**Abstract:** In paediatric ambulatory care, the speed of medication infusion can have major impact on healthcare staff workload and the number of children able to be treated by services designed to reduce inpatient length of stay. In many regions of the world, local and/or supra-regional guidelines allow ceftriaxone infusions of ≥50mg/kg in infants and children up to 12 years of age to be given over 10 minutes. The generic European summary of product characteristics (SPC) for ceftriaxone does not state a specific infusion time for this dose range, although one manufacturers’ SPC in the United Kingdom states a 30 minute minimum infusion time. We conducted a formal service evaluation of a change in practice at a large UK paediatric children’s hospital and demonstrated the clinical feasibility, safety and high parent satisfaction of 10-minute ceftriaxone infusions for prescribed doses ≥50mg/kg. This approach can improve patient flow within hospital based ambulatory services as well as by community nursing teams administering antibiotics at home.

**Introduction**

Ceftriaxone is the most commonly used intravenous antibiotic in children being ambulated from hospital in the UK.(1, 2) In a one year period between 1st October 2018 and 30th September 2019, 1029 children had 3081 doses of ceftriaxone at our hospital. The current UK summaries of product characteristics (SmPC) state that doses of ≥50mg/kg in infants and children up to 12 years of age should be administered as an infusion (60 minute infusion in neonates) although slow intravenous push may be used in people over 12 years of age.(3, 4) However, it is common practice in other countries, including the USA and Australia (5, 6), to give doses of ≥50mg/kg over a shorter period and doses of 100mg/kg have been given over 10-15 mins in clinical trials involving children with no adverse effects.(7) In the UK meningococcal epidemic in the mid 1990s, emergency care and intensive care clinicians regularly used slow IV push to deliver the first dose of 80 mg/Kg ceftriaxone, but SmPCs from this era are no longer available. We recognised that administering ceftriaxone 80mg/kg (max 4 grams) would significantly improve the flow of patients though the secondary care ambulatory paediatric medical clinic, and feedback from parents suggested that they would prefer more rapid infusions of antibiotics. As the current European Medicines Agency (EMA) SmPC does not stipulate that doses ≥50mg/kg are given over 30 minutes (8), we received agreement from the hospital (NHS Trust) Drug and Therapeutics Committee and the children’s hospital governance committee to administer ceftriaxone 80mg/kg over 10 minutes in children being managed within our paediatric ambulatory out-patient parenteral antimicrobial therapy (pOPAT) service on the understanding that we kept a database of patients receiving this therapy and reported any serious clinical side effects to the internal governance committee.

**Methods**

All children aged > 4 weeks of age managed on IV ceftriaxone within the ambulatory outpatient antibiotic (p-OPAT) service at a tertiary UK children’s hospital between March 2018-February 2019 were considered for 10-minute ceftriaxone administration. We included children up to and including 17 years of age as managed in the hospital paediatric clinical service. The routine ceftriaxone dose for all children was 80 mg/kg (max 4 grams) diluted to 50mg/ml in 0.9% saline as per local empirical antimicrobial guidelines and local administration practice respectively. A syringe driver was used to achieve the 10-minute infusion. Children excluded from receiving ceftriaxone over 10 minutes included all specific ceftriaxone infusion contraindications, specifically the receipt of Hartmann’s solution, parenteral nutrition or any other calcium-containing solution in the preceding 24 hours; or severe/life-threatening allergy to ceftriaxone. Those with a non-severe penicillin allergy receiving ceftriaxone for the first time were also given the drug via 30 minute infusion. All antibiotic doses were administered as per usual clinical practice, by pOPAT specialist nurses. Observations (temperature, heart rate and respiratory rate) were measured 10 minutes before and 10 minutes after the infusion as per routine practice. The local Drug and Therapeutics Committee asked that the clinical team a) record any systemic symptoms or side effects (SE) during the infusion and within 10 minutes of infusion completion were recorded; and b) provide all parents/carers with written and verbal explanation about the faster infusion change in practice. This formal hospital committee also agreed that specific ethics committee approval was not required. Parent/carer feedback was collected throughout the period of this service evaluation, as is routine for all patients managed directly by the paediatric antibiotic stewardship team.

**Results**

We administered a total of 213 10-minute ceftriaxone 80mg/kg (max 4 grams) infusions in 159 children. (Table 1, median age 3 year, IQR 1-8 years, range 4 weeks to 17 years).

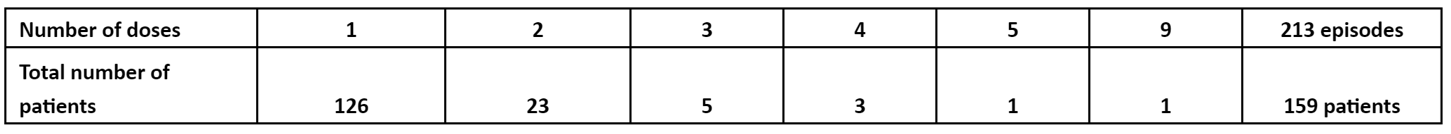


Table 1.

Most doses were administered via a peripheral cannula (n=155, 73%), with the remainder administered via a percutaneous intravenous central catheter (n=22), Hickman line (n=10) or portacath (n=6). There were no episodes of phlebitis or extravasation injuries.

193 (90.6%) of the 10-minute doses were successfully administered. 26 (12.2%) of doses were associated with side effects, all of which might be expected according to the SmPC.(3, 4) 22 children experienced pain at the infusion site and 4 had nausea and/or vomiting. 20 administrations (9.4%) were not completed within 10 minutes. Of these, 19 patients experienced pain at the IV cannula site (median 5 years, IQR 2.5-6 years) which was resolved by slowing the infusion to between 15 and 30 mins. One 17 year-old patient vomited –which was resolved by slowing the infusion to 30 minutes. No drug side effects required any other clinical intervention apart from slowing of the infusion. There were no clinically significant abnormal observations beyond those present at the start of infusions.

Parent/carer feedback

All families were sent a questionnaire by post within 7 days of completing their course of IV ceftriaxone. 83 responses out of 159 were received (52%) and all were reported back to the local Drug and Therapeutics Committee. 73 (88%) felt that the infusion over 10 minutes was better compared to 30 minutes and 9 (11%) felt that administering the ceftriaxone over 10 minutes was no different to a 30-minute infusion. The questionnaire and a selection of free text comments from parents about the 10 minute infusions are presented as Supplemental Digital Content.

**Discussion**

Despite guidelines in other countries (5, 6), there are no published data demonstrating the safety of administering an infusion of ceftriaxone 80mg/kg over 10 minutes in children. Evaluation of our change in practice to that used in other global geographical regions suggest that this approach is well tolerated in the majority of children and is associated with improved parent/carer satisfaction. There were no safety concerns in any recipients of the 10-minute infusion. Although approximately 15% administrations (22 of 155) given via a peripheral cannula were associated with mild pain at the infusion site, these were overcome by slowing the infusion. Overall, 149 out of 159 children (94%) received only one or two doses of drug. The administration of ceftriaxone ≥50mg (up to 80mg/kg) over 10-minutes is therefore likely to improve patient flow within the emergency room and hospital based ambulatory services as well as by community nursing teams administering antibiotics at home, enabling a greater number of children to be managed. This approach could therefore also be used for in-patients, reducing the time that children need to be connected to an IV infusion, with reduced infusion times associated with high rates of parent/carer satisfaction. Clinicians may wish to use these data to develop institutional or regional guidelines appropriate to their own clinical setting.

**Funding**

No funding was obtained to conduct this service evaluation. SNF is an UK National Institute for Health Research (NIHR) Senior Investigator.

**Transparency declarations**

None to declare

**References**

1. Patel S, Burzio V, Green H, et al. The Impact of Pediatric Outpatient Parenteral Antibiotic Therapy Implementation at a Tertiary Children's Hospital in the United Kingdom. *Pediatr Infect Dis J*. 2018;37:e292-e297.

2. Hodgson KA, Huynh J, Ibrahim LF, et al. The use, appropriateness and outcomes of outpatient parenteral antimicrobial therapy. *Arch Dis Child*. 2016;101:886-893.

3. <https://www.medicines.org.uk/emc/product/1361/smpc#POSOLOGY> (accessed 9/9/19).

4. <https://www.medicines.org.uk/emc/product/7933/smpc#POSOLOGY> (section 4.2) (accessed 9/9/19).

5. <https://www.umassmed.edu/globalassets/anesthesiology/files/resources/2016-resources/pediatric-guidelines-for-medications.pdf> (accessed 9/9/19).

6. <https://www.kemh.health.wa.gov.au/~/media/Files/Hospitals/WNHS/For%20health%20professionals/Clinical%20guidelines/NCCU/Drug%20Protocols/Ceftriaxone.pdf> (accessed 9/9/19).

7. Goldwater PN. Cefotaxime and ceftriaxone cerebrospinal fluid levels during treatment of bacterial meningitis in children. *Int J Antimicrob Agents*. 2005;26:408-411.

8. <http://mri.cts-mrp.eu/download/NL_H_1622_003_FinalSPC.pdf>.