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CLINICAL STUDY

Our experience using primary oral antibiotics in the management of orbital cellulitis in a tertiary referral centre

PS Cannon, D Mc Keag, R Radford, S Ataullah and B Leatherbarrow

Abstract

Aims/Purpose **Orbital cellulitis is conventionally managed by intravenous (i.v.) antibiotic therapy, followed by oral antibiotics once the infection shows signs of significant improvement. We report 4 years of experience using primary oral ciprofloxacin and clindamycin in cases of orbital cellulitis. Oral ciprofloxacin and clindamycin have a similar bioavailability to the i.v. preparations and provide an appropriate spectrum of antibiotic cover for the pathogens responsible for orbital cellulitis.**

Methods **A retrospective review was performed that identified all patients with orbital cellulitis and treated with primary oral antibiotic therapy admitted to the Manchester Royal Eye Hospital between March 2003 and March 2007. Age, stage of disease, surgical intervention, hospital duration, and complications were obtained. A comparison was made with patients admitted to our unit with orbital cellulitis and treated with primary i.v. antibiotics between March 2000 and March 2003.**

Results **Nineteen patients were included in the review for the period March 2003 to March 2007, which comprised of 7 children and 12 adults. Five patients required surgical intervention. All patients responded to the oral regimen, 18 patients had no change to their oral antibiotic therapy. Mean hospital stay was 4.4 days. There were no complications.**

Discussion **Empirical oral ciprofloxacin and clindamycin combination may be as safe and effective as i.v. therapy in the management of orbital cellulitis. Oral treatment can offer the advantages of rapid delivery of the first antibiotic dose, fewer interruptions in treatment, and simplified delivery of medication particularly in children.**

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Oculoplastic and Orbit Department, Manchester Royal Eye Hospital, Oxford Road, Manchester, UK

Correspondence:
PS Cannon,
Oculoplastic and Orbit Department,
Manchester Royal Eye Hospital,
Oxford Road,
Manchester M13 WH,
UK
Tel: +0044 161 276 5565;
Fax: +0044 161 272 6618.
E-mail: pscan05@yahoo.co.uk

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Introduction

Orbital cellulitis is an inflammation of the orbital or periorbital tissues. The most common cause is the spread of bacterial infection from the paranasal sinuses but other causes include trauma, dental abscesses, primary bacteraemia, or the spread of contiguous skin infections. Chandler *et al*[1] modified the staging of orbital cellulitis into five categories depending on the tissues involved. Although the morbidity and mortality associated with orbital cellulitis have dramatically improved since the advent of antibiotics, serious complications may still occur including blindness, meningitis, cavernous sinus thrombosis, brain abscess, and death.[2–4] Swift investigations and appropriate management are therefore required to minimise such complications. The role of computerised tomography imaging in the assessment of this condition has long been established.[4,5] There remains significant debate with regard to the appropriate management of orbital cellulitis.[6–8] All publications to date provide a consensus that intravenous (i.v.) antibiotics are required to manage the most likely causative organisms,

namely *Streptococci* species, *Staphylococcus aureus*, *Haemophilus influenzae*, and the anaerobic bacteria of the upper respiratory tract.[9]

There is growing interest in the role of oral antibiotics where the oral bioavailability is similar to the i.v. preparation. The oral form of ciprofloxacin is practically bioequivalent to the i.v. form (70–80%).[10] In adults, an oral dose of 500 mg and an i.v. dose of 400 mg have been found to provide an equivalent serum level. The oral bioavailability of clindamycin is 90%. Both ciprofloxacin and clindamycin have a broad spectrum of activity against Gram-positive and Gram-negative organisms, with clindamycin having additional activity against Gram-negative anaerobic organisms.

In 2003, we introduced a protocol for the management of orbital cellulitis at the Manchester Royal Eye Hospital. The protocol advocated the use of primary oral ciprofloxacin and clindamycin. We share the experience of our protocol in this paper.

Materials and methods

We reviewed the hospital case notes of patients admitted to the Manchester Royal Eye Hospital with orbital cellulitis from March 2003 to March 2007. We identified patients treated with primary oral antibiotic therapy and recorded their age at the time of admission, the stage of the orbital cellulitis on admission, whether surgical intervention was required, the duration of hospital stay, and any complication that occurred. We compared these findings with patients admitted to our centre from March 2000 to March 2003, who received primary i.v. antibiotic therapy. All patients were admitted for close observation involving hourly visual acuities and pupil reactions. The empirical antibiotic regimen did not influence any surgical intervention that was deemed to be necessary in the management of the patient.

The staging of the disease is based on the modified Chandler's[1] classification of orbital cellulitis. Stage I is preseptal cellulitis. Stage II is classified as orbital oedema with any evidence of chemosis, proptosis, restricted eye movements, or optic neuropathy. Stage III includes stage II with a subperiosteal abscess, while stage IV is classified as an orbital abscess. Stage V is an extension of the infection to the cavernous sinus, subdura, meninges, or brain.

Results

We identified 46 patients admitted to the Manchester Royal Eye Hospital with orbital cellulitis from March 2003 to March 2007. Patients who received primary i.v. therapy were excluded. The primary i.v. group had five patients whose degree of nausea precluded oral therapy, three patients commenced on i.v. therapy prior to admission to our unit, two patients with dental abscesses, one patient with an extradural abscess, and one patient who required i.v. antifungal therapy. One patient in the primary oral antibiotic group had i.v. therapy prior to admission to our unit and was excluded. All 14 patients with Chandler's[1] stage I orbital cellulitis were excluded. Thus 19 patients who received primary oral antibiotics were included for comparison.

We identified 17 patients in the 2000–2003 group who received primary i.v. therapy without having had i.v. therapy prior to admission and did not have stage I orbital cellulitis as defined above. Table 1 outlines the demographic data of the 2003–2007 primary oral group and the 2000–2003 primary i.v. group. The staging of the disease is presented in Table 2.

Table 1 Demographic details for the 2000–2003 primary intravenous group and the 2003–2007 primary oral group

	2000–2003 primary intravenous antibiotic group	*2003–2007 primary oral antibiotic group*
Total number of patients	17	19
Number of patients younger than 9 years of age	1 (6%)	5 (26%)
Number of patients aged 9–16 years	5 (29%)	2 (11%)
Number of patients aged 16 years or older	11 (65%)	12 (63%)
Mean age of patients	34.1 years	29.9 years
Range of ages	1–77 years	2–73 years

Table 2 Comparing the stage of orbital cellulitis, the number of patients for surgery, and the surgical procedures for the 2000–2003 primary intravenous group with the 2003–2007 primary oral group

Stage of orbital cellulitis	*Primary i.v. group (2000–2003)*	*Primary oral group (2003–2007)*
II	6	8
III	6	10
IV	5	1
Number of patients for surgery	9	5
Type of surgery		
SPA drainage	7	5
Sinus washout	5	2
OA drainage	4	0
Type of surgical approach		
Lynch incision	5	0
Trans-caruncular incision	1	5
Infra-brow incision	3	0

Abbreviations: OA = orbital abscess; SPA = subperiosteal abscess.

In the primary oral group, 10 patients were found to have a medial orbital wall subperiosteal abscess and one patient had a lateral orbital wall subperiosteal abscess. In the primary i.v. group, subperiosteal abscesses were found in the following locations: orbital roof in five patients, medial orbital wall in five patients, and the lateral orbital wall in one patient.

Surgical intervention was required for five patients in the primary oral group compared to nine in the primary i.v. group; some patients had more than one surgical procedure performed in the same session. The types of surgical procedures and incisions are recorded in Table 2. No patient in the primary oral group required a second surgical procedure, whereas one patient in the primary i.v. group required a second surgical procedure. This patient had reformation of a medial orbital wall subperiosteal abscess. The mean duration of hospital stay was similar for the two groups. This was 4.4 days in the primary oral group and 5 days in the primary i.v. group. Neither group had any associated complications recorded. In the primary oral group, 18 patients had no alteration to their antibiotic therapy, one patient was changed to an alternative oral medication, and three patients had an antiviral medication added to their antibiotic regimen. No patient in the primary oral group required subsequent i.v. therapy.

Microbiology results from the abscess aspirates were obtained for the five patients who had surgical intervention in the primary oral group and for the nine patients in the primary i.v. group. In the primary oral group microbiology cultures grew *Streptococcus anginosus* in two patients, *H. influenzae* in one patient, and *S. aureus* in one patient. The fifth patient had no growth recorded. This compares with the growth of *S. anginosus* in four patients, *Streptococcus constellatus* in one patient, *Streptococcus pneumonia* in one patient, *S. aureus* in one patient, and *H. influenza* in one patient in the primary i.v. group. The ninth patient had no growth recorded.

Discussion

All publications to date relating to the management of orbital cellulitis have used i.v. antibiotics.[6–9,11–16] Kagel *et al*[17] have described the potential complications associated with i.v. cannulation, which range from thrombophlebitis, cellulitis, haematomas with skin necrosis to compartment syndrome. There is also the psychological impact of i.v. cannulation to consider, particularly in children. Al-Nammari *et al*[18] posed the question 'should a child with preseptal periorbital cellulitis be treated with i.v. or oral antibiotics?'. They conducted a search involving 395 papers and were unable to find any published evidence to answer their question. The aim of this paper was to investigate whether or not oral antibiotic therapy was similar to i.v. therapy in outcome and safety.

Table 3 The MREH protocol on the management of orbital cellulitis

Initial management
1. Hospital admission
2. Urgent CT scan of the paranasal sinuses, orbit and brain
3. Full blood count, urea, and electrolytes
4. Monitoring of the vision and pupil reactions hourly
5. Frequent monitoring to detect proptosis and reduced ocular motility
6. Empirical antibiotic cover of oral ciprofloxacin and clindamycin

Indications for surgical intervention include
1. Signs of optic nerve dysfunction
2. Orbital or subperiosteal abscess on CT (particularly if a roof abscess is present)
3. Failure to improve on medical treatment
4. Gas within the abscess space (anaerobic infection)
5. Concurrent chronic sinusitis
6. Dental infection

After careful discussion with our hospital pharmacists and microbiologists, we introduced a protocol to manage orbital cellulitis in 2003 (Table 3). It advocates the use of oral ciprofloxacin and clindamycin as first-line antibiotic cover in both children and adults. Intravenous antibiotics are used in patients whose nausea precludes the use of oral antibiotics, where the patient had been commenced on i.v. therapy elsewhere and subsequently referred to our tertiary referral centre, or when advised to use i.v. therapy by the microbiology department in specific clinical scenarios. In the 2003–2007 group, 12 patients received i.v. antibiotic therapy for the reasons previously described. The protocol allows for the antibiotic regimen to be modified according to the patient's microbiology results and/or the patient's clinical condition.

The protocol also sets out indications for surgical intervention (Table 3), which are in accordance with current published studies.[1,7,8,11,16] Garcia *et al*[7] concluded from their experience that children under 9 years of age with a subperiosteal abscess are likely to improve without surgical intervention, provided certain criteria are met. We concur with their conclusions. We found that all five children under 9 years of age did not require surgical intervention in the primary oral group compared with two children aged 9 years or older. In the primary i.v. group, one child under 9 years required surgery to drain a subperiosteal abscess compared to all three children who were 9 years or older. Harris[19] maintains a more aggressive approach involving surgical drainage in

older children and adults with subperiosteal abscess due to the polymicrobial nature of their infection and the increased complications encountered in this age group. The primary i.v. group had more surgical intervention than the primary oral group. This can partially be accounted for by assessing the location of the subperiosteal abscess. The primary i.v. group had five patients with an orbital roof subperiosteal abscess, which is more likely to require surgery. There were no incidences of orbital roof subperiosteal abscesses in the primary oral group.

Primary oral preparations of antibiotics, particularly ciprofloxacin, have gained popularity in the management of serious infections. Ramirez-Ronda *et al*[20] performed a comparative, double-blind study on the use of oral ciprofloxacin and i.v. cefotaxime in skin and soft tissue infections. They found that oral ciprofloxacin was as effective and safe as i.v. cefotaxime. Tuncer *et al*[21] found similar results for the management of spontaneous bacterial peritonitis. The combination of ciprofloxacin and clindamycin offers a wide spectrum of activity against the most likely organisms involved in orbital cellulitis. The spectrum of bacteria isolated in our series, albeit small, is consistent with the spectrum noted in other publications such as *Streptococci*, *Staphylococci*, and *H. influenzae*.[6,9,11,14]

The most commonly prescribed i.v. antibiotics in the 2000–2003 group were third-generation cephalosporins, metronidazole, flucloxacillin, and ciprofloxacin. The use of i.v. antibiotics often resulted in delayed delivery of the first dose and missed doses while waiting for the i.v. cannula to be re-sited. The change to primary oral therapy did not appear to result in prolonged hospitalisation or additional complications. The majority (94.7%) of patients tolerated the combination of oral ciprofloxacin and clindamycin, with only one patient requiring a change in the antibiotic regimen. There were no cases of diarrhoea secondary to *Clostridium difficile* in our small group.

In summary, we found that the primary usage of oral ciprofloxacin and clindamycin as the antibiotic treatment for orbital cellulitis yielded results that were no different to those achieved with primary i.v. antibiotic therapy. Although the number of patients in this study was small, the results suggest that primary oral antibiotic therapy has a role in the management of orbital cellulitis provided that its bioavailability is similar to that of i.v. preparations. The antibiotic must have a spectrum of activity against the bacteria responsible for the orbital cellulitis. The oral preparations can offer more rapid delivery of the first dose, can result in fewer interruptions in the treatment delivery, and can simplify treatment delivery especially in children.

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