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Experience with a Physician-Directed, Clinic-Based Program for Outpatient Parenteral Antibiotic Therapy in the USA

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The experience with 538 patients who received outpatient parenteral antibiotic therapy (OPAT) in 1993 in a private institute in Tacoma, Washington, USA, is reviewed here. Clinical outcomes suggested a successful resolution of infection in 99 % of cases. Bacteriological outcomes showed that eradication of the organism had occurred in 92 % of patients by the end of therapy. The success of the program indicates that 91 % of properly selected patients can be treated without adverse events. Antibiotics were changed in 45 (8 %) instances, but only half of these changes were made because of an adverse event. The development of rash was the most frequent adverse event and resulted in hospitalization in only 1 instance. Hospitalization was necessary before the OPAT program was completed in 42 cases – 20 of those were for surgery and 13 for medical reasons unrelated to the infection or antibiotic therapy. In 8 cases, patients were hospitalized because of failure of home care or inability to administer the antibiotics effectively. Three patients were taken off the program because of failure to comply. Patient satisfaction surveys suggested that 99 % of patients were satisfied with the program. With careful patient selection and a well-developed program, OPAT can be safe, effective and beneficial to patients and can save costs in healthcare services.

Currently, more than 250,000 patients with serious infections are treated each year with intravenous antibiotics in nonhospital settings in the USA (data published by Cowen & Co., Boston, MA, USA). A broad spectrum of diseases has been treated, including an increasing number of infections related to the evolving AIDS epidemic. Mainly as a result of the growing financial pressure on US healthcare services, the use of outpatient parenteral antibiotic therapy (OPAT) has grown at a rate of 10–20 % per year, and is likely to continue to do so. The increasing use of OPAT has resulted in cost savings and patient benefits (1). For these reasons, it will be an important part of healthcare reform in the USA.

How far the move to outpatient care can and should go is not known; the limits of cost cutting and patient safety are being tested. One of the most critical areas in understanding the safety and effectiveness of OPAT programs is the selection of appropriate patients for outpatient therapy.

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Administering OPAT

Appropriate selection of patients for OPAT must include not only individual patient factors but also aspects of the treatment models, facilities and expertise available. There are three basic models for outpatient parenteral therapy in the USA (2): these are the visiting nurse model, the infusion center model and the model for self-administration. The relative advantages and disadvantages of each are reviewed here.

Visiting Nurse Model. In this model, the nurse visits the patient's home to give the injection or administer the infusion. This model offers the advantages of supervised administration of parenteral medication by a nurse, as well as an opportunity to see the patient and ensure that his or her home circumstances are adequate for treatment. Its disadvantages include the cost for the

nurse's time and travel. Some patients may also have concerns about privacy.

Infusion Center Model. With this model, treatment may be administered in a hospital clinic, a doctor's office or an independent infusion center. Among the advantages of this model are the easy accessibility of medical equipment, medications and healthcare personnel. If problems arise with, for example, difficult venous access, an adverse reaction or a need to change antibiotic therapy, they can be easily dealt with. The presence of the physician is an added advantage in such circumstances. Disadvantages of the clinic infusion model include the overhead costs of maintaining the facility and the need for patients to travel to the facility. The latter may cause difficulties if the patient is experiencing significant pain upon movement, has other limitations in function or lives far from the infusion center.

Self-Administration Model. In this model, the patient or a family member administers the antibiotic infusions, usually in the patient's own home. This model is significantly lower in cost than the others because of savings in healthcare personnel and overhead expenses. So far, patients and family have been willing to work for free. The obvious disadvantages include the lack of medical knowledge on the part of the patient or family members, a lack of medical supervision and minimal availability of medical equipment. Self-administration also requires careful training of the patient and his or her family, which may be time consuming. It is, nevertheless, the least costly method if parenteral antibiotics are needed for more than a few days.

Before safe and effective OPAT can be provided, a team of medical personnel is needed for the treatment program (3, 4). Such a team should consist of a physician, nurse and pharmacist as well as necessary administrative support personnel. The responsibilities of each member of the team should be clearly defined. The physician is responsible for the initial diagnosis, formulation of the treatment plan and for subsequent follow-up of the patient. Responsibilities for treatment outcome as well as overall liability for patient care also lie with the physician. The nurse's clinical assessment is also important in the formulation of a treatment plan. In addition, nurses are usually responsible for establishing and maintaining venous access, training patients in self-administration and ensuring patient follow-up or home visits. The pharmacist may also help in the development of the treatment plan and is responsible for mixing and dispensing the antibiotic and for providing any infusion-related devices, such as pumps.

A physician-directed, clinic-based OPAT program was started at Infections Limited, a private institution in Tacoma, Washington, USA, that serves a population of approximately 500,000 people. Although originally a self-contained practice, it has since developed into an outpatient infectious diseases unit with a clinic providing consultation and follow-up for serious infection problems as well as OPAT when appropriate. Over 2,500 patients have been treated with OPAT since 1981 (5). Personnel at the unit include six infectious diseases physicians, all of whom are board-certified in internal medicine and one of whom is also board-certified in pediatrics. There are also five specialist intravenous therapy nurses, two pharmacists and various administrative and support staff, as well as a research nurse for investigational studies of new antibiotics. The clinic has an on-site microbiology laboratory with equipment for hematological and chemical analysis. Between 30 and 40 patients participate in the OPAT program at any one time, although only a limited number attend the clinic each day. Patients are routinely seen at the clinic twice a week for follow-up. At these visits, in addition to the patients' seeing their physician and nurse and obtaining more antibiotics if required, any necessary laboratory studies and cultures are carried out.

The main infections treated at the clinic are soft tissue infections which range from cellulitis to postoperative infections to diabetic feet. The proportion of osteomyelitis cases treated by OPAT has declined in recent years with the advent of the quinolones, which has allowed many cases of gram-negative osteomyelitis to be treated orally (6). During the same period, however, there has been a gradual increase in the number of skin and soft tissue infections seen at the clinic, due, in part, to previous referrals of patients with cellulitis and wound infections. Increasingly, patients are referred to our clinic for intravenous antibiotic therapy in lieu of hospitalization. Virtually every type of bacterial infection has been treated in this clinic, at least in part on an outpatient basis.

Ceftriaxone was the first parenteral antibiotic to be used for outpatient treatment at this clinic. This drug was examined in investigational studies for both intravenous and intramuscular administration with lidocaine when the OPAT program was started in 1981 (5). Ceftriaxone is well tolerated and eminently suitable for OPAT use.

When the center's research studies with ceftriaxone ended in 1984, other antibiotics were tested and it has been found that virtually any antibiotic can be provided via this OPAT program. Ceftriaxone remains the antibiotic of choice at this clinic, however, because of its broad spectrum of activity and its once-daily dosing. Among the other antibiotics, vancomycin has proved to be particularly valuable because of the increasing incidence of methicillin-resistant staphylococcal infections among patients treated at the clinic.

During the early stages of the OPAT program, all patients were hospitalized for assessment and initiation of treatment before being discharged early to complete a course of parenteral therapy with the support of the clinic. Increasingly, however, patients are referred directly to the clinic where OPAT treatment is initiated without any hospitalization. More recently, as a result of the growing pressure within the USA to reduce the number of patients hospitalized, the clinic has been receiving referrals from local physicians for outpatient therapy after patients have failed on oral medications, and there is an increasing trend toward patient referral from hospital emergency rooms. Emergency room referrals are either for direct initiation of OPAT in lieu of hospitalization or for follow-up of patients given parenteral antibiotics in the emergency room the previous day.

Patient Selection

Careful patient selection is an essential prerequisite for safe, effective outpatient therapy (7, 8). Many factors should be considered at the time of initial evaluation before the subject of outpatient parenteral therapy is discussed with the patient (Table 1). One key factor is whether the infection is appropriate for outpatient therapy. Patients with diseases such as meningitis and endocarditis should be hospitalized to initiate the course of parenteral therapy, though in many cases, the final days of treatment may be successfully completed on an outpatient basis. Consideration should also be given to whether parenteral therapy is truly necessary; if oral antibiotics are appropriate and can be given, they should be used. In addition, any other medical or nursing needs should be determined on an individual basis. Many patients with serious infections also have underlying disorders, for example, diabetes, heart disease or lung disease. Patients who are hospitalized for reasons other than infection should continue to be treated there.

Once a patient has been assessed by the physician as a reasonable candidate for outpatient therapy, further individual factors regarding outpatient therapy should be considered. These include whether the patient is clinically stable and well enough to be treated outside a hospital. The patient must also be willing to try outpatient therapy without undue persuasion. Patients should be physically and mentally able to attend a clinic on a regular basis or to administer the medication in their home. Other family members, particularly spouses or parents, can often provide support if the patient has difficulty. Patients must have ready access to transport in case of adverse reactions to antibiotic therapy and must ensure that they will be able to attend the clinic to see their physician for venous access procedures and to receive additional medication. Finally, a history of alcohol and drug abuse may contraindicate outpatient therapy, especially if an intravenous catheter is to be left in place. Patients with a history of intravenous drug abuse may receive medication intramuscularly or by intravenous infusion, providing the needle is removed after each visit to the clinic.

Home circumstances must also be evaluated carefully. Family support is particularly important if self-administration or family administration of

Table 1: Patient selection criteria for OPAT.

Selection criteria	Individual circumstances	Home situation
Seriousness of infection	Clinical stability	Family support
Suitability for oral therapy	Willingness to try	Transportation
Presence of other diseases	Physical ability Mental ability	Telephone
Need for nursing	Drug or alcohol abuse	Running water Refrigerator

OPAT is planned. The presence of another person in the family who can be trained to recognize the potential difficulties that can arise with OPAT and can help evaluate the day-to-day condition of the patient is valuable for both patient and physician. The distance between a patient's place of residence and the medical facility may also be important. For example, a patient living several hours' drive from a medical center would not usually be considered a suitable candidate for outpatient therapy (by Infections Limited) unless arrangements could be made to provide it locally. Depending upon the circumstances, it may be necessary for a patient to have access to a telephone at home, and in the USA, this is considered essential. A supply of running water to ensure careful hand-washing and a refrigerator to store the medication are essential if self-administration is planned.

Program Outcome

The clinic treatment population is characterized in Table 2. A total of 538 patients, with a mean age of 45 years, were treated with OPAT during 1993. The model used during 1993 was primarily that of self-administration with family support, which accounted for 56 % of the cases. Clinic infusion was used in 43 % of patients. Visiting nurses were only necessary for the few patients who were unable to attend the clinic (1 %). Approximately 60 % of the patients were started directly on OPAT in the clinic without being hospitalized.

The infections treated in 1993 are shown in Table 3. The primary type of infection was that of skin and soft tissues, with cases ranging from cellulitis to lymphangitis to postoperative infections to diabetic feet. The total of 10,002 days of outpatient treatment is likely to amount to a cost savings of at least US$300 per day. The antibiotics used in 1993 are shown in Table 4. Some patients received more than one intravenous antibiotic at a time.

Table 2: Patient population profile of the 1993 OPAT program (Infections Limited, Tacoma, USA).

	Number of patients
Male	282
Female	256
Total	538
Mean age	45 years
Model used	
Self-administration	56 %
Clinic infusion	43 %
Visiting nurse	1 %
Started intravenous therapy in clinic	60 %

Table 3: Infections treated and overall duration of treatment on the OPAT program during 1993 (Infections Limited, Tacoma, USA).

Infections	No. of patients	No. of days
Skin/soft tissue infection	236	3,436
Osteomyelitis	102	2,935
Joint infection	43	805
Gynecologic infection	35	702
Ear-nose-throat infection	25	655
Bacteremia	14	302
Pulmonary infection	12	173
Other	71	994
Total	538	10,002

Table 4: Antibiotics used and overall duration of administration in the 1993 OPAT program (Infections Limited, Tacoma, USA).

Antibiotic	No. of patients	No. of days
Ceftriaxone	292	3,562
Vancomycin	113	1,888
Cefazolin	44	777
Clindamycin	42	780
Ceftazidime	39	835
Oxacillin	36	849
Tobramycin	28	515
Gentamicin	29	329
Other	112	1839
Total	735	11,374

Table 5 presents the clinical and bacteriological outcome of treatment during 1993. Clinical outcome was determined at the end of therapy as either improvement or failure. Of the 491 patients who could be evaluated, clinical improvement was reported in 484 (98.6 %) and failure in 7. Bacteriological outcome at the end of therapy was classified as eradication (repeat cultures were negative or not able to be cultured because of healing), persistence or superinfection. For the 265 cases that could be assessed, eradication of the infecting organism was reported in 244 cases (92 %), persistence in 17 and superinfection in 4. These outcomes are probably better than those of hospitalized patients because patients receiving OPAT are generally healthier than those who must remain confined to the hospital.

The outcome of the OPAT program is listed in Table 6. Four hundred ninety-two (91 %) patients

Table 5: Clinical and bacteriological outcome at the end of therapy in the 1993 OPAT program.

	No. (%) of patients
Clinical outcome (n = 491)	
Improvement	484 (98.6 %)
Failure	7 (1.4 %)
Bacteriological outcome (n = 265)	
Eradication	244 (92.0 %)
Persistence	17 (6.4 %)
Superinfection	4 (1.5 %)

Table 6: *Overall outcome of the 1993 OPAT program.*

Uneventful completion of therapy	492 (91 %)
Death on therapy	1
Hospitalization	
Surgery	20
Medical reasons	13
Poor response at home	8
OPAT-related adverse events	1
Failure to comply	*3*

Table 7: Reasons for changes in antibiotic therapy.

	No. of patients
Clinical failure	21
Microbial resistance	5
Superinfection	3
Adverse event	16
Rash	11
Leukopenia	1
Neuromuscular disturbance	1
Renal toxicity	1
Laryngeal edema	1
'Red man' syndrome	1
Total	45

completed the program without problems. Only one death occurred during treatment. In this instance, the patient, who had advanced AIDS, requested to die at home rather than in the hospital but wished to continue therapy with ganciclovir. Forty-two (7.8 %) patients were hospitalized after OPAT was begun. Of those, 20 (3.7 %) were hospitalized for surgery that could not be performed at an outpatient surgery center. A further 22 (4.1 %) were hospitalized for other reasons, including poor clinical response (n = 5), inadequate home care (n = 3), neurological problems (n = 3), cardiac disease (n = 2), bleeding (n = 2), chest disease (n = 2), vomiting (n = 2), leukopenia and fever (n = 1), reimbursement problems (n = 1) and drug rash (n = 1). Only the patient with drug rash was hospitalized due to adverse reaction to the OPAT program or medications related to it. Three patients were taken off the program because of failure to comply. Four patients were transferred to another OPAT program for insurance reasons.

Table 7 shows the reasons for changing antibiotics after initiation of OPAT therapy. Medication was changed because of an adverse effect in 16 cases. As expected, rash was the primary reason for change (2 % of cases). Other reactions included leukopenia, neuromuscular symptoms, renal toxicity, laryngeal edema and intractable 'red man' syndrome. In 21 cases, antibiotics were changed because of apparent clinical failure. Approximately half of these turned out to not have an infectious etiology, but this was not known at the time. Antibiotics were altered because of the determination of antimicrobial resistance in 5 cases, 1 of which apparently occurred during treatment. Superinfections occurred in 3 cases and required a change of intravenous therapy. Hospitalization was required in 1 case of erythema multiforme due to imipenem.

Patient reaction to outpatient therapy was also assessed using questionnaires distributed on the last day of therapy. A total of 294 questionnaires were returned to the clinic. In these, 262 (89.9 %) patients said they would definitely undergo outpatient therapy instead of being hospitalized if the need arose again; 28 (9.5 %) patients said they would probably undergo outpatient therapy again; 2 (0.7 %) said they probably would not. Only 2 (0.7 %) respondents said they would definitely not undergo outpatient therapy again.

Discussion

The preceding information has been collected for this specific OPAT program, and it is important to remember that other programs may differ considerably in the resources, models, technology, patient population and expertise available. In this program, the selection of patients was clearly appropriate as 92 % of patients completed therapy without event, thus justifying the chosen selection process. It is uncertain to what extent unwanted or unexpected outcomes could have been avoided in patient selection. Some errors are unavoidable, and in many situations, it is worth trying OPAT as patients can be transferred to hospi-

tal at any time. Thus far, there are no established outcome guidelines for OPAT, as there is a need for further multicenter studies. The one death that occurred during therapy in this program was anticipated and consistent with both the patient's and family's wishes. The incidence of compliance failures (3 patients) was not unexpected. Two of these patients had refused hospitalization before they began OPAT; however, in both cases, the patients had received enough intravenous therapy to be able to complete their treatment with oral antibiotics.

If hospitalization is regarded as a possible adverse outcome for OPAT, the 20 patients admitted for surgery should perhaps be eliminated from the figures because the surgery was no more or less likely to happen on an outpatient than inpatient basis. Hospitalization for medical reasons is, however, an area of some potential concern. Often these patients are ill and have multiple diseases in addition to the infections for which they are receiving intravenous antibiotic therapy. In our study, one death occurred in a patient who had been hospitalized with leukemia and thrombocytopenia and whose death had been anticipated. There was no indication that her treatment as an outpatient significantly delayed hospital care or intervention, though this is an area of continued concern. Hospitalization for clinical failures in eight instances (1.5 %) was not unexpected, and this small number was considered a good result. While earlier hospitalization may have been of some benefit in these patients, it is not always possible to know this in advance. It appears reasonable to at least try outpatient therapy first with the option of hospitalization if it is unsuccessful. Only a single case of hospitalization occurred due to an adverse antibiotic effect and this was less than expected. It occurred in a child who developed erythema multiforme together with dehydration and vomiting. The child was quickly returned to OPAT after the antibiotic was changed, and the eruption responded to corticosteroid therapy.

Changes in antibiotic therapy are an expected part of outpatient therapy, as indeed they are in the hospital. The incidence of adverse effects (3 %) reported in this program was lower than expected, and the recognition or development of resistant isolates in five instances as a reason to change therapy was also not unusual. In such cases, empirical therapy was begun and patients switched to a more suitable agent once full microbiologic identification and sensitivity profiling were performed. The incidence of superinfection (only 3 cases) was lower than would be expected in a hospital setting and may be related to the less resistant organisms found in the home. While a change in antibiotics because of poor clinical response is also not unusual, it underscores the need for close clinical follow-up by a physician and the need to alter therapy based on such assessments.

Conclusions

The results of this analysis and of this center's experience in providing outpatient treatment in Tacoma indicate that OPAT is beneficial to and largely appreciated by patients. OPAT also provides cost savings for hospitals and healthcare services. Given the expertise and resources of such programs, it seems possible to treat at least part of the course of any infection with outpatient parenteral therapy and with any of a wide range of antibiotics. Patient selection criteria are particularly important because not all patients will be appropriate for an OPAT program. Although specific factors may vary from region to region, they will quickly become clear once an effective team of healthcare personnel is assembled.

Patient selection criteria, however, should be strictly applied and are essential in gaining insight and understanding of whether or not patients are suitable for OPAT. The limits of available treatment on an outpatient basis are unknown but are being tested in many centers around the world. Further studies need to investigate which factors are most critical in patient selection as well as to increase understanding of safety issues in outpatient treatment.

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