REVIEW ARTICLE

The management of septic arthritis in children

SYSTEMATIC REVIEW OF THE ENGLISH LANGUAGE LITERATURE


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We performed a systematic review of the optimal management of septic arthritis in children as recommended in the current English literature using MEDLINE, EMBASE, CINAHL, the Cochrane Library and reference lists of retrieved articles without date restrictions up to 31 January 2009. From 2236 citations, 227 relevant full-text articles were screened in detail; 154 papers fulfilled the inclusion criteria, from which conclusions were drawn on the management of infected joints in children.

Our review showed that no single investigation, including joint aspiration, is sufficiently reliable to diagnose conclusively joint infection. The roles of aspiration, arthrotomy and arthroscopy in treatment are not clear cut, and the ideal duration of antibiotic therapy is not yet fully defined. These issues are discussed. Further large-scale, multi-centre studies are needed to delineate the optimal management of paediatric septic arthritis.

Although uncommon, septic arthritis must be ruled out in the child with a painful joint. Delay or failure in instituting appropriate management may be due to several factors, such as difficulties in obtaining an accurate history and problems encountered examining young children in pain. We performed a systematic review of the literature to identify the best available evidence on the diagnosis and treatment of paediatric septic arthritis. The aims were to identify relevant diagnostic factors, and to review the current evidence underlying the most commonly used treatment strategies.

Materials and Methods

We used the following electronic bibliographic databases: MEDLINE (Medical Literature Analysis and Retrieval System online, Bethesda, Maryland), EMBASE (Excerpta Medica Database, Amsterdam, The Netherlands), CINAHL (Cumulative Index to Nursing and Allied Health Literature, Ipswich, Massachusetts) and the Cochrane Library without date restrictions up to 31 January 2009. In order to avoid missing contemporary studies that remain unpublished the Google Scholar search engine was also used. The keywords and Medical Subject Heading (MeSH) terms which were used were paediatric, ‘joint infection’, ‘septic arthritis’, ‘antibiotics’, ‘surgery’ and ‘joint aspiration’. We screened the reference lists of included articles to identify any further relevant studies. We then reviewed the titles, abstracts and full texts of apparently relevant articles to determine their eligibility.

Eligibility criteria. Only comparative studies, analytical studies and case series written in English were included. We excluded studies with fewer than 20 cases, abstract-only publications and review articles (Table I). A total of 154 papers fulfilled the inclusion criteria (Fig. 1).

Extraction of data. Data were extracted from the eligible articles and differences were resolved by discussion. Each study was also reviewed for the quality of its methodology. Comparative studies were assessed using Detsky et al.’s scoring system for randomised controlled trials, and case series were assessed using Bland-Altman analysis, which allowed assessment of inter-rater agreement for the quality of studies. A descriptive summary of the results is presented.

Results

Incidence. Paediatric articular infection is uncommon. Studies performed over two different decades in Dallas demonstrated an unchanging incidence of 1 in 100 000. In Israel, an incidence of 37 in 100 000 has been noted. However, in the developing world the situation is different. The incidence of septic arthritis in children in Malawi has recently been reported to be 1 in 3000. Another prospective African study reported an incidence of 1 in 20 000.

Causative organisms. The most common organism causing septic arthritis in children is
Staphylococcus aureus, followed by group A Streptococcus and Enterobacter.\textsuperscript{9-14} Haemophilus influenza has been virtually eliminated by vaccination,\textsuperscript{15} but given the decrease in uptake of childhood immunisation as a result of the recent erosion of public confidence in vaccine safety, this organism should be reconsidered. Children with sickle-cell disease are at risk for salmonella-related osteoarticular infections\textsuperscript{16} and salmonella is the most common cause of septic arthritis in infants in Kenya,\textsuperscript{17} Malawi\textsuperscript{18} and Zambia.\textsuperscript{19} Improved techniques have led to the detection of unusual organisms such as Kingella kingae.\textsuperscript{6,20} Recent reports have emphasised the changing microbiological patterns in musculoskeletal infections, especially with respect to the emergence of methicillin-resistant Staphylococcus aureus (MRSA).\textsuperscript{5,21}

**Risk factors.** Several risk factors for septic arthritis in children have been recognised (Table II). Prematurity and low birth weight have been excluded as risk factors.\textsuperscript{22}

**Clinical symptoms and signs.** Children with acute septic arthritis typically have a painful, swollen joint. Parents may ascribe this to a preceding minor injury. Physical examination is likely to demonstrate an effusion, a restriction in the range of movement of the affected joint, tenderness and increased local warmth.\textsuperscript{9} With later presentations the child may be systematically unwell, with swelling of the entire extremity or associated cellulitis or abscess formation. Unfortunately, in infants and neonates typical symptoms and signs may be lacking.\textsuperscript{23} Signs may be as subtle as irritability or limited spontaneous movement in one limb (pseudo-paralysis).\textsuperscript{23}

Any joint may be affected, although the hips and knees are the most commonly involved.\textsuperscript{24,25} Owing to the variation in defining the presence or absence of pyrexia, direct comparison between papers is difficult. All the studies reviewed concluded that other clinical signs, imaging and inflammatory markers were necessary in combination with pyrexia to exclude septic arthritis.\textsuperscript{26-32}

**Laboratory findings.** White cell count. The response of the white cell count is related to age and is usually elevated in...
older children, sometimes elevated in younger children and only rarely elevated in neonates. In one study, only a third of patients with infected hips had an elevated white cell count.

**Erythrocyte sedimentation rate (ESR).** In a retrospective review of the medical records of 138 children, including neonates, presenting with acute hip pain, the ESR alone had a sensitivity of 79%. The ESR in isolation is of variable sensitivity, but in combination with an elevated temperature, white cell count and an inability to bear weight, it is an important exclusion parameter, with sensitivities consistently above 98%.

**C-reactive protein (CRP).** In one prospective trial the CRP level had the highest predictive value for septic arthritis and was the only risk factor strongly associated with outcome at a 5% level of significance. This is borne out by other studies that advocate a more conservative approach to treatment for limping children with a proven hip effusion and CRP < 10 mg/ml, as septic arthritis is very unlikely.

**Management algorithms.** Several studies have attempted to define algorithms to improve the diagnosis and subsequent treatment of septic arthritis, especially of the hip. The algorithms include clinical and serological parameters such as weight-bearing status, the presence of pyrexia, and raised white cell count, ESR and CRP. They are not necessarily applicable in all settings, and their validity must be tested locally.

However, other than weight-bearing status, the currently published clinical algorithms do not include physical examination. Algorithms should supplement and not substitute clinical decision-making in all cases.

**Microbiological culture.** The rate of positive identification of pathogens from blood and synovial fluid culture ranges from 34% to 82% in the current literature. Synovial fluid Gram stains may only be positive in 30% of aspirates. Synovial fluid white cell count > 50 000 must be correlated with the clinical picture to exclude other diagnoses, such as juvenile idiopathic arthritis.

Three studies have looked at the prognosis related to the findings of blood and synovial cultures, and two of these found that culture-negative patients ran a milder clinical course, although the third found no difference. Synovial fluid cultures were more sensitive than blood cultures in these studies. However, in several cases blood cultures but not joint aspirates were positive, and should therefore be performed in tandem.

**Imaging. Plain radiographs.** Plain radiographs are required to differentiate septic arthritis from other diagnoses, such as established osteomyelitis, fractures and neoplasia. An increase in joint space may reflect an effusion.

**Ultrasound.** Ultrasound remains the most sensitive tool for detecting an effusion in the hip. However, there is a false-negative rate of 5%. Ultrasound-guided aspiration of the hip evacuates pus, reduces damage to the articular surfaces, differentiates joint sepsis from other arthritides and helps direct antibiotic treatment. A negative ultrasound result when excluding septic arthritis in children must be interpreted with caution when symptoms have been present for less than 24 hours, or when there is bilateral disease.

**Magnetic resonance imaging (MRI).** MRI is extremely sensitive and specific in diagnosing septic arthritis of the hip and differentiating it from osteomyelitis and non-infective causes of hip pain in children. Statistically significant MRI findings in transient synovitis are an effusion in the contralateral (asymptomatic) joint and the absence of signal intensity abnormalities of the bone marrow.

**Bone scintigraphy.** This is particularly useful in identifying multifocal musculoskeletal infections, but lacks sensitivity and specificity in distinguishing septic arthritis from nearby osseous or soft-tissue infections.

**Management. Antibiotics.** Early administration of antibiotics is widely supported in the literature, and although microbiological evidence of infection is preferred, antimicrobials should not be withheld once diagnostic procedures have been performed. Conversely, there is little consensus on the choice of antibiotic, the choice often being made locally based on the most likely infecting organism. Suggested or recommended regimens include the septic arthritis Clinical Practice Guideline algorithm and the current British Society for Antimicrobial Chemotherapy guidelines (Table III).

Although there is agreement that antibiotics should be initially given intravenously and then orally once clinical improvement is evident, there is debate on the recommended duration of intravenous (IV) therapy, varying greatly from two to six or seven weeks. However, there is growing evidence in the recent literature for short-course IV therapy.
that short-course IV antibiotic treatment (seven days) is adequate, and that longer term treatment should be reserved for patients who failed to respond to the shorter regimen or who otherwise presented with clear clinical and microbiological counter-indicatory criteria. An earlier study found that shortened IV therapy in accordance with a patient’s response to treatment resulted in no recurrence or persistence of infection.

There are no publications on the use of intra-articular antibiotics in children.

**Joint aspiration versus arthrotomy and washout.** As the sequelae of paediatric hip sepsis can be devastating, arthrotomy has been advocated as the best method of treatment. It may also provide an opportunity to obtain specimens for microbiology and histology. Arthrotomy for infants diagnosed with a septic hip, and joint aspiration for older children presenting within four days of the onset of symptoms, have also been advocated.

Aspiration under ultrasound guidance has been proposed for the diagnosis of hip sepsis, although doubt remains as to both the adequacy of decompression and the need for further aspiration. In a prospective, randomised study, aspiration of septic shoulder joints showed no significant difference in clinical and radiological outcome at one year compared to open arthrotomy and washout.

There are no studies comparing aspiration **versus** arthrotomy for septic arthritis of hip in children.

**Arthroscopy.** A prospective controlled study comparing the outcome of formal arthrotomy of the hip **versus** arthroscopic drainage showed the only significant difference to be a shortened in-patient stay (6.4 days vs 3.8 days). There are currently no studies examining the role of arthroscopy in the treatment of infection of the knee joint in children.

**Prognosis.** The advances in diagnosing and treating septic arthritis, including the use of antibiotics, have led to a significantly reduced mortality, from 50% in 1874 to < 1% in 1973. Indicators of poor prognosis include:

1. **Young age.** This is due to difficulties in diagnosing septic arthritis, leading to a delay in initiating treatment, and to the presence of transphyseal vessels in neonates seeding bacteria from adjacent osteomyelitis. This may be compounded by the immaturity of the immune response.

2. **Delay in initiating treatment.** An excellent outcome is obtained in 75% of cases if symptoms are present for less than four days; this falls to 15% if symptoms are present for more than four days.

3. **Organism.** Many studies indicate a worse prognosis for infections with *Staphylococcus aureus*, which may be related to the virulence of this organism and an associated cell-mediated immunological reaction in response to the bacterial exoprotein. The presence of collagen receptors may account for the tropism of *Staphylococcus aureus* to septic joints.

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**Table III.** Empirical therapy guidelines from the British Society for antimicrobial chemotherapy

Because of the potential for permanent joint damage if suboptimal treatment is given, treatment should be discussed with your microbiologist.

The following are suitable empirical antibiotic regimens:

**Non high-risk patients**

- High-dose, μg flucloxacillin plus benzylpenicillin (plus either fusidic acid or rifampicin, depending on the severity of infection)

If the patient is in a high-risk group, has pre-existing rheumatoid arthritis, or Gram-negative organisms were identified on Gram stain, treatment can be modified as follows:

- High-dose, intravenous flucloxacillin plus either an aminoglycoside such as gentamicin or a quinolone such as ciprofloxacin (plus either fusidic acid or rifampicin depending on severity)

or

- A second-generation cephalosporin such as cefuroxime (plus either fusidic acid or rifampicin depending on severity)

**In penicillin-allergic patients:**

- Clindamycin plus a quinolone such as ciprofloxacin

or

- Vancomycin plus a quinolone such as ciprofloxacin

If MRSA is suspected, consult your microbiologist, as treatment will depend on local antibiotic susceptibilities. The following general principles usually apply:

- Intravenous vancomycin should be used instead of flucloxacillin

- Gentamicin or a quinolone such as ciprofloxacin can be added to vancomycin, subject to local policies and the advice of your microbiologist

If clinical signs indicate gonococcal septic arthritis, suitable treatments include:

- High-dose IV second- or third-generation cephalosporin such as cefuroxime or cefotaxime

or

- A quinolone such as ciprofloxacin plus flucloxacillin

* MRSA, methicillin-resistant *Staphylococcus aureus*
4. Site. The hip has the worst outcome of all joints, as elevated intracapsular pressure causes occlusion or thrombosis of retinacular and transphyseal vessels, and also because sepsis induces subluxation of the femoral head.8,78,79

Discussion
This paper is a comprehensive review of the current English language literature on the management of septic arthritis in children. Systematic reviews are useful as a tool in clinical decision making, especially in orthopaedic surgery where primary studies of small sample size predominate, provided the review is performed with strict methodological criteria. For this study, broad eligibility criteria were chosen for generalisability. However, restricting the study selection to English language journals was a potential source of bias. Conclusions based on English language studies has been shown to lead to significant overestimation of effects.80,81 As there was only one randomised controlled trial, the other studies carried the risk of ascertainment bias, as they were retrospective and narrative in nature. Outcome measures are difficult to compare between studies included in this review because of their considerable heterogeneity.

This review of current evidence identified key findings related to the management of septic arthritis in children. Given the low incidence of this condition in the antibiotic era, recognising and diagnosing septic arthritis is difficult. This may be compounded by the lack of clear clinical signs and symptoms, especially in younger, less co-operative patients. Unfortunately, a single gold standard test for diagnosing septic arthritis in children does not exist. However, current studies27,32,36,37 have emphasised the importance of normal CRP levels as having a high predictive value for excluding septic arthritis.

The hip is the only joint that has been extensively evaluated with respect to imaging, and although there are several drawbacks with respect to all imaging modalities, ultrasound appears to be the investigation of choice.10,18,50 The implementation of diagnostic algorithms,27,29,31,38,39 does not guarantee detection of all cases. Careful examination by an experienced clinician is therefore mandatory.

The problem of low sensitivities of blood and synovial cultures can be addressed by newer techniques such as real-time polymerase chain reaction for detecting organisms such as Kingella kingae,6,20 but this requires a high level of awareness. The causative pathogen in most children is a Gram-positive micro-organism.10-14 β-lactam antibiotics can therefore be commenced as first-line treatment in the absence of allergy. If there is doubt, or the child is at high risk for less typical organisms, then consultation with a microbiologist is advised.82

Once a diagnosis of septic arthritis is made, questions remain about the optimal method of treatment. Although literature exists regarding the efficacy of antibiotic therapy,33,57-60 no articles prospectively comparing outcomes following the use of antibiotics alone versus arthroscopy and/or arthrotomy provide the clinician with an opportunity to obtain specimens that identify the pathogen(s) where other culture samples may have failed.

The length of antibiotic therapy should be based on responses of clinical and serological parameters. Arthroscopy and/or arthroscopy provide an opportunity to obtain specimens that identify the pathogen(s) where other culture samples may have failed.

A multidisciplinary approach to management of septic arthritis in children is required.

Table IV. Summary findings

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<thead>
<tr>
<th>Organism</th>
<th>Summary</th>
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<tr>
<td>Staphylococcus aureus and group A streptococci are among the most common organisms associated with septic arthritis in children</td>
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<td>Typical signs and symptoms may be absent, particularly in neonates and infants</td>
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<td>C-reactive protein combined with weight-bearing status, temperature and white cell count is a useful tool in the diagnosis of septic arthritis in children</td>
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<td>Ultrasonography is a quick, non-invasive technique that aids diagnosis, especially for the hip joint</td>
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<td>Early initiation of intravenous therapy is recommended, although choice of therapy is a local decision based on the most likely pathogen</td>
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of stringent evidence, which is likely to be multifactorial in origin. The low incidence of septic arthritis in children and its presentation to different specialties creates difficulties in recruiting sufficient numbers of patients into prospective, randomised controlled trials. The establishment of a national registry would help provide a source of continuous data, which could be used to benchmark care. Important findings from this review are summarised in Table IV.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References


60. Yuan HC, Wu KG, Chen CJ, Tang RB, Hwang BT. Duration of antibi-...