Less than 28 Days of Intravenous Antibiotic Treatment Is Sufficient for Suppurative Thrombophlebitis in Injection Drug Users

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Data about the required duration of intravenous therapy for suppurative thrombophlebitis is lacking. Among 36 episodes of proven suppurative thrombophlebitis requiring hospital admission, no relapses occurred when treatment was given for >7 days intravenously and followed by oral therapy. A <4-week course of intravenous antibiotics may be sufficient.

Suppurative thrombophlebitis of proximal veins caused by nonsterile injections is a potentially life-threatening condition that is common among injection drug users (IDUs) [1]. In contrast with catheter-related thrombophlebitis and Lemierre syndrome [2, 3], little attention is paid to the antibiotic management of suppurative thrombophlebitis [4]. *Staphylococcus aureus* is the predominant bacteria in suppurative thrombophlebitis of IDUs [5, 6]. In general, conservative antibiotic treatment is recommended for suppurative thrombophlebitis of large veins [5, 6]. However, the duration and route of administration of antibiotic treatment are uncertain, and experts recommend that therapy be given according to published endocarditis-treatment guidelines [7]. However, a 4-week course of intravenous therapy is often not feasible for IDUs [6]. A 2-week course of intravenous therapy followed by oral ciprofloxacin plus rifampicin, administered according to the guidelines for treatment of right heart endocarditis due to *S. aureus* in IDUs [8], seems to be an alternative [6], but widespread use of this regimen may be difficult, because IDUs are frequently noncompliant to regimens that require that they reliably take oral medications.

In a retrospective survey of infectious complications among 344 admissions of IDUs at our hospital (University Hospital Basel; Basel, Switzerland), we diagnosed a suppurative thrombophlebitis in 36 cases (11%). In the present study, we analyze the clinical course, duration of antibiotic therapy, and outcome in these 36 cases of suppurative thrombophlebitis.

Methods. We included all IDUs who were hospitalized for suppurative thrombophlebitis from January 2001 through December 2006 and evaluated by the infectious diseases service of the University Hospital Basel, a 780-bed primary and tertiary care center with ∼27,000 hospital admissions annually. Demographic and clinical data were extracted from hospital charts, laboratory results, and separate reports of the infectious diseases service. The study was approved by the ethics committee of University Hospital Basel. The diagnosis of suppurative thrombophlebitis was defined by either ≥2 positive blood culture results or bacteria detected in the thrombus in a patient with negative blood culture results and detection of a thrombus by CT or ultrasonography [3, 9].

Results. Thirty-six hospital admissions for suppurative thrombophlebitis were identified among 29 IDUs (2 readmissions to the hospital were considered to be relapses, and 5 readmissions were not). Patient characteristics at hospital admission are listed in table 1. Twenty-nine cases (80.6%) met ≥2 systemic inflammatory response syndrome criteria [10] at hospital admission.

Thrombosis was detected on the basis of ultrasonographic findings in 32 cases (89%) and on the basis of CT findings in 4 cases (11%). Transthoracic echocardiography was performed in 31 (86%) of 36 cases; additional transesophageal echocardiography was performed in 5 of these 31 cases. Infective en-

Table 1. Demographic and clinical characteristics at hospital admission of 29 patients with 36 episodes of suppurative thrombophlebitis.

Variable	Value
Age, median years (range)	33 (20–45)
Male sex, no. (%) of episodes	22 (61.1)
Chronic hepatitis C, no. (%) of episodes	30 (88.9)
HIV positivity, no. (%) of episodes	4 (11.1)
C-reactive protein level, median mg/dL (range)	162.5 (6–417)
Leukocyte count, median cells $\times 10^9$ (range)	12 (5.2–31)
Temperature, median °C (range)	39.1 (35.3–41.3)

docarditis was diagnosed in 3 cases. Because transthoracic echocardiography cannot definitely rule out endocarditis, some cases of infective endocarditis may have been missed.

Thromboses were located mainly in the femoral and the iliac vein (table 2). The left side of the body was affected more frequently (21 cases; 58.3%).

In 160 (71.4%) of a total of 224 blood samples obtained within 48 h after hospital admission, the predominant pathogen was cultured. In all but 10 cases, ≥3 blood samples with positive culture results were obtained. *S. aureus* was the most frequent predominant pathogen (in 19 [53%] of the cases), followed by streptococci (table 2). No methicillin-resistant *S. aureus* isolates were identified. In 12 cases, polymicrobial sepsis was diagnosed. In 1 case with negative blood culture results (in which only 1 pair of blood samples was obtained), a thrombectomy was performed, and *S. aureus* was cultured from the biopsy specimen. In all cases, intravenous antibiotic therapy was administered as first-line therapy. All but 1 case received β-lactam antibiotics as the main antibiotic therapy (i.e., the antibiotic given for the longest period intravenously) (table 3).

The duration of intravenous therapy varied greatly (table 3). Four patients were treated for ≤7 days; 2 of these patients experienced relapse leading to readmission (after 3 days and after 5 days). There were no relapses among the patients who were treated intravenously for >7 days. Six patients were treated for 8–14 days, and 10 patients were treated for 15–21 days. Altogether, in 20 (56%) of the episodes, the patients received an intravenous therapy for ≤21 days. The median duration of intravenous therapy was 19.5 days. In 9 cases, therapy was continued >28 days because of additional complications. A subsequent regimen of oral antibiotic therapy was administered in 34 of 36 cases. The median duration of oral treatment was 9.5 days (range, 0–180 days), and the overall duration of antibiotic therapy was a median of 28.5 days (range, 7–220 days). There was no significant difference in the duration of intravenous therapy between patients treated for *S. aureus* infection and those treated for non–*S. aureus* infection. Documented negative blood culture results at day 3 of therapy did not influence the duration of intravenous antibiotic treatment (median duration of therapy was 22 days and 21.5 days for patients with negative and patients with positive blood culture results, respectively).

In 33 (91.7%) of the cases, anticoagulation therapy was initiated. In 10 cases (27.8%), oral anticoagulation therapy was abandoned at hospital discharge because of compliance concerns.

Additional complications associated with IDU were as follows: local skin abscesses in 14 cases (22.2%; incisions were made in 8 cases); septic arthritis in 2 cases (5.6%; lavage was necessary); 1 case of necrotizing fasciitis after suppurative thrombophlebitis of the subclavian vein, resulting in amputa-

Table 2. Characteristics of suppurative thrombophlebitis.

Variable	No. (%) of episodes (*n* = 36)
Location	
Femoral vein	21 (58.3)
Iliac vein	7 (19.4)
Great saphenous vein	2 (5.6)
Internal jugular vein	5 (13.9)
Subclavian vein	1 (2.8)
Predominant pathogen[a]	
Staphylococcus aureus	19 (52.8)
Streptococcus pyogenes	7 (19.4)
Viridans streptrococci	3 (8.3)
Streptococcus dysgalactiae	3 (8.3)
Streptococcus agalactiae	1 (2.8)
Peptostreptococcus asacharolyticus	2 (5.6)
Arcanobacterium hemolyticum	1 (2.8)

[a] Additional pathogens in polymicrobial infections were *Fusobacterium necrophorum, Micromonas micros, Actinomyces* species, and *Veillonella* species.

tion of the limb; 2 cases of acute osteomyelitis; 5 cases of pulmonary abscesses; and 2 cases of empyemas. In addition to these 11 cases that required surgical intervention because of additional complications, only 1 case involved a patient who underwent surgery of the involved vein; this patient experienced a local abscess formation that required excision of the internal jugular vein.

The median duration of hospitalization was 20 days (range, 6–58 days), and the median time to defervescence was 2 days (range, 0–17 days). Negative blood culture results were obtained at follow-up in 28 cases (77.8%). The median time from start of therapy to the first negative blood culture result was 4.5 days (range, 2–167 days).

The overall readmission rate was high (table 4). However, only 2 readmissions were attributable to relapses of suppurative thrombophlebitis. According to the death records of the local authorities, no patient died after hospital discharge.

Discussion. Suppurative thrombophlebitis is a potentially dangerous complication in IDUs. No studies or clinical trials have investigated the optimal duration of intravenous antibiotic treatment. Four weeks of therapy is recommended according to expert opinions [7]. A long hospital stay for intravenous therapy may not be feasible because of compliance and adherence problems in IDUs [11]. In our study, the intravenous antibiotic treatment duration was quite variable, ranging from <7 days to >28 days. No relapse occurred in cases treated intravenously for >7 days. In more than one-half of the episodes (20 episodes; 56%), the patient received intravenous therapy for ≤21 days. The present data suggests that a 2–3-week course of intravenous therapy followed by therapy with oral antibiotics was safe for suppurative thrombophlebitis. Adherence in IDUs

Table 3. Therapy for suppurative thrombophlebitis.

Variable	Suppurative thrombophlebitis episodes ($n = 36$)
Main antibiotic[a]	
Amoxicillin-clavulanate	12 (33.3)
Penicillin	12 (33.3)
Flucloxacillin	9 (25.0)
Piperacillin-tazaobactam	1 (2.8)
Imipenem-cilastatin	1 (2.8)
Vancomycin	1 (2.8)
Duration of intravenous therapy	
Overall	
Median days (range)	19.5 (6–85)
≤7 Days	4 (11.1)
8–14 Days	6 (16.7)
15–21 Days	10 (27.8)
22–28 Days	7 (19.4)
>28 Days	9 (25)
For *Staphylococcus aureus* infection[b]	
No. of episodes	19
Median days (range)	23 (6–85)
For non–*S. aureus* infection[b]	
No. of episodes	17
Median days (range)	18 (7–41)
Duration of oral therapy, median days (range)	9.5 (0–180)

NOTE. Data are no. (%) of episodes, unless otherwise indicated.

[a] Main antibiotic was considered to be the antibiotic given for the longest period intravenously.

[b] $P = .837$ for differences between groups, using 2-tailed Mann-Whitney U test.

is known to be limited. Therefore, it remains uncertain whether the oral medications were taken.

Two or more systemic inflammatory response syndrome criteria [10] were met by 29 cases (80.6%) at hospital admission, emphasizing the severity of illness and confirming that IDUs tend to present late in the course of illness. In accordance with the literature, we found no attributable mortality. A recent review involving 115 patients showed a mortality rate of <2% [4].

We identified *S. aureus* as the pathogen most frequently cultured, which is in accordance with the findings of other studies [5]. *S. aureus* is one of the most frequently isolated pathogens in infective right-heart endocarditis among IDUs [8]. Therefore, empirical therapy for IDUs with suspected suppurative thrombophlebitis or infective endocarditis should cover this pathogen. In our region, methicillin-resistant *S. aureus* is rare [12]; therefore, empirical treatment with amoxicillin-clavulanate or flucloxacillin is sufficient.

Most septic thromboses were identified in veins of the lower limbs (83.3%). This might be explained by the use of less hy-

gienic injection techniques when injecting in the lower limbs, compared with injection techniques used in the upper limbs. Only 1 suppurative thrombophlebitis was identified in the upper subclavian vein, which may reflect metastatic infection.

An excision of the vein was performed in only 1 patient who presented with an abscess formation. The other 35 cases were successfully treated with antibiotic and anticoagulation therapy. In the literature, conservative management is proposed for suppurative thrombophlebitis of large veins, whereas the failure of conservative therapy and catheter-related or suppurative thrombophlebitis of small peripheral veins are indications for surgical intervention [5, 6].

Our data are not sufficient to make a recommendation concerning anticoagulation in IDUs with suppurative thrombophlebitis, which is still under discussion. A recently published systematic review showed that there is a lack of comparative trials studying the effectiveness and toxicity of heparin in patients with suppurative thrombophlebitis [4]. In our study, all but 3 patients received anticoagulation therapy during hospitalization; the 3 patients who did not receive anticoagulation therapy received low–molecular weight heparin in prophylactic doses.

A limitation of our study is the use of a retrospective analysis with a limited number of cases. Nevertheless, our study is, to our knowledge, the largest case series reported to date. A further strength of our study is the exact information about outcome parameters: IDUs in our area are not likely to be admitted to any other hospitals, and death records from local authorities were available, precluding the possibility that any deaths occurred as consequences of relapses without our knowledge. Also, it is extremely unlikely that we have missed any IDUs with suppurative thrombophlebitis during the observation period in our hospital, because the infectious diseases service evaluates all patients with positive blood culture results. Therefore, any selection bias is unlikely.

The present data suggest that suppurative thrombophlebitis could be sufficiently treated with an intravenous antibiotic course of 14–21 days followed by oral therapy. This observation should be evaluated in a prospective randomized study comparing short regimens versus longer regimens.

Table 4. Outcome of suppurative thrombophlebitis.

Variable	No. (%) of episodes ($n = 36$)
Negative blood culture results	
Available	28 (77.8)
Obtained during therapy	23 (63.9)
Hospital readmission	
Overall	28 (77.8)
Relapse	2 (5.6)

Acknowledgments

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