Improving paediatric antimicrobial stewardship in hospital-based settings; why, where and how?

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**Short title**: Improving paediatric antimicrobial stewardship in hospital-based settings

**Abstract**

**Background**

Antimicrobial resistance (AMR) is being recognised as a priority by healthcare organisations across the world. However, many children are managed on intravenous antimicrobials in hospital with very little consideration of antimicrobial stewardship issues.

**Objectives**

A nurse-led paediatric ambulatory outpatient parenteral antimicrobial (OPAT) service, managing children with common infections being ambulated on short courses of IV antimicrobials, was introduced within Southampton Children’s Hospital in January 2018. We evaluated the impact of this service in terms of the quality of antimicrobial prescribing and timing of ambulation in children presenting with common infections.

**Methods**

All cases managed within the service were reviewed in two separate 2-month time periods; prior to introduction of the service (Sept-Oct 2016), and then prospectively after its introduction (Sept-Oct 2018).

**Results**

96% of IV antibiotic management decisions at 48 hours were deemed appropriate in 2018, compared to 75% in 2016. 64% of patients were ambulated on IV antibiotics at some point during their treatment course in 2018, compared to 19% in 2016. However, a significant proportion of antimicrobial decisions made at the point of presentation to hospital remained suboptimal in 2018.

**Conclusions**

Children are commonly managed with intravenous antibiotics in hospital. We demonstrate marked improvements in appropriate antimicrobial use through the introduction of a nurse led ambulatory OPAT service. In addition, such a service can promote a greater proportion of children being ambulated from hospital, freeing up valuable in-patient beds and potentially delivering cost savings that can be used to fund such services.

**Introduction**

Antimicrobial resistance (AMR) is an increasing threat, recognised as a priority by healthcare organisations all over the world.1-3 It is understood that one primary driver of resistance to antimicrobials is antibiotic prescribing, with increased rates of inappropriate prescribing driving resistance by increasing selection pressures on bacteria.4 Although attention has focused on adults, there are increasing data to suggest a high burden of antimicrobial-resistant infections in young infants.5 One of the most important ways to reduce AMR in healthcare settings is antimicrobial stewardship, defined by the National Institute of Health and Care Excellence (NICE) as a process which, “embodies an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness”.6 Paediatric clinicians have an important role in assuring appropriate and judicious antibiotic use, as up to 40% of UK hospitalised children receive antibiotics at any one time, either as in-patients or administered on an ambulatory basis.7 Data from the USA demonstrate that there is much room for improvement in paediatric hospital prescribing, especially in regards to inappropriate initiation of intravenous (IV) therapy or prolonged IV therapy when oral step down would have been appropriate.8,9 There has recently been a move towards much shorter courses of antibiotics for infections, with earlier step down from IV to oral being advocated in adult practice for conditions such as bone and joint infections, Gram negative bacteraemia and endocarditis.10-12 A recent systematic review has highlighted where high quality evidence supports these practices in children.13

However, there are conflicting clinical pressures when deciding if children presenting with fever and infective symptoms require prompt initiation of empirical IV antibiotics. With ever more emphasis being placed on the recognition and early treatment of sepsis to reduce morbidity and death, as yet unpublished national data from the UK suggest that broad spectrum antibiotic treatment in Emergency Departments has risen by almost 30% in the last five years. Initiating empirical antibiotic treatment in only the sickest patients at high risk of death remains an important challenge.

At our regional children’s hospital in the UK, which serves a regional population of about 500,000 children and has approximately 9000 admissions per year, the paediatric infectious diseases and antimicrobial stewardship (PID/PAS) team has been proactive in managing children with complex infections requiring prolonged courses of IV antimicrobials at home (≥5 days following discharge from hospital), through the implementation of a tertiary paediatric outpatient parental antimicrobial therapy (tertiary p-OPAT) service in July 2012.14,15 In January 2018, this programme was expanded to include children with common infections requiring short courses of IV antimicrobials lasting <5 days (ambulatory p-OPAT), through the introduction of a nurse led clinic where children on IV antibiotics returned to a hospital-based ambulatory unit for daily review. The nurses were trained by the PID/PAS team and were directly supported by the patient’s primary clinical team (general paediatrics or other paediatric specialities) on the suitability of children to stop or step-down antibiotic therapy. The PID/PAS team had overall oversight of the service and reviewed management of all cases managed within the service. This short report describes how setting-up a formalised service for this large cohort of children presenting to hospital with common infections not only provides opportunities for admission avoidance and early discharge through the delivery of safe ambulatory care, but also ensures that antimicrobial stewardship principles are adhered to.

**Methods**

We evaluated the impact of our ambulatory p-OPAT service by carrying out a review of antibiotic prescribing and ambulation in two separate 2-month time periods; one carried out prior to introduction of the service (Sept-Oct 2016), and a second carried out prospectively after its introduction (Sept-Oct 2018). All children initiated on IV antibiotics for non-complex infections likely to be primarily managed in local as well as regional hospitals were included in each time period. The appropriateness of antibiotic prescribing and ambulation decisions were assessed following the completion of each episode of care by a general paediatrician (MA) and a consultant in paediatric infectious diseases (SP). In addition, the two assessors estimated the likely impact on rates of ambulation and antimicrobial use if optimal decisions had been made at the time of presentation to hospital (t=0). The data were extrapolated to provide an estimate of the impact of the service over a 12-month time period. Ethical approval to conduct this service evaluation was granted by the Ethics Committee of the University of Southampton (ERGO 42242).

**Results**

67 patients were identified in the retrospective group (2016) and 78 in the prospective group (2018). Table 1 outlines the pathologies managed in 2018. Ceftriaxone was the most commonly used empirical IV antibiotic during both periods (66% of cases in 2016 and 91% in 2018). In 2018, 96% of IV antibiotic management decisions made at 48 hours were deemed appropriate, compared to 75% in 2016, the most common reason being failure to stop IV antibiotics at 48 hours when no longer indicated. No adverse events occurred after cessation of antibiotics in either patient cohort. In 2018, 50 (64%) of all paediatric presentations/admissions started on IV antibiotics for non-complex infections were ambulated at some point during their treatment course, compared to only 13 (19%) in 2016, despite the opportunity for children to return to the acute paediatric ward for daily IV antibiotics existing in 2016. Although the total number of IV antibiotics days was similar in both time periods (205 in 2016 and 201 in 2018), inpatient days on IV antibiotics dropped from 172 in 2016 to 106 in 2018.

However, despite the ambulatory OPAT service having a significant impact on decision making at 48 hours, a significant proportion of antibiotic prescribing decisions made at the time of presentation to hospital (t=0 decisions) could have been improved in 2018. 21 (27%) of children started on IV antibiotics were deemed to have been managed suboptimally, with no antimicrobial therapy required in 9 (43%) and oral antibiotics being indicated in 9 (43%). The main presentation for which antimicrobials were commenced inappropriately was lower respiratory tract infections; of the 13 children managed with IV antibiotics for LRTIs, antibiotic therapy was not indicated in 6 (46%) and oral antibiotics rather than IV antibiotics would have been more appropriate in 3 (13%). In terms of ambulation, although a far greater proportion of children were ambulated on IV antibiotics at some point during their admission in 2018 compared to 2016, there was almost no change in the proportion being immediately ambulated (admission avoidance); 35% in 2016 compared to 43% in 2018. Evaluation of the impact of optimised t=0 decision-making suggested a 23% reduction in courses of total IV antibiotics, 33% increase in children being ambulated on IV antibiotics without admission (admission avoidance) and a 16% reduction of in-patient bed days for children on IV antibiotics (table 2).

**Discussion**

This report describes the management of a cohort of children with common infections within a nurse-led ambulatory antibiotic service. This differs from the model of care currently offered in most hospitals, in which children being ambulated on IV antibiotics return daily for administration of their medication outside of a formalised antimicrobial service. The range of pathologies managed within our service is representative of those routinely seen in local hospitals. We have demonstrated that introducing a dedicated cohort of nurses to deliver this service, trained and supported by infection experts, has proven effective in improving the quality of antibiotic prescribing and encouraging timely ambulation of children from hospital. The increase in ambulation is likely to reflect clinician confidence in the service. However, there is room for improvement; although the service has resulted in a marked improvement in decision-making at 48 hours, it has had less of an impact on decisions made when a child presents to hospital (t=0 decisions). If t=0 antibiotic prescribing decision-making was to be optimised, significant benefits could be realised in terms of reducing unnecessary exposure to antibiotics as well as reducing rates of admission to hospital.

Focusing on antimicrobial prescribing in children is especially timely because of the recent emphasis being placed on sepsis. This message has emerged at a time when rates of invasive bacterial infections in children is extremely low, due to the introduction of highly effective vaccines against pathogens such as Streptococcus pneumoniae (pneumococcus), Neisseria meningitidis (meningococcus) and Haemophilus influenzae b (Hib).16,17 Unfortunately this focus on sepsis, along with high profile medicolegal cases, has resulted in clinicians becoming increasingly risk averse when managing children presenting with infection. This is likely to have contributed to the almost 30% rise in broad spectrum antibiotic treatment in UK Emergency Departments in the last five years (unpublished data). Aligning approaches to sepsis and antimicrobial stewardship needs to be a priority, especially in children.18,19**Limitations**

One of the major limitations of this study is the relatively small number of patient episodes observed over a short period of time. Another of the limitations is the location in which this study was conducted; we recognise that the resources and personnel available in a tertiary Children’s hospital differ significantly from those available in local hospitals. Although there are a number of barriers to the successful implementation of ambulatory p-OPAT services in local hospital settings, including a lack of funding and lack of formalised training opportunities for healthcare professionals to perform this role, we think that many of these can be overcome through the development of regional infection networks, in which PID/PAS teams within tertiary children’s hospitals train and support general paediatricians, clinical pharmacists, microbiologists and nurses working in local hospitals. Funding could be obtained through savings made from admission avoidance and reduced length of in-patient stays. To address the current knowledge gap, evidence-based UK and Ireland good practice recommendations, focusing on antimicrobial stewardship and ambulation of children presenting to hospital with common infections, are being drafted by the British Society of Antimicrobial Chemotherapy (BSAC) and the Royal College of Paediatrics and Child Health (RCPCH). These will support clinicians in local hospitals to shorten the duration of antibiotic courses, encourage earlier step down from IV to oral therapy and facilitate timely ambulation from hospital when appropriate.

**Conclusion**

We hope that the success of our paediatric ambulatory p-OPAT service, which has relied on collaboration between nurses, general paediatricians, paediatric specialitists and tertiary infectious diseases specialists, will prompt other tertiary Children’s Hospitals to implement similar services. More importantly, we hope that it will encourage PAS teams in regional Children’s hospitals to support their colleagues working in local hospitals. This could be achieved by introducing in-reach or out-reach educational programmes, collaborating on regional antimicrobial guidelines and setting up regional paediatric antimicrobial stewardship networks. Only by doing this can we ensure high quality antimicrobial prescribing adhering to the principles of antimicrobial stewardship in all hospital settings, reducing the emergence of antimicrobial resistance in children.

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**Transparency declarations**

None to declare

|  |  |
| --- | --- |
| Working Diagnosis | Number of Patients (%) |
| Query sepsis | 15 (19) |
| LRTI | 13 (16) |
| Pyelonephritis / upper UTI | 9 (12) |
| Cellulitis | 8 (10) |
| Fever without source | 7 (9) |
| URTI | 7 (9) |
| Lymphadenitis | 3 (4) |
| Meningitis | 2 (3) |
| Scalded Skin Syndrome | 2 (3) |
| Gastroenteritis | 2 (3) |
| Infected eczema | 2 (3) |
| Seizure | 2 (3) |
| Scarlet fever | 1 (1) |
| Glomerulonephritis | 1 (1) |
| Subcutaneous abscess | 1 (1) |
| Query endocarditis | 1 (1) |
| Rash | 1 (1) |
| Conjunctivitis | 1 (1) |

Table 1. Pathologies managed with IV antibiotics (2018)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | 2018 data | Estimated impact of optimised decision making | Extrapolation over 12 Months | Total activity over 12 months |
| Admission Avoidance | 21 | 28 (🡹**33%)** | **41 extra admissions avoided** | **164 patients** |
| Inpatient Bed Days | 106 | 90 (🡻**15%)** | **93 extra bed days saved** | **524 bed days saved** |
| Potential IV Antibiotic Courses Avoided | 78 | 60 (🡻**23%)** | **104 courses of IVAbs avoided** | **346 IVAb courses administered** |

Table 2. Potential impact of improved decision making at the time of presentation to hospital (t=0 decisions) on antimicrobial use and admissions

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