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Cold Agglutination is a Concern in the Collection and Processing of Hematopoietic Progenitor Cell Products

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Abstract

Similarly, cry globulins can precipitate from plasma when temperatures fall below the central body temperature, resulting in erythrocyte agglutination. Unfortunately, such temperature ranges are commonly encountered outside of the body's circulation, such as in an extracorporeal circuit during hematopoietic progenitor cell collection or human cell therapy laboratory processing. Ex vivo agglutination may cause issues with the collection of product, resulting in adverse effects or product loss. In this section, we hope to share our experience in preventing and responding to recognized incidents of HPC agglutination in our human cell therapy facility.

Keywords: Agglutination; Cold agglutinin; Cryoglobulin; Hematopoietic progenitor cell

Introduction

During collection and processing, spontaneous hematopoietic progenitor cell product agglutination can occur for a variety of reasons. Insufficient anticoagulation in the collection/processing bag, cold-reacting autoantibodies, and cell-free DNA from excess white blood cell lysis are all known causes of spontaneous HPC agglutination. Cold autoantibodies are frequently detected in transfusion laboratories during pretransfusion examination. These autoantibodies are classified as cold agglutinins or cry globulins based on their immunoglobulin subtype and illness potential [1].

CG is another source of HPC agglutination. Immunoglobulin's precipitate from plasma when temperatures fall below 37°C, causing cryoglobulinemia. CGs are more prevalent than CAD, affecting one out of every 100,000 people, with the majority of instances caused by viral infections such as HIV or hepatitis C. After washing with prewarmed reagents, agglutination resolved in one of two cases.

Preprocessing and product changes, such as those indicated in, can avoid HPC product agglutination due to cold autoantibodies, CA and CG, according to limited case studies.

Agglutination is the process by which particles bind together as a result of molecules on the particle's surface interacting with other particles, which is frequently related with an antibody on the cell's surface.

When antibody molecules build a network of cross-linked antigens, insoluble precipitates occur. As the amount of antigen grows in relation to the amount of antibody, the amount of insoluble precipitate increases to a maximum. At this moment, the antibody-to-antigen ratio is optimal, allowing for the greatest number of cross-linking contacts. This is referred to as the equivalency zone, and if the amount of antigen increases any further, the system is said to be in antigen excess. When there is an excess of antigen, less precipitate is created as a result of the excess antigen smothering the antibody, preventing it from cross-linking numerous antigens and so limiting the amount of insoluble precipitate formed.

Antibody-coated latex or magnetic particles can improve agglutination detection and broaden the range of the positive dosage response before antigen excess precludes particle cross-linking. There are numerous examples of particle agglutination being utilised to detect and quantify chemicals and microorganisms in illness research [2-4].

Materials and Methods

The study was carried out over a four-year period at a tertiary care hospital in Western India, with the approval and ethical clearance of the institutional ethical committee. All participants provided written informed consent, and their participation was entirely voluntary, with the ability to withdraw from the study at any time.

The trial included 1020 Rh-negative ANCs who were assessed between February 2018 and March 2022 [5].

From 2019 to 2021, we analyzed planned and unplanned process modifications for occurrences involving HPC product agglutination, and we identified four incidences of product agglutination for patients ranging in age from 51 to 66 years old, with a male to female ratio of 3:1. Medical records were evaluated to determine the reason for the transplant, the type of transplant, planned process improvements during collection, processing, and infusion, and extra laboratory testing [6].

Micromod Partikeltechnologie GmbH in Germany provided surface modified PS and silica particles. According to the provider, the nominal particle sizes of the PS and silica particles were 200 and 220 nm, respectively. According to earlier research, the latex agglutination test can be performed with any particle size, but particles with sizes ranging from few nanometers to submicrons appear to be routinely used. Biotin was used to coat PS and silica particles, respectively.

A total of 182 individuals on maintenance dialysis three times per week were studied. Dialysis was performed on 48 patients at Tokyo Women's Medical University and 134 patients at Nerima Sakuradai Clinic. The blood was drawn right before the first hemodialysis session of the week. The LIA technique and quantitative LC-MS/MS were used to measure hepcidin-25[7, 8].

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Discussion

Other reasons of spontaneous agglutination known to HCT laboratories include product clotting due to inadequate anticoagulation or prolonged transit time, and cell-free DNA due to excessive cell lysis due to age or cryopreservation.

The attribution of an agglutination score based on image analysis makes it difficult to use in practise without prior training. Although computer software to facilitate and simplify this process is possible, a large number of samples, including convalescent plasma with different levels of SARS-CoV-2 antibodies determined by an orthogonal method, would need to be tested by the agglutination assay to obtain enough data for training. When unprocessed blood was used in the current setting, the latex agglutination experiment produced considerable background signals. Before the agglutination assay can be evolved into a home test, this issue must be handled [9,10].

Conclusion

While uncommon, cold agglutination of HPC products can interrupt routine collection and processing methods. Protocol changes can help to avoid negative donor events and reduce product loss. Such procedural changes should be considered in persons with known agglutination risks that are undergoing HPC donation/collection.

Conflict of Interest

None

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None

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