SHORT REPORT

Taurolidine lock: The key to prevention of recurrent catheter-related bloodstream infections

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Received 19 January 2005; accepted 8 February 2005

Summary The literature shows that repeated courses of antibiotics and catheter removals in a subset of patients suffering from multiple catheter-related bloodstream infections (CRBSI), are unlikely to prevent recurrence. In acceding to preventative strategies, we report our application of the antimicrobial chemotherapeutic Taurolidine used as a daily flush solution in seven home TPN patients suffering from multiple episodes. A pretreatment infection rate of 10.8 infections per 1000 catheter days decreased to 0.8 after treatment.

Introduction

The literature shows that a management consisting of repeated courses of antibiotics and catheter removals in a subset of patients suffering from multiple catheter-related bloodstream infections (CRBSI), is unlikely to prevent recurrence. Recent Hospital Infection Control Practices Advisory Committee (HICPAC) guidelines considers the use of antibiotic lock technique to be acceptable in judiciously selected patients in whom vascular access is indefinitely required. We report the first case series of Taurolidine as a single agent lock in seven home TPN patients for a total of 5500 catheter days.

Repeated catheter removals and re-insertions can lead to limited vascular access such that future catheter removal may be ill-advised. Furthermore, on-going thrombosis is sponsored by staphylococci coagulase strains which promote local coagulation which is resistant to the customary heparin lock, left to dwell when the catheter is not in use. In determining which patients to initiate on lock technique, consideration need be given to the total number of catheter re-insertions due to either mechanical or infectious reasons in addition to the frequency of presentation with peripheral and retrograde blood culture positivity supporting a diagnosis of CRBSI. Clinical findings may be unreliable for establishing a diagnosis of CRBSI because of their poor specificity and sensitivity. A positive...

KEYWORDS
Taurolidine; Lock solution; Catheter infection; Bloodstream infection

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retrograde culture does require clinical interpretation to distinguish between colonization and infection, however, a negative result is unequivocal at ruling out CRBSI. The luminal colonization mechanism of progression to catheter-related bloodstream infection figures more prominently in the home TPN population as opposed to the extraluminal route.\(^2\)

An important limitation in the application of conventional antibiotics as flush solutions is whether or not microbes develop resistance including subpopulations of skin microbes after prolonged exposure and this may necessitate population analysis as part of clinical studies. Taurolidine would appear to be strategically positioned as a flush solution or for intraluminal and extraluminal application to catheters. Adverse effects or the emergence of microbial resistance or superinfection have not been noted with the systemic use of Taurolidine.

### Patients and methods

Seven out of 30 patients from the Home Parenteral Nutrition Unit of St. Michael’s Hospital presented every 1–6 months with malaise and/or chills and fevers, usually with escalating frequencies (Table 1). After a positive diagnostic workup for CRBSI, management of these seven patients consisted of conventional antibiotic administered systemically in addition to intraluminal antibiotic delivery in accordance with blood culture and sensitivity results. The need to remove the catheter materialized on numerous occasions either because of overwhelming infection or due to failure to achieve negative follow-up cultures. The number and nature of infections and their treatments in accordance with cultures, the catheter site condition, the number and nature of line exchanges, line hesitancy either ante or retrograde, as well as number of days of infection-free cannulization were all tracked.

CRBSI was defined as positive peripheral cultures which collated with positive retrograde cultures in addition to either leukocytosis or patient symptomatology consistent with bloodstream infection. These seven patients were targeted out of 30 patients, as the frequency with which they would present with CRBSI, would lead to limited vascular access rapidly, which was in contrast to the stasis with the remaining 23 patients.

After informed consent was obtained, these seven patients were instructed to instill daily 3 ml of Taurolidine into their central line after infusing TPN. The commercially available product, at a

### Table 1: Patient summary of episodes of catheter-related bloodstream infections and catheter exchanges pre-and posttaurolidine lock treatment.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Duration of cannulization before therapy (months)</th>
<th>No. of total removals (mechanical+infectious) before treatment</th>
<th>No. of line removals due to CRBSI</th>
<th>No. of catheter salvages attempted with conventional antibiotic lock technique before treatment</th>
<th>Interval between presentations with CRBSI with (+) blood cultures preceding Taurolidine lock (months)</th>
<th>CRBSI while on Taurolidine lock</th>
<th>Initiation of Taurolidine lock coincided with new line insertion (Y or N)</th>
<th>Subsequent line removals+reinsertions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;10 yrs</td>
<td>10</td>
<td>2</td>
<td>4</td>
<td>10 yrs</td>
<td>1 CRBSI</td>
<td>Y</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>2</td>
<td>2 yrs 3 mos</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>6 yrs</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>3</td>
<td>10 yrs</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2 yrs</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>4</td>
<td>4 yrs 8 mos</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4 yrs</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>5</td>
<td>1 yr 1 mo</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1 yr</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>6</td>
<td>1 yr 11 mos</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1 yr</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
<tr>
<td>7</td>
<td>&gt;6yrs</td>
<td>12</td>
<td>12</td>
<td>18</td>
<td>5 yrs</td>
<td>1 CRBSI</td>
<td>N</td>
<td>1 CRBSI</td>
</tr>
</tbody>
</table>

CRBSI, Catheter-related bloodstream infection; CNS, Coagulase-negative staphylococcus; S. Milleri, Streptococcus milleri; K. pneumoniae; R. pneumoniae; S. aureus, Staphylococcus aureus; E. coli, Escherichia coli; CRBSI, Catheter-related bloodstream infection; TPN, Total Parenteral Nutrition.
concentration of 2% (Taurolin®, Geistlich Pharma, Wolhusen, Switzerland), is left indwelling for 12 h and is flushed in when it is time to hook up for TPN. For the initiation of cannulization as well as subsequent line insertions and/or exchanges, all patients primarily received the procedure at St. Michael’s Hospital Department of Interventional Radiology. All patients received single lumen Hickman catheters with the subclavian vein the vessel of choice although Peripherally Inserted (PIC) lines were also engaged.

The underlying diagnoses of the patients (age range 33–75 over the years 1995–2002) were as follows:

- two out of seven patients with intestinal pseudoobstruction/dysmotility,
- short bowel syndrome postresection for Crohn’s disease/bowel infarction for the rest.

Evaluation of patients’ aseptic technique was ongoing and deemed to be satisfactory in all cases. In all patients, the protocol and frequency of site care and technique, including alcohol swabbing of the catheter hub, remained unchanged over the patients’ TPN course in the home to date. All patients flushed their lines daily and the frequency of infusion of TPN (including lipid emulsion) varied over the course. Radiologic investigation of the exact volume of each of the patients’ catheters was not done except for Patient #7 who had the implanted device at the time (PASport®, Pharma/cia/Deltac, USA) plus an extension to a total of 1.5 ml and this served as a guide to the volume to be used.

### Results

The mean infection rate of the seven Taurolidine patients before the intervention was 10.8 infections per 1000 catheter days (see Table 2) with infection being defined as CRBSI exclusive of exit site/pocket involvement. After intervention with Taurolidine, the mean infection rate decreased significantly to 0.8 infections per 1000 catheter days. The mean infection rate for these seven patients before treatment plus 14 other patients matched for diagnosis out of total 30 patients in the unit, was 4.1 infections per 1000 catheter days.

The number of infection-free days of cannulization for the Taurolidine patients significantly increased when compared with an equivalent trial period before treatment ($P = 0.0156$, Wilcoxon signed rank test). Taurolidine was started with fresh catheters inserted in only two of the Patients—nos. 1 and 5 and the latter has remained infection-free to date. Despite having previously infected catheters, four out of the five patients started on Taurolidine with salvaged lines have not been presented with CRBSI.

None of our patients have reported experiencing any adverse reactions from flushing the Taurolidine after its dwelling or presented with line hesitancy. Biases may emerge from the comparison and aggregation of this data in patient selection, co-morbidity, and the duration of treatment that are all quite heterogenous. However, noteworthy is that Taurolidine is successful in interrupting the pattern of recurrent infection even in lines which have been previously salvaged with conventional antibiotic lock technique. The decision to calculate an infection rate per patient and then a mean was

<table>
<thead>
<tr>
<th>Patient</th>
<th># Infection/1000 catheter days pre Taurolidine</th>
<th># Infections/1000 catheter days Taurolidine</th>
<th># Taurolidine treatment days</th>
<th># Infection-free* days Taurolidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.6</td>
<td>2.5</td>
<td>780</td>
<td>752</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>0</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>4.8</td>
<td>0</td>
<td>1230</td>
<td>1230</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>0</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0</td>
<td>730</td>
<td>730</td>
</tr>
<tr>
<td>6</td>
<td>8.7</td>
<td>0</td>
<td>570</td>
<td>570</td>
</tr>
<tr>
<td>7</td>
<td>6.9</td>
<td>3.2</td>
<td>1860</td>
<td>1770</td>
</tr>
<tr>
<td>Mean</td>
<td>10.8 infections Per 1000 catheter days</td>
<td>0.8 infections Per 1000 catheter days</td>
<td>5500</td>
<td></td>
</tr>
</tbody>
</table>

*INFECTION-FREE DAY is defined as a day which is not part of a 2 week IV antibiotic/intraluminal therapy course for a discrete episode of CRBSI.
based on the fact that four out the seven Taurolidine patients did not have adequate number of pretreatment days of being cannulated to make up a trial period before the treatment similar to a period of maximum duration of Taurolidine treatment.

Discussion

Taurolidine, in addition to having a broad-spectrum bactericidal activity, prevents or reduces the adherence of bacterial cells to the epithelium by altering the bacterial cell wall structures and by destroying the fimbriae and flagellae. Anti-adherence is achieved when either the bacterial and the epithelial cell is exposed to Taurolidine. With respect to pretreated catheter surfaces, it cannot be discounted that the drug prevents both the process of surface conditioning with associated fibrous matrix as well as receptor-mediated attachment by microbes, both figuring so prominently in the pathogenesis of device-related infection.

Chemically derived from the aminosulphonic acid taurine, the drug is metabolized to water and carbon dioxide. Its bactericidal mechanism of action is attributed to reactive methylene iminium ions, the conversion to which occurs in an aqueous medium. Bacteria and fungi cell wall constituents are then methylolated and killing is affected.

Resistance for a vast array of microbes as well as superinfection with the use of Taurolidine have never been reported. The promising initial results of others using Taurolidine in combination with a local anticoagulant and without, as a lock, support our initial and current observations that this drug is safe and is an effective preventative therapy for CRBSI.

References