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Review

Nurses best practices for the management of thrombotic thrombocytopenic purpura

Pamela Harmon[a,*], Eduard Cojocari[a], Catherine Lynn Mader[b], Charlene Galloway[b], Megan Buchholz[c], Brenda Lewis[d], Susan Sinclair[e]

[a] University Health Network, Apheresis, Toronto, Ontario, Canada
[b] Nova Scotia Health Authority (NSHA), Halifax, Nova Scotia, Canada
[c] Saint Michael's Hospital, Toronto, Ontario, Canada
[d] Health Sciences Centre, Winnipeg, Manitoba, Canada
[e] Apheresis Department, Health Sciences Centre, London, Ontario, Canada

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ABSTRACT

A group of Canadian apheresis nurses developed best practice for in the management of thrombotic thrombocytopenic purpura (TTP). The recommendations address issues related to infusion protocols, preventing and managing adverse events, comprehensive patient assessments, treatment procedures, as well as pre- and post-treatment care. The Canadian group encourages institutes to include nurses on committees that examine recommendations for TTP management.

1. Introduction

Thrombotic thrombocytopenic purpura (TTP) is a particular form of thrombotic microangiopathy originally characterized by a pentad of thrombocytopenia, microangiopathic hemolytic anemia (MAHA), fever, neurological abnormalities, and renal impairment. The modern diagnostic criteria state, however, that TTP should be considered in the presence of thrombocytopenia and MAHA alone [1]. TTP is both rare and fatal, with a reported incidence of six cases per million per year in the UK and an untreated mortality rate of 90% [2]. Congenital and acute TTP is due to a deficiency of von Willebrand factor (VWF) cleaving protein known as ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) [3]. Aquired TTP has also been related to low ADAMTS-13 levels. In the absence of ADAMTS-13, ultra large multimers of VWF (ULVWF) released from endothelium are not cleaved appropriately, causing spontaneous platelet aggregates in the microvasculature of the brain, heart and kidneys.

Daily sessions of therapeutic plasma exchange (TPE) are the primary form of treatment for TTP and these significantly reduce mortality [4]. TPE is hypothesized to replenish the missing enzyme ADAMTS-13, thus removing the ULVWFM and ADAMTS13 inhibitors/proteolytic inactivators. Historically, transfusions of whole blood, which contains ADAMTS13, were used as a plasma therapy. Since the 1980s, however, fresh-frozen plasma (FFP) and cryoprecipitate poor plasma, also known as cryosupernatant (CSP), have been used [1]. Solvent/detergent-treated plasma (SDP) is another replacement fluid that has increasingly been used in Canada in recent years for plasma exchange in TTP patients. In Canada, SDP is available as Octaplasma®, which is the only standardized pathogen-inactivated, prion removed and cell-free SDP and, in our country is largely used for patients allergic to FFP/CSP or with pre-existing lung disorders. Over 60,000 bags of Octaplasma® have been transfused in Canada since 2012. Despite TPE efficiency, some patients with TTP fail to respond to TPE alone. Therefore, other treatment modalities including steroids, vincristine, cyclophosphamide, Rituximab, antiplatelet agents and splenectomy have all been used in combination with TPE for the treatment of TTP [5,6].

Optimal plasma exchange protocols for patients with TTP – including the choice of fluid to use during TPE – remain unstandardized. In Canada, all TPEs take place in hospitals; therefore, the nursing group's objective was to create recommendations for the administration and management of TTP using TPE.

2. Methods

The nursing group convened virtually to discuss key features of these recommendations. These meetings allowed the advisors to raise questions and provide feedback regarding infusion protocols, preventing and managing adverse events, comprehensive patient

* Corresponding author.
E-mail addresses: Pamela.Harmon@uhn.ca (P. Harmon), Eduard.Cojocari@uhn.ca (E. Cojocari), Catherine.Mader@nshealth.c (C.L. Mader), Charlene.Galloway@nshealth.ca (C. Galloway), BuchholzM@smh.ca (M. Buchholz), BLewis@exchange.hsc.mb.ca (B. Lewis), Sue.Sinclair@lhsc.on.ca (S. Sinclair).

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assessments, treatment procedures, as well as pre- and post- treatment care. After various discussion periods, the advisors reached consensus on the recommendations that form the backbone of this article.

3. Recommendations

3.1. Develop infusion protocols for the treatment of TTP

Currently, no uniform approach to the management of TTP exists in Canada. The treatment regimen is generally determined by a physician based on various clinical criteria. Our group of Canadian apheresis nurses recommend that in order to optimize and standardize TTP management, health care organizations should develop protocols that will provide clinical practice guidance for the treatment of TTP. The protocols may include information regarding recommendations for replacement solution choice and recommendations for the TPE regimen.

Protocol recommendations from the group of Canadian apheresis nurses are as follows:

3.1.1. Choose a replacement fluid that is best for the patient

The use of FFP versus CSP as the best replacement fluid for plasma exchange remains debated. Compared to FFP, CSP contains less von Willebrand factor (VWF) and fewer of the higher molecular weight forms ; therefore, some hypothesize that thrombotic events in TTP may be reduced. One small Canadian study comparing the two fluids in 58 patients demonstrated better outcomes for TTP patients treated with CSP [7]; however, a small American randomized control trial did not confirm these findings [8]. Similarly, a 2005 Canadian study had insufficient numbers to show a difference between CSP versus FFP in the outcome of TTP patients [9]. One common limitation across these studies is the small sample size. In Canada, when patients present with TTP, CSP has historically been the replacement fluid of choice.

Emerging pathogens, transfusion-related infections and reactions are an ongoing concern for patients receiving TPE. For these reasons, many European countries have switched their main plasma use to SDP [10]. In the UK, Octaplasma® is the product of choice for children and for all patients with TTP or for those using high volumes of plasma. Based on clinical experience, and the availability of Octaplasma®, the Canadian Apheresis Group (CAG) recently updated its TTP treatment algorithm which includes Octaplasma®. Octaplasma® has been added as a first line plasma option, alongside CSP, FFP or other suitable fluid. The choice of replacement fluid should be at the discretion of the treating physician [11]. The Network of Rare Blood Disorder Organizations (NRBDO) also advocates for unrestricted access of SDP for all patients with TTP or other blood disorders that require large volume of plasma exchanges, which leave them at a higher risk of adverse events and viral transmission [12]. Recommendations for TPE regimens are shown in Fig. 1.

The Canadian apheresis nursing group recommends that robust transfusion medicine support should be in place at each institution's blood bank to ensure that these replacement solutions are readily available for emergent TPE procedures.

3.2. Develop standard operating procedures for adverse events

The development and implementation of organizational standard operating procedures (SOPs) for adverse event prevention and management can minimize the risk to patients as well as improve patient care. Currently, TPE is generally well tolerated; however, the risk of adverse events associated with these procedures cannot be eliminated. Therefore, apheresis centres should be prepared for potential adverse events. For this purpose, all apheresis centres should have policies and SOPs that ensure effective management of adverse events in case they occur. The group of Canadian apheresis nurses provide recommendations for the management of adverse events during TPE in Table 1.

During the apheresis procedure, the apheresis nurse should monitor the patient for potential clinical complications. If any signs and symptoms of adverse reactions are detected, the nurse should initiate corrective action as it is specified in the organizational SOPs. If applicable, the physician will prescribe additional medical interventions and determine if the procedure should be continued. In accordance with SOPs, the apheresis nurse should report blood transfusion reactions, inform the patient regarding the adverse reaction, and document all information regarding the adverse reactions (including treatment and outcome). The apheresis physician should regularly review all severe adverse reactions related to the apheresis procedure to determine if corrective actions were adequate.

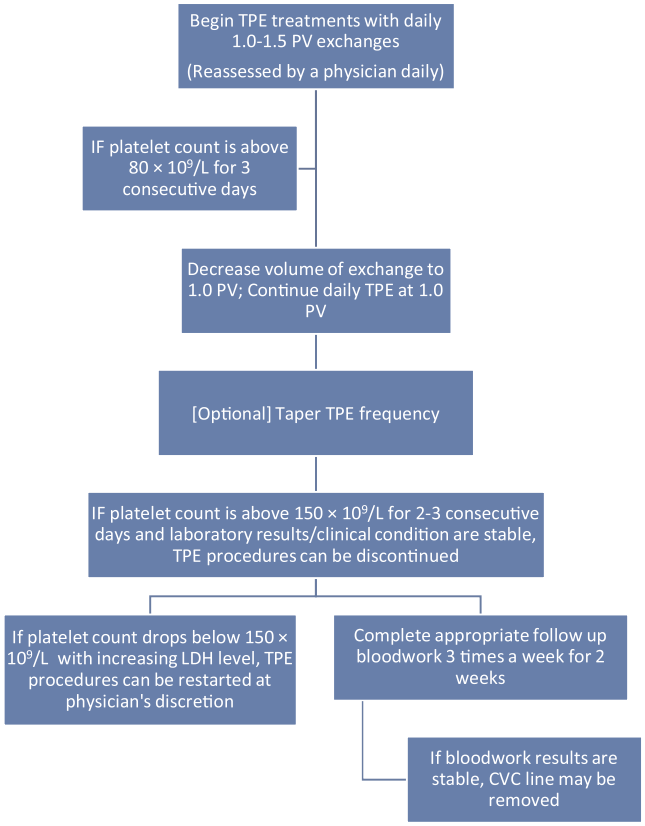

Fig. 1. Recommendations* for Therapeutic Plasma Exchange (TPE) Regimen.
*Recommendations may vary institutionally.
PV = plasma volumes, LDH = Lactate dehydrogenase, CVC = Central Venous Catheter.

3.3. Complete a comprehensive patient assessment

The Canadian apheresis nurses agreed that TTP patients should receive a comprehensive nursing assessment prior to treatment, which is an urgent priority. This assessment would include a physical assessment and past medical history, a review of the patient's current medications, blood work, providing patient education, a review of current treatment orders, an assessment of venous access, and a psychosocial assessment.

3.3.1. Urgency and priority of TTP patients

Suspected patients with TTP should be treated as soon as possible once a diagnosis is suspected, and are considered an urgent priority. Importantly, while a low (less than 5–10%) ADAMTS level is consistent with a diagnosis of TTP, a level higher than 10% does not rule out the disease. Recent reports confirm that relapsing patients who have ADAMTS levels greater than 10% will respond to plasma exchange [13]. Plasma exchange should be initiated if thrombotic microangiopathy is present. Bridging with plasma infusion may be required until TPE can be arranged. All patients with presumed or confirmed TTP