Editorial

Thrombocytopenia in critically ill patients

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Thrombocytopenia is one of the most common hematologic complications found in critically ill patients. The incidence and prevalence of thrombocytopenia in critically ill patients are varied due to various reasons. First, the definition of thrombocytopenia applied in individual studies is different. Although thrombocytopenia is usually defined when platelets are $\leq 150x10^9$/L, a number of reports choose a platelet threshold of $\leq 100x10^9$/L, as used by the author of this article. Second, the underlying diseases of patients and types of intensive care units also contribute to the mixed incidence and prevalence of thrombocytopenia. Williamson DR, et al[1] reported the incidence and prevalence of thrombocytopenia, defined by platelet $\leq 100x10^9$/L, of critically ill patients, admitted to any type of intensive care unit, of 13.3% and 7.8%, respectively. However, the incidence or prevalence of thrombocytopenia varied depending on each study's population. A report focusing on pediatric patients with bloodstream infection in the intensive care unit demonstrated a thrombocytopenia incidence of 3.8%[2]. Another data of patients who underwent continuous renal replacement displayed a greater incidence of thrombocytopenia in the cardiac intensive care unit patients, as high as 22.5%, in comparison with those in the medical intensive care unit, which had an incidence of 13.1%[3]. The author also reported the prevalence of thrombocytopenia in Thai patients admitted to medical intensive care units of 8.3% which was similar to the previous ones.[4]

Impact of thrombocytopenia in critically ill patients

One of the major concerns regarding thrombocytopenia in these particular patients is an endowment of a grave prognosis. The mortality rate of critically ill patients who have thrombocytopenia is 1.25 times (odd ratio 1.25, 95%CI: 1.20-1.31; $p < 0.001$) greater than ones with normal platelet numbers.[1] Lillemäe K, et al, reported that patients with traumatic brain injuries who had platelet of $\leq 100x10^9$/L and $> 100x10^9$/L had a mortality rate of 26%, and 9%, respectively.[5] Moreover, patients with infection in the intensive care unit who had a platelet of $\leq 50x10^9$/L had a mortality rate 3.6 times higher than those with a platelet count of $> 130x10^9$/L.[6] Apart from the platelet number and underlying diseases of patients, pattern of platelet recovery also contribute to their mortality rate. Regarding the platelet recovery pattern of critically ill patients, one study showed that the survivors usually had platelet recovery time by day 7-9, whereas the non-survivors seldom had normal platelet count at the end of the first week.[7] Nevertheless, the relationship between the degree of thrombocytopenia and the mortality rate of the patients admitted to medical intensive care units was not studied in this report.

Causes of thrombocytopenia

The typical causes of thrombocytopenia in critically ill patients are infection, drugs, disseminated intravascular coagulation (DIC), massive transfusion, extracorporeal membrane circuits exposure such as extracorporeal membrane oxygenation (ECMO), intra-aortic balloon pump (IABP) or hemodialysis etc. The other causes are unusual, however, should be considered as delayed diagnosis could lead to fatal complications. Those conditions include heparin-induced thrombocytopenia/thrombosis (HIT/T), hemophagocytic syndrome (HPS), thrombotic thrombocytopenic purpura (TTP) and post-transfusion purpura (PTP) etc. In line with this study results, infection is the predominant cause of thrombocytopenia

in critically ill patients which could be attributed to a wide range of mechanisms such as direct infection to megakaryocytes, immune complex formation binding against platelet, DIC, macrophage activation and HPS. Certain medications result in thrombocytopenia by either direct bone marrow suppression or increased platelet destruction by either immune or non-immune processes. The notorious ones include ranitidine, β-lactam antibiotics, vancomycin, furosemide and linezolid etc. DIC is a complication following infection diseases especially Gram-negative bacteremia, blood group incompatibility, massive transfusion etc. After an intense activation of platelet and coagulation cascade, platelets decline to a variable degree. Patients with DIC may acquire thrombosis as well as bleeding complications. Heparin, a commonly used medication in intensive care units, can lead to thrombocytopenia, namely HIT/T, by certain mechanisms.[8] Platelets usually are greater than 40-50x10^9/L, as such HIT/T patients would rather have thrombotic than bleeding complications. The Onset of thrombocytopenia, the presence of thrombosis and a platelet number are valuable parameters in supporting the diagnosis of HIT/T. HPS, a complication associated with infection or malignancies, is characterized by pancytopenia, hyperferritinemia, hypofibrinogenemia and evidence of hemophagocytosis in bone marrow. However, its mechanism is not well elucidated. Lastly, PTP is a scarce but serious post-transfusion complication. It typically occurs in multiparous women and appears within 10-14 days after blood transfusion. The exact mechanism is uncertain but hypothesized that patients produce platelet antibody against both donor and their platelet. Platelets could decrease to < 10x10^9/L and bring about bleeding complications.

Diagnosis

The diagnostic approach to thrombocytopenia in critically ill patients should begin with a history review focusing on the onset of thrombocytopenia, underlying diseases, and current medications. If thrombocytopenia occurs prior to admission, pre-existing hematologic diseases such as immune thrombocytopenia or myelodysplastic syndrome should be considered. HIT/T is suspected if there is a history of heparin usage within an appropriate duration. DIC and HPS should be taken into account if patients exhibit fever with or without sepsis. Complete blood count (CBC), a most valuable screening investigation, provide information not only on the presence of thrombocytopenia but also on the severity of thrombocytopenia. Moreover, CBC occasionally assists in diagnosing the causes of thrombocytopenia. Fragmented red cells or schistocytes found in macroangiopathic hemolytic anemia suggest the diagnosis of either DIC or TTP. Coexisting leucopenia, especially neutropenia, raise the suspicion of drug-induced thrombocytopenia from bone marrow suppression or HPS. Low plasma fibrinogen can be found in DIC and HPS. Overall, it is important to note that thrombocytopenia causes in critically ill patients may be multifactorial.

Treatment

Treatment of thrombocytopenia depends on the underlying diseases of patients and the causes of thrombocytopenia. Treatment of the underlying diseases is vital and frequently improves thrombocytopenia afterward. Together with treatment of underlying disease, specific treatment of thrombocytopenia of individual cause is considered. For example, immunosuppressive agents such as steroids or etoposide are recommended in the treatment of HPS[9] and intravenous immunoglobulin (IVIg) is indicated in PTP.[10] Plasma exchange is the standard treatment of TTP.[11] Nonetheless, platelet can sometimes be lower than the safety margin. In addition to platelet number, the presence of bleeding complications and invasive procedure schedule are needed to be evaluated for the decision of platelet transfusion.[12,13]

Conclusion

Thrombocytopenia in critically ill patients is a common problem. Its incidence and prevalence are varied. Thrombocytopenia reflects a poor prognosis and correlates with a higher mortality rate. Treatment options are based on underlying diseases, causes and severity of thrombocytopenia. Platelet transfusion is indicated if patients develop bleeding complications or undergo invasive procedures.

Reference

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