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Transfusions in Critically Ill Pediatric Patients

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Transfusion therapy is a common intervention in pediatric intensive care unit (PICU) patients. Anemia is present in one third of children on admission to PICU, and in addition, approximately 40% of critically ill children become anemic during their intensive care course [1]. The causes of anemia are multifactorial and include direct inhibitory effects of inflammatory cytokines, erythropoietin deficiency, poor endogenous erythropoietin response, altered iron metabolism, pathogen-associated hemolysis, overt and occult bleeding, iatrogenic blood loss through diagnostic phlebotomy, nutritional deficiencies, renal insufficiency and treatment causing bone marrow suppression. These causes may be grouped into three main categories: decreased red blood cell (RBC) production, increased RBC destruction, and blood loss [2]. Different types of anemia frequently coexist in critically ill pediatric patient.

The most important consequences related to anemia involve the reduction of delivered oxygen (DO_2) and subsequent tissue hypoxia. Global DO_2 is dependent primarily upon hemoglobin (Hb) concentration, cardiac output, and the relative proportion of oxyhemoglobin. In PICU patients, the relationship between DO_2 and the consumption of oxygen by the tissue seems to be more important than the actual oxygen delivery [3]. The main physiological responses to acute isovolemic anemia are increased cardiac output and increased oxygen extraction by the tissues. Tissue hypoxia is common during critical illness. Significant anemia requires compensatory responses that place an extra burden on critically ill patients, many of whom have preexisting cardiopulmonary disease. Moreover, critical illness can reduce the capability of cells to utilize oxygen even despite an adequate oxygen supply. This may be caused by inhibition of mitochondrial oxidative phosphorylation by pro-inflammatory cytokines and other substances such as nitric oxide [4].

The impact of anemia on the outcome of PICU patients has not been studied extensively. Some data suggest that severe anemia may be detrimental to critically ill children with septic shock or hemodynamic compromise [5]. The largest studies of the association between anemia and critically ill children involve pediatric patients with malaria, who had increased mortality with severe anemia (Hb<5 g/dL). In the adult population, anemia has been strongly associated with adverse outcomes, including failure of liberation from mechanical ventilation, type 2 myocardial infarction, and increased risk of death. It is difficult to ascertain whether anemia is an independent predictor of poor outcomes or merely a marker of more severe underlying disease not captured in chosen parameters of disease severity [6].

Anemia in critical illness has traditionally been treated with RBC transfusions. The primary goal of transfusion is to improve oxygen delivery to the tissues. Up to 50% of children who are hospitalized in PICU receive at least one RBC transfusion at some point during their stay, most frequently during the first 2 days after admission. The most transfused are neonates, with transfusion rates usually inversely related to the weight and/or maturity [3]. However, transfusion practice is an area of controversy in pediatric critical care and the optimal Hb threshold for RBC transfusion in critically ill children is unknown. Historically, transfusion recommendations were based upon the "10/30 rule", according to which RBC transfusions were indicated to maintain Hb concentration above 10 g/dL and a hematocrit level above 30 percent. Over the last two decades, pediatric intensivists and hematologists have become much more restrictive in the use of transfusions. There is a general agreement that the only indication for RBC transfusion is to provide a child with sufficient RBCs to prevent or reverse tissue hypoxia due to limited DO_2 [5].

Transfusion guidelines for children have been established by taking standards from adults and modifying them according to clinical experience, and are based principally upon child's age and clinical status. Pediatric transfusion practices are usually divided into two age periods, infants from birth to 4 months and children older than 4 months. Infants less than 4 months of age are considered separately because of their small blood volume and decreased production of erythropoietin. Neonates require special considerations. Premature infants suffer more readily than term infants from anemia, and 90% of infants with a birth weight of less than 1000 g are transfused. Premature babies have diminished erythropoietin levels, reduced RBC life span of 35 to 50 days, and a relatively hyporegenerative bone marrow. Beside physiologic factors, iatrogenic blood loss remains a significant source of anemia of prematurity [1]. The guidelines for children older than 4 months of age are similar to those used in adults. In general, RBC transfusion is recommended for Hb levels <7 g/dL (hematocrit<21 percent), since most anemic children have symptoms at this level. In children with Hb>10 g/dL (hematocrit >30 percent), RBC is generally not indicated. In children with underlying specific medical conditions, particularly cyanotic congenital heart disease and sickle cell disease, it may be preferable to maintain higher Hb levels. However, the decision to give RBC transfusion should not be based solely on Hb concentration, but upon the clinical situation. Accordingly, pediatric healthcare professionals should assess individually any critically ill anemic child, and take into consideration the risks of anemia versus the risks of transfusion. For children with symptomatic anemia or active bleeding, RBC transfusion is often warranted regardless of Hb level [6,7].

Although RBC transfusion therapy is a cornerstone in managing many critically ill children, it is no longer perceived as merely lifesaving. There is growing evidence that RBC transfusions are associated with complications and unfavorable outcomes. Most of the complications associated with pediatric transfusions are similar to those encountered in adults; however, metabolic complications occur more readily and with a greater frequency in children (e.g. hypocalcemia, hyperkalemia,

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hypochloremia, metabolic alkalosis and hypothermia). Other transfusion risks include acute and delayed hemolytic reactions, febrile non-hemolytic reactions, alloimunization, allergic reactions, transmission of infections (human immunodeficiency virus, hepatitis viruses, cytomegalovirus, human T-cell lymphotrophic viruses, parvovirus B19, West Nile virus, Plasmodium malariae, Trypanosoma cruzi, Babesia microti, Leishmania donovani, prions), volume overload, transfusion-related acute lung injury, and immunosuppression. At present, bacterial contamination of blood products presents the greatest risk for transfusion-transmitted infection, ranging from 0.2 to 7.4 events per million RBC units. Additional risks include the development of transfusion-associated graft-versus-host disease and transfusion-associated microchimerism in severely injured patients [8].

These risks and complications support a restrictive rather than liberal transfusion strategy in stable critically ill children. Transfusion in pediatrics should be considered as high-risk treatment that requires careful individual clinical assessment.

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