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Original article

Impact of an outpatient parenteral antimicrobial treatment (OPAT) as part of a paediatric-specific PROA program

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ABSTRACT

Introduction: Outpatient parenteral antimicrobial treatment (OPAT) is an alternative to in-patient care in carefully selected patients. This study presents a self-administration OPAT program integrated within the pediatric antibiotic stewardship program (ASP) in a pediatric tertiary care center.
Material and methods: Descriptive, retrospective and unicentric study. Data from all patients under 20 years of age who were prescribed treatment by a pediatric unit during 2019 and 2020 were included. Data regarding number of saved beds and estimating the opportunity cost of the OPAT program for the hospital were analyzed.
Results: Fifty-seven patients received 106 episodes of treatment. Favorable clinical outcome occurred in 74.5% of the episodes. The main cause of premature interruption was unfavorable clinical outcome of the infection (37.1%). A total of 2.62 beds/day were saved, resulting in an economic benefit of 1,069,963 €.
Conclusion: A self-administration OPAT program integrated within the pediatric ASP has proven to be safe and effective and provides economic benefits.

Impacto del tratamiento antimicrobiano domiciliario endovenoso (TADE) como parte de un programa de optimización del uso de antimicrobianos (PROA) específico para pediatría

Palabras clave:
Tratamiento antimicrobiano domiciliario endovenoso (TADE)
Enfermedades infecciosas
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RESUMEN

Introducción: El tratamiento antimicrobiano domiciliario endovenoso (TADE) es una alternativa a la hospitalización para pacientes pediátricos bien seleccionados. Presentamos un programa TADE basado en un modelo de autoadministración e integrado en el programa de optimización del uso de antimicrobianos (PROA) de un hospital pediátrico de tercer nivel.
Material y métodos: Estudio descriptivo, retrospectivo y unicéntrico que incluye todos los pacientes menores de 20 años tratados con TADE prescrito en un hospital pediátrico entre 2019 y 2020. Se analizaron los datos sobre los días de ingreso ahorrados y una estimación económica del coste oportunidad que supone el programa TADE para el hospital.
Resultados: Cincuenta y siete pacientes realizaron un total de 106 episodios de tratamiento. En el 74,5% hubo una evolución clínica favorable. El principal motivo de interrupción prematura fue una mala evolución de la infección (37,1%). Se liberaron 2,62 camas diarias, suponiendo un beneficio económico de 1.069.963 €.

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Conclusión: Un programa TADE integrado en el PROA pediátrico de nuestro hospital y basado en un modelo de autoadministración se ha mostrado un programa seguro y efectivo y aporta importantes ventajas a nivel económico.

Introduction

The growing complexity in the diagnosis and treatment of infectious diseases and the increase in resistances have necessitated the implementation of Antimicrobial Stewardship Programmes (ASP). These institutional *antimicrobial stewardship programmes* have been introduced to improve clinical outcomes in patients with infections, minimise adverse effects and guarantee the use of cost-effective treatments.[1] The need for a paediatric-specific ASP has been recognised in recent years.[2] In this population group, there is less scientific evidence about the use of the new antibiotics, there is a different profile of adverse effects and the dosage regimen is also different. In addition, there are differences in the epidemiology of infections and patterns of antimicrobial resistance in paediatrics. For all these reasons, the "PROA-NEN" ASP multidisciplinary working group was established in 2015 at the Barcelona Hospital Campus Vall d'Hebron Children's Hospital in Barcelona.

In the context of the ASPs, and consequently with the aim of improving the use of antimicrobials, there are Outpatient Parenteral Antimicrobial Treatment (OPAT) programmes that permit the administration of an antibiotic parenterally to a patient on an outpatient basis. The term was first described in 1974 by Rucker et al. in paediatric patients with cystic fibrosis.[3]

OPAT seeks to achieve faster patient recovery, since it avoids the complications associated with the hospital setting and enables the patient to return to their family, social and work/school environment sooner.[3,4] It also represents significant savings in hospital beds and associated costs. Different studies have demonstrated that it is a safe, effective and more efficient care modality than conventional hospitalisation.[4–8] However, most of these works focus on adult pathology and there are fewer works in paediatrics.[9,10]

Our centre's OPAT programme comprises a multidisciplinary team of paediatric infectologists, other paediatric specialties, nursing professionals and pharmacists. One important factor in the programme's success is to ensure an adequate patient screening based on the following inclusion criteria[3]: there must be no other oral options with equivalent efficacy, the patient must be clinically stable, the caregiver and/or patient must feel safe and understand the indications for at-home administration, which must be adequate, and good communication between families and health personnel must be guaranteed. The correct selection of venous access is also important. The self-administration model is used in our hospital. The nursing team is responsible for training and educating the patient/caregiver in the drug administration technique and there is also a Guide available for the home administration of intravenous antibiotics created by our hospital.

This paper is intended to present an OPAT project in paediatrics integrated in the "PROA-NEN" ASP programme in a high-complexity paediatric hospital.

Patients and methods

A retrospective, descriptive and single-centre study was carried out, including all patients under 20 years of age who had received OPAT treatment prescribed by a specialised paediatric unit between January 2019 and December 2020.

The data collected included: therapeutic indication, antimicrobial administered, duration of the treatment episode, treatment modality (monotherapy or multiple therapy), microbiological result (type of culture and isolated microorganism), final clinical result, appearance of adverse effects and reason for discontinuation of the treatment. A financial estimate of the opportunity cost for the hospital involved in carrying out the treatment on an inpatient basis compared to treatment with the OPAT programme was also analysed. The cost of providing the treatment during admission was calculated by taking into account the cost per day of hospitalisation according to the public prices established by the Servei Català de Salut 2020[11] (Table 1) per hospital stay. The cost of treatment with the OPAT programme included direct costs, the cost of the outpatient clinical follow-up of each OPAT episode, plus the median cost of medications and administration material.

Table 1
Public prices of healthcare activities recorded according to the Servei Català de la Salut in 2020.[11]

Services	Rates
First-stage medical stay (1st–5th day)	€751
Second-stage medical stay (6th day onwards)	€597
Medical visit	€48
Nursing visit	€48
Pharmaceutical care visit	€80

The clinical data were obtained from the hospital's computerised clinical history. They were collected in a RedCap database and the statistical analysis consisted of calculating medians with their interquartile ranges (IQR) or means and their standard deviations (SD) according to the type of variable. This study was submitted to and approved by the Medicines Research Ethics Committee (mREC) of the Hospital Universitari Vall d'Hebron under code PROA-NEN/HUV-ANT-2017-01.

Results

Fifty-seven (57) patients were included, 34 males (59.6%), with a median age of 10.5 years (IQR: 5.5–16.0). These patients received a total of 106 treatment episodes, 77 in 2019 and 29 in 2020, with a median OPAT duration of 13 days (IQR: 9.0–17.3). On average, each patient had 1.9 OPAT episodes (SD: 1.4), all according to the self-administration model.

The most commonly treated infections were respiratory superinfections in patients with cystic fibrosis (n = 37; 36 in 2019 and 1 in 2020 [34.9%]), cholangitis (n = 29; 16 in 2019 and 13 in 2020 [27.4%]), osteoarticular infections (n = 10; 6 in 2019 and 4 in 2020 [9.4%]) and complicated urinary tract infections (n = 8; 7 in 2019 and 1 in 2020 [7.5%]).

The most commonly used antibiotics were piperacillin-tazobactam (n = 23; 15.6%), colistin (n = 19; 12.9%), ceftazidime (n = 14; 9.5%), teicoplanin (n = 13; 8.8%) and meropenem (n = 13; 8.8%). The drugs were mostly administered as monotherapy (n = 71; 67.0%), although bitherapy (n = 30; 28.3%), triple therapy (n = 4; 3.8%) and even quadruple therapy (n = 1; 0.9%) were used on some occasions. The most utilised venous accesses were the midline venous catheter or Midline and the peripherally inserted central catheter (PICC). No patients had a peripheral venous catheter (PVC).

The microbiological data analysed demonstrated significant variability in the microorganisms isolated and in the types of microbiological tests performed. A positive result was obtained in 79 of

Table 2
Microorganisms isolated on more than one occasion in infections treated with OPAT.

Microorganism isolated	Positive isolates	Sample type	% of the number of episodes
Pseudomonas aeruginosa	28	Sputum (19) Pharyngeal swab (7) Urine culture (1) Bile fluid (1)	26.4
Staphylococcus aureus (MRSA)	23 (9)	Sputum (16) Pharyngeal swab (2) Blood culture (2) Pus from abscess (2) Bronchial aspirate (1)	21.7 (39.1)
Candida albicans	10	Sputum (7) Pharyngeal swab (2) Bronchial aspirate (1)	9.4
Escherichia coli (ESBL)	8 (3)	Urine culture (3) Blood culture (1) Sputum (1) Drainage fluid (1) Fluid collection (1) Middle ear exudate (1)	7.5 (37.5)
Stenotrophomonas maltophilia	7	Sputum (5) Bronchial aspirate (1) Pharyngeal swab (1)	6.6
Klebsiella pneumoniae *(ESBL)*	7 (6)	Urine culture (6) Sputum (1)	6.6 (85.7)
Streptococcus anginosus	4	Brain abscess pus (2) Skin exudate (1) Peritoneal fluid (1)	3.8
Plasma coagulase-negative staphylococci	4	Blood culture (2) Skin exudate (1) Catheter tip (1)	3.8
Aspergillus fumigatus	4	Sputum (4)	3.8
Achromobacter xylosoxidans	3	Sputum (3)	2.8
Aspergillus citrinoterreus	3	Sputum (2) Bronchial aspirate (1)	2.8
Enterococcus faecium	2	Bile fluid (1) Drainage fluid (1)	1.9
Enterobacter cloacae	2	Urine culture (1) Blood culture (1)	1.9
Serratia marcescens	2	Pharyngeal swab (2)	1.9
Candida glabrata	2	Sputum (2)	1.9
Scedosporium apiospesmum	2	Sputum (2)	1.9
Other	21	[a]	19.8
Negative	24	–	22.6
Not performed	3	–	2.8
Total	159[b]	–	–

ESBL: Extended-spectrum β-lactamases; MRSA: Methicillin-resistant *Staphylococcus aureus*

[a] Microorganisms isolated only on one occasion are included (*Achromobacter insuavi*, *Aspergillus flavus*, *Borrelia* spp., *Candida parapsilosis*, *Citrobakter braaki* ESBL, *Citrobacter freundii*, *Corynebacterium striatum*, *Enterococcus faecalis*, *Haemophilus haemolyticus*, *Haemophilus influenzae* serotype b, *Klebsiella aerogenes*, *Leclercia adecarboxylata*, *Mycobacterium tuberculosis*, *Nocardia cyriacigeorgica*, *Prevotella loescheii*, *Prevotella* spp., *Shewanella algae*, *Streptococcus constellatus*, *Streptococcus dysgalactiae*, *Streptococcus mitis*group, *Streptococcus pyogenes*).

[b] The number of isolates is higher than the number of episodes, since more than one microorganism was isolated in some of them.

the episodes (74.5%). In 24 of the cases, all the microbiological analyses were negative (22.6%) and they were not performed in the remaining 3 (2.8%). The most frequently isolated microorganisms were *Pseudomonas aeruginosa* (n = 28; 26.4%), *Staphylococcus aureus* (n = 23; 21.7%) — in 9 cases (n = 39.1%) methicillin-resistant — and *Candida albicans* (n = 10; 9.4%) (Table 2).

Clinical evolution was favourable in 79 episodes (75.4%), while the OPAT was discontinued prematurely in 27 (25.5%). These interruptions were mainly due to poor evolution of the infection (n = 10; 37.1%), the need to optimise antibiotic treatment (n = 8; 29.6%), catheter occlusions (n = 6; 22.2%) or the appearance of adverse effects (n = 3; 11.1%). Rehospitalisation was required on 9 occasions (8.5%) and no catheter-associated bacteraemia was observed.

In total, during the study period, 1,913 days of hospitalisation were avoided, a figure that represents a free-up of 2.62 beds per day in the 2 years analysed. The estimated cost associated with total hospitalisation would have been €1,158,940, while the estimated cost of outpatient clinical follow-up related to OPAT was €23,744, and the cost of drugs and material for administration was €65,233, constituting a difference of €1,069,963 in terms of cost.

Discussion

OPAT programmes were first described more than four decades ago, and since then their use has been improved and their application has been protocolised through the publication of different clinical practice guidelines.[3,7,8] The publication of some centres' experience has also helped to expand knowledge of these treatments. Nevertheless, most of these works focus on adult pathology and there are fewer works on paediatric OPAT.[9,10]

Among the latter, Patel el al.[9] present data from a paediatric OPAT programme in a UK tertiary care hospital between 2012 and 2015. Their results show a total of 130 episodes in 123 patients, and practically half of the treatments administered are for osteoarticular infections. These data contrast with our own results, with an average of almost 2 episodes per patient and a majority of respiratory infections in patients with cystic fibrosis and cholangitis

in patients with liver disease, indicating a different patient profile between both centres, and OPAT is indicated more frequently and repeatedly in our patients with complex pathology. On many occasions, the complexity of these patients requires more prolonged intravenous treatment and a later sequential switch to the oral route. On the other hand, a large number of patients with cystic fibrosis can be started on OPAT on an outpatient basis, therefore hospitalisation is completely avoided in these cases.

The characteristics of the patients treated and the types of infections and causative microorganisms account, at least partially, for the high use of broad-spectrum antibiotics in our study. However, the fact that OPAT is not a valid option for all drugs may lead the spectrum of certain home treatments to be extended. As presented by Gilchrist and Seaton[12], this may conflict with ASP programmes, often focused on reducing the spectrum of antibiotics used. The stability of the drug, the speed of administration and the dosage regimens, as well as the OPAT model (self-administration vs. administration by health professionals) are factors that can condition the choice of drugs with a broader spectrum for the home setting, which is why these same authors say that the OPAT team must be formally represented in the hospital's ASP programme. Although both programmes work together in our centre, the OPAT self-administration model means that in most cases the antibiotic spectrum does not need to be expanded to facilitate home administration.

To date, several articles discussing the safety of OPAT have been published. For example, the Australian paediatric cohort study published by Sriskandarajah et al.[10] analyses the complications of OPAT and their possible relationship with clinical factors. One of the components that they detected as a risk factor for suffering up to twice as many complications was the self-administration model. In this regard, it is important to note that in our centre the self-administration model is always used in conjunction with training sessions for families, and our rates of complications are similar or even lower than those described by the aforementioned study and the different OPAT clinical guidelines.[3,7,8] The Guide for home intravenous antibiotic therapy in paediatrics[13], a multidisciplinary effort with graphic support and featuring the participation of patients and families, has contributed significantly to this model's success.

The fall in OPAT treatment episodes in our hospital between 2019 and 2020, with 2020 regarded as an exceptional year due to the COVID-19 pandemic, is also worthy of note. The best part of this change can be explained by a major reduction in treatments for patients with respiratory exacerbations in cystic fibrosis. The non-pharmacological protection measures implemented on account of the pandemic and the initiation of modulating and enhancing *cystic fibrosis transmembrane conductance regulator* (CFTR) treatments may possibly have contributed to this group presenting fewer superinfections.

Finally, as suggested by several studies, OPAT is an alternative that favours the financial sustainability of the health system.[4,5,14,15] The results published by Chapman et al.[4] show that the cost of OPAT represents 41% of the estimated hospital cost. In contrast, our results show that the cost of OPAT represents just 7.7% of the estimated cost if the patient had been hospitalised. This difference is possibly due to the self-administration model used, related to a significant decrease in healthcare personnel costs. In addition, it should be noted that our study only examined direct costs and OPAT represents a saving in indirect costs, such as optimisation in the management of hospital beds and less need for families to travel, hence the benefit is possibly even greater.

We would conclude that a OPAT programme integrated into the paediatric ASP programme of a tertiary paediatric hospital and based on the self-administration model has been shown to be a safe and effective programme that enables multiple infections to be treated in complex patients and is associated with a significant financial advantage.

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Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this article.

Appendix A. TADE-PEDIATRÍA Group

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References

1. Rodríguez-Baño J, Paño-Pardo JR, Alvarez-Rocha L, Asensio Á, Calbo E, Cercenado E, et al. Programas de optimización de uso de antimicrobianos (PROA) en hospitales españoles: documento de consenso GEIH-SEIMC, SEFH y SEMPSPH. Enferm Infecc Microbiol Clin. 2012;36, 22.e1–22.e23.
2. Gerber J, Jackson MA, Tamma P, Zaoutis T. Policy statement: antibiotic stewardship in pediatrics. J Pediatric Infect Dis. 2021;10:641–9.
3. López LE, Mujal Martínez A, Fernández Martínez De Mandojana M, Martín N, Gil Bermejo M, Solà Aznar J, et al. Resumen ejecutivo del tratamiento antimicrobiano domiciliario endovenoso (TADE): Guía de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) y la Sociedad Española de hospitalización a domicilio (SEHAD). Enferm Infecc Microbiol Clin. 2019;37:405–9.
4. Chapman ALN, Dixon S, Andrews D, Lillie PJ, Bazaz R, Patchett JD. Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective. J Antimicrob Chemother. 2009;64:1316–24.
5. Mitchell ED, Murray CC, Meads D, Minton J, Wright J, Twiddy M. Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. BMJ Open. 2017;7:e013560.

6. Williams DN, Baker CA, Kind AC, Sannes MR. The history and evolution of outpatient parenteral antibiotic therapy (OPAT). Int J Antimicrob Agents. 2015;46:307–12.
7. Chapman ALN, Seaton RA, Cooper MA, Hedderwick S, Goodall V, Reed C, et al. Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement. J Antimicrob Chemother. 2012;67:1053–62.
8. Norris AH, Shrestha NK, Allison GM, Keller SC, Bhavan KP, Zurlo JJ, et al. 2018 Infectious Diseases Society of America clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. Clin Infect Dis. 2019;68:e1–35.
9. Patel S, Burzio V, Green H, Rees S, Tebruegge M, Jones C, et al. The impact of pediatric outpatient parenteral antibiotic therapy implementation at a tertiary children's hospital in the United Kingdom. Ped Infect Dis J. 2018;37:e292–7.
10. Sriskandarajah S, Ritchie B, Sluggett JK, Hobbs JG, Reynolds KJ. Safety of nurse- and self-administered paediatric outpatient parenteral antimicrobial therapy. Antibiotics. 2020;9:761.
11. Departament de Salut. ORDRE SLT/63/2020, de 8 de març, per la qual s'aproven els preus públics de Servei Català de la Salut. 2020. Available from: https://www.gencat.cat/dogc. [Accessed 13 May 2021].
12. Gilchrist M, Seaton RA. Outpatient parenteral antimicrobial therapy and antimicrobial stewardship: challenges and checklists. J Antimicrob Chemother. 2015;70:965–70.
13. Vall d'Hebron Barcelona Hospital Campus. Guía de administración domiciliaria de antibióticos intravenosos en pediatría; 2018. Barcelona. Available from: https://hospital.vallhebron.com/sites/default/files/guia_antibiotics_esp.pdf?_ga=2.191092386.929507841.1620469476-2020166409.1620469476. [Accessed 30 January 2021].
14. Wai AO, Frighetto L, Marra CA, Chan E, Jewesson PJ. Cost analysis of an adult outpatient parenteral antibiotic therapy (OPAT) programme. A Canadian teaching hospital and Ministry of Health perspective. Pharmacoeconomics. 2000;18:451–7.
15. Vargas-Palacios A, Meads DM, Twiddy M, Czoski Murray C, Hulme C, Mitchell ED, et al. Cost-effectiveness of outpatient parenteral antibiotic therapy: a simulation modelling approach. J Antimicrob Chemother. 2017;72:2392–400.