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Original Article

Pre-transfusion testing for Ebola virus disease patients in serious communicable infectious diseases hospitals in Tokyo: A cross-sectional study☆

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ABSTRACT

Background: Ebola virus disease (EVD) was endemic to Africa in 2014–2016. Supportive therapies have been shown to improve the outcome of EVD, and additional supportive therapy including blood transfusion therapy and external circulation could be needed in the event of a future global outbreak. However, pre-transfusion testing policies and guidelines have not yet been established in Japan.
Methods: We conducted a cross-sectional study of blood transfusion therapy for EVD patients at three designated hospitals for serious communicable diseases in Tokyo. In each hospital, we surveyed blood transfusion therapy policy, blood transfusion protocol, presence of a specialist in the department of transfusion medicine, facility capacity for pre-transfusion compatibility testing, and types of personal protective equipment available.
Results: One hospital had a cross-matched compatible blood transfusion policy, one had a cross-matched compatible blood transfusion policy only when the patient's ABO and RhD type is previously known, and the third had not created a policy. Two hospitals had a department of transfusion medicine. These two hospitals had a special testing unit for serious communicable diseases, while the other had a portable unit for testing. There were no major differences noted in available personal protective equipment.
Conclusion: Policies and protocols differ among hospitals. The choice of blood transfusion policy and pre-transfusion testing is largely dependent on equipment and human resources. Further discussion is required to develop national guidelines for blood transfusion therapy in patients with serious communicable diseases, including countermeasures against complications and ethical issues related to the safety of patients and healthcare workers.

1. Introduction

Ebola virus disease (EVD) was endemic to Western Africa in 2014–2016 [1]. Although EVD is a severe hemorrhagic disease frequently resulting in death, intensive care, such as mechanical ventilation and continuous renal-replacement therapy, have been shown to improve the outcome of EVD in some cases [2,3]. Additional supportive therapy including blood transfusion could be needed for future outbreaks. Moreover, although not yet supported by evidence, convalescent plasma and whole blood transfusion therapy have also been tried as a treatment option for EVD patients [4,5]. Before initiating intensive supportive care, such as blood transfusion therapy, convalescent plasma, or whole blood transfusion, pre-transfusion compatibility testing is necessary, and the World Health Organization (WHO) has provided interim guidance for transfusion therapy for EVD patients [6]. However, in Japan, there are neither national guidelines for blood transfusion therapy

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in EVD patients nor research regarding blood transfusion policy and pre-transfusion testing in EVD patients. As a result, designated hospitals for serious communicable infectious diseases develop their own approach for providing blood transfusion therapy to EVD patients. Of note, because Tokyo metropolitan area will host the Olympic games in 2020, and has a geographical relationship with the two main international airports of Japan (Haneda and Narita international airport), large numbers of people from foreign countries will visit and serious communicable diseases could be brought into Japan. To prepare for the event of a future outbreak of a serious communicable disease in Japan, more information is needed regarding the current situation. Thus, we aimed to assess and evaluate the current status of blood transfusion therapy for EVD patients, comparing three designated hospitals in Tokyo to understand current concerns regarding pre-transfusion testing and facility settings.

2. Material and methods

We completed a cross-sectional study of blood transfusion therapy for EVD patients at three hospitals designated for treating serious communicable diseases in the Tokyo metropolitan area (Tokyo Metropolitan Bokutoh General Hospital, Tokyo Metropolitan Komagome Hospital, and Tokyo Metropolitan Health and Medical Corporation Ebara Hospital). All three hospitals have a department of infectious diseases. The study was approved by the institutional review boards of all three hospitals.

Evaluation items were developed prior to investigation; subsequently, three researchers systematically conducted a review and visit survey at all hospitals following the same procedure at all hospitals. We surveyed the transfusion procedure manual for EVD patients in each hospital, interviewed doctors and pre-transfusion testing personnel, and reviewed the blood transfusion therapy policy and blood transfusion protocol for EVD patients. Additionally, we investigated whether a specialist in the department of transfusion medicine was present, whether facilities for pre-transfusion compatibility testing were available, and the types of personal protective equipment that were used by testing personnel.

3. Results

3.1. Blood transfusion policy

The blood transfusion policy for EVD patients differed between the three hospitals. One hospital had the policy of doing cross-matched compatible blood transfusion in all EVD patients. Another hospital had the policy of doing cross-matched compatible blood transfusion only if the patient's ABO and RhD blood type was previously mentioned in their medical record. If the EVD patient had not visited the hospital previously and/or had not reported their blood type, the hospital would complete cross-matched incompatible blood transfusion. The third hospital did not have a policy for blood transfusion, instead deciding whether or not to do a transfusion after assessing the patient's severity.

3.2. Blood transfusion protocol

Regarding blood transfusion protocol, one hospital discerned ABO and RhD type by visual judgment and did a computer cross-match if transfusion was necessary. One hospital did computer cross-matching if the patient's ABO and RhD type was already known, or, if unknown, would do an O and RhD-positive transfusion. The third hospital did not have a transfusion protocol for EVD patients.

3.3. Department of transfusion medicine

Two hospitals had a department of transfusion medicine with a blood transfusion specialist. The other hospital did not have a department of transfusion medicine. Both hospitals that had a blood transfusion specialist also had clear policies regarding transfusion therapy for EVD patients.

3.4. Testing units for serious communicable diseases

Two hospitals had a special testing unit for serious communicable diseases, including EVD, and these units were isolated from the other facilities (Fig. 1). The third hospital had no special unit for testing, but used a portable unit (Fig. 2) for testing patients. Ideally, this portable testing unit would be used in a room beside the room where the patient with the serious communicable disease is isolated.

3.5. Personal protective equipment

Two hospitals had gowns, goggles, face shields, gloves, and N95 masks. The third hospital had gowns, goggles, gloves, and N95 masks.

4. Discussion

Although cross-matched compatible blood transfusion is the ideal blood transfusion therapy for patient safety, both cross-matched compatible and cross-matched incompatible blood transfusion should be reasonable options within the capacity of designated hospitals. Cross-matched compatible blood transfusion is safer for patients than cross-matched incompatible blood transfusion. Furthermore, cross-matched blood transfusion can provide the treatment option of using convalescent whole blood and plasma in patients recovering from EVD. Although evidence and guidelines for convalescent plasma and whole blood transfusion therapy have not yet been established, these therapies could be future options for EVD management [2,3].

Cross-matched incompatible blood transfusion is also a reasonable option for EVD patients because omitting pre-transfusion testing would decrease the risk of exposing laboratory personnel to infected blood, and all designated hospitals could not equally complete ideal cross-matched blood transfusions, due to insufficient human resources and facility settings. According to the WHO recommendation [6], blood transfusions that are ABO and RhD type compatible should be the first line of treatment, but if ABO and RhD types are unknown—as in many emergency cases—O and RhD-negative red blood cells and AB type plasma should be the second choice. However, although blood transfusion policies and protocols vary between hospitals, complications regarding blood transfusion therapy are important concerns for physicians. In Japan, it is difficult to get RhD-negative blood type quickly, because the majority of Japanese people (as many as 99.5%) have RhD-positive blood type [7]. Therefore, according to guidelines for critical bleeding in Japan [8], O and RhD positive blood transfusion is permitted. The frequency of the RhD-negative blood type differs among populations and races. While RhD-negative blood type is less common (1–10%) in Asian and African populations [9–11], Britain and the United States have a higher number of people (17–40%) with RhD-negative blood type [12,13]. Therefore, as RhD-negative blood type cannot be immediately accessed in Japan, hospitals need to have an existing plan for responding to possible complications of RhD-incompatible blood transfusion, such as hemolytic transfusion reactions, particularly if a patient with EVD is from a foreign country and more likely to have RhD-negative blood type. In these situations, transfusion specialists are necessary for

Fig. 1. The isolated unit for serious communicable diseases. This unit is located near the patient room, and nearly all types of tests that use blood samples are possible in the unit.

dealing appropriately with complications and to provide consultation services to other medical personnel. Although not a blood transfusion, a case of EVD with acute respiratory distress syndrome possibly caused by convalescent plasma use has been reported [14], indicating risks associated with the use of biological products.

In this study, two of three hospitals had a department of transfusion medicine and a transfusion specialist, with a system in place for providing consultation to other medical staff. Japan has many designated hospitals for serious communicable diseases, but all designated hospitals do not have a department of transfusion medicine and a transfusion specialist. A national system, such as a national consultation service, is needed to provide support for transfusion-related complications in hospitals that do not have a department of transfusion medicine or a transfusion specialist. Appropriate transfusion policies and protocols for EVD patients are needed in each hospital, and should be developed according to the staff and settings.

A significant improvement of facility settings is not expected in all designated hospitals in Japan, due to limited space and high costs. In the hierarchy of control [15], which has been used as a means of determining how to implement feasible and effective control solutions, the hierarchy of engineering controls includes the facility setting improvement. Although, the initial cost could be higher than the cost in other hierarchies, long-term operating costs could be lowered. In the present study, the facility setting was different in each hospital. Two hospitals had an isolated unit for

Fig. 2. Portable unit for serious communicable diseases. This unit is used when the patient with a serious communicable disease is on admission in the room beside the unit. The testing is limited, but the unit is easy to move and maintain.

testing. These units were ideal for testing specimens of patients with serious communicable diseases, but more space and a dedicated testing machine were needed. The other hospital did not have an isolated unit. This hospital had a portable unit for testing, which was less expensive and more useful than an isolated unit for hospitals that had limited space.

On the other hand, cross-matched blood transfusion introduces an increased risk of exposing laboratory personnel to infected blood from EVD patients during pre-transfusion compatibility testing. Thus, the risk of infection to laboratory personnel should be minimized during pre-transfusion testing. The WHO and the Centers for Disease Control and Prevention provide guidelines for healthcare workers regarding personal protective equipment (PPE) during exposure to EVD [16,17], recommending the use of appropriate equipment, such as gloves, gown, and goggles. PPE is the lowest measure in the hierarchy of control [15].This process is frequently used with existing processes, but requires significant effort by the relevant workers. As laboratory personnel exposed to EVD are also at risk for EVD, eye protection is essential. In an interview of laboratory personnel in this study, we found that judging ABO and RhD type by sight is difficult due to goggle clouding, and that clouded goggles can cause difficulty in handling blood samples. These findings suggest that preventing goggle clouding is important to allow personnel to determine blood type by sight and to safely handle blood specimens.

Adding to rules and guidelines is important, and training is also important. Although national transfusion guidelines for EVD patients are needed to show a management plan to designated hospitals in Japan, each hospital should make their own plans to manage EVD patients based on the national guideline. As reported by Oladimeji et al., gaps could occur in knowledge and practice [18]; therefore, training should be available and any subsequent problems that occur after training should be dealt with individually. As mentioned above, goggle clouding can be improved with appropriate training that can solve this problem immediately. In the hierarchy of control [15], the hierarchy of administrative controls involves training. This process could be relatively inexpensive to establish and easy to initiate.

To determine a transfusion policy for patients with serious communicable diseases such as EVD, greater discussion of the risk-benefit between the safety of patients and healthcare workers is needed in Japan, which leads to issues with professional ethics. In terms of patient safety, if the biological product may cause adverse reactions as mentioned above, the decision to not perform transfusion therapy may be made [14]. This choice is favorable for the safety of healthcare workers. On the other hand, as transfusion therapy could improve outcomes for EVD patients, the choice to perform transfusion therapy is also acceptable if the safety of healthcare workers is considered. However, because PPE and training is lower in the hierarchy of control, these processes might be less effective than other measures [15]. In such a high-risk situation, it should be considered that not all healthcare workers may wish to be exposed to potential hazards at work. Each hospital in the present study has not adequately discussed this risk-benefit problem between the safety of patients and healthcare workers, and further discussion with all involved staff, including administrators, is required to develop a transfusion policy for EVD patients.

An important limitation of this cross-sectional study is that only three designated hospitals in Tokyo were included. Therefore, the Results may not be generalizable to other designated hospitals in Japan.

In summary, our findings demonstrate that each hospital in this study was seeking transfusion policies and protocols for pre-transfusion testing that were appropriate in their own settings. The choice of blood transfusion policy and pre-transfusion testing is largely dependent on equipment and human resources. Although cross-matched compatible blood transfusion is ideal, if cross-matched incompatible blood transfusion cannot be avoided in an emergency, hospitals in Japan should prepare countermeasures against potential complications, for example through identifying or creating consultation services by transfusion therapy specialists. Moreover, there should be a discussion about the ethical issues involved with patient and healthcare worker's safety in Japan. The Results of this study support a possible need for the development of national guidelines for blood transfusion therapy in Japan, to ensure that hospitals are better prepared for the event of future outbreaks of serious communicable diseases.

Declarations of interest

None.

Authorship contributions

NS wrote the initial draft of the manuscript. AK, SI, NUF, and IA contributed to collecting and analyzing the data, and assisted in the preparation of the manuscript. HF performed critical review of the manuscript. NS revised the manuscript. All authors contributed to the final version of the manuscript.

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