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# Evaluation of a Probabilistic Antibiotherapy Protocol for Community Osteoarticular Infections in Children

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## Abstract

**Objective:** To evaluate a protocol of empirical intravenous antibacterial treatment amoxicillin-clavulanate (age <2 years), or cloxacillin (age >2 years) for Bone and Joint Infections (BJI) in children.

**Patients and Methods:** Retrospective observational study in a referral center for complicated BJI. Data collected through medical files, and contact with parent(s)/general practitioner for one year-follow-up.

**Results:** From 2011 to 2014, 63 children have been admitted for community-acquired acute BJI (mean age, 5.2+4.3 years): Arthritis (n=42), osteomyelitis (n=14) or osteoarthritis (n=7), mainly involving the knee (n=22), the hip (n=21) or the ankle (n=10), mostly due to *Staphylococcus aureus* (n=14) and *Kingella kingae* (n=9). All children were cured at one-year follow-up, with a mean hospital stay duration of 5.0 ± 2.4 days, a change of antibacterial treatment outside of the protocol in 11 cases (16%), and secondary surgery in 9 cases (11.5%).

**Conclusion:** The protocol is well adapted to community-acquired BJI in our population.

**Keywords: Osteoarticular infections; Antibiotic; Empirical; *Kingella kingae*; *Staphylococcus aureus***

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## Introduction

Osteoarticular Infections (OAI) in children are frequent and potentially serious pathologies with the risk of repercussions on bone growth. Advances in microbiological diagnosis have made it possible to better define the epidemiology of IOA in children and to develop therapeutic recommendations [1-3]. Early multidisciplinary, diagnostic and therapeutic treatment often allows healing without sequelae [4-7]. Strategies to reduce length of hospital stay, associated with a reduction in the duration of intravenous antibiotic therapy have multiple advantages for the patient (reduction in exposure to nosocomial risk, reduction in distance from the environment family and school), and for the system (cost reduction, hospital accommodation needs) [8,9]. In this context, a multidisciplinary working group established a probabilistic antibiotic therapy protocol for the management of acute community pediatric AOI in our establishment, taking into account data from the literature and local epidemiology, with early oral relay. This protocol, validated by all the disciplines concerned, has been applied since January 01st, 2013. The objective was to assess the performance of this protocol by analyzing its application during the first three years.

## Materials and Methods

This is a retrospective observational study of all confirmed or suspected cases of community-based AOI in children aged 0 to 16 years, hospitalized in the pediatric surgery department of a reference center for complex IOA (CRIOAC) from 01/01/2013 to 31/12/2016. All medical records of children diagnosed with arthritis, osteoarthritis or osteomyelitis were admitted to hospital during the study period been studied. The data were collected by a standardized questionnaire. We excluded patients with chronic IOA (duration >4 weeks at diagnosis), care-related IOA or inflammatory rheumatic disease.

In our establishment, a suspicion of acute AIO leads to the realization of a joint or metaphyseal

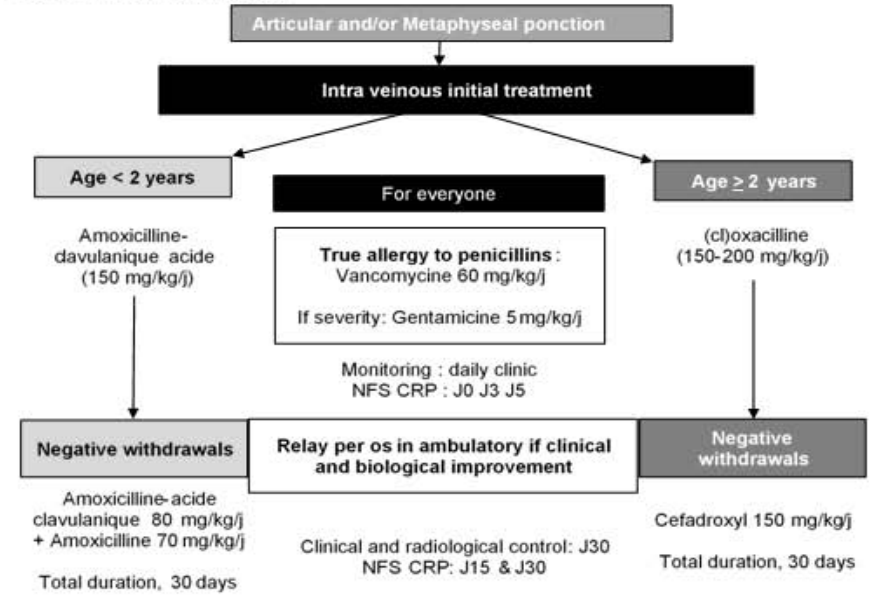


**Figure 1:** Treatment protocol.

puncture under general anesthesia in emergency, as well as blood cultures. A standard microbiological analysis was carried out for all the osteo-articular samples (direct examination after Gram staining, aero- and anaerobic cultures), associated with a systematic search for *Kingella kingae* by PCR. Intravenous antibiotic therapy was started immediately after sampling according to the protocol (Figure 1). In the event of favorable evolution, the oral relay was envisaged from the first days, according to the sensitivity profile of the pathogen identified when microbiological documentation had been obtained or probabilistically in the absence of documentation, by amoxicillin-acid clavulanic before the age of 2 years, or cefadroxil beyond. In the absence of clinical and biological improvement, revision surgery was discussed. The operating technique was left to the operator.

The protocol provided for adaptation to the most common situations. In the event of an unusual allergy or pathogen, an infectious disease opinion was obtained in order to define relay antibiotic therapy. The children were seen again 1 month and 1 year after diagnosis to make sure there were no complications, including growth problems. Adverse events were collected from medical records, classifying as severe any adverse event requiring hospitalization or prolongation of hospitalization. The parents of the children who were not seen by the attending physician or the pediatric surgery department one year after the diagnosis were contacted by one of the investigators (AB) in order to collect progress data. The primary endpoint was healing at one year. Secondary endpoints were length of hospital stay, recovery surgery, changes in antibiotic therapy not provided for in the protocol and the occurrence of complications. The study was approved by the ethics committee of our institution. The quantitative variables were analyzed by a Student test with normal distribution or non-parametric Mann-Whitney Wilcoxon tests. Qualitative variables were analyzed by nonparametric Fisher tests. The analyzes were performed with SAS software, version 9.4.

## Results

During the study period, 63 children were cared for the main characteristics are detailed in Table 1. Microbiological documentation was obtained from 36 children (60%). The main bacteria identified were *Kingella kingae* before the age of 2 years (7/12, 58%) and Staphylococcus aureus after 2 years (14/24, 58%). The average length of hospital stay was 5.0 ± 2.4 days (2.0 to 13.0). Three children (4%) experienced a relapse. Surgical revision was necessary in 9 cases (14%): Joint puncture-lavage (n=4), arthrotomy (n=3) and arthroscopic lavage (n=2). The average time between initial puncture and recovery was 3 days (range, 2 to 5). An adaptation of the antibiotic therapy outside the protocol was necessary in 11 cases (16%) (spectrum unsuitable given the microbiological documentation (n=4), clinical failure (n=3) and intolerance (n=2)). Two serious adverse events have been reported (anemia requiring transfusion (n=1) and metacarpophalangeal epiphysiodesis (n=1)). Three children (5%) presented with a non-serious adverse event (femoro-cutaneous hypoesthesia (n=1), deep-adherent scar (n=1) and persistent gonalgia after infection of the knee (n=1)). All IOA were cured at one year with a follow-up >6 months at the end of treatment. The identification of a pathogen during joint puncture has been associated with a duration prolonged hospitalization (average 5.6 days *vs.* 4.1 days; P=0.004) and the need for repeat surgery (9/36 *vs.* 0/27; P=0.008). All relapses (3/36 *vs.* 0/27) concerned children with isolation of bacteria during joint puncture.

## Discussion

This study suggests that this antibiotic therapy protocol is suitable for the majority of situations with a modification of the antibiotic therapy not provided for in the protocol in 16% of the cases, and a cure at one year in 100% of the cases. In addition, these results are obtained with an average hospital stay of 5 days. Two pediatric series report comparable lengths of hospital stay. The need for repeat surgery for AIO control is low in our series and few complications are noted. The value of a systematic initial surgical wash remains controversial [10]. In our experience, initial surgical abstention is reasonable subject to close monitoring during the first days and early drainage in the event of poor progress. The low relapse rate under treatment (5%) and the absence of recurrence at the end of treatment in all children, testify to

**Table 1:** Acute community osteoarticular infections in children (n=63).

| **Demographic data** | |
|---|---|
| Age (years) | 5.2 + 4.3 |
| - Age <2 years | 44 (69.8%) |
| - Age >2 years | 19 (30.2%) |
| **Sex ratio girls/boys** | 26/37 (0.70) |
| Type of infection | |
| Arthritis | 42 (66.7%) |
| Osteoarthritis | 7 (11.1%) |
| Osteomyelitis | 14 (22.2%) |
| **Localizations** | |
| Knee | 22 (34.9%) |
| Hip | 21 (33.3%) |
| Ankle | 10 (15.9%) |
| Others* | 11 (17.5%) $ |
| **Microbiology** | |
| *Staphylococcus aureus* | 14 (58.3%) |
| *Kingella kingae* | 9 (14.3%) |
| *Staphylococcus coagulase*-negative | 4 (6.3%) |
| *Streptococcus pyogenes* | 4 (6.3%) |
| *Cutibacterium acnes* | 3 (4.8%) |
| Others € | 2 (2.2%) |

the effectiveness of this management, with an evolution comparable to that reported in the literature [8].

The microbiological documentation, obtained in 60% of cases, is in agreement with recent series, with the predominance of *Kingella kingae* during the first years of life, well covered by probabilistic antibiotic therapy with amoxicillin-clavulanic acid [10]. The predominance of *S. aureus* beyond the age of 2 years and the potential severity of infections with this pathogen justify the initial use of an intravenous anti-*Staphylococcal penicillin*, cloxacillin or oxacillin, as a probabilistic treatment in this group of age [10]. The evolution still favorable in the absence of microbiological documentation in our series, in the absence of a relapse or the need for a repeat surgery, confirms these choices of probabilistic antibiotic therapy, even if the etiology of these cases remains undetermined. The choice of oral relay in these situations is complex. Beyond 2 years, we offer cefadroxil as a probabilistic oral relay, in accordance with French and European recommendations, especially taking into account a dosage form suitable for young children (oral solution), a good tolerance and a low prevalence of methicillin resistance in community strains of *S. aureus* in France [3]. Our study has limitations: It is a retrospective observational study, with possible biases in the collection of variables. The quality of data regarding the duration of antibiotic treatment and compliance is not guaranteed, with many data missing for these variables in medical records. The monocentric nature, in a region with a low prevalence of antibiotic resistance, does not allow the extrapolation of the results to all contexts. The lack of microbiological documentation in one in four children, even if it is found in most series, is a weakness. On the other hand, the systematic inclusion of all the cases taken care of in our CRIOAC with a large number of staff in light of the data in the literature and a systematic collection of follow-ups at one year are assets allowing to give a good overview of the characteristics, management, and the evolution of acute community AOI in children. Our center is the only referral center in the department and all patients depending on our geographic area are referred there. This provides a representative sample of the population studied.

## Conclusion

The antibiotic therapy protocol that we are proposing seems well suited to acute community AOI in children in regions with a low prevalence of methicillin-resistant *S. aureus* and a high prevalence of *Kingella kingae* infection below the age of 2 years. By offering standardized treatment, adapted to microbiological particularities according to age, it allows a favorable development in the vast majority of cases with a short hospital stay and little recourse to surgical recovery.

## Authors' Contribution

Bourgoin Antoine, Common Harold: Data collection, article writing Arvieux Cédric and Violas Philippe: Study methodology, proofreading and criticism of the article Marleix Sylvette, Lucas Grégory, Fraisse Bernard, Josse Antoine, Jolivet-Gougeon Anne, Tattevin Pierre: Review and criticism of the article.

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