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Review Article

Blood Transfusion: A Powerful Process of Saving Anaemic Patients

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Abstract

Blood transfusion is very important in saving lives especially in anaemic states. Haemoglobin is needed for daily metabolic processes and for continued existence. Anaemic patients depending on the severity can face life threatening situations and may lead to loss of life in an environment there is no availability of blood for transfusion and trained experts. The paper was reviewed using different search engines like Pubmed, Google Scholar, Scopus, Researchgate, etc. It was shown that blood transfusion is helpful in anaemic patients to improve their lives and save them.

Keywords: *Blood Transfusion; Anaemic Patient; Hypoxia; Erythropoietin; Haemoglobin*

Introduction

Anemia is a normally met clinical case in the strictly sick [1]. Erythrocyte blood infusions are strongholds in the management of anaemic patients, resulting in a better list of routine medical approaches in admitted patients [2]. About 95% of seriously sick persons who are admitted in the intensive care unit (ICU) for 3 days or higher undergo from anaemia and measured to be 40% of them obtain packed erythrocyte blood infusion [3]. It was reported in 2001, almost 14 million units of packed erythrocytes were infused, but the physiologic source for transfusion in the serious sick is not with no challenge [4]. It was reported in the last 2 decades that blood infusion exercises have changed into extra restrictive possibly in reaction to future study.

A lot of blood infusions are recommended for sick persons with moderately low concentration of haemoglobin and only in checked condition. The first thought is that the blood infusion will raise oxygen availability and so lower insufficiencies thus reducing low tissue oxygen.

Insufficiency of oxygen to tissues can lead to many organ crash and high epidemiological disasters.

Dangers of blood transfusion in anaemic patient

The threats of blood infusion in patient with low haemoglobin concentration encompasses: the transmission of contagious ailment, immune repression, acute respiratory distress syndrome, circulatory overload and anomalies in blood infusion.

It has been deduced that after faced with liberal or defensive traditional blood infusion attributes, more restricting blood infusion procedures are adopted in line with a better practice of varied therapies. Although, we must be careful as this design can mount to causing patients unnecessarily to risks of anaemia and low oxygen by not giving blood infusions.

Weiskopf opined that while millions of units of erythrocytes are given, the biological potency of this approach has not been documented, regulated researches, nor do extra features be present by which one might determine the potency of the blood infusion of mass erythrocytes [5].

Study showed that blood infusion to patient with haemoglobin level leads to higher threat than help to patients and in the transfused group it presented an elevated level of horrible occurrences than it did to those without blood infusions [6].

Also, in clinical randomized checked studies determining the potency of red blood cell infusion [7], it is shown that the hindrance of blood infusion in patients with no bleeding has no main side effect on patient results, and it could yet get better results among some people. These researches suggest that blood transfusion for patient with low haemoglobin level gives little gain for serious sick patients with haemoglobin levels greater than 8 - 9 g/dl [8].

Etiology of anemia

The cause of low haemoglobin is many and dense. Recapped phlebotomies, gastrointestinal bleeding, and extra surgical approaches affix importantly to the development of low haemoglobin level [9].

Additional features included in etiology encompass coagulopathies, pathogen-linked haemolysis, hypoadrenalism and nutritional insufficiencies [10].

Correctible nutritional deficiencies in severely sick patients, as well as deficiencies of iron, B12 and folate.

These insufficiencies can lead to ineffective erythropoiesis with resultant anaemia [11].

Low erythropoietin synthesis and/or weakened bone marrow reaction to erythropoietin may also have a major role in the formation of low haemoglobin level. These effects are heightened by a diverse of inflammatory cytokines such as Interleukin-1 (IL-1) and tumor necrosis factor- (TNF), which prevent erythropoietin (EPO) formation. In addition, IL-1, IL-6, and TNF- impair synthesis of erythrocytes by direct inhibitory effects on bone marrow.

The hyperadrenergic situation after critical destruction may also stimulate bone marrow anomaly and crash of red blood cell formation. This result may be caused by IL-6 and interferon- (IFN-), which are released next to severe destruction and have been shown to hamper the differentiation and proliferation of erythroid progenitors [12].

Elevated echelons of hepcidin have been opined to have a major effect in the cause of low haemoglobin in anaemia of chronic disease [13]. The major usual factors of anaemia of chronic disease are acute or chronic inflammatory cases like infections, cancer, autoimmune diseases, and chronic renal illness. It is illustrated by confiscation of iron in macrophages, hypoferremia, and iron-restricted erythropoiesis. Anaemia of chronic disease is linked to increased degrees of inflammatory cytokines such as IL-1, IL-6. These cytokines stimulate surplus hepcidin formation, which has been reported to downregulate ferroprotein, an iron export protein on the cell exterior of duodenal enterocytes, macrophages, and hepatocytes [14]. Thus, elevated serum degrees of hepcidin reduce intestinal iron absorption and prevent iron export from tissue stores, leading to functional iron deficiency.

Other causes include: bleeding, frequent blood draws, a chronic condition or disease, medications, kidney disease, chronic infections, cancer.

Indications for transfusion

The purpose of blood infusion in the anaemic patient is to increase oxygen supply to and also utilisation by tissues. An increase in haemoglobin should improve patient's oxygen carrying ability and help supply oxygen to low oxygen tissues. Lactate, a clinically used surrogate of tissue low oxygen, should lower with improved oxygen utilisation. Enough of published works over the past 3 decades show that this clinical consumption is mostly not realized with transfusion in the severely sick. Dietrich et al. in a superior research in the early nineties transfused volume resuscitated severely sick persons to a haemoglobin of 10 g/dl [15]. These sick persons again had increased measured oxygen supply but no increased oxygen uptake; no reduction in lactate, and no increase in cardiac index.

Marik and sibbald studied 23 severely sick persons with sepsis in a future research and showed that transfused patients had no elevation in oxygen usage [16]. Also, Mazza., *et al*. in a likely research in 2005 showed that transfusing patients to a haemoglobin above 9 g/dl was not linked to a considerable reduced lactate or raised mixed venous oxygen saturation, sign of no benefit in meeting earlier unmet tissue oxygen necessities [17].

The mean age of blood transfused in the USA is 17.9 days and wide documentation exists about age-related alterations of packed erythrocytes [18]. Stored blood cells have reduced levels of 2,3-diphosphoglycerate which shifts the oxygen disassociation curve to the left, reducing haemoglobin's capacity to deliver oxygen at the tissue level. Stored erythrocytes have been transported to lose their deformability leading in raised aggregation, haemolysis and the following discharge of systemic factors associated to organ anomaly [19]. Fitzgerald., *et al*. showed in rats that transfused blood which was less than 3 days old was linked to an elevated systemic oxygen uptake as opposed to blood that was 28 days old [20].

Complications of transfusion

Infection

Historically, the AIDS menace obliged the critical care community to re-measure the gains of blood transfusion in the ICU. Due to these worries blood is now screened for a diverse of viral and bacterial infections as well as HIV and Hepatitis A, B, and C. In the United Kingdom, the danger of acquiring infection due HIV secondary to transfusion is less than one in 2 million [21].

The spread of infection is only one of the methods blood can affect its possible recipient. In the early seventies, it was noticed that kidney transplant patients who received a transfusion prior to transplant had elevated allograft survival. This outcome led to extra hypothesis in the medical literature that the transfusion of blood may affect the recipient's immune system. Over the past forty years numerous studies have weighed the effect of transfusing on transplant survival, cancer recurrence, and host predisposition to infection [22].

Taylor et al. in a past research of 1711 patients shown that transfused patients were 6 times more probable to form a hospital acquired infection than non-transfused patients [23].

Also, each unit of packed red blood cell transfused raised patients odds of forming infection by 1.5. Claridge., *et al*. showed in a future research of 1593 trauma patients that 33.6% of transfused patients formed infection versus 7.6% patients who did not receive transfusions [24]. They also opined that a linear, dose-response pattern existed, as patients who received more packed red blood cell were more possible to form infection. Univariate analysis of their data revealed that the most indicator of forming infection was the transfusion of packed red blood cell in the first 48 hours. Shorr., *et al*. carried a crucial secondary analysis of the CRIT study involving 284 ICUs and 4,892 patients to determine blood stream infections (BSIS) in the severely sick [25]. These researchers showed that 3 factors were linked to new BSI in the ICU: the early work of cephalosporins, higher order organ collapse evaluation rating, and packed red blood cell transfusion. The relevance of their study is that the data came from multiple ICUs unlike single-center researches cited previously and the patient populations were mixed. Shorr., *et al*. carried another secondary analysis of the CRIT study and showed that both small (1 - 2 units) and large (> 2 units) volume transfusions were independent risk factors for the formation of ventilator-related pneumonia [26].

In cardiac surgery patients the transfusion of packed red blood cell has been likewise linked to raises risk of infection [27]. Though, Ali., *et al*. in a prospective, single-center study of 234 patients showed that packed red blood cell was not linked to elevated risk of infection in postoperative cardiac surgery patients [28]. Multiple large well-designed trials show that blood transfusion in anaemic patient expose patients to infection may be due to the immunomodulation of the patient's immune system.

Impact of blood transfusion on clinical outcomes

A developing body of proof now shows that correcting anaemia by transfusion often either gives no benefit or is harmful. The TRICC trial revealed a considerable elevation in cardiac and pulmonary impediments and a pattern toward increased mortality in the liberal transfusion group during patients intensive care stay. In subgroup analysis, younger (age < 55 yrs) or less critically sick (APACHE II scores < 20) patients randomized to a liberal strategy had a statistically considerable elevation in mortality [29].

The CRIT study showed that the number of blood transfusions was independently associated with both length of stay and mortality in ICU patients. A cohort analysis within the CRIT study revealed blood transfusion to be independently linked to formation of acute respiratory distress syndrome (ARDS) [30].

In 2002, Vincent., *et al*. opined a prospective observational study measuring the blood sampling, haemoglobin status, and transfusion rates in 146 Western European ICUs [31]. They concluded that receipt of a blood transfusion increased patients odds of dying and increased patients length of stay in the ICU.

In 2008, Vincent., *et al*. published another prospective observational study that included 198 European ICUs [32]. This study revealed that transfused patients had a reduced mortality than non-transfused patients at 30 days when patient populations were compared to propensity scores. Considerable argument exists about the use of a propensity score for statistical analysis involving the inability to balance unquantified clinical factors in the studied populations. Vincent et al. have encouraged additional debate about the need for another prospective trial comparing a liberal versus conservative blood transfusion plan in the severely sick, particularly in the period of leukodepletion of packed red blood cell transfusions.

Transfusion impact on cardiac disease

Statistics from the first TRICC trial showed that patient in the liberal transfusion arm (i.e. those transfused at a threshold haemoglobin of 9 g/dL versus 7 g/dl for the restrictive group) had a superior frequency of both pulmonary edema and MI [33]. Then, a subgroup analysis of patients from the TRICC trial with heart disease failed to show any considerable mortality results between groups. Though, patients in the liberal transfusion group had a greater incidence of organ dysfunction [34].

Sabatine., *et al*. [35] found varying outcomes for patients with STEMI and those with non-ST-elevation ACS. Patients with STEMI and haemoglobin levels < 12 g/dl had enhanced results when transfused. Equally, patients with non-ST-elevation ACS were established to have poorer results if transfused, not minding their haemoglobin level.

Many researches in cardiac surgery patients have showed blood transfusion to be independently linked to elevation in infectious impediments, myocardial infarction (MI), stroke, kidney failure, prolonged mechanical ventilation, atrial fibrillation, hospital length of stay, and mortality [36].

Blood conservation

Patients in the ICU on average have 41 ml of blood drawn over a 24-hour period with sicker patients requiring extra recurrent blood draws causing even higher blood loss [3]. Older literature has shown that patients with an arterial catheter may lose higher than 900 ml during their stay [37]. Educational programs about lowered sampling, point of care testing, and closed arterial line system have all been recommended [3].

Alternatives to transfusion

Usually, processes would exist to reduce or get rid of the need of blood transfusion altogether. Severely sick patients with anaemia have been reported to have an inappropriately low erythropoietin reaction to their disease. Corwin et al. in two works showed that infusion markers were reduced in severely sick patients treated with erythropoietin. However, in their third work erythropoietin therapy did not considerably change the rate of transfusion in the severely sick patients. Mortality was non-significantly unlike in the medical population, but considerably reduced in trauma patients at 140 days, though this reduction in mortality was not connected to any variation in transfusion rates in the groups that received and did not receive erythropoietin. This observation led the researchers to hypothesize that erythropoietin reduces mortality in trauma patients by mechanisms other than the decrease in packed red blood cell requirements [38].

One other process for lowering packed red blood cell transfusion is artificial oxygen carriers or haemoglobin alternatives. Haemoglobin alternatives can be categorised into 2 categories, perfluorocarbons and modified haemoglobins. Perfluorocarbons carry both oxygen and carbon dioxide but need patients to be on 100% oxygen. The gains of perfluorocarbons over PRBC are their lack of potential infection transmission and their long half-lives. They have been reported to reduce the need for blood transfusions in patients with elective noncardiac surgeries.

Though, bovine, old human, and recombinant-based haemoglobin-based oxygen carriers (HBOC) have been majorly researched for 30 years only one HBOC is approved for clinical use. The utility of these haemoglobin-based blood units recently is thought to be the power to lower allogenic PRBC infusion and provide a blood substitute in cases where blood is unavailable.

Conclusion

Anaemia is common in critically ill patient. The blood transfusion is a mainstay in the treatment of anemic patients. These blood transfusions are not without risks. The risk-benefit profile for blood transfusions to treat anaemia is uncertain, but they may contribute to adverse patient outcomes in some situations.

However, despite growing evidence that risk of blood transfusion outweighs its benefit, but significant numbers of critically ill patients still receive blood transfusion during their intensive care unit (ICU) stay.

Red blood cells transfusions are widely used in the treatment of anemia, although adequate thresholds for its use remain controversial. Although therapeutic approaches should be subject to a rigorous monitoring of its efficacy and safety before use in clinical setting, red blood cell transfusion has not been subjected to a similar examination. Besides the already known challenges from transfusions, numerous works show that red blood cell infusion may be linked with different side effects.

The few results and non-controversial data have not overcome the challenges that have hindered previous works to establish a policy or step for red blood cell infusion. Despite these challenges and the lack of exact solutions, clinicians often have no other choice but the agreed procedure [39]. Almost 2/3 of clinicians report regularly transfusing red blood cell in probably unnecessary cases, and there is a big gap in transfusion approaches with respect to weight that is linked to clinical factors used in decision making, which also hinders the characterization of current practice.

A high priority for future clinical works should be discovering the efficacy of red blood cell infusion those conditions grouped as uncertain. In the absence of data, it is good that red blood cell infusion begiven with carefulness in these clinical cases. Hence, we should carry it out on an individual basis, i.e. carefully weighing the risks of low haemoglobin level and the risks and benefits to be derived from each of these units of blood for each patient, caring for them with the appropriate dosage and checking the expected therapeutic outcome.

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