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 non-sterile 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-

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>33 (20–45)</td>
</tr>
<tr>
<td>Male sex, no. (%) of episodes</td>
<td>22 (61.1)</td>
</tr>
<tr>
<td>Chronic hepatitis C, no. (%) of episodes</td>
<td>30 (88.9)</td>
</tr>
<tr>
<td>HIV positivity, no. (%) of episodes</td>
<td>4 (11.1)</td>
</tr>
<tr>
<td>C-reactive protein level, median mg/dL (range)</td>
<td>162.5 (6–417)</td>
</tr>
<tr>
<td>Leukocyte count, median cells × 10^9 (range)</td>
<td>12 (5.2–31)</td>
</tr>
<tr>
<td>Temperature, median °C (range)</td>
<td>39.1 (35.3–41.3)</td>
</tr>
</tbody>
</table>
docarditis was diagnosed in 3 cases. Because transthoracic eche-
cardiography 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 a thrombectomy was
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blood samples was obtained), a thrombectomy was
performed, and a thrombectomy was performed, and a thrombectomy was
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performed.

In 7 (19.4%) of the episodes, the patient received intravenous
therapy for 8–14 days, and 10 patients were treated for 15–21 days.

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 an-
tibiotic therapy was a median of 28.5 days (range, 7–220 days).

There was no significant difference in the duration of intra-
venous 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 in-
fluence the duration of intravenous antibiotic treatment (me-
dian 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 ini-
tiated. 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 supplicative
thrombophlebitis of the subclavian vein, resulting in amputa-
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 experi-
cenced 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 supplicative
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 ad-
herence 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 in-
travenously 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 supplicative thrombophlebitis. Adherence in IDUs

Table 2. Characteristics of supplicative thrombophlebitis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of episodes (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Femoral vein</td>
<td>21 (58.3)</td>
</tr>
<tr>
<td>Iliac vein</td>
<td>7 (19.4)</td>
</tr>
<tr>
<td>Great saphenous vein</td>
<td>2 (5.6)</td>
</tr>
<tr>
<td>Internal jugular vein</td>
<td>5 (13.9)</td>
</tr>
<tr>
<td>Subclavian vein</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Predominant pathogens</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>19 (52.8)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>7 (19.4)</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>Streptococcus dysgalactiae</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Peptostreptococcus asacharolyticus</td>
<td>2 (5.6)</td>
</tr>
<tr>
<td>Arcanobacterium hemolyticum</td>
<td>1 (2.8)</td>
</tr>
</tbody>
</table>

* Additional pathogens in polymicrobial infections were Fusobacterium nec-
rorophorum, Micromonas micros, Actinomyces species, and Veillonella species.
Table 3. Therapy for suppurative thrombophlebitis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Suppurative thrombophlebitis episodes (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main antibiotic&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>12 (33.3)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>12 (33.3)</td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td>9 (25.0)</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Imipenem-cilastatin</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Duration of intravenous therapy</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>Median days (range) 19.5 (6–85)</td>
</tr>
<tr>
<td>≤7 Days</td>
<td>4 (11.1)</td>
</tr>
<tr>
<td>8–14 Days</td>
<td>6 (16.7)</td>
</tr>
<tr>
<td>15–21 Days</td>
<td>10 (27.8)</td>
</tr>
<tr>
<td>22–28 Days</td>
<td>7 (19.4)</td>
</tr>
<tr>
<td>&gt;28 Days</td>
<td>9 (25)</td>
</tr>
<tr>
<td>For &lt;i&gt;Staphylococcus aureus&lt;/i&gt; infection&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No. of episodes 19</td>
</tr>
<tr>
<td>Median days (range)</td>
<td>23 (6–85)</td>
</tr>
<tr>
<td>For non-&lt;i&gt;S. aureus&lt;/i&gt; infection&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No. of episodes 17</td>
</tr>
<tr>
<td>Median days (range)</td>
<td>18 (7–41)</td>
</tr>
<tr>
<td>Duration of oral therapy, median days (range)</td>
<td>9.5 (0–180)</td>
</tr>
</tbody>
</table>

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

<sup>a</sup> Main antibiotic was considered to be the antibiotic given for the longest period intravenously.

<sup>b</sup> 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 <i>S. aureus</i> as the pathogen most frequently cultured, which is in accordance with the findings of other studies [5]. <i>S. aureus</i> 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 <i>S. aureus</i> 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 hygienic 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.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of episodes (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative blood culture results</td>
<td></td>
</tr>
<tr>
<td>Available</td>
<td>28 (77.8)</td>
</tr>
<tr>
<td>Obtained during therapy</td>
<td>23 (63.9)</td>
</tr>
<tr>
<td>Hospital readmission</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>28 (77.8)</td>
</tr>
<tr>
<td>Relapse</td>
<td>2 (5.6)</td>
</tr>
</tbody>
</table>

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Potential conflicts of interest. All authors: no conflicts.

References