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Letter to the editor

Antibiotic Lock Therapy (ALT) for the prevention of Catheter Related Blood Stream Infection (CRBSI) in neurological patients treated with Therapeutic Plasma Exchange (TPE)

Dear Editor.

Neurological disorders frequently require therapeutic plasma exchange (TPE) treatment and non-tunneled temporary catheter insertion [1,2]. Catheter-related bloodstream infection (CRBSI) is a well-known complication for chronic hemodialysis (HD) catheters that account for approximately 30- 40 % of cases [1]. On the other hand, patients receiving TPE experienced a high incidence of infectious complications (reached 48 % in ICU, mainly pneumonia) in a median time of 5 days after the TPE initiation [3]. Surprisingly, CRBSI was only reported in 5-10 % of patients receiving TPE [2,3].

In our two University Hospitals from 2021 to 2022, we found a high incidence of CRBSI (approximately 70- 90 % of patients) in neurologic patients who received TPE with or without concomitant immunosuppressive drugs. CRSBI was noticed in a median time of 3 to 6 days after receiving two to three sessions of TPE. This complication was associated with prolonged hospital stays, worse outcomes, and higher morbidity rates, however, no mortality was reported. Also, CRBSI was followed by high medical care costs including intravenous (IV) antibiotic treatment, blood and catheter cultures, catheter exchanges, and monitoring the inflammatory tests such as C-reactive protein until patient recovery. The medical literature defined several etiologies that are implicated in catheter-related infection (CRI). Most often, infection results from contamination of the catheter connectors, catheter lumens, and infused solutions during TPE sessions [1]. CRBSI and exit-site infections may also result from the migration of organisms through the puncture site from the skin flora and colonization of the outer catheter surface, sutures, or rarely from other remote sites during bacteremia [1]. Indeed, infections related to TPE could also result from decreased circulating immunoglobulins and complement proteins, in addition to concomitant immunosuppressive drug regimens [3]. Non-tunneled and femoral temporary catheters that were used during the TPE also increased the risk of CRI [1,3].

In our condition, we believed that the main reasons for CRI were non-compliance with disinfection and hygiene procedures from the nurse staff and patients. Also, the femoral insertion is the main site that was preferred by neurological patients, which also increased CRI. On the other hand, CRBSI was otherwise rarely reported in nephrological patients receiving TPE. This might result from more catheter care approaches or prescribing trimethoprim/sulfamethoxazole prophylaxis in the context of immunosuppressions that were applied by nephrologists.

So, several approaches were introduced to reduce the incidence of CRBSI in patients receiving TPE. Firstly, the internal jugular vein was used as the main insertion site unless the patients preferred the femoral site. Secondly, restricted disinfection protocols were reconfirmed by retraining and observing the nurse staff and also followed by daily disinfection procedures by residents in each department.

The main approach was the use of antibiotic lock therapy (ALT), definitely amikacin or vancomycin, which was introduced for all patients receiving TPE despite the admission department. In this practice, we used amikacin at a dose of 25- 50 mg/mL and vancomycin at a dose of 5- 20 mg/mL, which were both mixed with heparin after each TPE session. The amikacin ampule is available at doses of 100 mg and 500 mg per ampule, which costs 3700 and 5400 Syrian pounds per ampule; respectively. Meanwhile, the vancomycin vial is available in 0.5 g and 1 g per vail, which costs 35 and 70 thousand Syrian pounds per vial; respectively. Since the vancomycin vial could be used within 48 h of mixation with cold preservation, the single vial was used for 2 consecutive TPE sessions. When the patient received a median of 5 TPE sessions during 10 days, this needed 5 amikacin ampules (cost between 18 to 27 thousand Syrian pounds) or 3 vancomycin vails (cost between 105 to 210 thousand Syrian pounds).

These approaches reduced the incidence of CRBSI to less than 1–2 % in the following two years. Additionally, this also significantly reduced medical care costs by preventing the incidence of CRBSI, which -if happened- needs a minimum of two weeks of IV broad-spectrum antibiotic therapy in addition to cultures, catheter exchange, and monitoring tests. In this regard, if we use an empirical antibiotic therapy by meropenem (1 g/ 3 times daily; costs 70 thousand Syrian pounds per vial) and vancomycin (1 g/ once daily; costs 70 thousand Syrian pounds per vial), the costs of 14 days CRBSI treatment would cost 2.94 million Syrian pounds for meropenem and 980 thousand Syrian pounds for vancomycin.

IDSA guidelines 2022 recommended ALT for preventing long-term central venous catheters (CVCs) only in patients with high risk for CRBSI, defined by a history of recurrent CRBSI or recently implanted intravascular devices [4]. The concern was regarding the potential risk for increased resistance in exposed organisms to ALT [4]. In our experience, the ALT did not increase the susceptibility to resistance infections. This could be explained by the short-term ALT application in TPE catheters (maximum 10- 14 days); however, this approach could be concerning if applied in long-term CVCs.

Several studies have been performed to evaluate the efficacy of ALT for the prevention of CRI, and almost 10 meta-analyses have concluded that ALT substantially reduced CRI [5]. In a New Zealand survey from 2011 to 2015, inpatient costs were significantly higher several times in isolated heparin lock (due to higher incidence of CRBSI) compared with gentamycin lock mixed with heparin or citrate [6]. Also, the annual cost of caring for patients with CRI ranges from $296 million to $2.3 billion

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[7].

Another recommended approach is to infuse IV immunoglobulin (IVIG) at a dose of 100–400 mg/kg post-TPE in cases of severe infections following TPE initiation or in aggressive TPE if serum IgG levels reduced to less than 500 mg/dL [1].

KIDOQI 2006 guidelines recommended that non-tunneled temporary catheters for use in dialysis are not acceptable beyond one week, and femoral catheters should be placed no more than 5 days [1]. In these situations, the recommendations mandate the replacement of non-tunneled catheters with tunneled or cuffed catheters, which are associated with less incidence of CRI [1]. On the contrary, a non-tunneled catheter is generally an accepted option for short-term TPE sessions, and there is no recommendation to place a tunneled catheter [1].

In our opinion, it is not reasonable to insert a tunneled catheter for TPE in an attempt to reduce CRI due to the high costs and short-term sessions. Also, IgG monitoring after each TPE session and IVIG infusion is not practical to use for TPE patients, especially in developing countries, which further increases the costs and adverse reactions that are known in IVIG infusions.

In summary, CRBSI is associated with several debilitating consequences for patients and medical institutions, including increased hospital stays, morbidity, and medical care costs. The ALT shows a great benefit in reducing medical costs that introduced after the incidence of CRI and if compared with preventive IVIG infusion or tunneled catheter insertion, especially in developing countries. So, ALT should be considered an acceptable and reasonable approach for patients receiving TPE to prevent and reduce CRBSI and further reduce its following consequences.

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Marwa Kliea: Writing – original draft, Validation, Data curation. **Qussai Hassan:** Writing – review & editing, Visualization, Validation, Supervision. **Mohammad Alsultan:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Data curation.

Declaration of Competing Interest

The author declares that they have no conflicts of interest regarding this study.

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Authors' contribution

Mohammad Alsultan and Marwa Kliea: wrote the letter, literature search, submitted the article, and patient follow-up. Qussai Hassan; corrected the manuscript and supervisor.

Consent for publication

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Mohammad Alsultan [*,1]
Internal Medicine Department, Nephrology, Damascus University, Faculty of Medicine, Damascus, Syria

Marwa Kliea
Internal Medicine Department, Neurology, Damascus University, Faculty of Medicine, Damascus, Syria
E-mail address: marwakl96@gmail.com.

Qussai Hassan
Internal Medicine Department, Nephrology, Damascus University, Faculty of Medicine, Damascus, Syria
E-mail addresses: qussai.hassan@damascusuniversity.edu.sy, Abo_joseph2003@yahoo.fr.

[*] Correspondence to: Internal Medicine Department, Nephrology, Damascus University, Faculty of Medicine, Omar Ibn Abdulaziz Street, Al Mezzeh, Damascus, Syria.
E-mail addresses: mohalsultaan@gmail.com, mohammad.alsultaan93@damascusuniversity.edu.sy (M. Alsultan).

[1] ORCID; https://orcid.org/0000–0001-9113–5338