Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis

Spanish Multicenter Study

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Background: Acute osteoarticular infection (OAI) is a potentially severe disease. The aim of this study was to evaluate the etiology, clinical characteristics and therapeutic approach of OAI in children in Spain.

Methods: Medical records from children <14 years with OAI from 25 hospitals between 2008 and 2012 were reviewed. Confirmed osteomyelitis (OM) and septic arthritis (SA) required a positive bacterial isolate; otherwise, they were considered probable. Probable SA with <40,000 cells/mm^3 in joint fluid was not included.

Results: A total of 641 children were evaluated. Two hundred and ninety-nine cases (46%) were OM, 232 (36%) SA, 77 (12%) osteoarthritis and 33 (5%) spondylodiscitis. Children with OM were older (63 vs. 43 months for SA; $P < 0.001$). Magnetic resonance imaging and bone scintigraphy had the highest yield for OM diagnosis (94%). Arthrocentesis was performed in 96% of SA. A microorganism was isolated in 246 patients (38%: 33% OM vs. 55% SA; $P < 0.001$): *Staphylococcus aureus* was the most common (63%), followed by *Kingella kingae* (15%) and *Streptococcus pyogenes* (9%). Ninety-five percent of children initially received IV antibiotics, mostly cefotaxime + cloxacillin (60%) or cloxacillin (40%). Total treatment duration was 38 (±31) days for OM and 28 (±16) days for SA ($P < 0.0001$). Twenty percent of children with OM (46% because of complications) and 53% with SA (95% initial arthrotomy) underwent surgery. Patients with SA were compared according to initial arthrotomy (n = 123) versus arthrocentesis (n = 109), and no clinical differences were observed, except for higher rate of hip SA in the former (50% vs. 9%; $P < 0.001$). Children with arthrocentesis had less sequelae [6.6% vs. 1%; $P = 0.03$, odds ratio = 0.58 (95% confidence interval: 0.45–0.76)], but not in the multivariate analysis.

Conclusions: This is the largest pediatric cohort of OAI in Spain. *S. aureus* was the most common isolate, although *K. kingae* was recovered in a high proportion of cases. Conservative management was applied in half of the patients. There was a low rate of sequelae, even with nonsurgical approaches.

Key Words: septic arthritis, osteomyelitis, spondylodiscitis, arthrotomy, arthrocentesis

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Osteoarticular infections (OAI) are a relatively common and potentially a severe disease in children. Septic arthritis (SA) has an estimated incidence of 4 cases per 100,000 children per year, occurring more frequently in males under 5 years of age.[1] In the case of osteomyelitis (OM), an incidence of 2–13 cases per 100,000 children is estimated.[2] Overall, males are affected between 1.2 and 3.7 times more than females.[3]

Despite the potential severity of OAI in children, there are no well-established protocols about the management of these infections. A correct and early diagnosis together with appropriate antibiotic treatment is the cornerstone that will lead to prompt recovery of children with such infections without sequelae.

The management of OAI in children has changed significantly in recent years, and some groups are managing these infections less aggressively than in the past. For example, needle aspiration has been described as an alternative to surgical drainage SA,[4,5] and shorter antibiotic courses have also been evaluated in both SA and OM.[6,7] Nevertheless, these practices have not been widely adopted yet, in part due to the lack of large epidemiological, clinical and management studies of OAI in children.

The objectives of this study were to evaluate the epidemiology, etiology, management and outcome of OAI in children in Spain, before the publication of a consensus document on the etiology, diagnosis and treatment of uncomplicated SA and OM by the Spanish Society for Pediatric Infectious Diseases (SEIP), the Spanish Society of Pediatric Rheumatology (SERPE) and the Society of Pediatric Orthopedic (SEOP) Infections.[8,9]

MATERIALS AND METHODS

A retrospective, multicenter study was designed in a large number of hospitals from different geographical areas of Spain from 2008 to 2012. Medical records were reviewed, and a specific questionnaire was completed. Variables analyzed included demographics, clinical and laboratory parameters at presentation, imaging studies, surgical procedures, antibiotic treatment, duration of hospitalization, complications, total duration of therapy and sequelae. The study was approved by the Ethical Committee of the participating centers. Data were analyzed to evaluate factors that may be related to the outcome of these infections.

Inclusion Criteria

All children ≤14 years diagnosed with acute OAI at any of the participating hospitals during the inclusion period were included. Acute infection was considered when the duration of symptoms was <14 days.

Osteomyelitis (OM) was defined as the presence of (1) clinical features (fever, pain, restriction of movement), (2) radiological study that identified the location of the infection [bone scan, magnetic resonance imaging (MRI), computerized tomography (CT) or ultrasound] and with or without (3) bacterial isolation

from blood or bone sample. Spondylodiscitis (SpD) was included in this definition.

Confirmed septic arthritis (CSA) was defined as the presence of (1) clinical features (fever, joint swelling, functional disability or pain), (2) joint effusion demonstrated by ultrasound or by physical examination performed by an experienced physician and (3) bacterial isolation from joint fluid or blood culture. Probable septic arthritis (PSA) was considered when a microbiological isolation was not obtained, but the joint fluid showed more than 40,000 cells/mm^3, and there was a favorable response to antibiotic treatment with a minimum of 6 months follow-up. A lower count than the classical 50,000 cells/mm^3 was chosen to improve the sensitivity of SA recruitment.[10]

Osteoarthritis (OA) was considered when the disease met criteria of both OM and SA, according to the above definitions.

Exclusion Criteria

Children with immunodeficiencies, underlying bone diseases, carriers of prosthetic materials, those with hospital-acquired infections and newborns (<1 month of age) were excluded from the study.

Outcome

Complications and sequelae were considered surrogate markers to evaluate the outcome of AOI and, therefore, to determine risk factors associated with a poorer evolution. Complications were defined as any clinical condition developed in these children not present on admission or that required additional therapy, such as pyomyositis, abscess, hospital-acquired infections or deep venous thrombosis. Sequelae were considered as any clinical feature that significantly affected the quality of life of the child (pain, limping, stiffness or dysmetria) as a direct consequence of an OAI, lasting longer than 6 months.

Statistical Analysis

Values were expressed as percentages for discrete variables or as mean and standard deviation for continuous variables. Median and interquartile ranges were used for nonparametric variables. Continuous variables were compared using the Student *t* test or nonparametric tests, where appropriate. Categorical variables were compared by the χ^2 test and Fisher exact test. The Pearson or Spearman tests were performed to study correlations and logistic regression for multivariate analysis according to the distribution and characteristics of the variables. A 2-sided value of $P < 0.05$ was considered statistically significant. Odds ratio (OR) was used as association measurement, with 95% of confidence interval (CI) to assess its precision. All analyses were performed using the Statistical Package for the Social Sciences (SPSS, IBM. Version 21.0, IBM Corp, Armonk, NY). Spondylodiscitis was analyzed independently because of the specific characteristics of this type of OAI.

RESULTS

A total of 38 hospitals were invited to participate, and 25 of them completed the survey.

Epidemiology and Clinical Data

A total of 641 children that met the inclusion criteria were evaluated. Two hundred and ninety-eight cases (46%) had OM, 232 (36%) SA (111 CSA), 78 (12%) were considered OA and 33 (5%) SpD. Sixty percent of the patients were male. The mean age was 53 ± 50 months. Patients with OM were older than those with SA (63 vs. 42 months; $P < 0.001$). Days of symptoms before diagnosis were 6.7 ± 11 (7.7 ± 12 and 14.5 ± 18 for OM and SpD, respectively; $P < 0.001$). Fever was present in 70% of children. Foot bones, tibia and femur were the most common locations (79%), whereas the knee was the most frequent joint involved (56%), followed by the hip (26%). There were no differences in inflammatory indices among infections. Only 48 (7.4%) children had an erythrocyte sedimentation rate (ESR) <20 mm/h, whereas 127 (20%) had a C-reactive protein (CRP) <10 mg/L [OR = 3.12 (95% CI: 2.19–4.45)]. Epidemiological and clinical data of the patients are described in Table 1.

Microbiology

Overall, a microorganism was isolated in 252 (39%) patients, more commonly in OA (61% vs. 33% in OM and 55% in SA; $P < 0.001$). A blood culture was performed in 80% of cases: 25% were positive in SA and 29% in OM. An arthrocentesis was done in 96% of SA, and a sample of synovial fluid sent for culture or bacterial polymerase chain reaction (PCR) analysis in 90% and 15% of cases, respectively. A pathogen was isolated from the synovial fluid in 112/272 (41%) of cases: (103) 38% by culture, (15) 5.5% by PCR and 6 (2%) by both methods. Only 23 (3.5%) of children underwent a bone puncture for diagnostic purposes. *S. aureus* was the most common isolate [159, 63%; 4 (2%) methicillin resistant],

TABLE 1. Epidemiologic and Clinical Characteristics Associated With Different Osteoarticular Infections

Clinical Feature	OM (n = 298)	SA (n = 232)	OA (n = 78)	SpD (n = 33)	*P*	Total (n = 641)
Male (%)	181 (60) 132 (57)	50 (64)	19 (58)	NS		382 (59)
Mean age in months (SD)	**63 (52)***	42 (43)	55 (53)	**33 (41)**	**<0.001**	53 (50)
Temperature >37.9°C (%)	201 (67)	163 (71)	61 (78)	21 (68)	NS	446 (70)
Symptoms (%)					**0.04**	
Limping (%)	135 (45)	105 (45)	27 (35)	**9 (12)**		276 (43)
Pain (%)	201 (67) 113 (49)	113 (49)	**57 (73)**	21 (68)		392 (61)
Swelling (%)	92 (31) **110 (47)**	**110 (47)**	30 (38)	-		232 (36)
Days until diagnosis; Mean (SD)	**7.7 (12)**	**4.7 (8.1)**	**5.1 (5.8)**	**14.5 (18)**	**<0.001**	6.7 (11)
Leucocytes/mm^3; Mean (SD)	17,700 (30,500)	14,600 (5034)	13,700 (6500)	11,900 (4200)	NS	13270 (5260)
CPR mg/L, Mean (SD)†	**63 (73)**	**63 (63)**	**87 (84)**	**23 (50)**	**0.03**	64 (71)
ESR mm/h Mean (SD)†	51 (27)	56 (26)	62 (29)	44 (19)	NS	53 (27)
Bone/joint affected (%)	OM		SA and OA	SpD	**0.042**	
	Foot bones 76 (25)		Knee 189 (61)	Lumbar 28 (85)		
	Tibia 65 (22)		Hip 88 (28)	Dorsal 3 (9)		
	Femur 62 (21)		Ankle 28 (12)	Cervical 2 (6)		

*Significant differences in bold.

†A total of 127/641 (19.8%) of children had <10 mg/L of PCR, whereas only 48/641 (7.5%) had a ESR <20 mm/h ($P < 0.001$).

NS indicates not significant.

TABLE 2. Comparison of Microbiologic Results of Different Osteoarticular Infections

	OM (n = 298)	SA (n = 232)	OA (n = 78)	SpD (n = 33)	*P*
Microbiologic isolation (%)	98 (33)	104 (45)	48 (61)	2 (8)	<0.001
Total isolations*					
S. aureus (%)	78 (28)	52 (26)	28 (38)	1 (3.8)	0.005
K. kingae (%)	1 (0.7)	29 (15)	5 (7)		<0.001
S. pyogenes (%)	10 (3.5)	7 (3.5)	5 (7)		NS
Positive blood culture (%)	71/245 (29)	48/189 (25)	25/62 (40)	2/26 (8)	NS
S. aureus (%)	57 (80.3)†	24 (50)	18 (72)	1 (3.8)	
K. kingae (%)	1 (1.4)	2 (4.2)	-	-	
S. pyogenes (%)	8 (11.3)	6 (12.5)	3 (3.9)	-	
Positive synovial culture (%)	81/211 (38)	24/45 (53)			0.064
S. aureus (%)	-	42 (52)	12 (50)	-	
K. kingae (%)	-	19 (23.5)	2 (8.3)	-	
S. pyogenes (%)	-	8 (10)	1 (4)	-	
Positive synovial fluid PCR (%)	14/26 (55)	4/9 (44)			
K. kingae (%)	-	11/14 (79)	4/4 (100)	-	

*Other agents: *Streptococcus pneumoniae* (15), *Streptococcus agalactiae* (6), *Enterobacteriaceae* (10), *Haemophilus influenzae* (1), *Sphingomonas* (1).
†Of the total of positive isolates.
NS indicates not significant.

followed by *Kingella kingae* (35, 14%) and *S. pyogenes* (22, 9%). *K. kingae* was mainly isolated from synovial fluid, with a high proportion detected by PCR (15/35; 43%). There were only 3 cases (8.6%) of this bacterium isolated from blood culture. Therefore, *K. kingae* was more frequently isolated in SA than in other entities (15% vs. 7%; $P < 0.001$). A summary of the different microbiological results is shown in Table 2.

Imaging Studies

Radiological studies are summarized in Table 3. Conventional radiography was performed in 82% (336/409) of patients with AOI, excluding the SA group, where it was performed much less frequently (146/232, 61%; $P < 0.0001$). The diagnostic yield of the initial radiography was low (27% for OM and 39% for SpD). MRI and bone scan had the highest yield for the diagnosis of OM, displaying a compatible image in 94% of the cases. In the SpD group, MRI was the most frequently used technique (88%), being diagnostic in 93% of cases. Regarding SA, ultrasound was performed in 70% of cases, with effusion being the most common finding (90%). CT was marginally used.

Treatment and Prognosis

A total of 607 (94.7%) children were initially hospitalized and received intravenous (IV) antibiotics. The most frequently administered IV antibiotics were the combination cefotaxime–cloxacillin (44%), followed by cloxacillin (20%), amoxicillin–clavulanate (10%), cefazolin (8.1%) and cefuroxime (7.4%). When antibiotic use was analyzed according to age, children <5 years received the combination of cefotaxime–cloxacillin (60%) more frequently, whereas children >5 years more frequently received cloxacillin (40%).

The duration of intravenous therapy was 12.8 ± 7.5 days (13.6 ± 8 for OM and 11 ± 6.6 for SA; $P = 0.014$). The length of hospitalization was related to inflammatory parameters on admission, such as CRP ($r = 0.2$; $P < 0.001$), procalcitonin ($r = 0.35$; $P = 0.015$) and ESR ($r = 0.1$; $P = 0.042$). There was no correlation with the grade of fever or leucocytes in blood.

First and second generation cephalosporins were the most common oral antibiotics administered (53.2%) followed by amoxicillin–clavulanate (25%). Total treatment duration was 35 ± 25 days, with a shorter for the SA group 28.9 ± 16 days ($P < 0.001$). Treatment differences among groups are described in Table 4.

A total of 219 children (34%) underwent surgery: 20% of children with OM (46% because of complications) and 53% of patients with SA (only 5% because of complications). Children who underwent surgery at any time had a more prolonged hospital stay and duration of therapy. In addition, children with hip involvement underwent initial arthrotomy more frequently than children with other joint involvement [84% vs. 16%; OR = 4.6 (95% CI: 2.8–8.6)]. Complications were diagnosed in 72 patients (11.8%), mainly abscess and pyomyositis, whereas sequelae developed in 26 (4.1%) children, dysmetria being the most frequent (34.8%). The group of patients with OA had the highest proportion of sequelae (10.3%, $P = 0.02$).

In the univariate analysis, the parameters associated with complications were surgical procedure, older age and positive bacterial isolation, especially when *S. aureus* was involved. When a multivariate analysis was performed, only surgical procedure

TABLE 3. Imaging Studies Performed for the Diagnosis of Different Osteoarticular Infections

	OM (n = 298)	SA (n = 232)	OA (n = 78)	SpD (n = 33)	*P*
Radiograph* (%)	241 (80.6)	146 (61.6)	65 (85.5)	30 (91)	<0.001
Compatible (%)	80 (27)	14 (6)	15 (23)	13 (39)	
Ultrasound (%)	138 (46)	162 (70)	57 (74)	5 (15)	<0.001
Compatible (%)	29 (23)	150 (93)	14 (24)	0	
Bone scan (%)	157 (54)	33 (14)	25 (33)	16 (48.5)	<0.001
Compatible (%)	142 (94)	17 (51)	21 (84)	14 (87.5)	
MRI (%)	174 (58)	34 (15)	49 (64.5)	29 (88)	<0.001
Compatible (%)	162 (93)	19 (56)	47 (95)	27 (93)	
CT	15 (5)	3 (1.3)	0	3 (9.4)	0.042
Compatible (%)	14 (93)			2 (66)	

*The first line refers to the percentage of tests performed.

TABLE 4. Treatment and Prognosis of Different Osteoarticular Infections

	OM (n = 298)	SA (n = 232)	OA (n = 78)	SpD (n = 33)	*P*
Hospitalization (%)	279 (93.6)	219 (94.4)	77 (98.7)	32 (97)	NS
IV therapy days (SD)	12.9 (7.9)	**11.3 (6.6)**	15.8 (7.9)	14.7 (6)	**0.016**
Oral therapy days (SD)	26.5 (30.9)	**18.9 (14.8)**	24.4 (20.4)	26.6 (18.8)	**0.014**
Total treatment days (SD)	38 (31.5)	**28.9 (16.4)**	38.5 (21.9)	40.4 (19.6)	**0.001**
Hospitalization days (SD)	13.5 (7.8)	**12.1 (7.1)**	17 (9.3)	14.9 (5)	**0.03**
Surgery (%)	**60 (20)**	123 (53)	36 (46.2)	0	**0.0001**
Types of surgery					
Arthrotomy (%)	8 (2.7)	111 (48)	28 (36)	-	
Arthroscopy (%)	2 (0.7)	3 (1.3)	2 (2.6)	-	
Abscess drainage (%)	27 (9.1)	2 (1.9)	7 (5)	-	
Diagnosed puncture (%)	22 (7.4)	-	-	-	
Complications (%)	40 (13.4)	20 (8.6)	**14 (18)**	6 (18.2)	**NS**
Abscess (%)	13 (4.4)	3 (1.3)	3 (3.8)	2 (6.1)	
Pyomyositis (%)	12 (4)	6 (2.6)	7 (9)	2 (6.1)	
Others (%)	15 (5)	11 (4.8)	4 (5.1)	2 (6.1)	
Sequelae (%)	7 (2.3)	9 (3.9)	**8 (10.3)**	2 (6.1)	**0.02**
Dysmetria (%)	7 (2.3)	5 (2.2)	4 (5.1)	2 (6.1)	
Pain (%)	4 (1.3)	1 (0.4)	-	-	
Limited movement (%)	1 (0.3)	4 (1.7)	5 (6.4)	-	
Others (%)	5 (1.7)	2 (0.9)	7 (9)	2 (6.1)	

NS indicates not significant.

remained significant with older age showing a trend toward significance [OR = 1.7 (95% 0.98–2.9); *P* = 0.056; Table 5).

Parameters associated with sequelae in the univariate analysis were surgical procedure, infants, a positive bacterial isolate, especially when *S. aureus* was involved [OR = 1.8 (95% CI: 1.1–3)], and OA group [OR = 2.8 (95% CI: 1.4–5.3)]. When multivariate analysis was performed, surgical procedure, age and OA remained significant (Table 5).

Complications and Sequelae in Children With SA

Patients with SA were compared according to the initial procedure performed [arthrotomy (n = 123) vs. arthrocentesis (n = 109)] to evaluate if an elective surgical drainage may have an impact on the outcome. In the multivariate analysis between these two groups, only a higher rate of hip involvement [42% vs. 9%; OR = 7.2 (95% CI: 3.4–15.2)] and the presence of fever [77% vs. 64%; OR = 1.38 (95% CI: 1.01–1.88)] were associated with elective arthrotomy.

It is also shown in the multivariate analysis that only hip SA was significantly associated with complications [OR = 2.8 (95% CI: 1.2–4.8)]. No other parameters, such as age, an isolated pathogen or elevated inflammatory markers, were different between groups in the multivariate analysis.

Children with arthrocentesis had less sequelae 1% versus 6.6% [*P* = 0.03, OR = 0.58 (CI: 0.45–0.76)], whereas hip involvement was a risk factor for development of sequelae [OR = 5.2 (CI: 1.3–20.5), *P* = 0.07]. No other risk factors were associated.

DISCUSSION

The present study is an analysis of the epidemiological characteristics and therapeutic approach of a large national cohort of children with OAI in Spain. The main results found in this study are as follows: (1) the main microorganism involved in OAI in these children was methicillin–susceptible *S. aureus*, and *Kingella* was found to be the second most common isolate, especially because of an increasing use of diagnostic PCR; (2) OM was the most common OAI in these children with longer duration of symptoms before diagnosis and of therapy compared with SA; (3) the management of these infections in children in our setting tends to be conservative, with long duration of IV therapy and high proportion of surgical interventions; (4) parameters associated with complications and sequelae were mainly OA, hip involvement and surgical intervention; (5) children with SA who initially underwent arthrocentesis did not seem to have a worse outcome, although hip involvement, the only parameter associated with worse outcome in

TABLE 5. Factors Associated With Complications and Sequelae in the Univariate and Multivariate Analyses in the Total Cohort

	Univariate analysis		Multivariate analysis	
	OR (CI)	*P*	OR (CI)	*P*
Complications				
Bacterial isolation	1.8 (1.4–2.3)	0.0001		NS
S. aureus positive	2 (1.4–2.8)	0.0001		NS
Age >3 years	1.4 (1.1–1.8)	0.002	1.7 (0.98–2.9)	0.056
Surgery	1.7 (1.4–2.2)	0.0001	2.5 (1.3–2.7)	0.002
Sequelae				
Bacterial isolation	1.8 (1.3–2.5)	0.002		NS
S. aureus positive	1.8 (1.1–3)	0.023		NS
Age <1 year	2.1 (1.2–3.5)	0.008	2.5 (1.05–5.9)	0.039
Surgery	2.1 (1.6–2.7)	0.0001	3.1 (1.2- 7.9)	0.015
Osteoarthritis	2.8 (1.4–5.3)	0.002	2.8 (1.07–7.6)	0.035

NS indicates not significant.

the multivariate analysis in SA, was more frequently found in children who received arthrotomy.

The epidemiological characteristics of this cohort are somewhat similar to other studies previously published in children.[1,2,11] Thus, OM was more frequently diagnosed than SA, with a low rate of OA. Also, according to the literature, the knee was the most frequently involved joint followed by the hip.[2,3] Symptomatology was similar to that reported in other series as well,[3] with absence of fever in 30% of cases and males being more frequently diagnosed with OAI than females. The mean age of the children with OAI was under 5 years, and the SA group was younger. The youngest group of the children studied had SpD, which comprised a small proportion of cases. There were not many cases of older children with SpD, which may be in agreement with other authors who believe that this disease affects mainly young children, whereas in older children and adolescents it may reflect more of an inflammatory condition.[8,12] Lumbar vertebrae were the most frequent location for this type of OAI.[12] In a previous series of SpD in our country, the age distribution was similar with a high proportion of infants.[13]

As universally recognized, *S. aureus* was the most prevalent etiological agent (63%),[3,14] but there was a low proportion of methicillin-resistant *S. aureus* (MRSA; only 4 patients), as reported from other Western European countries, which is different to the high rates of MRSA reported in the US.[15] This may certainly contribute to the good outcome of our cohort. Although the isolation rate of *S. pyogenes* (9%) was close to *K. kingae* (14%), this was probably not a reflection of the true situation because *K. kingae* was mainly detected by PCR in the synovial fluid in SA, and only 15% of the samples were analyzed by this technique. Many of the participant hospitals did not have the bacteria PCR available, and thus this analysis could not be performed. This certainly may underestimate the actual proportion of *K. kingae* infections because this bacteria is difficult to grow in standard culture media.[16,17] OA were the infections with higher yield of a positive culture (61%), which may be related to a higher load of microorganisms, which the joint achieved from the adjacent bone.

Imaging techniques performed to diagnose OM in this study were mainly MRI and bone scan, with a high yield for both diagnostic tools (around 94%). Other authors have also found that both techniques may be useful for this diagnosis with a benefit in using MRI when a complication is suspected.[18,19] Conventional radiography was still used widely in this cohort, especially to differentiate OM from other pathologies[20] because the yield of diagnosis was low. Radiography had a higher diagnostic yield in children with SpD, possibly because these children are usually diagnosed later in the course of the infection. Finally, ultrasound was the imaging technique of choice for SA with a high diagnostic yield (90%), also useful for the diagnosis of 23% of the OM cases, as it has been reported before.[21]

Most of the patients were hospitalized and received IV antibiotics, with only 34 children initially treated with oral antibiotics. IV cloxacillin and IV and oral (PO) first/second generation cephalosporins were the most frequently used antibiotics in agreement with the most common etiology and the low rate of MRSA strains isolated in this cohort. According to this study, almost 50% of children received an initial combination therapy with IV cloxacillin and cefotaxime, even though most of the microorganisms isolated in these children were susceptible to narrow-spectrum antibiotics, which may be related to standard protocols still used in some centers.[9]

In relation to the duration of the IV treatment, the data presented here are somewhat far from the new recommendations proposed mainly by Peltola group[6,22] and acquired by the Spanish guidelines.[9] These guidelines proposed a short initial course of IV antibiotics with prompt switch to oral therapy in noncomplicated OAI.[6,22–25] In this cohort, there was an average of 11.3 days for AS and 12.9 for OM of IV antibiotics, and a total duration of therapy of 28 and 38 days for SA and OM, respectively, which is considerably longer than the above-mentioned recommendation.

Patients with OM were generally managed without surgery, with only a small group of them receiving elective bone puncture for diagnostic purposes. Complications were present in 13% of OM (abscess and pyomyositis) and this was the main reason for surgery, particularly drainage. The initial approach to SA was different among centers. Thus, some hospitals had a more conservative approach and managed the patients with arthrocentesis, whereas in others, arthrotomy was the main therapeutic approach. Some authors have reported that arthrotomy may be suitable to avoid complications in case of >5 day delay in the diagnosis, ESR >50 mm/h and CRP >100 mg/L.[26] However, in this study, the choice of initial elective surgery was associated only with the center, where patients were treated (data not shown) and with hip involvement. Children treated with initial arthrocentesis had a lower percentage of sequelae in this cohort (1.1% vs. 6%, $P = 0.03$), but the multivariate analysis showed that only hip involvement was associated with sequelae. Therefore, arthrotomy may be related to an increase in sequelae because of its high association with hip involvement and not by itself. This may indicate that health care providers tend to surgically drain the hip and more severe SA, probably because of a potentially worse prognosis. Therefore, whether there is a direct association between surgery and worse outcome in these children or that this link is a matter of a more complicated, or severe infection remains unclear. Several studies have observed that conservative treatment may be safe and leads to faster recovery of children with SA, even when hip or shoulder are involved.[27–30] Nevertheless, there are no randomized clinical studies performed, and thus this therapeutic approach has not yet been adopted by many groups, including the institutions participating in this study. Therefore, although in a great proportion of cases a more conservative approach may be safe, further research to evaluate this management is warranted.

Of particular note is that the OA group had the highest proportion of surgical intervention (46%), complications (18%) and sequelae (10% vs. 3, 2% for the rest of infections; $P = 0.02$), showing that this is probably the group with the most severe disease. Furthermore, OA was a risk factor for complications in the multivariate analysis. All of this leads us to recommend special care for this group of children who tend to be very young.

This study has several limitations, because of its retrospective nature and the fact that not all the infections were confirmed by a microbiological isolate. However, all OM had compatible imaging, and all SA had rigorous inclusion criteria, with a minimum follow-up period of 6 months, which reasonably allowed ruling out inflammatory diseases. Furthermore, most of the infections in children from this cohort had a favorable outcome with treatment. Among the strengths of this study are the multicenter national character and the high number of cases reported, being the largest study ever performed in our setting.

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