Mediterranean Journal of Hematology and Infectious Diseases

Original Article

Antibiotic Lock Therapy for Port Catheter-Related Infections of Children with Acute Leukemia

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Competing interests: The authors declare no conflict of Interest.

Abstract. ***Introduction:*** **Port catheters facilitate the administration of chemotherapy, antibiotics, blood products, fluid, and parenteral nutrition to pediatric patients with hematological malignancies. However, as its use has become widespread, local and systemic, catheter-related infections have emerged as important causes of morbidity and mortality. In our study, we aimed to evaluate the success of antibiotic lock therapy in port catheter-related infections of pediatric patients followed up with acute leukemia.**
Methods**: Port catheter cultures taken from a total of 182 pediatric patients with acute lymphoblastic/myeloblastic leukemia who were followed up at Ankara City Hospital Pediatric Hematology Clinic between August 2019 and August 2023 were evaluated retrospectively.**
Results**: Bacterial growth was identified in 739 port catheter culture specimens of 182 patients. Closure or removal of the port was required in 91, and removal of the port catheters in 49 patients due to port catheter-related infections. Antibiotic lock therapy was started in 56 patients with bacterial growth in the port catheter. With antibiotic lock therapy, port catheter-related infections of 42 patients were eradicated, and their catheters began to be used again. As a result, the port catheter-related infections of 42 of 56 (75%) patients whose ports were closed and also received systemic antibiotic therapy were eradicated, and no infection recurrence was observed.**
Conclusion**: Adding antibiotic lock therapy to systemic antibiotics in pediatric patients may be beneficial in terms of catheter salvage.**

Keywords: Leukemia; Port catheter; Antibiotic Lock therapy; Infection.

Citation: Kurtipek F.B., Yozgat A.K., Yüksek S.K., Kaçar D., Bayhan T., Gökçebay D.G., Parlakay A.Ö., Yaralı N. Antibiotic lock therapy for port catheter-related infections of children with acute leukemia . Mediterr J Hematol Infect Dis 2024, 16(1): e2024072, DOI: http://dx.doi.org/10.4084/MJHID.2024.072

Published: September 01, 2024 **Received: June 24, 2024** **Accepted: August 17, 2024**

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Introduction. Intravascular catheter-related bloodstream infections (CRBSI) are significant complications for leukemia patients with increased risk of morbidity and mortality, longer hospital stays, and higher costs.[1,2] *Coagulase-negative Staphylococci* (CoNS), *Staphylococcus aureus*, *Enterococcus spp., and Klebsiella spp.* are the most common pathogens responsible for CRBSI in children.[3] Microorganisms may be transmitted through the infected closure sites during catheter insertion or via hematological routes.[4] The risk of CRBSI is high in children receiving intensive chemotherapy and those carrying external or double-

lumen catheters.[5] Although catheter removal is preferred to prevent the development of CRBSI, catheter salvage may be attempted in patients whose alternative venous access is challenging to construct and who continue to need a catheter for infusions.

Antibiotic lock therapy (ALT) is a treatment method in which high concentrations of antibiotics are delivered through the lumen of the catheter.[2] Microorganisms can migrate into the intraluminal space, forming a pathogenic biofilm resulting in the onset of CRBSI. In ALT, the catheter lumen is filled with a high concentration of antibiotics to maximize bactericidal activity and penetrate the pathogenic biofilm. The antibiotic concentration required to destroy causative microorganisms in the catheter lumen should be 100-1000 times the minimum inhibitor concentration.[6] Re-catheterization complications and costs can be prevented with the use of ALT**.** However, the catheter should be removed if the systemic intravenous antibiotics and ALT are unable to destroy the microorganisms.[1,7]

Data concerning the efficacy and safety of ALT in children are limited. In this study, we aim to determine its effectiveness in children with leukemia and identify factors affecting treatment outcomes.

Methods. This retrospective study assessed 182 children with acute leukemia treated in the Ankara Bilkent City Hospital Pediatric Hematology Clinic between August 2019 and August 2023. The patient demographic and clinical characteristics, isolated microorganisms, and antibiotics used in lock therapies were examined. Duration, success or failure of ALT, catheter-related reinfections, catheter removal, and mortality data were collected from patients' electronic medical files.

In cases of febrile neutropenia (FN) (body temperature >37.5 ºC persisting for at least 2 hours or >38 ºC once), a blood sample was drawn from the peripheral vein and port catheter lumen for culture and empirical antimicrobial treatment was started. Systemic empiric antibiotic therapy was administered according to the Infectious Diseases Society of America (IDSA) guidelines that recommend the use of antipseudomonal broad-spectrum beta-lactamase antibiotics like piperacillin-tazobactam or cefepime.[8] After the causative microorganism was identified, the treatment might be modified if necessary. Glycopeptides were added to the treatment protocol in patients with severe mucositis, pneumonia, soft tissue infections, and methicillin-resistant *S. aureus* colonization.

Diagnosis of CRBSI was based on the updated 2009 version of IDSA Clinical and Practice guidelines for the diagnosis and management of intravascular catheter-related infections.[8] Accordingly, in cases where the same microorganism was detected in both the cultures of blood samples drawn from the catheter tip and peripheral blood if the microorganism was identified at least two hours earlier in the cultures of the blood samples drawn from the catheter, then the presence of CRBSI was considered. If nonpathogenic microorganisms of normal skin flora (CoNS, *S. viridans*, *Propionibacterium spp*., *Bacillus spp.*) were isolated from at least two blood cultures, it was accepted as CRBSI. The clinical signs of infection were noted simultaneously at the time when the blood culture samples were obtained.

Catheter removal was performed in catheter-related infections associated *with S. aureus, Pseudomonas spp., fungi, and mycobacteria*, all tunnel infections, complicated catheter-related infections, and severely septic patients. If the patient was clinically stable and the catheter removal was not required, ALT combined with systemic intravenous antibiotic therapy was used. In ALT, heparin (100 U/mL) with saline and vancomycin (5 mg/mL), gentamicin (1 mg/mL), amikacin (2 mg/mL), colistin (0.1 mg/mL) or trimethoprim-sulfamethoxazole (10 mg/mL) were used according to identified microorganisms.[8,9] The locking solution was introduced into the catheter lumen (usually 3 mL), and then the catheter was locked. This solution was renewed every 24 hours. Duration of ALT varied depending on the causative microorganisms as follows: *Enterococcus spp.*: 7-14 days; *CoNS*: 10s-14 days; gram-negative bacilli: 10-14 days.[8] Control catheter and peripheral blood cultures were taken after 72 hours of ALT.

Treatment failure was defined as persistent bacterial growth of the same microorganism in blood cultures obtained within 72 hours of ALT. If the same pathogen was isolated from the blood culture within three months, it was accepted as a relapse.[9] The catheter was removed if the fever persisted or a sterile blood culture could not be obtained. All patients were followed for at least six months after CRBSI was diagnosed.

This study was approved by the University of Health Sciences Ankara City Hospital Ethics Committee (ethics approval number: E2-23 -3816) and performed according to the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research involving Human Subjects and its latest amendments.

Statistical analysis. Statistical analyses were performed using SPSS for Windows 16. Categorical variables were expressed as numbers and percentages, and numerical variables were defined using mean ± standard deviation, minimum–maximum, and median values. Survival curves were estimated according to the Kaplan-Meier method. Adjusted hazard ratio and 95% confidence interval were used to estimate survival. The level of statistical significance was set at $p < 0.05$.

Results. The febrile neutropenia (FN) episodes of 182 children with acute leukemia were examined. Bacterial growth was detected in port catheter cultures in 91 FN episodes of 79 patients, including cases with acute

Table 1. Demographic and Clinical Characteristics of Patients with CRBSI

Characteristics	
Total number of patients	79
Age, mean (range), year	7 (1-17)
Gender	45M/34F
Acute lymphoblastic leukemia (n)	65
Acute myeloid leukemia (n)	14
WBC, mean± SD	924.6±1170.9/mm^3
ANC, mean± SD	410.2±745.7 /mm^3
CRBSI (n)	91
Antibiotic lock therapy (n, %)	56 (61%)
Therapeutic success rate (n, %)	42/56 (75%)
Catheter removal rate	14/56 (25%)
Relapse rate	1 (1.09%)
Mortality	7 (8%)

WBC: White blood cell, ANC: Absolute neutrophil count, CRBSI: Catheter-related bloodstream infection, ALT: Antibiotic lock therapy.

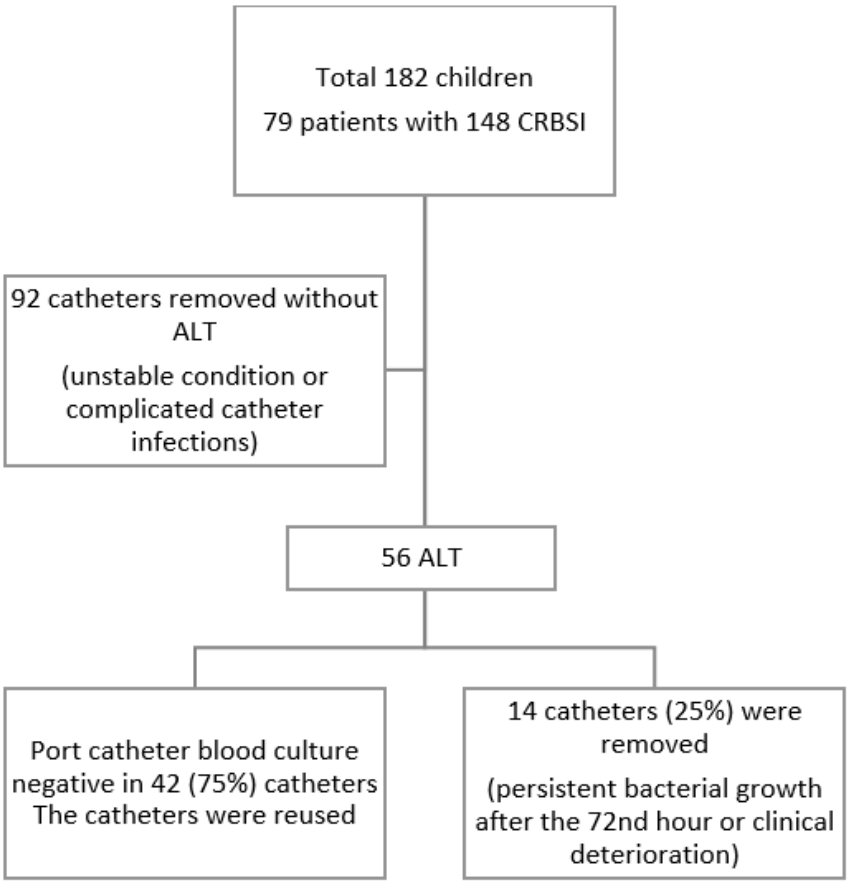

Figure 1. Algorithm of patients with catheter infection.

myeloid leukemia (AML) (n:14) and acute lymphoblastic leukemia (ALL) (n:65). Demographic and clinical characteristics of patients are summarized in **Table 1**. CRBSI was detected in 34 female and 45 male patients. The mean age of the patients with CRBSI was 6.8 years (min-max: 1- 17 years).

Patient management was individualized depending on the causative microorganism, the patient's clinical condition, and the catheter type. Ninety-two catheters of 35 patients (44.3%) were removed as soon as possible without using ALT due to the patient's unstable condition (hypotension, resistant fever, detection of fungal microorganisms) or the development of complicated catheter infections such as tunnel infection. The treatment algorithm for patients with catheter-related infections is summarized in **Figure 1**.

Microorganisms growing on the catheters are listed in **Table 2**. The most frequently isolated pathogens were

Table 2. The outcome of ALT therapy for CRBSI and related microorganisms.

Microorganisms identified in cases with CRBSI	Antibiotics used for ALT	ALT failure (n, %)
Staphylococci: 26	Vancomycin	11.5
S. epidermidis: 13		2 (15.3)
S. haemolyticus:7		-
S. hominis:3		-
S. aureus: 3		1 (33.3)
E. Coli: n:11	Amikacin, Gentamicin	4 (36.3)
Klebsiella pneumoniae, n:8	Amikacin, Gentamicin	4 (50)
Acinetobacter baumanii, n:3	Amikacin	2 (66.6)
Enterobacter, n:2	Gentamicin, Colistin	1 (50)
Enterococci, n: 1	Vancomycin	-
Achromobacter xylosoxidans, n:1	Amikacin	-
Pseudomonas aeroginosa, n:1	Amikacin	-
S. sanguis, n:1	Vancomycin	-
Chrysobacterim indologenese, n:1	TMP-SMX	-
Raoultella ornithinolytica , n:1	Amikacin	-

CRBSI, Central line -related bloodstream infection; ALT, Antibiotic Lock Therapy.

Staphylococci (46%), *E. coli* (19.6 %), and *Klebsiella spp*. (14.2 %). ALT was started against 56 catheter-related infections. Microorganisms growing in the catheter cultures are listed in **Table 2**. Upon identification of gram-positive bacteria in 28 and gram-negative bacteria in 28 catheters, vancomycin (n:28), amikacin (n:21), gentamicin (n:5), colistin (n:1), TMP-SMX (n:1) were used in the respective patients for the treatment of ALT. All patients also received appropriate systemic intravenous antibiotics together with ALT.

Fourteen catheters (25%) were removed due to persistent bacterial growth after the 72nd hour of ALT or clinical deterioration of the patients while receiving ALT. A number of patients, indicated in bracket, infected with *K. pneumonia* (n:5), *Staphylococcus spp* (n:3), *and P. aeruginosa* (n:2), *Achromobacter spp*. (n:1), *E. coli* (n:1) required intensive care treatment due to hemodynamic instability. Seven of these patients died due to sepsis. Antibiotic lock treatment was applied to one patient in whom pseudomonas growth was detected in the catheter, and the port catheter was removed directly because the other patient had clinical instability. Port catheter blood culture became negative in 42 (75%) patients treated with ALT, and these catheters were reused. Recurrent infection with *S. epidermidis* was observed in one (1.7 %) patient. As a result, the therapeutic success rate of ALT was 75 percent. The outcomes of CRBSI and identified microorganisms are shown in **Table 2**. ALT was successful in the treatment of CoNS infections but failed in the treatment of infections caused by *Acinetobacter spp*.

Discussion. Antibiotic lock therapy has been described in the prevention of CRBSI, and treatment guidelines to sterilize the catheter lumen so as to prevent its removal have been stated.[10] However, a limited number of studies have investigated the efficacy and safety of ALT' in children with leukemia.[11] In most guidelines, eradication of CRBSI that persists despite 72 hours of appropriate antimicrobial therapy, infections with *S. aureus*, *P. aeruginosa*, fungi, or mycobacteria, and tunnel infections, port abscesses has been recommended. Salvage of the catheter is essential in many children who need continuous intravenous chemotherapies, antibiotics, and fluids and for whom it is difficult to create a new peripheral venous access. However, guidelines specify that for children affected with CRBSI under “unusual extenuating circumstances," the attempt to salvage the CVC is allowed. Therefore, the decision to salvage the catheter must be assessed on a case-by-case basis.[8] There are also reports of successful antibiotic lock therapy in cases of CRBSI caused by the pathogens mentioned above.[1,13] In our study, we also obtained successful results with antibiotic lock therapy in infections caused by S. *aureus, Pseudomonas aeruginosa,* and *Acinetobacter baumanii.*

In our study, CoNS, *E. coli*, and *Klebsiella spp*. were the most frequently isolated pathogens. Gram-positive and gram-negative microorganisms were identified in equal percentages (50%) of patients receiving ALT. *S. epidermidis* and other CoNSs were reported as the most common causative microorganisms in CRBSI due to skin contamination during catheter manipulations.[1,2,9,14]

In a meta-analysis involving adult and pediatric patients with CRBSI, coadministration of systemic antibiotic therapy and ALT achieved better outcomes than single systemic antibiotic therapy.[15] Catheter removal rate was higher (33%) in patients receiving the

sole systemic antibiotic therapy than in those treated with sole ALT (10%) and the recurrence rates in patients in the ALT group were significantly lower than those in the non-ALT group (30% vs 20%).[15] In a pediatric study, Kara et al. reported CoNS as the most common organism, and the therapeutic success rate of the ALT was 81 percent.[16] In Lafaurie et al. prospective adult study, continuous vancomycin lock therapy was administered for 88 patients and intermittent vancomycin lock therapy for 9 patients due to coagulase-negative staphylococci infection. This therapy was successful in 44 patients. They recommended that continuous lock therapy should be preferred to intermittent therapy because of recurring infection risk.[17] In the Okur et al. study, teicoplanin lock therapy was administered for port-related Coagulase-negative Staphylococci in pediatric oncology patients, and the overall port survival rate was found to be 72.7%. The author suggested that this therapy is effective and safe for catheter-related infections caused by methicillin-resistant coagulase-negative staphylococcus.[18]

In our study, 42 of 56 catheters of patients who received ALT were reused, and our ALT success rate was 75 percent. ALT might be given without systemic antibiotics for patients with multiple positive catheter blood cultures demonstrating the growth of CoNS and concurrent negative peripheral blood cultures.[19] ALT was used with systemic antibiotics in our patients with CoNS infection. The therapeutic success rate of ALT was 70% for CoNS infection; however, for gram-negative infections, the ALT was successful in 57 of the cases. In a retrospective pediatric study, 37 febrile attacks in 28 patients were examined. Gram-negative bacilli were determined to be the most common causative agent, and the therapeutic success rate of ALT was 67.6 percent. [20] In that study conducted by Signorino et al., the most common causative gram-negative agent was *K. pneumoniae* (n:6), and 3 catheters infected with this agent were saved. In our study, the most frequently detected gram-negative pathogen was *E. coli* (n:11), and we successfully eradicated *E. coli* from 7 contaminated catheters with ALT.

In our study, the catheter removal rate was 53 percent. In a pediatric study, Adler et al. reported that catheters were removed in 46% of their patients during 207 CRBSI episodes.[3] Another study reported that removal of the catheters was necessitated in 56.4% of CRBSI episodes.[12] The mortality rate has been reported to range from 1.9% to 11% in children with CRBSI.[2,21,22] In our study, the mortality rate was 7.6 percent.

Our study's limitations were its retrospective nature and small sample size. However, the most powerful aspect of this study is that we included only pediatric patients with hematological malignancies to ensure the homogeneity of the patient population.

Conclusions. CRBSI is a significant cause of morbidity and mortality in pediatric patients with acute leukemia. ALT is a safe strategy and helps prevent unnecessary catheter removals when administered with systemic therapy in pediatric patients with acute leukemia. Multi-center randomized controlled trials are required to support the available data.

References:

1. Wolf J, Allison KJ, Tang L, Sun Y, Hayden RT, Flynn PM: No evidence of benefit from antibiotic lock therapy in pediatric oncology patients with central line-related bloodstream infection: results of a retrospective matched cohort study and review of the literature. Pediatric blood & cancer 2014, 61(10):1811-1815. https://doi.org/10.1002/pbc.25101 PMid:24923808
2. Adler A, Yaniv I, Solter E, Freud E, Samra Z, Stein J, Fisher S, Levy I: Catheter-associated bloodstream infections in pediatric hematology-oncology patients: factors associated with catheter removal and recurrence. Journal of pediatric hematology/oncology 2006, 28(1):23-28.
3. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, Kallen A, Limbago B, Fridkin S: Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infection control and hospital epidemiology 2013, 34(1):1-14. https://doi.org/10.1086/668770 PMid:23221186
4. Flynn PM: Diagnosis and management of central venous catheter-related bloodstream infections in pediatric patients. The Pediatric Infectious Disease Journal 2009, 28(11):1016-1017. https://doi.org/10.1097/INF.0b013e3181bf7bfc PMid:19859018
5. Yacobovich J, Ben-Ami T, Abdalla T, Tamary H, Goldstein G, Weintraub M, Yaniv I, Toren A, Kenet G, Revel-Vilk S: Patient and central venous catheter related risk factors for blood stream infections in children receiving chemotherapy. Pediatric blood & cancer 2015, 62(3):471-476. https://doi.org/10.1002/pbc.25281 PMid:25327811
6. Ceri H, Olson ME, Stremick C, Read RR, Morck D, Buret A: The Calgary Biofilm Device: new technology for rapid determination of antibiotic susceptibilities of bacterial biofilms. Journal of clinical microbiology 1999, 37(6):1771-1776. https://doi.org/10.1128/JCM.37.6.1771-1776.1999 PMid:10325322 PMCid:PMC84946
7. De Sio L, Jenkner A, Milano GM, Ilari I, Fidani P, Castellano A, Gareri R, Donfrancesco A: Antibiotic lock with vancomycin and urokinase can successfully treat colonized central venous catheters in pediatric cancer patients. The Pediatric Infectious Disease Journal 2004, 23(10):963-965. https://doi.org/10.1097/01.inf.0000141740.82420.e6 PMid:15602201
8. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad, II, Rijnders BJ, Sherertz RJ, Warren DK: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 2009, 49(1):1-45. https://doi.org/10.1086/599376 PMid:19489710 PMCid:PMC4039170
9. Tsai HC, Huang LM, Chang LY, Lee PI, Chen JM, Shao PL, Hsueh PR, Sheng WH, Chang YC, Lu CY: Central venous catheter-associated bloodstream infections in pediatric hematology-oncology patients and effectiveness of antimicrobial lock therapy. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi 2015, 48(6):639-646. https://doi.org/10.1016/j.jmii.2014.07.008 PMid:25311403
10. Justo JA, Bookstaver PB: Antibiotic lock therapy: review of technique and logistical challenges. Infection and drug resistance 2014, 7:343-363. https://doi.org/10.2147/IDR.S51388

PMid:25548523 PMCid:PMC4271721
11. Castagnola E, Ginocchio F: Rescue therapy of difficult-to-treat indwelling central venous catheter-related bacteremias in cancer patients: a review for practical purposes. Expert review of anti-infective therapy 2013, 11(2):179-186.
https://doi.org/10.1586/eri.12.160
PMid:23409823
12. Ford WJH, Bundy DG, Oyeku S, Heo M, Saiman L, Rosenberg RE, DeLaMora P, Rabin B, Zachariah P, Mirhaji P et al: Central Venous Catheter Salvage in Ambulatory Central Line-Associated Bloodstream Infections. Pediatrics 2021, 148(6).
https://doi.org/10.1542/peds.2020-042069
PMid:34814175
13. Buonsenso D, Salerno G, Sodero G, Mariani F, Pisapia L, Gelormini C, Di Nardo M, Valentini P, Scoppettuolo G, Biasucci DG: Catheter salvage strategies in children with central venous catheter-related or -associated bloodstream infections: a systematic review and meta-analysis. The Journal of Hospital Infection 2022, 125:1-20.
https://doi.org/10.1016/j.jhin.2022.03.010
PMid:35390396
14. Celebi S, Sezgin ME, Cakır D, Baytan B, Demirkaya M, Sevinir B, Bozdemir SE, Gunes AM, Hacimustafaoglu M: Catheter-associated bloodstream infections in pediatric hematology-oncology patients. Pediatr Hematol Oncol 2013, 30(3):187-194.
https://doi.org/10.3109/08880018.2013.772683
PMid:23458064
15. O'Horo JC, Silva GL, Safdar N: Anti-infective locks for treatment of central line-associated bloodstream infection: a systematic review and meta-analysis. American journal of nephrology 2011, 34(5):415-422.
https://doi.org/10.1159/000331262
PMid:21934302
16. Kara TT, Özdemir H, Erat T, Yahşi A, Aysev AD, Taçyıldız N, Ünal E, İleri T, İnce E, Haskoloğlu Ş et al: Is antibiotic lock therapy effective for the implantable longterm catheter-related bloodstream infections in children? The Turkish journal of pediatrics 2019, 61(6):895-904.
https://doi.org/10.24953/turkjped.2019.06.011
PMid:32134584
17. Lafaurie M, Montlahuc C, Kerneis S, de Lastours V, Abgrall S, Manceron V, Couzigou C, Chabrol A, de Raigniac A, Lescure X, Longuet P, Lesprit P, Vanjak D, Lepeule R; Groupe des référents en Infectiologie d'Ile de France (GRIF). Efficacy of vancomycin lock therapy for totally implantable venous access port-related infection due to coagulase-negative staphylococci in 100 patients with cancer. J Antimicrob Chemother. 2023 May 3;78(5):1253-1258.
https://doi.org/10.1093/jac/dkad083
PMid:37014800
18. Okur Acar, Sultan MD*; Tahta, Neryal MD*; Böncüoğlu, Elif MD†; Odaman Al, Işik MD*; Kiymet, Elif MD†; Gözmen, Salih MD*; Demirağ, Bengü MD*; Karapinar, Tuba H. MD*; Oymak, Yeşim MD*; Vergin, Canan MD*; Devrim, İlker MD†. Efficacy of Teicoplanin Lock Therapy in the Treatment of Port-related Coagulase-negative Staphylococci Bacteremia in Pediatric Oncology Patients. Journal of Pediatric Hematology/Oncology 45(1):p e17-e20, January 2023.
https://doi.org/10.1097/MPH.0000000000002502
PMid:35700426
19. Tural Kara T, Erat T, Yahşi A, Özdemir H, İleri T, İnce E, Taçyıldız N, Ünal E, Çiftçi E, İnce E: Bloodstream infections in pediatric hematology/oncology patients: Six years' experience of a single center in Turkey. Turkish journal of medical sciences 2019, 49(4):1157-1164.
https://doi.org/10.3906/sag-1812-101
PMid:31342734 PMCid:PMC7018311
20. Signorino C, Fusco E, Galli L, Chiappini E: Effectiveness of Antimicrobial Lock Therapy for the Treatment of Catheter-Related and Central-Line-Associated Bloodstream Infections in Children: A Single Center Retrospective Study. Antibiotics (Basel, Switzerland) 2023, 12(5).
https://doi.org/10.3390/antibiotics12050800
PMid:37237703 PMCid:PMC10215690
21. Eggimann P, Pittet D: Overview of catheter-related infections with special emphasis on prevention based on educational programs. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 2002, 8(5):295-309.
https://doi.org/10.1046/j.1469-0691.2002.00467.x
PMid:12047407
22. van de Wetering MD, Poole J, Friedland I, Caron HN: Bacteraemia in a paediatric oncology unit in South Africa. Medical and pediatric oncology 2001, 37(6):525-531.
https://doi.org/10.1002/mpo.1246
PMid:11745891