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Outpatient parenteral antimicrobial therapy

Ann L N Chapman

Department of Infection and Tropical Medicine, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundations Trust, Sheffield S10 2JF, UK
ann.chapman@sth.nhs.uk

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Outpatient parenteral antimicrobial therapy (OPAT) allows patients to be given intravenous antibiotics in the community rather than as an inpatient. First developed in the 1970s in the US for the treatment of children with cystic fibrosis,[1] OPAT has expanded substantially and is now standard practice in many countries.[2 3] In the UK, uptake has been much slower, although OPAT is now being increasingly used in both primary and secondary care, driven by a national focus on efficiency savings in healthcare, improving patient experience, and provision of care closer to home. It is important that medical practitioners are aware both of the opportunities that OPAT presents and of the potential risks of treatment outside hospital for patients with serious and often complex infections. This article aims to describe the clinical practice of OPAT, highlight potential risks, and explore how these may be reduced.

What is OPAT?

OPAT is the administration of intravenous antimicrobial therapy to patients in an outpatient setting or in their own home. It can be used for patients with severe or deep seated infections who require parenteral treatment but are otherwise stable and well enough not to be in hospital; these patients may be discharged early to an OPAT service or may avoid hospital admission altogether.

What type of infections can be treated?

Cellulitis

OPAT is most widely used for patients with soft tissue sepsis, mainly cellulitis.[4 5] Cellulitis accounts for 1-2% of emergency hospital admissions in England and Wales, or about 80 000 admissions annually.[6] Around 30% of patients presenting to hospital with cellulitis have moderately severe infection that requires intravenous antibiotics but do not have severe systemic sepsis necessitating inpatient care.[7 8] One randomised controlled trial of twice daily intravenous cefazolin administered by a nurse at home compared with standard inpatient care showed no significant difference in duration of intravenous or subsequent oral antibiotic therapy, patient functional outcomes, or complications but reported improved patient satisfaction with home treatment.[9]

SUMMARY POINTS

- Outpatient parenteral antimicrobial therapy (OPAT) allows patients requiring intravenous antibiotics to be treated outside hospital
- OPAT is suitable for many infections, especially cellulitis, bone and joint infections, and infective endocarditis
- Antibiotics can be administered in an outpatient unit, at home by a nurse, or at home by the patient or a carer
- Patients should be assessed by a doctor and specialist nurse to determine medical and social suitability
- Evidence suggests that OPAT is safe as long as it is administered through a formal service structure to minimise risk

SOURCES AND SELECTION CRITERIA

References were sourced through a systematic review of the literature undertaken for the UK OPAT Good Practice Recommendations in 2012. The search included all English language articles between 1998 and 2010, and was further updated with a search of PubMed, Medline, and Cochrane databases. Published OPAT guidelines from other countries and key reviews were also used, as well as the author's knowledge of the literature.

Data from several large retrospective case series show that outpatient treatment with once daily ceftriaxone is also safe and effective, with good short and long term clinical outcomes, and this is now the predominant antibiotic used for outpatient intravenous treatment of cellulitis in the UK.[4 5 10] If there is concern about possible meticillin resistant *Staphylococcus aureus* (MRSA) infection, teicoplanin or daptomycin are alternatives.[5] Increasingly a nurse led model of care is being used for management of cellulitis outside hospital, with treatment set out in a protocol and limited input from doctors.[11]

Bone and joint infections

Patients with bone and joint infections invariably require prolonged parenteral antibiotic courses, and several large retrospective case series have shown that outpatient treatment can be used successfully in this group.[12-14] Patients may receive outpatient antibiotics within a two stage revision of an infected joint or as sole therapy for septic arthritis or osteomyelitis. One UK study reported outcomes for 198 patients with a range of bone and joint infections treated by OPAT. Seventy three per cent of patients were disease free at median follow-up of 60 weeks; patients with advanced age, MRSA infection, and diabetic foot infections were more likely to have a relapse or recurrence.[12]

Infective endocarditis

US, European, and UK guidelines now recommend OPAT as part of routine clinical care for patients with infective endocarditis.[15-17] Although initially recommended only for uncomplicated native valve infections with low risk organisms, there is increasing evidence that OPAT is safe in more complex patients after an initial period of inpatient care, as long as the potential risks are assessed on a case by case basis and treatment is administered through a formal OPAT service with the appropriate safeguards to minimise risk.[18 19] Such safeguards include daily nurse review, once or twice weekly physician review, and the establishment of an escalation pathway for medical staff familiar with the case to be informed of potential problems.[15 16]

Other uses

Use of OPAT has been described for numerous other infections, including resistant urinary tract infections, central

nervous system infections, and low risk neutropenic sepsis.[20-22] The availability of long acting antibiotics such as ceftriaxone, teicoplanin, and daptomycin and the diversity of models for delivering OPAT allows most stable patients requiring intravenous antimicrobials to be considered for outpatient treatment. However, there are some situations where it is less useful—for example, patients with pneumonia are best managed either with outpatient oral therapy for mild infection or intravenous antibiotics in hospital for more severe cases.[23]

Which patients are suitable?

Patients referred for outpatient treatment need to be clinically stable, both in terms of their general condition and their infection. Thus they should have stable vital signs and be at low risk of their infection progressing or developing serious complications.[2 3 24] Patients with a diagnosis of cellulitis, for example, need to be assessed by a healthcare practitioner competent to exclude other more serious conditions that could potentially be confused with cellulitis, such as septic arthritis or necrotising fasciitis. Patients with endocarditis are more likely to develop potentially life threatening complications in the first two weeks of therapy, and outpatient administration is therefore not recommended until after this period.[16] Determination of suitability will generally require a medical review, unless a protocol is in place for assessment by another trained healthcare practitioner.[11]

Other health and social issues also need to be explored. OPAT requires the patient to engage actively and reliably with therapy, and thus patients with substance misuse or serious mental health problems may not be suitable. In addition, there must be no other barrier to discharge from hospital. For example, although diabetic foot infections may be suitable for OPAT, many patients will require other care that has to be provided in hospital, including adjustment of diabetic control, vascular assessment, and surgical intervention.[25] Finally, home based care must be suitable from a social perspective—for example, an acceptable home environment, access to a telephone, adequate transport, and support from family or carers, In general the OPAT nurse, in collaboration with other professional teams, is best placed to assess these additional factors, and current OPAT guidelines recommend that patients should be assessed by both a doctor and nurse before being accepted for outpatient administration.[2 3 24]

How is OPAT delivered?

Three service models can be used to deliver OPAT, all of which have been shown to be effective: an ambulatory care centre, a nurse attending the patient's home, or self administration. The approach used varies among countries—for example, infusion centres have been the dominant model in the US whereas services in Australia tend to follow the "hospital in the home" visiting nurse model. However, it is becoming increasingly common for individual OPAT services to offer all three models, allowing treatment to be tailored to each patient's circumstances.[2] Most OPAT services described in the literature are based in acute hospitals, predominantly in specialist infectious diseases units.[4 5 13 18] Services may also be established by other inpatient specialist teams or in frontline emergency or acute medicine units[9]: in the UK, the Society of Acute Medicine has recently established a working group to promote the development of OPAT in this setting.

In the ambulatory care centre model, the patient attends a healthcare facility daily, or as required, with antibiotics administered by a healthcare practitioner. Treatment in the patient's home may be administered by community nurses, outreach nurses from the acute hospital, or nurses provided through a private healthcare company. In the third model patients (or carers) are taught to administer therapy; this has the advantages of engaging patients in their care, allowing more flexibility of dose frequency and timing, and reducing staffing costs. Despite theoretical concerns about line infections, two large retrospective studies have shown that self administration is as safe as administration by a healthcare worker in the community.[14 26]

The model of OPAT used largely determines the type of intravenous access. Options include temporary "butterfly" needles that are inserted and removed for each dose, short term peripheral cannulas, or, for longer antibiotic courses, peripherally inserted central cannulas or tunnelled central lines. Bolus injections or infusions may be used, depending on the choice of antimicrobial agent(s). Infusions allow higher doses to be administered but require additional administration time and training.[27] Novel delivery devices allow patients greater freedom to continue normal daily activities. For example, portable elastomeric infusion devices can be carried in the patient's pocket or a carrying pouch and deliver continuous infusions over 24 hours.[3]

What are the benefits?

The clinical effectiveness of OPAT has been established for a wide range of infections through numerous retrospective case series, as outlined above. However, there have been few randomised controlled trials comparing OPAT with inpatient care. Furthermore, there are no published data on clinical efficacy of OPAT services based entirely in a community setting, although there are descriptions of collaborative services across primary and secondary care sectors.[9]

OPAT has been shown to be cost effective in many healthcare contexts. One retrospective study from a UK service compared the actual costs of OPAT over two years with the theoretical costs of inpatient care for the same patient cohort and found that OPAT cost 47% of equivalent inpatient national average costs.[4] However, in reality there is a wide range of funding arrangements for OPAT in operation across the UK, and in some instances OPAT may offer little cost advantage to commissioners over inpatient care. A national tariff for OPAT would allow consistency and equity and support wider use.

In addition to reducing direct costs, OPAT frees inpatient capacity, which can then be used either to admit further patients or as part of a planned reduction in bed capacity. More detailed modelling of these downstream benefits has not been undertaken but might provide added evidence of OPAT's cost effectiveness.

Finally, there is increasing evidence that OPAT is associated with a very low rate of healthcare associated infection. Despite theoretical concerns about the use of broad spectrum agents such as ceftriaxone, the risk of *Clostridium difficile* infection seems to be low: a meta-analysis of three

large UK OPAT cohorts found the rate of *C difficile* infection to be 0.1%,[10] although there are no published prospective data.

What are the risks?

Despite these benefits, OPAT is associated with increased clinical risk compared with inpatient care because of the reduced level of supervision. At least 25% of patients having OPAT experience an adverse reaction of some type, ranging from mild antibiotic associated diarrhoea to severe line infections.[24] The treatment pathway—from patient selection, determination of the therapeutic regimen and intravenous access device to communication with other teams and ongoing monitoring during therapy—provides numerous opportunities for error.[28] In addition, as OPAT is used increasingly for more complex infections in patients with serious comorbidities, the likelihood of adverse events unrelated to the infection increases. A retrospective survey of US physicians involved in OPAT found that 68% had seen at least one major adverse event in their patients in the preceding year,[29] highlighting the importance of a formal governance structure. The adverse events included unexpected death, line related bacteraemia, air embolism, drug hypersensitivity, and drug induced blood dyscrasia.

About 10% of patients will require readmission, with higher rates for patients with more complex infections.[4 5 14 18 19] In addition, many patients require further unplanned input during therapy: one study found that 12% of OPAT patients needed urgent advice or an unscheduled home visit.[30] Thus it is essential that the service has an established system for 24 hour access to clinical support and a formal (re)admission pathway to secondary care.

One further potential risk is overuse of intravenous antimicrobial therapy as an alternative to oral agents purely because an OPAT service exists. Similarly, there is also a risk that a broad spectrum once daily parenteral antimicrobial agent could be chosen in preference to a potentially more efficacious agent requiring multiple daily doses for reasons of convenience alone. OPAT should therefore operate within the context of an antibiotic stewardship programme, and it is essential that a microbiologist or infectious diseases physician is involved in both the initial design of antibiotic protocols and ongoing patient care. Several studies have found that assessment of referred patients by an infection specialist results in reduced use of intravenous therapy, improved clinical care, and substantial cost savings.[31-33]

How can the risks be reduced?

It is clear that OPAT delivered through a formal service structure is safer than when delivered through ad hoc arrangements. Several bodies have published recommendations on delivery of OPAT[2 3 34] and the aim of these is to ensure that the risks associated with OPAT are minimised. In the UK a consensus statement on the use of OPAT was recently published as a joint initiative between the British Society for Antimicrobial Chemotherapy and the British Infection Association.[24] It covers service structure, patient selection criteria, antimicrobial selection and delivery, frequency and type of clinical and blood test monitoring, monitoring of outcomes, and clinical governance.

ADDITIONAL EDUCATION RESOURCES

E-OPAT (http://e-opat.com)—an online resource for setting up OPAT services from the British Society for Antimicrobial Chemotherapy

It recommends the core OPAT team should comprise, as a minimum, an OPAT specialist nurse, doctor, infection specialist (either an infectious diseases physician or a microbiologist), and a pharmacist. A doctor with suitable training and experience (who may also be the infection specialist, when he or she delivers hands-on clinical care) should take responsibility for management decisions for each patient, in collaboration with the team. Although patients on prolonged courses of antimicrobials can be reviewed weekly, or less frequently if stable, those receiving treatment for cellulitis should be reviewed daily to allow switching from intravenous to oral therapy as soon as clinically appropriate.

What is the future of OPAT in the UK?

OPAT offers a rare opportunity not only to improve patient choice while maintaining service quality but also to reduce healthcare costs and improve service efficiency. Use of OPAT is likely to continue to expand in the UK, as in many other countries, driven by enthusiasm for increasing care delivery in the community as well as by cost pressures and patient choice. OPAT was recently cited as one of five antimicrobial prescribing decision options in Department of Health guidance on antibiotic stewardship.[35] Services will continue to be developed both in primary and secondary care, and it is likely that integrated services across sectors will be established in order to combine primary care's capacity and expertise in home treatment with the specialist knowledge and back-up of secondary care.

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ANSWERS TO ENDGAMES, p 36

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STATISTICAL QUESTION

Intraclass correlation coefficient

Statements *a* and *c* are true, whereas *b* is false.

PICTURE QUIZ

A dangerous complication of thoracocentesis

1 The fluid at the underwater seal should oscillate and bubble.
2 Yes. The left lung has fully reinflated, suggesting that the drain is functioning correctly.
3 The re-expanded left lung shows widespread airspace opacification. In this clinical context, this signifies re-expansion pulmonary oedema.
4 Management is supportive. This may include supplemental oxygen, analgesia, diuretics, continuous positive airways pressure, or invasive ventilation in severe cases.
5 After a pneumothorax, advise patients to return if symptoms recur, to avoid flying in the short term, and to avoid diving for life.

CASE REPORT

Preparing a Jehovah's Witness for major elective surgery

1 In the United Kingdom and United States, the autonomy of competent patients must be respected above other ethical principles (this is not the case in all countries) and an individual management plan agreed and formalised with a legally binding advanced directive. The beliefs and opinions of Jehovah's Witnesses may differ regarding blood derived products and procedures.
2 A thorough history, examination, and appropriate investigations to identify chronic disease, anaemia, and clotting abnormalities are essential. This patient's normocytic anaemia was attributed to her chemotherapy because no other cause was identified, and she had normal renal function and blood tests. She was treated with erythropoietin in conjunction with intravenous iron before elective surgery was scheduled.
3 Perioperative measures that aim to reduce and replace blood loss are managed by both the anaesthetist and surgeon. Intraoperatively, this patient's anaesthetist used permissive hypotension and careful temperature regulation and would have used autologous transfusion if needed. The surgeon designed a minimally invasive technique with meticulous haemostasis.
4 For immediate advice the on-call haematologist can be contacted. In addition, every UK hospital has a transfusion committee and can access one of the 33 national hospital liaison committees. Furthermore, local or national societies may be able to offer support and advocate for the beliefs of Jehovah's Witnesses. Strong emphasis is placed on seeking the advice of experienced multidisciplinary teams.
5 Yes. Evidence suggests that the use of extreme blood management strategies has an equal or better outcome in the short and long term than giving allogeneic blood transfusion. Patient selection is key, communication and consultation are essential, and planning is crucial to optimise outcome.