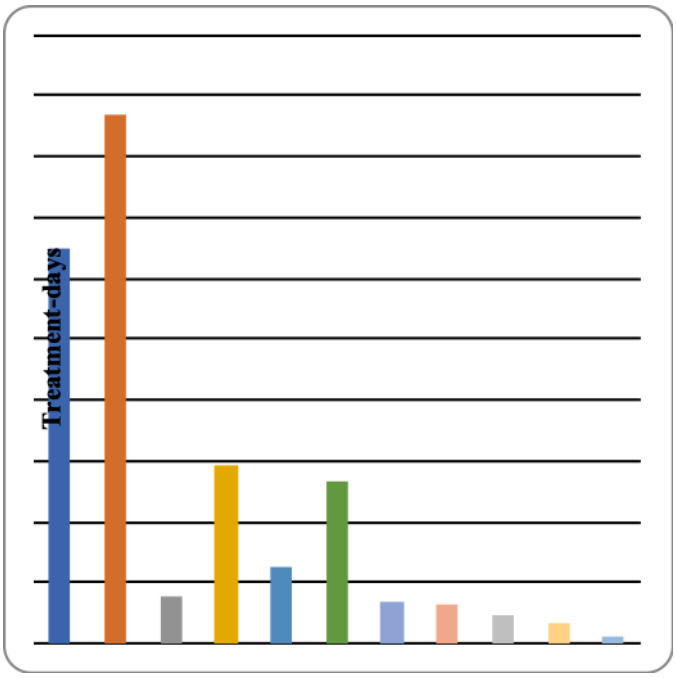

Fig. 1B Infections treated in terms of treatment-days administrated (n = 2533)

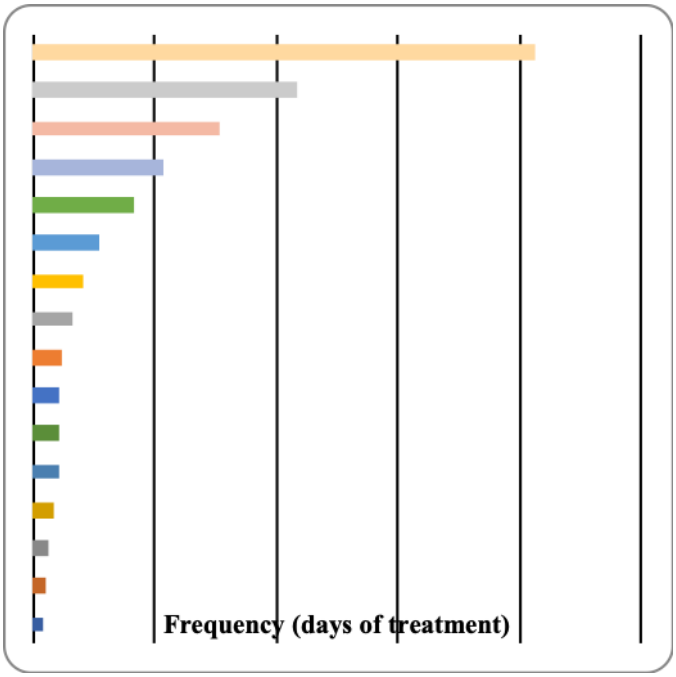

Fig. 2 Antimicrobials used

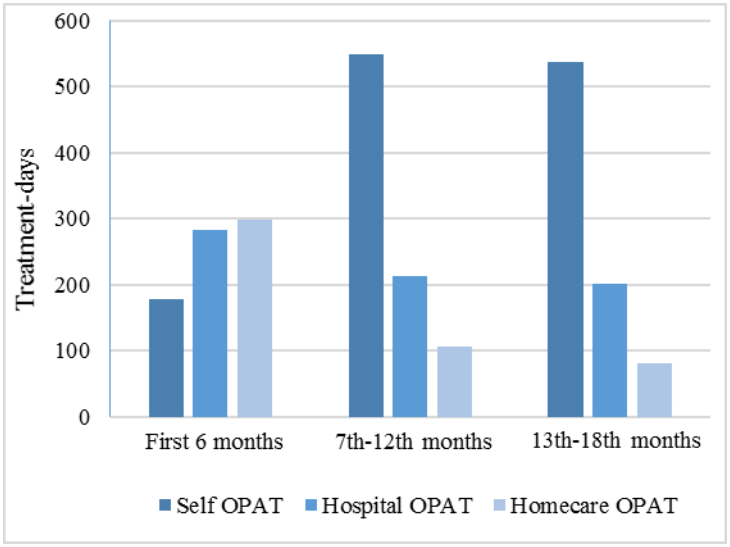

Fig.3 Evolution over 18 months of the service models used in term of treatment-days (n=2533)

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Re-admissions	No (%) of patients	Cumulative risk per 1000 OPAT treatment-days
Total	24 (13%)	9.5
Planned	7 (4%)	2.8
Unplanned	17 (9%)	6.7
Treatment failure	3	
Adverse drug reaction	3	
PICC line infections	3	
Other medical complications	8	

Specific adverse events	No (%) of patients	Cumulative risk per 1000 OPAT treatment-days
Total	16 (9%)	6.4
Adverse drug reaction	10 (5.5%)	4.0
Rash	3	
Thrombopenia	2	
Acute hepatitis	2	
Neutropenia	1	
Acute renal insufficiency	1	
Fever	1	
Line-related adverse events	6 (3.5%)	2.4
Line infections	4	
Line thrombosis	2	

Treatment failures	No (%) of patients	Cumulative risk per 1000 OPAT treatment-days
Total	11 (6%)	4.4
Unplanned surgery	5 (2.8%)	2.0
Surgical drainage of an abscess	3	
Removal of material of osteosynthesis	2	
Relapse after treatment completion	6 (3.2%)	2.4

331 **Table 1** Outcomes and adverse events