Our study has several limitations. The first limitation is that we could not account for many factors that may contribute to acute mastoiditis, such as antecedent OM, antibiotic use, vaccination status and underlying health. Although we can contextualize our findings with published data on these factors, we cannot directly correlate incidence with these factors in our study population. Another limitation is that estimates are only available every 3 years from KID (next release 2016 data in mid-2018). This may impede our ability to see year-over-year shifts, which is potentially important in identifying trends. A third limitation is that KID aggregates state-level data with variability in the number of states submitting data and in the data fields submitted over time. A strength of our study is the ability to estimate national incidence of this rare disease. The inclusion of a sensitivity analysis is also a strength as it allows us to account for both changes in true incidence and coding practices.

This study of mastoiditis among US children from 2000 to 2012 estimated incidence rates over time and across regions, sexes and age groups in the PCV era. These estimates may serve as a baseline for public health surveillance of this rare complication and could be used to monitor for unintended consequences of reducing antibiotic use for AOM, potentially informing antibiotic stewardship efforts.

REFERENCES


TAUROLIDINE–CITRATE LINE LOCKS PREVENT RECURRENT CENTRAL LINE–ASSOCIATED BLOODSTREAM INFECTION IN PEDIATRIC PATIENTS

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**Abstract:** This study describes a successful, targeted intervention in central venous access device routine care to decrease central line–associated bloodstream infection. Taurolidine–citrate locks significantly reduced the rate of central line–associated bloodstream infection, particularly Gram-negative organisms without adverse events.

**Key Words:** Healthcare-associated infection, central line–associated bloodstream infection, catheter lock, children, taurolidine

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Central venous access devices (CVADs) are essential for the management of acutely, critically and chronically ill children.1 CVAD-associated complications, especially infections, remain prevalent2 and are a significant cause of morbidity and mortality for children who are reliant on their function.2 Central line–associated blood stream infection (CLABSI) develops because of intra- or extraluminal contamination by organisms, especially *Staphylococcus aureus*. CLABSI most commonly occur because of contamination of the catheter hub, subsequently growing within a luminal biofilm layer which develops rapidly (<24 hours) after insertion. The presence of biofilm complicates the ability of antimicrobials to completely resolve CLABSI, often resulting in premature catheter removal and treatment delays.3

Implanted CVADs including totally implanted devices (TID; eg, port-a-cath) and tunnelled cuffed CVADs are used for children who require long-term and sometimes lifelong vascular access.2 Repeated catheter removal and subsequent replacement may result in venous insufficiency for future device placement, thus catheter salvage is the ultimate goal when CLABSI is suspected. Novel line salvage techniques include ethanol, antibiotic, hydrochloric acid and fibrinolytic locks4,5; however, eliminating CLABSI continues to be challenging.

Taurolidine/citrate (Taurolock; TauroPharm GmbH, Germany) is a catheter lock solution that may prevent biofilm formation in vitro6 and has broad-spectrum bactericidal and antifungal activity.7,8 With the antiadherence properties of taurolidine and the anti-clotting and chelator activities of both taurolidine and citrate, this lock solution is postulated to disrupt bacterial surface adherence and consequential biofilm production.1 Contemporary pediatric literature, including a prospective cohort study7 and 2 randomized controlled trials8 of children with cancer, and a prospective cohort study of children receiving parental nutrition (PN),9 has consistently reported a reduction in CVAD-related bloodstream infection (BSI) when using Taurolock, in comparison to other lock solutions, without obvious adverse effects or bacterial resistance. A systematic review and meta-analysis of taurolidine lock solutions (6 randomized controlled trials, 431 patients, 86,078 catheter days) reported a significant reduction in the incidence of CVAD-related BSI in comparison to heparin lock solutions (risk ratio: 0.34; 95% CI: 0.21–0.55).

In response to higher than local average CLABSI rates in a cohort of children with CVAD, and after review of the above literature, a targeted implementation of Taurolock was initiated by an interdisciplinary collaboration of pediatric infectious disease, gastroenterology and oncology physicians, pharmacy, vascular access specialists and home healthcare nurses.

This study aimed to compare the incidence of CLABSI in children identified at high risk of CLABSI before and after the
introduction of Taurolock into routine clinical care, and to demonstrate a process by which Taurolock can be implemented outside of a clinical trial.

**MATERIALS AND METHODS**

This study was undertaken at the Royal Children’s Hospital (Brisbane; subsequently incorporated into Lady Cilento Children’s Hospital), tertiary referral pediatric hospitals in Queensland, Australia. Taurolock was introduced as the sole interventional change into routine clinical care in selected, high-risk patients between April 2013 and September 2015. In routine care, CVADs were locked intermittently with heparin with the volume based on line length; 10 units/mL if less than 3 days of inactivity, 100 units/mL if greater than 3 days of inactivity. Retrospective data regarding participant CLABSI results were collected from March 2011 to March 2013 to enable comparison.

Children presenting with recurrent CLABSI throughout the course of their treatment were considered for suitability of Taurolock. Children were eligible if they met all the following criteria: (1) had a new or previously inserted CVAD; (2) had a history of recurrent (2 or more) CLABSI from a CVAD or were on home PN; (3) could have a Taurolock dwell time of at least 6 hours. Children were excluded if they had a peripherally inserted central catheter, were unable to have a minimum Taurolock dwell time of at least 6 hours or did not have a skilled or trainable carer to provide treatment.

Taurolock (tauroline 1.34% with citrate 4%) was administered daily with the volume/dose calculated to either the length of the line (if line length unknown) or 2 mL for tunneled cuffed CVAD and 4 mL for TID. Taurolock was left to dwell for at least 6 hours or did not have a skilled or trainable carer to provide treatment.

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The primary outcome of Taurolock implementation was CLABSI defined in accordance with the Centers for Disease Control Device-associated Module BSI.12 This is a laboratory-confirmed BSI that is not secondary to an infection at another body site (excludes mucosal barrier injury laboratory-confirmed BSI), with the CVAD in place for greater or equal to 2 days on the day of the BSI and on the date of the event or the day. Confirmation of CLABSI was by a pediatric infectious disease specialist using clinical and microbiologic data. While receiving Taurolock, calcium levels (corrected for hypoalbuminemia) were monitored to ensure safety, with values of less than 2.1 mmol/L indicating an adverse event. Clinical data were collected via patient chart audit and microbiologic and biochemistry data were collected from laboratory information systems.

Statistical analysis was performed with GraphPad Prism Statistical package 2017 (La Jolla, CA). Descriptive statistics have been used to describe the participant cohort, including frequencies and percentages for categorical variables and mean, median, interquartile range and range for continuous variables. CLABSI results are expressed as rates per 1000 catheter days, with time-to-first CLABSI between groups described using Kaplan–Meier survival curves, with comparisons made via the log-rank test. CLABSI data were compared using paired t tests, where each patient acted as their own control. Significance was set at P < 0.05.

**RESULTS**

Nineteen children were identified who met the inclusion and exclusion criteria and were commenced on Taurolock. None were

<table>
<thead>
<tr>
<th>TABLE 1. Central Line–associated Blood Stream Infection Episodes and Pathogens Pre- and Post implementation of Taurolock</th>
</tr>
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<tr>
<td><strong>Children = 19</strong></td>
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<tr>
<td><strong>Pre-Taurolock</strong></td>
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<td><strong>Post-Taurolock</strong></td>
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<tr>
<td>CLABSI episodes</td>
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<tr>
<td>Total catheter days</td>
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<tr>
<td>Participant catheter days (median, interquartile range, range)</td>
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<tr>
<td>CLABSI rate per 1000 catheter days</td>
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<tr>
<td>Individual CLABSI rate per 1000 catheter days (mean, range)</td>
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<tr>
<td>Staphylococcus epidermidis [N (%)]</td>
</tr>
<tr>
<td>Klebsiella pneumoniae [N (%)]</td>
</tr>
<tr>
<td>Enterobacter sp. [N (%)]</td>
</tr>
<tr>
<td>Staphylococcus aureus [N (%)]</td>
</tr>
<tr>
<td>Staphylococcus warnerii</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
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<tr>
<td>Methicillin-resistant S. aureus</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Micrococcus sp.</td>
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<tr>
<td>Streptococcus mitis [N (%)]</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
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<tr>
<td>Pantoea sp.</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
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<tr>
<td>Streptococcus parasanguinis</td>
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</tbody>
</table>

*Paired t test.
†Positive blood culture in hematopoietic stem cell transplant recipient and patient with acute lymphoblastic leukemia, respectively, with neutropenic sepsis. At time of neutropenic sepsis, patient not receiving Taurolock due to limited CVAD access.
‡Positive blood culture in parenteral nutrition–dependent patient with short gut syndrome.
withdrawn from treatment. Mean age at trial commencement was 6.2 years [standard deviation (SD) 5.5 years, range 0.3–17] with 9 (47%) males. Oncologic malignancy (47%; n = 9) or intestinal failure (53%; n = 10) were the indication for CVADs with 15 (79%) being tunneled, cuffed CVAD and 4 (21%) TID. A total of 17,436 catheter days were studied across both phases: 7077 catheter days pre-Taurolock implementation; 10,359 catheter days postimplementation.

Pre-Taurolock, 19 children had 39 episodes of CLABSI (7077 catheter days), and 5 episodes of CLABSI (10,359 catheter days) post-Taurolock. The cumulative CLABSI rate decreased from 5.5 to 0.5 per 1000 catheter days (P = 0.0001), compared with the overall hospital CLABSI rate which was 1.8 and 1.5 in the equivalent time periods. Individual mean CLABSI rates decreased from 20.39 per 1000 catheter days (SD 23.77, range 0.76–71.43) to 2.26 per 1000 catheter days (SD 4.98, range 0–18.2; P = 0.0001) (Table 1). The mean time to first CLABSI episode increased from 87 to 296 days after Taurolock implementation (P = 0.012). There were no episodes of hypocalcaemia observed during Taurolock implementation.

Before Taurolock implementation, Gram-positive pathogens were identified in 62% of CLABSIs with 38% Gram-negative organisms; post-Taurolock, all 5 (100%) were Gram positive (Table 1).

**DISCUSSION**

This study describes a successful intervention into routine care for a target group of children undergoing nutritional therapy, chemotherapy and/or bone marrow transplantation. The use of Taurolock catheter lock solution was associated with significantly reduced CLABSI, with no reported adverse events, consistent with previous pediatric studies in similar population groups.6–9

Consistent with previous literature, the pathogens resulting in CLABSI altered with the implementation of Taurolock. In vitro study has shown that after 24 hours contact, certain solutions of taurolidine–citrate were lethal for Candida albicans, Staphylococcus epidermidis, Pseudomonas aeruginosa and Enterococcus faecalis and after 72 hours there was no growth in the taurolidine–citrate–treated devices. A systematic review reported that taurolidine solutions were effective at reducing the rate of Gram-negative infections (P = 0.004), but were associated only with a nonsignificant decrease in Gram-positive infections (P = 0.07).4 Accordingly, this was demonstrated within this study, with all CLABSI identified as Gram positive after Taurolock implementation.

With a 78% decrease in the incidence of Gram-negative CLABSI per 1000 catheter days, Taurolock is promising as a viable intervention into routine care to decrease CLABSI rates in high-risk groups. The results are limited in the study’s retrospective comparison, lack of randomization, small sample size and varying follow-up time. However, the study provides a framework for clinicians to replicate the successful application of Taurolock solution to reduce CLABSI in high-risk patients. Although additional close surveillance, follow-up and more experience are required to observe the long-term benefits of using Taurolock CVAD locks and to test its independent effectiveness, our results suggest this could potentially reduce infectious complications, without adverse effect, resulting in improved quality of life for children with chronic illness.

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