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COMPLICATIONS OF BLOOD TRANSFUSION

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ABSTRACT

Blood transfusions are now a common medical procedure, and over time, many changes have been made to increase their safety. Procedures for blood transfusions may entail the transfer of the entire blood supply or the use of its various cellular (RBCs, WBCs, and platelets) and non-cellular components (Plasma or plasms derivatives). A few of the clinical issues that could develop during blood transfusion operations are discussed in this review. With a range of key words and Mesh terminology, the databases of Google Scholar, Pubmed, and J Gate were searched using Boolean operators. Additionally, reference lists for selected publications were examined, and snowballing was used to extract the needed data. Numerous complications from blood transfusions can occur, including circulatory overload (TACO), hyperkalaemia, hypothermia, haemolytic transfusion reactions (HTR), febrile non-haemolytic transfusion reactions (FNHTR), transfusion-related acute lung injury (TRALI), graft vs. host disease (TA-GVHD), febrile reactions, allergic reactions, and more.

KEYWORDS: Blood transfusion, Complications of blood transfusion, Allergic reactions.

INTRODUCTION

Blood transfusions have become a routine medical practice and has transformed overtime with a lot of improvements being made to enhance its safety. Blood transfusions procedures may involve transfer of whole or usage of its different cellular (RBCs, WBCs, Platelets) and no cellular components (Plasma or plasms derivatives). This technique dates back to a long ago history, with the first reported blood transfusion performed between animal by Richard Lower in 1665. In 1818 British Obstetrician James Blundell did the first Human to Human transfusion, until then blood typing was not developed and hence cross reactivity base severe immune responses were very common. ABO blood typing and RH typing significantly improved the safety of this technique and since then has saved innumerable lives. Enhanced methods in donor screening and modern equipment's have made the procedure hassle free decreasing the chances of infectious complications, but the non-infectious manifestations have always been a matter of concern for clinical practitioners. These non-infectious transfusions related events could occur due to a particular component of the blood, volume of transfusion or any other human errors which might occur during the procedure (Refer Table 1).

Since 1996, data on substantial adverse events brought on by the transfusion of blood components have been gathered from volunteer groups by the serious hazards of transfusion (SHOT) scheme. Although it is now required that all "Blood Establishments and Hospital Blood Banks report to the Secretary of State for Health all serious adverse reactions attributable to the safety or quality of blood," this is due to the European Union Directive on Blood Safety and Quality, which went into effect in 2005.[16] In 2004, 539 occurrences were voluntarily reported to SHOT, and 3.4 million blood components were distributed in the UK. Over 2003, this indicates an increase of 19%. The information gathered once reporting became required is not yet available.[16] This review discusses few of the clinical complications which might arise during blood transfusion procedures.

Table 1: Complications of Blood Transfusion.

Early	Late
• Haemolytic transfusion reactions (HTR) ○ Immediate, Delayed • Febrile Non-haemolytic transfusion reactions (FNHTR) • Allergic reactions to proteins, IgA • Air embolism • Thrombophlebitis • Hyperkalaemia • Citrate toxicity • Hypothermia • Transfusion-related acute lung injury (TRALI) • Reactions secondary to bacterial contamination • Transfusion associated circulatory overload (TACO) • Clotting abnormalities (after massive transfusion	• Transmission of infection ○ Viral (hepatitis A, B, C, HIV, CMV) ○ Bacterial (Treponeum pallidum, Salmonella) ○ Parasites (malaria, toxoplasma) • Transfusion associated Graft-vs-host disease (TA-GVHD) • Iron overload (after chronic transfusions) • Immune sensitization (Rhesus D antigen)

Complications of Blood Transfusion

Haemolytic Transfusion Reactions (HTR)

The most common yet avoidable cause of haemolytic reactions is the misidentification or mislabelling of the blood samples. ABO incompatibility arises due to the presence of pr-existing antibodies in a person's blood against its non-compatible antigens. Haemolytic Transfusion reactions can be acute (<24 hrs) or delayed (>24 hrs). Acute haemolytic transfusion reactions are very common in systems which handle trauma patients. Immunologic incompatibility leads to intravascular osmolysis of red cells. The free heme molecules scavenge excess nitric oxide which induces vasoconstriction. There is an incomplete activation of complement system which activates mast cells.[3] An acute response to cross reacting blood leads to anaphylactic shock responses with a wide spectrum of symptoms involving fever, chills, nausea, shock infusion site pain to be named a few. Prolonged severity of the symptoms can lead to acute kidney failure or death. Since, improper handling or human error is considered to be the main cause behind the occurrence of this condition, a well-established and robust screening of donors and receivers can cut down the risk to many folds.[5,7]

Febrile Non-Haemolytic Transfusion Reactions (FNHTR)

The occurrences of FNHTR are as common as HTRs but are usually not so severe and life threatening and only display mild symptoms. The manifestation of FNHTR is known to be caused by cross reactivity based immune reaction which happens between antigens in the donor leucocytes and antibodies that are present in the recipient's plasma[1]. This interaction leads to the formation of an antigen-antibody complex which in turn activates the complement system ultimately releasing endogenous pyrogens like IL-1 and IL6.[10] The visible symptoms of this reactivity includes fever, chills or headache leading to its confusing similarities with HTRs. However, a direct antiglobulin test can help draw a distinction between the two diagnosis. The leucocyte load in the blood to be donated determines the severity or likeliness of FNHTR and the onset of the symptoms occur several hours after the transfusion. Donor blood profiling for leucocyte count and subsequently subjecting it to leukoreduction is a key to preventing FNHTR incidences.[5,12]

Transfusion Related Acute Lung Injury (TRALI)

TRALI leads to non-cardiogenic permeability edema. The preliminary symptoms of TRALI is characterised by inflammation while the later occurrences are perturbed to be caused by anti-leucocyte antibodies or other molecules like lipids which might induce an immunogenic response.[1] These antibodies and pro-inflammatory factors accumulate in blood product during storage. Cellular profiling of TRALI have revealed neutrophils as the main perpetrators of this pathophysiology in lungs.[2] TRALI incidences are mainly correlated with high plasma volume transfusion. Hypoxemia, dyspnoea, rigors, low grade fevers, hypotension, hypothermia are some of the clinical representations of TRALI. Immediate respiratory support with supplemental oxygen, chest imaging and discontinuing the blood transfusion are some strategies which can be followed upon preliminary occurrence of TRALI related symptoms.[11,14]

Transfusion Associate Circulatory Overload (TACO)

TACO is frequently observed in critically ill patients and is related to medical conditions like heart failure. Patients with TACO show elevated levels of beta natriuretic peptide. Pulmonary hydrostatic edema is generated in TACO, the pathways involved in this manifestation is largely unknown.[8] The initial clinical symptoms mostly overlap with TRALI. Patients are found to have an elevated level of IL-10 (Interlukin 10) and pro inflammatory factors like IL-6 (Interlukin 6) in TACO. The occurrence of this disease is mostly attributed to an increased volume of blood transfusion, however lack of compensatory mechanisms in response to volume overload could also link to renal or cardiac failure. Performing the transfusion at lower volumes, splitting

the blood products and avoiding unnecessary transfusions can largely help avoid TACO incidences.[11]

Transfusion Associated Graft vs Host Disease (TA-GVHD)

TA-GVHD has been observed to occur in both immunocompetent and immunocompromised individuals. The clinical symptoms of the condition are known to show up in 1-2 weeks of transfusion. The main cause behind TA-GVHD is found to be the presence of active T-lymphocytes in blood products. The presence and proliferation of T lymphocytes in the recipient leads to erythema, diarrhoea, aplasia among several other immune responses. Patients are generally found to have elevated transaminases, bilirubin and alkaline phosphatase.[13] Blood transfusion from close first relatives are known to enhance the recipient's susceptibility to develop TA-GVHD due to partial Human Leucocyte Antigen (HLA).[5,6] Cellular products of blood have chances of carrying T-lymphocytes but not plasma products. The use of immunosuppressant in case of TA-GVHD is known to help in some cases but there is no systematic treatment available. Irradiation of blood products help eliminate the presence of T lymphocytes.[9]

Febrile Reactions

The most frequent adverse transfusion reaction is febrile reactions. Leukocyte-reduced blood products, which make up the majority of blood products in the US, can help lessen febrile symptoms during transfusion. If this happens, the transfusion should be stopped, the patient should be assessed because a hemolytic reaction can at first seem similar, and you should consider completing an infectious or hemolytic workup. Acetaminophen is used as a therapy together with diphenhydramine if necessary for symptomatic relief. The transfusion might restart at a slower pace after treatment and the rule-out of other reasons.[15]

Allergic Reactions

Less than 1% of transfusions result in an allergic reaction, which frequently takes the form of urticaria and pruritis. Rarely do people experience more serious symptoms such bronchospasm, wheezing, or anaphylaxis.[15]

Patients with IgA deficiencies may experience allergic reactions because donor goods containing IgA might trigger severe anaphylactoid reactions. By cleaning the plasma from the cells before transfusion, this can be prevented. Antihistamines can be used to treat mild symptoms including pruritis and urticaria. A combination of bronchodilators, steroids, and epinephrine can be used to treat more severe symptoms.[15]

Hyperkalaemia

During storage, the blood's potassium level rises by up to 5 to 10 mmol u1. After transfusion, the Na-K ATPase pumping mechanism on the RBC membrane is restored, and cellular potassium reuptake proceeds quickly. Massive transfusions rarely result in hyperkalaemia unless the patient is both acidotic and hypothermic.[16]

Hypothermia

At 4° C, RBCs are kept. The recipient's core temperature will drop quickly after a rapid transfusion at this temperature, significantly compromising haemostasis. Hypocalcaemia, metabolic acidosis, and cardiac arrhythmias are all made more likely by hypothermia, which also slows down the metabolism of lactate and citrate. The oxyhaemoglobin dissociation curve swings to the left with a drop in core temperature, limiting tissue oxygen delivery at a time when it should be maximised. All intravenous fluids should be warmed, and forced air convection warming blankets should be used to limit radiative heat loss.[16]

Massive Blood Transfusion

A large blood transfusion occurs when all of the patient's blood is replaced in less than 24 hours. Acid-base balance, serum biochemistry, coagulation status, and temperature homeostasis are only a few of the anomalies that follow.[16]

CONCLUSION

Blood transfusions continue to be effective therapeutic interventions, but extreme caution must be exercised to prevent any potential side effects. Blood transfusions can result in a number of complications, including febrile reactions, allergic reactions, haemolytic transfusion reactions (HTR), febrile non-haemolytic transfusion reactions (FNHTR), transfusion-related acute lung injury (TRALI), graft vs. host disease (TA-GVHD), circulatory overload (TACO), and more.

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