Success Rates of First-line Antibiotics for Culture-negative Sub-acute and Chronic Septic Arthritis

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A combination of surgical and medical treatment is normally required for patients with septic arthritis[1]. Antibiotics selected for use on these patients are normally based on tissue culture results[2]. However, in sub-acute and chronic septic arthritis cases, the results of the culture are usually negative as a result of prior treatment. The present study will investigate the incidence of culture-negative septic arthritis and the outcomes based on the use of first-line drug antibiotics for the treatment of sub-acute and chronic septic arthritis.

For the present study, the authors retrospectively reviewed medical records of surgically treated septic arthritis cases over the past 10 years at Siriraj Hospital. The patient culture results, the antibiotics used, and the results of treatment were all recorded and analyzed.

One hundred fifty-three septic arthritis patients were reviewed. Sixty-two patients were classified as having been diagnosed with either sub-acute or chronic septic arthritis. Thirty-six of 62 patients (58.1%) had a negative culture result. In the culture-positive patients, 42.3% had Streptococcus, 26.9% had Staphylococcus aureus, 11.5% had other gram positive bacteria, 15.4% had gram-negative bacteria, and 3.8% had tuberculus infection. In the culture-negative sub-acute and chronic group (36 of 62), 23 patients received Cefazolin, nine patients received Cloxacillin, and four patients received Clindamycin. Successful results were 69.9%, 66.7% and 75%, respectively.

The present study reflects that the incidence of culture-negative, sub-acute and chronic septic arthritis is approximately 58.1%. The first-line class of antibiotics remains the appropriate antibiotic choice for these patients because they are still effective for treatment of septic arthritis in up to 70% of all cases.

Keywords: *Septic arthritis, Culture negative, Antibiotic, Chronic septic arthritis*

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Septic arthritis is a common, but very serious orthopedic condition that results in high rates of morbidity and mortality[3,4]. Patients who do not receive appropriate and timely treatment will likely experience irreversible joint damage perhaps leading to permanent disability. Both accurate diagnosis and precise treatment are necessary to preserve joint longevity and function[5,6]. In the past, study findings reported that gram-positive bacteria, most notably *Streptococcus* and *Staphylococcus aureus*, were the common pathogens found in septic arthritis in adults. Gram-positive bacteria were followed in levels of incidence by gram-negative bacteria, anaerobic bacteria, and rarely, mycobacteria and fungal infection[7]. To date, the "gold standard" for diagnosing septic arthritis is still based on a synovial fluid culture. However many studies have reported that only 30-60% of the bacterial cultures taken in cases of sub-acute and chronic septic arthritis come out as positives[4,8,9]. This negative result sometimes misleads physician as to whether the antibiotic used is appropriate or not.

Therefore, the present study was designed to assist in answering two questions: 1) what is the incidence rate of culture-negative septic arthritis in a tertiary referral hospital and, 2) what is the rate of effectiveness of first-line antibiotics for the treatment of sub-acute and chronic septic arthritis.

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Material and Method

The present study was undertaken at the orthopedic surgery department in a tertiary care hospital in Bangkok, Thailand. The researchers retrospectively

reviewed the medical records of patients who were surgically treated for septic arthritis over the past 10 years.

One hundred fifty-three patients were identified and included in the study. Septic arthritis was diagnosed using 2 of the 3 following laboratory criteria: positive joint gram stain, Joint WBC >50,000 cell/ml[10], gross joint purulent (thick, cloudy joint fluid). Sub-acute and chronic septic arthritis are characterized by either or both: onset of painful joint swelling and/or a fever that came on more than 2 weeks before patient hospitalization. The exclusion criteria include any one of the following conditions: open wound deep to the joint, infection close to prosthetic implant, and patients with concurrent osteomyelitis. Sixty-two patients met the inclusion criteria and were included in the present study.

All patients received surgical debridement and drainage within 24 hours and a routine bacteria culture was taken and sent to the lab for analysis. All patients in this group were treated with first-line antibiotics, including Cloxacillin, first generation cephalosporins (Cefazolin), or Clindamycin, if the patient had a history of allergy to penicillin. Antibiotics were started immediately after specimens were collected intra-operatively.

The present then reassessed clinical outcome 1 week after surgery. If clinical symptoms were not improved after 1 week, the antibiotic was changed to 3rd generation cephalosporin, Vancomicin, or Meropenam. The patient was then re-evaluated 1 week later, consistent with the initial assessment protocol.

Successful treatment was declared if the patient met 3 of 4 clinical criteria: 1) no fever (37.8 degree Celsius), 2) improved pain with more than 5 of 10 VAS score, 3) no joint effusion, and 4) no joint inflammation (wound warm and red). Clinical outcomes were assessed at 1 week, 6 weeks, and 3 months after surgery. 72 hours to 1 week after surgery, the culture (negative or positive) was identified. In the culture-positive group, we changed the antibiotic as indicated by this finding. In the culture-negative group, first-line antibiotic therapy was continued as long as the patient was improving according to 4-point criteria, as outlined immediately above. However, if the patient did not improve, again according to the 4-point criteria assessment, then the antibiotic was changed to another group, such as 3rd generation cephalosporin, Vancomycin or Meropenam.

Results

One hundred fifty-three patients were diagnosed with septic arthritis. Sixty-two of 153 patients were diagnosed as sub-acute or chronic septic arthritis (21 sub-acute and 41 chronic).

Joint fluid culture was positive in 26 of 62 patients (41.9%) and negative in 36 of 62 patients (58.1%). The result for culture positive were 11 *Streptococcus* (42.3%), 7 *Staphylococcus aureus* (26.9%), 3 other gram positive bacteria (11.5%), 4 gram negative bacteria (15.4%), and 1tuberculus infection (3.8%).

In culture-negative sub-acute and chronic septic arthritis (36 patients), 23 patients received Cefazolin, 9 patients received Cloxacillin and 4 patients received Clindamycin.

Patients who received first-line antibiotics that primarily cover gram-positive bacteria were clinically assessed at 1 week after treatment. Of the patients who received Cefazolin, 16 of 23 cases (69.6%) were defined as successfully treated. However, 7 of 23 cases (30.4%) in this group needed to change antibiotics: 4 to Vancomicin, 2 to Meronem, and 1 to Certriaxone. In the group of patients that was treated with Cloxacillin, 6 of 9 (66.7%) responded, 2 of 9 (22.2%) converted to Vancomicin, and 1 (11.1%) converted to Ceftriaxone. In the group of patients that received Clindamycin, 3 of 4 (75.0%) responded, with 1 patient (25.0%) being converted to Ceftriaxone. Overall, 25 of 36 patients (69.4%) diagnosed with sub-acute and chronic septic arthritis, were successfully treated with first-line antibiotics.

Discussion

Acute septic arthritis is common in general daily practice. The treatment for this condition is difficult because of many confounding factors[6,10]. Many patients suffer from acute septic arthritis that did not receive proper case management, such as inadequate antibiotic or drainage. Many of these cases progress to sub-acute and chronic septic arthritis, which are far more difficult to treat. From our study, the incidence of sub-acute and chronic septic arthritis is relatively high as compared to other studies[11,12], likely because Siriraj Hospital is a referral center. All cases that are referred are usually either complicated, delayed-in-treatment, or only partially treated. In this study, the incidence of culture negative sub-acute and chronic septic arthritis in all patients is about 58.1% (36 of 62 cases). However, if we compare the results of our study to investigations performed in other referral hospitals, the results are not different from any other reports[3,4,6].

In general, once a patient has been diagnosed

with septic arthritis, a treatment comprised of immobilization, surgical drainage, and antibiotic therapy would start immediately[2,6]. Physicians always suggest empirical antibiotics such as cloxacillin, first generation cephalosporin, or clindamycin[6,10], provided the patient does not have contraindications. This protocol is followed because 58.1% of cases of septic arthritis are culture-negative.

The present study found the effectiveness of first-line antibiotic drugs for the treatment of culture-negative septic arthritis to be 69.4%. These findings give us an overall assessment of the effectiveness of current treatment protocols for patients with culture-negative septic arthritis. In addition, we found that Cefazolin, Cloxacillin, and Clindamycin have response rates of about 69.57%, 66.7%, and 75%, respectively. These findings may provide added guidance regarding choice of antibiotic for patients with culture-negative septic arthritis.

Limitations of the present study include a limited sample size of patients and the fact that none of the septic arthritis patients in the present study had implants or prostheses. Indeed, the results of the present study may not necessarily apply to implant-related septic arthritis.

Conclusion

The present study reflects that the incidence of culture negative sub-acute and chronic septic arthritis is approximately 58.1%. Antibiotics such as Cefazolin, Cloxacillin, and Clindamycin are still recommended as appropriate first line antibiotics for the treatment of culture negative sub-acute and chronic septic arthritis, because they are still effective for the treatment of septic arthritis in up to 70% of all cases.

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Potential conflicts of interest

None.

References

1. Goldenberg DL, Reed JI. Bacterial arthritis. N Engl J Med 1985; 312: 764-71.
2. Gillespie WJ. Epidemiology in bone and joint infection. Infect Dis Clin North Am 1990; 4: 361-76.
3. Eder L, Zisman D, Rozenbaum M, Rosner I. Clinical features and aetiology of septic arthritis in northern Israel. Rheumatology (Oxford) 2005; 44: 1559-63.
4. Dubost JJ, Soubrier M, De Champs C, Ristori JM, Bussiere JL, Sauvezie B. No changes in the distribution of organisms responsible for septic arthritis over a 20 year period. Ann Rheum Dis 2002; 61: 267-9.
5. Stengel D, Bauwens K, Sehouli J, Ekkernkamp A, Porzsolt F. Systematic review and meta-analysis of antibiotic therapy for bone and joint infections. Lancet Infect Dis 2001; 1: 175-88.
6. Weston V, Coakley G. Guideline for the management of the hot swollen joint in adults with a particular focus on septic arthritis. J Antimicrob Chemother 2006; 58: 492-3.
7. Swan A, Amer H, Dieppe P. The value of synovial fluid assays in the diagnosis of joint disease: a literature survey. Ann Rheum Dis 2002; 61: 493-8.
8. Newman JH. Review of septic arthritis throughout the antibiotic era. Ann Rheum Dis 1976; 35: 198-205.
9. Coutlakis PJ, Roberts WN, Wise CM. Another look at synovial fluid leukocytosis and infection. J Clin Rheumatol 2002; 8: 67-71.
10. Shirtliff ME, Mader JT. Acute septic arthritis. Clin Microbiol Rev 2002; 15: 527-44.
11. Al Tawfiq JA, Babiker M. Incidence and bacteriologic causes of septic arthritis in a general hospital in Saudi Arabia. Ann Saudi Med 2013; 33: 116-8.
12. Al Arfaj AS. A prospective study of the incidence and characteristics of septic arthritis in a teaching hospital in Riyadh, Saudi Arabia. Clin Rheumatol 2008; 27: 1403-10.

ความสำเร็จในการใช้ยาปฏิชีวนะเบื้องต้นสำหรับผู้ป่วยข้ออักเสบติดเชื้อที่ผลเพาะเชื้อให้ผลลบ

บวรฤทธิ์ จักรไพวงศ์, ศราวุธ พุ่มพวง

ภาวะข้อติดเชื้อเป็นปัญหาที่พบได้บ่อยและจำเป็นต้องได้รับการรักษาอย่างถูกต้องและรวดเร็วไม่เช่นนั้นอาจจะส่งผลให้เกิดปัญหาตามมา โดยทั่วไปการรักษาทำได้โดยการผ่าตัดและให้ยาปฏิชีวนะตามเชื้อที่เพาะได้ มีบ่อยครั้งที่ผู้ป่วยที่มีภาวะข้ออักเสบติดเชื้อเรื้อรังได้รับการรักษาบางส่วน ตรวจไม่พบเชื้อจากการเพาะเชื้อจึงทำให้เลือกใช้ยาปฏิชีวนะได้ลำบาก งานศึกษานี้จึงจัดทำขึ้นเพื่อหาความชุกของผลเพาะเชื้อที่ให้ผลลบในผู้ป่วยข้ออักเสบชนิดกึ่งเฉียบพลันและเรื้อรังและศึกษาผลของการรักษาผู้ป่วยกลุ่มนี้ด้วยยาปฏิชีวนะกลุ่ม first-line

งานศึกษารวบรวมข้อมูลผู้ป่วยที่ได้รับการผ่าตัดย้อนหลังในช่วง 10 ปี ในโรงพยาบาลโรงเรียนแพทย์ขนาดใหญ่ที่รับการผ่าตัดรักษาข้ออักเสบติดเชื้อโดยบันทึกผลเพาะเชื้อจากเนื้อเยื่อที่ได้จากการผ่าตัดและผลการรักษา

จากผู้ป่วยทั้งหมด 153 ราย ที่ได้รับการผ่าตัดพบว่ามี 62 ราย เป็นกลุ่มข้ออักเสบติดเชื้อกึ่งเฉียบพลันและเรื้อรังพบผู้ป่วยในกลุ่มนี้ ผลเพาะเชื้อให้ผลบวกทั้งหมด 26 ราย (41.9%) โดยให้ผลเป็นเชื้อ Streptococcus 42.3%, Staphylococcus aureus 26.9%, other gram-positive bacteria 11.5%, gram-negative bacteria 15.4%, และ tuberculus 3.8%

ในผู้ป่วยที่ผลเพาะเชื้อให้ผลลบทั้งหมด 36 ราย ใน 62 ราย (58.1%) ได้รับยา Cefazolin 23 ราย, Cloxacillin 9 ราย และ Clindamycin 4 ราย ซึ่งผลตอบสนองรักษาสำเร็จเท่ากับ 69.6%, 66.7% และ 75% ตามลำดับ

ผลของการศึกษาดังกล่าวสามารถให้ข้อมูลที่มีประโยชน์ในการพยากรณ์ผลเพาะเชื้อในผู้ป่วยข้ออักเสบกึ่งเฉียบพลันและเรื้อรังและยังเป็นแนวทางในการรักษาผู้ป่วยกลุ่มนี้ซึ่งมักจะประสบปัญหาในการเลือกยาปฏิชีวนะและผลการเพาะเชื้อที่ให้ผลลบได้