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COMMENT

Variation in UK guidelines for the first-line antimicrobial management of paediatric orbital cellulitis—time for national recommendations

David McMaster[1] · Sanjay Patel[2] · Catherine Marsh[3]

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Orbital cellulitis is an emergency that may be life-threatening if it spreads to the intracranial space. It is an infection of the soft tissues of the orbit posterior to the orbital septum, usually caused by organisms originating in the upper respiratory tract or skin and although it can occur at any age, it is more common in the paediatric population [1–3]. CT imaging of the head is almost always indicated following empiric antimicrobial therapy due to the difficulty in clinically excluding the presence of a subperiosteal or orbital abscess [4]. Antimicrobial therapy is effective management in most patients, with source control requiring surgical intervention [2, 5].

There is significant variation in the antibiotic choice used to treat orbital cellulitis [1]. The largest complete data set of treatment outcomes of children diagnosed with orbital cellulitis included 1828 children reporting over 200 different variations of antibiotics used [6]. We searched local, national and international guidelines for the first-line management of orbital cellulitis in a patient without a penicillin allergy or suspected methicillin-resistant *Staphylococcus aureus* (MRSA) (Table 1). We identify variation in guidance for antimicrobial choice, dose and duration, highlighting the need for consistent UK recommendations for the treatment of orbital cellulitis.

✉ David McMaster
david.mcmaster@doctors.org.uk

[1] University of Nottingham School of Medicine, Nottingham, UK

[2] University Hospital Southampton NHS Foundation Trust, Southampton, UK

[3] The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust, Bournemouth, UK

Antimicrobial choice

Empiric antimicrobial therapy should cover the most common causative organisms, including *Streptococcus spp., Staphylococcus aureus* and in older children, polymicrobial infections with aerobic and anaerobic bacteria [1–3]. In areas with low rates of MRSA, such as the UK [7], intravenous co-amoxiclav is a single-drug therapy that provides adequate aerobic and upper respiratory tract anaerobic cover [1]. For infections with risk of intracranial spread, empiric antibiotics with high central nervous system penetration are required. Ceftriaxone (or cefotaxime in indicated groups) [8] provides aerobic cover, with good penetration of the blood–brain barrier; it should be used with metronidazole, which provides good anaerobic cover. In cases of suspected MRSA, a combination of a third-generation cephalosporin (e.g. ceftriaxone) with vancomycin may be indicated. Immunocompromised patients have greater risk of atypical infection and antimicrobial choice should be discussed closely with infectious disease specialists or microbiologists. In the UK there is significant variation in empiric antibiotic choice (and route of administration) between local NHS Trusts, national guidance and international standards (Table 1).

Dosing

Antibiotic dosing is more complex in paediatric patients than adults, with careful consideration needed with the safety profile of the antibiotic, pharmacodynamics between the drug and bacteria and the differences in pharmacokinetics between adults and children. A recent study identified marked heterogeneity in widely used paediatric antibiotic formularies in middle and high-income countries for commonly prescribed antibiotics, including those used to treat orbital cellulitis (Table 2) [9]. As well as variation between

Table 1 Orbital cellulitis guidelines.

Paediatric guidelines	Antibiotics	Duration
Manual of childhood infections: the blue book [12]	Ceftriaxone IV + metronidazole IV or co-amoxiclav IV	
Royal Children's Hospital Melbourne [13]	Cefotaxime IV or ceftriaxone IV + flucloxacillin IV	
Indian National Centre for Disease Control [14]	Cloxacillin IV + ceftriaxone IV + metronidazole IV	
Moorfields Manual of Ophthalmology [15]	Ceftriaxone IV + flucloxacillin IV	
ENT UK [16]	Co-amoxiclav IV	
UK NHS Trusts [17]		
Barking, Havering & Redbridge University Hospitals NHS Trust	Ceftriaxone IV + metronidazole IV	10–14 days
Barts Health NHS Trust	Ceftriaxone IV + flucloxacillin IV	Not available
Betsi Cadwaladr University Health Board	Ceftriaxone IV + metronidazole IV	7–10 days
Birmingham Women's and Children's NHS Foundation Trust	Cefotaxime IV or ceftriaxone IV + metronidazole IV	Treat until resolution
Brighton and Sussex University Hospitals NHS Trust [18]	Cefotaxime IV (<1 month) or ceftriaxone IV	Not available
Chesterfield Royal Hospital NHS Foundation Trust	Co-amoxiclav IV	10 days
East Kent Hospitals University NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	10–14 days
Epsom and St Helier University Hospitals NHS Trust	Ceftriaxone IV + flucloxacillin IV	Not available
Frimley Health NHS Foundation Trust	Cefotaxime IV or ceftriaxone IV	7 days
Gloucestershire Hospitals NHS Foundation Trust [19]	Cefotaxime (<1 month) or ceftriaxone IV + metronidazole IV	7 days (minimum)
Guy's and St Thomas' NHS Foundation Trust	Co-amoxiclav IV	7–10 days
Homerton University Hospital NHS Foundation Trust	Cefotaxime IV or ceftriaxone IV	10–14 days
Isle of Wight NHS Trust	Ceftriaxone IV + metronidazole IV	10 days
James Paget University Hospitals NHS Foundation Trust	Ceftriaxone IV + metronidazole IV (if abscess suspected) or Co-amoxiclav IV	14 days
Lewisham and Greenwich NHS Trust	Ceftriaxone IV + metronidazole IV	10-14 days
Mid Essex Hospital Services NHS Trust	Ceftriaxone IV + metronidazole IV	Not available
North Middlesex University Hospital NHS Trust	Cefotaxime IV or ceftriaxone IV + metronidazole IV	Not available
Northern Care Alliance NHS Group [20]	Cefotaxime (<3 months) or ceftriaxone IV + clindamycin IV	Not available
Northumbria Healthcare NHS Foundation Trust	Cefotaxime or ceftriaxone IV + metronidazole IV	Not available
North West Paediatric Allergy, Immunology and Infection Group (NWPAIIG) [21]	Ceftriaxone IV + metronidazole IV	14 days (minimum)
Poole Hospital NHS Foundation Trust	Cefotaxime (<4 weeks) or ceftriaxone IV + metronidazole IV	10 days (minimum)
Portsmouth Hospitals NHS Trust	Ceftriaxone IV + metronidazole IV	7–10 days
Royal Berkshire NHS Foundation Trust	Ceftriaxone IV + clindamycin PO	7 days
Royal Cornwall Hospitals NHS Trust	Cefotaxime IV (<4 weeks) or ceftriaxone IV + vancomycin IV + metronidazole IV	10–14 days
Royal Free London NHS Foundation Trust	Cefotaxime (<1 month) or ceftriaxone IV + metronidazole IV	10 days
Royal Surrey County Hospital NHS Foundation Trust	Cefotaxime IV or ceftriaxone IV + metronidazole IV	7 days
Royal United Hospitals Bath NHS Foundation Trust	Ceftriaxone IV + metronidazole IV (if strong suspicion of anaerobic infection)	Not available
Sandwell and West Birmingham Hospitals NHS Trust	Ceftriaxone IV ± metronidazole IV	10 days
Shrewsbury & Telford Hospital NHS Trust	Co-amoxiclav IV	14 days
St George's University Hospitals NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	7–10 days
The Royal Wolverhampton NHS Trust	Cefuroxime IV ± metronidazole	7–10 days
The Whittington Hospital NHS Trust	Ceftriaxone IV	14 days
University College London Hospitals NHS Foundation Trust	Co-amoxiclav PO (can tolerate oral medication and no intracranial involvement) or ceftriaxone IV	7–10 days
University Hospital Southampton NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	10 days (minimum)
University Hospitals Bristol NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	14 days
University Hospitals of Leicester NHS Trust [22]	Cefotaxime (<1 month) or ceftriaxone IV + metronidazole IV (if sinus involvement suspected)	Not available
West Suffolk NHS Foundation Trust	Ceftriaxone IV (consider addition of metronidazole IV)	10–14 days
Western Sussex Hospitals NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	7–14 days
Wrightington, Wigan and Leigh NHS Foundation Trust	Ceftriaxone IV + metronidazole IV	14 days (minimum)
Wye Valley NHS Trust	Ceftriaxone IV + metronidazole IV + flucloxacillin IV	10–21 days

Paediatric guidelines for the first-line antibiotic management of orbital cellulitis in patients without a penicillin allergy or suspected methicillin-resistant *Staphylococcus aureus* (MRSA).

IV intravenous administration, *PO* oral administration.

Table 2 Paediatric antimicrobial dosing guidelines.

	Intravenous antibiotics		
	Ceftriaxone	Metronidazole	Co-amoxiclav
BNFc[a]	<15 days: 20–50 mg/kg per day, q24h; 15–28 days: 50–80 mg/kg per day, q24h; 1 month–11 years (weight < 50 kg): 50–80 mg/kg per day, q24h; 9–11 years (weight ≥ 50 kg): 1000–2000 mg/day, q24h; 12–17 years: 1000–2000 mg/day, q24h	<1 month: 7.5 mg/kg per day, q24h (CGA: <26 weeks); 15 mg/kg per day, q12h (CGA: 26–34 weeks); 22.5 mg/kg per day, q8h (CGA: ≥34 weeks); 1 month–17 years: 22.5 mg/kg per day, q8h	<1 month: 60 mg/kg per day, q12h; 1–2 months: 60 mg/kg per day, q12h; 3 months–17 years: 90 mg/kg per day, q8h
Blue book[b]	<28 days: 25–50 mg/kg per day, q24h; 1 month–18 years: 50–80 mg/kg per day, q24h	<28 days: 15 mg/kg/ per day, q12h; 1 month–18 years: 22.5 mg/kg per, q8h	<28 days: 60 mg/kg per day, q12h; 1–3 months: 90 mg/kg per day, q8h; 3 months–18 years: 90–120 mg/kg per day, q6h–q8h
Red book[c]	>28 days: 50–75 mg/kg per day, q24h; 100 mg/kg per day, q12h–q24h (severe infection)	≤28 days: 7.5 mg/kg per day, q12h (PMA: ≤ 34 weeks); 7.5 mg/kg per day, q8h (PMA: 35–40 weeks); 10 mg/kg per day, q8h (PMA: >40 weeks); >28 days: 22.5–40 mg/kg per day, q6h–q8h	No information
Pocket book[d]	<2 months: 100 mg/kg per day, q12h–q24h; >2 months: 80 mg/kg per day, q24h	No information	No information
Indian National Centre for Disease Control[e]	50–100 mg/kg per day, q12h	22.5 mg/kg per day, q8h	40 mg/kg per day, q12h

Dosing recommendations from five widely used paediatric formularies for three commonly used antibiotics for the treatment of orbital cellulitis. Adapted from Mathur et al. [9].

CGA corrected gestational age, *PMA* postmenstrual age, *q6h* every 6 h, *q8h* every 8 h, *q12h* every 12 h, *q24h* every 24 h.

[a]British National Formulary for children [8].

[b]Manual of childhood infections: the blue book [12].

[c]Red book: 2018–2021 report of the committee on infectious diseases [23].

[d]Pocket book of hospital care for children [24].

[e]National treatment guidelines for antimicrobial use in infectious diseases [14].

these guidelines, there are also differences between some local NHS Trust dosing recommendations (where available) and British National Formulary for children recommendations. Correct dosing for paediatric patients is essential to effective treatment of infection, avoiding toxicity and reducing the risk of antimicrobial resistance.

Duration

Like other serious infections, intravenous antibiotics can be stepped down to an oral regimen when there are signs of improvement in orbital cellulitis. Oral antibiotics should continue for the shortest effective duration to reduce the risk

of antimicrobial resistance and adverse events. Local NHS Trust guidelines vary in total treatment duration, including both intravenous and oral antibiotics, from no specific time frame to up to 21 days (Table 1). McMullan et al. [10] recently reviewed the evidence to provide the shortest safe duration of antibiotic therapy to treat a range of paediatric infections, recommending a total duration of 7–10 days for orbital cellulitis.

Recommendations

We have identified significant national variation in antimicrobial choice, dose, total duration and when to step down from intravenous to oral antibiotics to provide the shortest effective duration of therapy for the first-line treatment of orbital cellulitis in children. This level of variation is hard to justify. Never has there been more emphasis on the threat antimicrobial resistance poses to the future of healthcare and the importance of antimicrobial stewardship. To achieve the WHO's Global Action Plan on Antimicrobial Resistance there must be efforts to optimise antibiotic use [11]. The variations identified here highlight the need for consensus-based UK guidelines for the treatment of paediatric infections such as orbital cellulitis, with an optimal antibiotic, dose and duration, as outlined above. This is being addressed through collaboration between the British Society for Antimicrobial Chemotherapy, Royal College of Paediatrics and Child Health, ENT UK and the Royal College of Ophthalmologists paediatrics sub-committee.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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