Clinical profile and outcome of antibiotic lock therapy for bloodstream infections in pediatric hematology/oncology patients in a tertiary care hospital, Karachi, Pakistan

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Background: Intravascular catheters are susceptible to infections, thus requiring catheter removal and leading to increased morbidity and costs. Antibiotic lock therapy (ALT) is a therapeutic technique that is used to salvage the catheter. The aim of this study was to evaluate the outcome of antibiotic lock therapy in bloodstream infections in pediatric hematology/oncology patients in a tertiary care hospital, Karachi. Methods: A retrospective review was performed from January 2013 to December 2017 of pediatric hematology/oncology patients with bloodstream infections and who received ALT at Aga Khan University Hospital. All cases of polymicrobial infections, catheter removal, or malfunction before the completion of ALT were excluded. Descriptive analysis was carried out using SPSS version 20.

Results: A total of nine hematology/oncology patients were eligible. The catheter was salvaged in 7/9 (77.8%) children, and in 2/9 (22.2%) cases, catheter was removed because of persistent bacteremia. The most common organism isolated was Staphylococcus non-aureus species (33.3%). Relapse with a similar pathogen occurred in 2 (22.2%) patients and 2 (22.2%) of them developed an exit-site infection.

Conclusion: In our experience, in almost two thirds of the cases, the catheter was salvaged, but disappointingly, relapses were high when the infection was due to Staphylococcus spp. Although this is a small study, our results show that ALT can be a potential safe adjunctive strategy to treat catheter-related bloodstream infections (CRBSI). However, we need larger prospective studies to test the safety and efficacy of ALT to develop specific ALT recommendations and guidelines particularly in children.

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expressed as mean ± SD or median (IQR) days of ALT was 4.0 (7.0) days. The median (range) dwell time was 48 h (24 h). The

2. Methods

A retrospective study was conducted from January 2013 to December 2017 in the department of pediatrics and child health. All hematology and oncology patients of age >1 year and either gender with bloodstream infections and having received ALT were included. Children with polymicrobial infections whereby the catheter was removed before the completion of ALT were excluded. Data were collected on participants’ demographics, medical history, primary diagnosis, treatment, laboratory parameters, and outcome of ALT on a structured proforma. All the individuals were followed up for a period of 1 month after the completion of ALT to assess the relapse rates. Descriptive analysis was carried out using SPSS version 20. Data were expressed as frequency and percentage for categorical variables such as gender, primary diagnosis, antibiotic used for lock therapy, pathogen isolated, relapse, persistent bacteremia, and mortality. For quantitative variables such as age, days, dose and volume of ALT, and length of hospital stay, data were expressed as mean ± SD or median ± interquartile range depending on data distribution. The chi-square test was used for comparing qualitative variables, and the t-test was used for comparing quantitative variables.

3. Results

A total of 9 hematology/oncology children fulfilled the eligibility criteria during the study period. The median (range) age was 5.0 (1.0–15.0) years. The majority of the patients, i.e., 5/9 (55.6%), were male. The most common underlying diagnosis was pre-B–cell acute lymphoblastic leukemia (Pre-B-ALL) in 4/9 (44.4%) children. Port-a-catheter was placed in 6/9 (66.3%) children who received ALT for bacteremia. Vancomycin was used in 7/9 (77.8%) children for ALT. All patients, i.e., 9/9 (100%), received systemic antibiotics along with ALT. The most common pathogen isolated was \( \text{Staphylococcus non-aureus} \) in 3/9 (33.3%) cases followed by each case, i.e., 1/9 (11.1%), of \( S. \) aureus, \( S. \) saprophyticus, \( Brevibacterium \) spp., \( Pseudomonas \) aeruginosa, \( Brevibacterium \) and \( Bacillus \). Persistent bacteremia was observed in 2/9 (22.2%) patients, and in 2/9 (22.2%) cases, exit site infection was present. Out of 9 children, 2 (22.2%) had a relapse, and in the remaining 7 (77.8%) children, a catheter was salvaged. None of the patients had a metastatic infection or septic shock. All of them survived (Table 2).

4. Discussion

In the current review, two thirds of the catheters were salvaged with the use of ALT. One fifth of the patients developed persistent bacteremia requiring removal of the catheter. Cases of catheter salvage included \( S. \) aureus as well as \( P. \) aeruginosa for which the current IDSA guidelines recommend removal. These results are comparable with those reported in previous studies conducted in Children’s Hospital of Michigan/Wayne State University, in a larger randomized, blinded, multicenter trial from Belgium and from studies conducted in India [12–15]. We observed that the most common pathogen isolated in our study was \( \text{Staphylococcus non-aureus} \). Further identification of the species was not reported. This is the most common pathogen of bacteremia and reinfection related to central venous carriage (CVC) in studies conducted in other countries as well. This trend is probably because the major microbial flora of the skin comprises staphylococci [16–18]. The organisms present in the skin migrate from the insertion site into the cutaneous catheter tract, thereby resulting in colonization of the tip of the catheter and formation of biofilms [17,19,20]. In several studies, the outcome of ALT is generally better in the less virulent organisms (coagulase-negative staphylococci and enterococci) than the gram-negative organisms and yeast [21]. In our study, the catheter was salvaged with ALT in patients infected with \( P. \) aeruginosa.
In a recent study, we observed that the catheter was removed in one of the two severely neutropenic patients and the type of catheter was peripherally inserted central catheter (PICC). Our study showed a high relapse rate of 28.6% compared to those reported in other studies, where the rates were 6.08% and 14.28% [14,22]. An attributing factor could be that one of the two patients had a *S. aureus* infection, for which IDSA guidelines do not recommend ALT. Hence, if we can recognize the risks of undesirable outcomes and eliminate them, then we might be able to further increase the catheter salvage rate.

There was no complication or death noted in the present study despite this being an immunocompromised population. None of the patients developed septic shock or metastatic infection. In a study conducted by Poole, C.V. et al., the rate of serious complications in ALT used for dialysis-catheter-related bacteremia was 7.3% [23].

To the best of our knowledge, this is the first study reporting the outcome of ALT in Pakistan. However, the small sample and retrospective single-centered nature of our study are the major limitations. Therefore, there is a need for sufficiently powered studies to conclusively demonstrate the role of ALT in CRBSI in children as well as in adults.

### 5. Conclusion

In our experience, in almost two thirds of the cases, the catheter was salvaged, but disappointingly, relapse rates were high when the infection was due to *Staphylococcus* spp. Although this is a small study, our results show that ALT can be a potential safe adjunctive/alternative strategy to treat CRBSI. However, we need larger prospective studies conducted in multiple tertiary healthcare centers to test the safety and efficacy of ALT to develop specific ALT recommendations and guidelines particularly in children.

### Conflict of interest

All the authors declare that we have no conflict of interest, whether financial or otherwise.

### Table 2

| No. | Age/sex | Organism isolated          | Type of catheter | ANC (mm³) | Name of ALT | Dose of ALT (mg) | Dwell time (hours) | No. of ALT doses | Days of ALT | Persistent bacteremia | Catheter salvage | Relapse |
|-----|---------|-----------------------------|------------------|-----------|-------------|-----------------|-------------------|------------------|-------------|----------------------|------------------|---------|
| 1   | 5 yr/M  | *Pseudomonas aeruginosa*    | Port-a-catheter  | 1915      | Ciprofloxacin | 0.6             | 48                | 5                | 10          | No                   | Yes              | No      |
| 2   | 5 yr/F  | *Staphylococcus aureus*     | Port-a-catheter  | 2869      | Cloxacillin  | 300.0           | 48                | 4                | 8           | No                   | Yes              | Yes     |
| 3   | 2 yr/F  | *Staphylococcus non-aureus* | Port-a-catheter  | 3542      | Vancomycin  | 7.5             | 24                | 1                | 1           | No                   | Yes              | No      |
| 4   | 7 yr/M  | *Staphylococcus non-aureus* | PICC line        | 5464      | Vancomycin  | 7.5             | 48                | 1                | 1           | No                   | Yes              | No      |
| 5   | 2 yr/M  | *Staphylococcus saprophyticus* | Port-a-catheter   | 1890      | Vancomycin  | 7.5             | 48                | 4                | 8           | No                   | Yes              | Yes     |
| 6   | 1 yr/M  | *Enterococcus species*      | Port-a-catheter  | 7724      | Vancomycin  | 7.5             | 48                | 2                | 4           | No                   | Yes              | No      |
| 7   | 4 yr/F  | *Brevibacterium*            | Port-a-catheter  | 539       | Vancomycin  | 7.5             | 48                | 3                | 7           | No                   | Yes              | No      |
| 8   | 12 yr/M | *Staphylococcus non-aureus* | PICC line        | 3060      | Vancomycin  | 5.0             | 24                | 3                | 3           | Yes                  | No               | No      |
| 9   | 15 yr/M | *Bacillus*                  | PICC line        | 245       | Vancomycin  | 5.0             | 24                | 1                | 1           | Yes                  | No               | No      |

### Declaration of interest

None.

### Ethical statement

The study was exempted from Ethical Review Committee of The Aga Khan University Hospital (ERC Ref # 5278-Ped-ERC-18). There are no identifiers of the participants in the manuscript.

### Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Acknowledgments

We would like to acknowledge Miss Ale Zehra, pharmacist at Aga Khan University hospital for providing us the data of children who received antibiotic lock therapy.

### References

[1] Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 2006;81(9):1159–71.

[2] Hord JD, Lawlor J, Werner E, Billett AL, Bundy DG, Winkle C, et al. Central line associated blood stream infections in pediatric hematology/oncology patients with different types of central lines. Pediatr Blood Canc 2016;63(9):1603–7.

[3] Thomas D, Parameswaran N, Harish BN. Catheter related blood stream infections in the paediatric intensive care unit: a descriptive study. Indian J Crit Care Med 2013;17(3):135–9.

[4] Advasi S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. Clin Infect Dis : Off Publ Infect Dis Soc America 2011;52(9):1108–15.

[5] Kleven RM, Edwards JR, Richards Jr CL, Horan TC, Gaynes RP, Pollock DA, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Publ Health Rep 2007;122(2):156–60.

[6] O’Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49(1):1–45.

[7] Justo JA, Bookstaver PB. Antibiotic lock therapy: review of technique and logistical challenges. Infect Drug Resist 2014;7:343–63.
[9] Carratalà J. The antibiotic-lock technique for therapy of ‘highly needed’ infected catheters. Clin Microbiol Infect 2002;8(5):282–9.
[10] Forrín J, Grill F, Martín-Díavila P, Blázquez J, Tato M, Sánchez-Corral J, et al. Treatment of long-term intravascular catheter-related bacteraemia with antibiotic-lock therapy. J Antimicrob Chemother 2006;58(4):816–21.
[11] Krzywda EA, András DA, Edmiston Jr CE, Quebbeman EJ. Treatment of Hickman catheter sepsis using antibiotic lock technique. Infect Control Hosp Epidemiol 1995;16(10):596–8.
[12] Onland W, Shin CE, Fustar S, Rushing T, Wong WY. Ethanol-lock technique for persistent bacteremia of long-term intravascular devices in pediatric patients. Arch Pediatr Adolesc Med 2006;160(10):1049–53.
[13] Valentine KM. Ethanol lock therapy for catheter-associated blood stream infections in a pediatric intensive care unit. Pediatr Crit Care Med 2011;12(6):e292–6.
[14] Rijnders BJ, Van Wijngaerden E, Vandecasteele SJ, Stas M, Peetermans WE. Treatment of long-term intravascular catheter-related bacteraemia with antibiotic lock: randomized, placebo-controlled trial. J Antimicrob Chemother 2005;55(1):90–4.
[15] Soman R, Gupta N, Suthar M, Kothari J, Almeida A, Shetty A, et al. Antibiotic lock therapy in the era of gram-negative resistance. J Assoc Phys India 2016;64(2):32–7.
[16] Miliaraki M, Katzikakis N, Chranioti I, Stratigaki M, Koutsaki M, Psarrou M, et al. Central line-associated bloodstream infections in childhood malignancies. In: Single-Center Experience; 2017.
[17] Cecinati V, Brescia I, Tagliaferri L, Giordano P, Esposito S. Catheter-related infections in pediatric patients with cancer. Eur J Clin Microbiol Infect Dis 2012;31(11):2869–77.
[18] Katsibardi K, Papadakis V, Charisiadou A, Pangalis A, Polychronopoulou S. Blood stream infections through the entire course of acute lymphoblastic leukemia treatment. Neoplasma 2011;58(4):326–30.
[19] De Sio L, Jenkner A, Milano GM, Ilari I, Fidani P, Castellano A, et al. Antibiotic lock with vancomycin and urokinase can successfully treat colonized central venous catheters in pediatric cancer patients. Pediatr Infect Dis J 2004;23(10):963–5.
[20] Oda K, Matsuo Y, Nagai K, Tsumura N, Sakata Y, Kato H. Sepsis in children. Pediatr Int 2000;42(5):528–33.
[21] Bailey E, Berry N, Cheesbrough JS. Antimicrobial lock therapy for catheter-related bacteraemia among patients on maintenance haemodialysis. J Antimicrob Chemother 2002;50(4):615–7.
[22] Fernandez-Hidalgo N, Almirante B, Calleja R, Ruiz I, Planes AM, Rodriguez D, et al. Antibiotic-lock therapy for long-term intravascular catheter-related bacteraemia: results of an open, non-comparative study. J Antimicrob Chemother 2006;57(6):1172–80.
[23] Poole CV, Carlton D, Bimbo L, Allon M. Treatment of catheter-related bacteremia with an antibiotic lock protocol: effect of bacterial pathogen. Nephrol Dial Transplant 2004;19(5):1237–44.