







Vancomycin vs teicoplanin antibiotic lock therapy for pediatric coagulase negative staphylococcal central line associated bloodstream infections

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ABSTRACT

Aims: Central line associated bloodstream infections (CLABSIs) are the major complication of central lines. Coagulase-negative *Staphylococcus* (CoNS) are the leading cause of CLABSI often necessitating line removal. While antibiotic lock therapy (ALT) is widely utilized in adults, pediatric specific data remains limited. In this study we aimed to evaluate the ALT outcomes in children with CoNS CLABSIs.

Methods: Children with CoNS CLABSIs who received ≥ 72 hours of ALT with either vancomycin or teicoplanin between January 2020-2023 were retrospectively reviewed. Data on demographic and clinical characteristics, management strategies, and outcomes were analyzed. ALT success was defined as clinical resolution, negative follow-up blood cultures, and catheter retention.

Results: Nineteen patients were included (median age 50 months; 58% female). Methicillin-sensitive CoNS (MSCoNS) were isolated in 4 (21%) cases and methicillin-resistant CoNS (MRCoNS) in 15 (79%). ALT regimens comprised vancomycin (n=9, 47%), teicoplanin (n=8, 42%), or sequential use (n=2, 11%). Overall, ALT success was 63% (12/19). Vancomycin-based ALT succeeded in 56% (5/9) vs. 62.5% (5/8) for teicoplanin (p=1.0). Success was higher in MSCoNS CLABSIs (100%) than MRCoNS (53%), though not statistically significant (p=0.245). Younger age (p=0.003) and persistent positive cultures (p=0.013) were associated with catheter loss. No infection-related mortality occurred. Recurrence occurred in 3 (16%) patients and reinfection in 5 (26%).

Conclusion: ALT achieved satisfactory catheter salvage rates in pediatric CoNS CLABSI, with comparable efficacy between vancomycin and teicoplanin. Younger age and persistent bacteremia predicted failure. Vancomycin or teicoplanin based ALT can be used in selected children with CoNS CLABSI.

Keywords: Catheter-related infections, coagulase, *Staphylococcus*, teicoplanin, vancomycin

INTRODUCTION

Central lines play an essential role in the care of hospitalized pediatric patients, facilitating the administration of medications, parenteral nutrition, and blood sampling over extended periods. However, bloodstream infections remain the most common complication, contributing significantly to morbidity, mortality, prolonged hospitalization, and increased healthcare costs.¹⁻⁴

Coagulase-negative *Staphylococcus* (CoNS) are the leading causative organisms of central line associated bloodstream infection (CLABSI), largely due to their capacity to adhere to catheter surfaces and form biofilms.⁴⁻⁷ These biofilms confer protection from host defences and systemic antimicrobial

agents, rendering eradication difficult without catheter removal.^{6,7}

Conventional management of CoNS CLABSIs often necessitates catheter removal, yet this is not always feasible in paediatric patients who rely on long-term vascular access.⁸⁻¹⁰ In such cases, antibiotic lock therapy (ALT) has emerged as a valuable adjunctive strategy. ALT, involving the instillation of highly concentrated antimicrobial solutions into the catheter lumen, has long been utilized as a targeted strategy to treat intraluminal infections and preserve catheter function in adults.^{8,11,12} ALT is typically used in combination with systemic antibiotics and aims to sterilize the catheter lumen,

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disrupt biofilms, and allow catheter salvage, particularly in stable patients without signs of metastatic infection.^{8,11,13} Despite growing clinical use, there is limited pediatric specific evidence to guide ALT protocols especially regarding optimal antimicrobial agents, dwell times, and treatment duration.¹²⁻¹⁴

In this study, we hypothesised that ALT with vancomycin or teicoplanin, when combined with parenteral therapy is an effective and safe strategy for managing CoNS CLABSI in children by enabling catheter salvage and reducing line removal. The study retrospectively evaluated the clinical outcomes of paediatric patients treated with this approach.

METHODS

Study Design

The study was approved by the Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.04.2023, Decision No: 09.2023.621). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective study evaluated patients aged 1 months to 18 years with CoNS CLABSI who received ALT between January 2020 and January 2023 at a tertiary hospital. Demographic, clinical and laboratory data were extracted from electronic medical records, including infection characteristics, management strategies, and treatment outcomes.

Clinical Management

According to the institutional policy, children with central lines and either peripheral or catheter-derived blood cultures positive for gram-positive organisms were empirically initiated with systemic vancomycin or teicoplanin. Following the detection of a positive blood culture, all cases were evaluated by the pediatric infectious diseases (PID) team, who determined whether the episode met criteria for CLABSI and made individualized decisions regarding the initiation of ALT. The choice of systemic antibiotic and lock solution was guided by the antimicrobial susceptibility profile of the isolated organism and clinical profile of the patient.

In line with hospital policy, C-reactive protein (CRP) levels were not routinely measured during febrile episodes in children receiving anti-cancer chemotherapy. Clinical assessment and complementary laboratory investigations were used to guide management, given that malignancy or chemotherapy can result in non-specific elevations in CRP, thereby limiting its diagnostic utility.

Patient Selection and Definitions

A central line associated bloodstream infection (CLABSI) was defined according to CDC guidelines as a primary bloodstream infection (BSI) occurring in a patient who had a central venous catheter (CVC) in place within the preceding 48 hours and in the absence of an identifiable source of infection elsewhere.¹⁵

Patients were eligible for inclusion if they met the following criteria: (1) confirmed CoNS CLABSI, (2) received systemic antimicrobial therapy with vancomycin or teicoplanin, and (3) received ALT for ≥ 72 hours.

Patients were excluded if they had Staphylococcal colonization without systemic infection signs, ALT administered for less than 72 hours, or polymicrobial infections. For children with multiple episodes of CoNS CLABSI during the study period, only the first episode was included in the analysis.

Treatment success was defined as clinical improvement and resolution of fever within 72 hours of ALT initiation with at least two consecutive sterile blood cultures obtained from the catheter, and retention of the long-term central line.¹⁶

Recurrence was defined as a new episode of CLABSI with the same pathogen ≥ 30 days after documented clearance. Reinfection was defined as a new CLABSI episode caused by a different organism following clinical resolution and sterile blood cultures.¹⁷⁻¹⁹

Antibiotic Lock Therapy (ALT)

ALT was administered in addition to the systemic therapy. Vancomycin lock solution was prepared by using vancomycin at 5 mg/ml with 2500 IU/ml heparin, and teicoplanin lock solution was prepared with teicoplanin at 10 mg/ml and 2500 IU/ml heparin according to local protocol. ALT was administered by instilling the antibiotic-heparin solution into the catheter lumen for at least 12 hours each day, and the solution was renewed every 24 hours. Patients who were on systemic vancomycin (60 mg/kg/day divided to four doses) therapy received vancomycin lock therapy while patients who were on systemic teicoplanin (10 mg/kg every 12 hours for three doses, then 10 mg/kg once daily) therapy received teicoplanin lock therapy.

Statistical Analysis

Data analyses were performed using SPSS Statistics Version 22.0 for Windows (IBM Corp., Armonk, NY). Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as either mean \pm standard deviation or median with interquartile range, depending on the normality of their distribution. Continuous variables were compared using the independent-samples T test or the Mann-Whitney U test based on normality of distribution. The Pearson Chi-square test or Fisher exact test was used to compare categorical variables, with statistical significance set at $p < 0.05$.

RESULTS

During the study period a total of 20 children with CoNS CLABSI were treated with ALT. One patient with a polymicrobial infection involving methicillin resistant coagulase negative *Staphylococcus* (MRCoNS) and *Enterococcus faecium* infection was excluded. The final analysis included 19 patients.

Of these, 11 (58%) were female. The median age of patients was 50 months [interquartile range (IQR): 16-116 months]. Underlying conditions included solid organ tumours (n=4), hematologic malignancies (n=9), of whom four had undergone hematopoietic stem cell transplantation (HSCT), and rare comorbidities (n=6), such as I-cell disease, short bowel syndrome, autoimmune enteropathy, epileptic encephalopathy, trichohepatoenteric syndrome, and combined cystic fibrosis with osteogenesis imperfecta.

The median duration of catheter use prior to infection onset was 29.5 days (IQR: 17.75-79 days). Catheter types included 15 (79%) skin tunnelled central venous catheters, and four (21%) implanted port catheters.

Microbiological testing identified methicillin sensitive CoNS (MSCoNS) in 4 (21%) patients and methicillin resistant CoNS (MRCoNS) in 15 (79%) patients. Species level identification was available in 10 (52.6%) cases, comprising *Staphylococcus epidermidis* in 7 (36.8%), *Staphylococcus haemolyticus* in 2 (10.5%), and *Staphylococcus hominis* in 1 (5.3%).

At the time of infection, 7 (36.8%) patients were neutropenic. Among the non-neutropenic group (n=12, 63.2%), the median leukocyte count was 6.900/mm³ (IQR: 2.225-13.550/mm³), and the median absolute neutrophil count was 4.000/mm³ (IQR: 1.500-7.600/mm³). CRP levels were measured in 9 (47.3%) patients with a median value of 11 mg/L (IQR: 8.5-74.5 mg/L).

ALT regimens included teicoplanin in 8 (42.1%) patients, vancomycin in 9 (47.4%) patients, and sequential use of both agents in 2 (10.5%) patients. The median duration of ALT was 7 days (IQR: 5-8 days), while systemic intravenous antibiotics were administered for a median of 13 days (IQR: 13-14 days).

ALT was successful in 12/19 (63.2%) patients. Among those treated with vancomycin-based ALT, 5/9 (55.6%) patients achieved catheter salvage, while teicoplanin ALT was successful in 5/8 (62.5%) patients. The difference was not statistically significant. (p=1.0) When stratified by methicillin susceptibility, ALT was successful in all 4 cases (100%) of MSCoNS CLABSI, compared with 8 of 15 (53.3%) cases of MRCoNS CLABSI. The difference was not found statistically significant (p=0.245).

Younger age and a higher number of repeated positive blood cultures were found significantly associated with catheter loss (p=0.003 and p=0.013, respectively). Catheter instillation duration and CRP levels were not associated with catheter loss. (p=0.44 and p=0.90, respectively)

Subgroup analyses for underlying conditions and catheter types was not performed due to the limited sample size.

One patient with port catheter developed concurrent endocarditis. No infection related mortality occurred during the study period. Recurrence of CoNS CLABSI was observed in 3 (15.8%) patients with implanted ports and all underwent port catheter removal. Reinfection occurred in 5 (26.3%) patients, caused by *Rothia mucilaginosa* (n=1), *Ralstonia pickettii* (n=1), *Pseudomonas aeruginosa* (n=1), *Stenotrophomonas maltophilia* (n=1), and *Ralstonia insidiosa* (n=1).

DISCUSSION

In this study, ALT achieved an overall success rate of 63% in children with CoNS CLABSI, allowing catheter salvage in the majority of cases. This finding is consistent with previously reported ALT success rates in children, which range from 50% to 80%, depending on pathogen type, underlying disease, and treatment protocol.^{16,18-21}

We found no significant difference in success between vancomycin and teicoplanin based ALT. Both regimens achieved comparable catheter salvage rates, suggesting that the choice between these glycopeptides may be guided by organism susceptibility, drug availability, and patient-specific considerations rather than anticipated efficacy. This aligns with prior studies in which both agents demonstrated similar outcomes against CoNS.^{13,17}

Only a limited number of studies in the literature have investigated the use of teicoplanin based ALT, and these have generally involved small case series. Del Pozo et al.²² examined 44 adults with CoNS related bacteremia, of whom 17 received teicoplanin based ALT and 27 vancomycin-based ALT. None of the teicoplanin-treated patients required catheter removal, whereas 23% of those treated with vancomycin failed therapy and subsequently required catheter removal. Okur Acar et al.²¹ recently reported a success rate of 72.7% with teicoplanin ALT in children with port related CoNS bacteremia. Conversely, Guédon et al.²³ found a considerably lower success rate of 37.5% in 24 adults with catheter related infections, which was attributed to the use of a low teicoplanin lock concentration (2.5 mg/ml).

Reported concentrations of teicoplanin based ALT vary considerably across studies. While Shan et al.,¹² in their review, recommended 10 mg/ml, and Okur Acar et al.²¹ employed a teicoplanin lock concentration of 2.0 mg/ml and Guédon et al.²³ used 2.5 mg/ml, and Blanco-Di Matteo et al.,²⁴ in their study on haemodialysis related catheter infections, also applied a 10 mg/ml concentration. In line with our institutional protocol, we adopted a 10 mg/ml teicoplanin based ALT in this study. By contrast, vancomycin-based ALT concentrations are more consistent in the literature, with most reports supporting effective catheter salvage at 5 mg/ml.^{12,24,25} Accordingly, this concentration was adopted in our protocol.

Methicillin resistance is a well-recognized predictor of poorer outcomes in CLABSI. Castagnola et al.¹³ reported that MRCoNS isolates required higher vancomycin minimum inhibition concentrations (MICs), with standard intravenous therapy achieving success in 75% of cases when the MIC was ≤1 mg/L, but in only 6% when the MIC was 2-4 mg/L; catheter salvage improved modestly with adjunctive vancomycin lock therapy at 3 mg/ml. Similarly, Buonsenso et al.,²⁶ in a systematic review, found lower success rates and higher recurrence in MR *Staphylococcus aureus* related CLABSI. We found higher success rate observed in MSCoNS CLABSI (100% vs. 53%) compared to MRCoNS CLABSI. While this trend is clinically relevant, our limited sample size may have restricted our ability to detect statistical significance.

Risk factor analysis identified younger age and repeated positive blood cultures as predictors of catheter loss aligning with other studies in literature.^{4,19,27} These findings likely reflect a combination of host and infection related factors, such as the immature immune response in younger children and the increased bacterial burden associated with persistent bacteremia, both of which may diminish the likelihood of successful catheter salvage. They underscore the importance of careful patient selection and vigilant monitoring, particularly

in younger children or in those who continue to have positive cultures during ALT.

Limitations

Our study has several limitations, including its retrospective design, small sample size, non-randomized selection of ALT agents, incomplete CRP data, and potential confounding from heterogeneous underlying conditions and catheter duration.

CONCLUSION

To the best of our knowledge this is the first pediatric study comparing outcomes of vancomycin vs teicoplanin lock therapy in CONS CLABSI. In conclusion, ALT achieved satisfactory catheter salvage rates in pediatric CoNS CLABSI, with similar outcomes for vancomycin and teicoplanin. Vancomycin or teicoplanin based ALT may be considered in selected children with CoNS CLABSI. Greater caution is warranted in younger patients, in those with persistent bacteraemia, and in cases caused by MRCoNS. Future prospective studies with larger sample sizes are needed to validate these risk factors, refine selection criteria, and optimize ALT protocols, including lock duration, concentration, and combination strategies.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Marmara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 07.04.2023, Decision No: 09.2023.621).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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