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Review Article

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Transfusion in Oncology

Carlos A. Gonzalez[1,2*] and Silvana Gonzalez[3]

[1]*Servicio de Hemoterapia, Hospital Muñiz, Buenos Aires, Argentina*

[2]*Dirección de Posgrado, Medical School, Pontificia Universidad Católica Argentina, Buenos Aires, Argentina*

[3]*Medical School, Pontificia Universidad Católica Argentina, Buenos Aires, Argentina*

[*]Corresponding author

Carlos A Gonzalez, Servicio de Hemoterapia, Hospital Muñiz, Buenos Aires, Argentina, Dirección de Posgrado, Medical School, Pontificia Universidad Católica Argentina, Buenos Aires, Argentina, E-mail: carlosgonzalez@buenosaires.gob.ar

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Abstract

Cancer patients often have hematological disorders which can affect erythrocytes, platelets, leukocytes or blood proteins. Therefore, transfusion support is essential in the treatment of oncological patients.

Keywords: Blood Transfusion – Red Blood Cells – Platelet Concentrates – Plasma

Introduction

Cancer patients often have hematological disorders which can affect erythrocytes, platelets or blood proteins [1].

Among these alterations, anemia is the most frequent cytopenia (30-90% oncological patients it at some point of their disease); being the frequency higher in patients with hematologic neoplasms (76 %) and those receiving chemotherapy (61%) [2].

The cause of anemia is often multifactorial, and can be caused by nutritional disorders, haemorrhage, autoimmune hemolysis, erythroid aplasia, chronic disease, or as a result of chemotherapy and radiotherapy [3].

Therefore, transfusional therapy is essential in the support of the treatment of cancer patients.

In fact, transfusions improve symptoms very quickly [4,5]. However, some complications may appear, most of them mild, and some of them severe which can lead to death.

In this brief review we will approach the most important aspects of transfusional support for cancer patients.

Components and Derivatives

The blood components are all those products obtained by mechanicals methods such as centrifugation or cellular processors (apheresis). These labile components are characterized by having a short expiration period and the need of strict conservation conditions, they are the red blood cell concentrates, platelet concentrates, plasma, cryoprecipitate and y granulocyte concentrates (Fig 1)

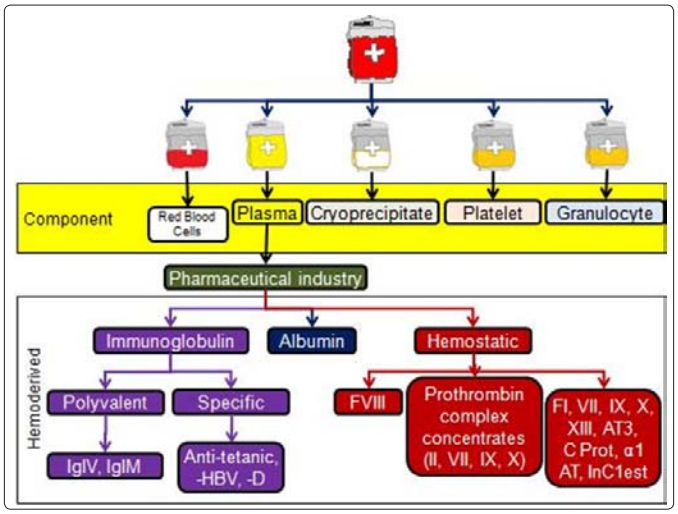

Figure 1: Blood product

IgIV: immunoglobulin intravenous
IgIM: immunoglobulin intramuscular
FVIII: Factor VIII
AT3: Antithrombin 3
C Prot: C Protein:
α1 AT: α1 antitrypsin
InC1est: C1 esterase inhibitor

On the other hand, the hemoderivates are those produced in large scale (pharmaceutical industry) and are obtained from large volumes of plasma. Their conservation is generally prolonged, such as Factor VIII concentrate, polyvalent intravenous immunoglobulins, hyperimmune anti-D globulin, etc.

Tranfusional Ethics

Prior to the transfusional act, the patient **must be informed** of:

- Steps of the transfusion process.
- The risks of transfusion.
- The benefits of transfusion.
- The alternative therapies available.
- The right to accept or refuse the procedure.
- The only reason to transfuse is a **legitimate clinical need**.

Therefore, the informed consent must be obtained, which is a process by which the patient/responsible family member is informed by the physician, and then agrees to the treatment.

As a result, the patient/responsible family member must understand why the physician recommends the transfusion, its risks and benefits, and appreciate the possible consequences of not receiving the recommended transfusion.

Recommendations

The recommendation to transfuse patients with anemia is based on levels of evidence:

- Grade 1: Strong recommendation
- Grade 2: Weak recommendation
  - Level A: High methodological quality (Randomized control trial)
  - Level B: Moderate methodological quality (No randomized)
  - Level C: Low methodological quality (expert committee)

Red Blood Cell Concentrate

The red blood cell concentrate (RBC) is the component that is obtained by extracting the plasma of a donated blood unit. Each administrated unit can raise the level of haemoglobin (Hb) by 1 g/dl and the hematocrit (Ht) by 3 percent points.

In pediatric patients the transfusion of 8 ml/kg increases the level of Hb by 1 g/dl.

The objective of transfusional treatment is to improve the oxygen transport capacity and avoid its symptomatology. Only the patient with symptoms of moderate severity caused directly by anemia must be transfused. It's important to consider that the transfusion will only temporarily improve the anemia, since the underlying disorder persists.

The indication of RBC transfusion shall take into account:

- The age and cardiovascular state of the patient
- The speed of onset and progression of the anemia
- The symptoms dependent on anemia
- The concentration of Hb
- The probable efficacy of other treatments

In a general way, it can be established that transfusion is indicated to maintain a 7-8 g/dl level of Hb. If the level of Hb is 5-8 g/dl, clinical judgement is essential to make the decision of whether to transfuse or not. If Hb is less than 6 g/dl, most patients require repeated transfusion (Fig 2) [6-8].

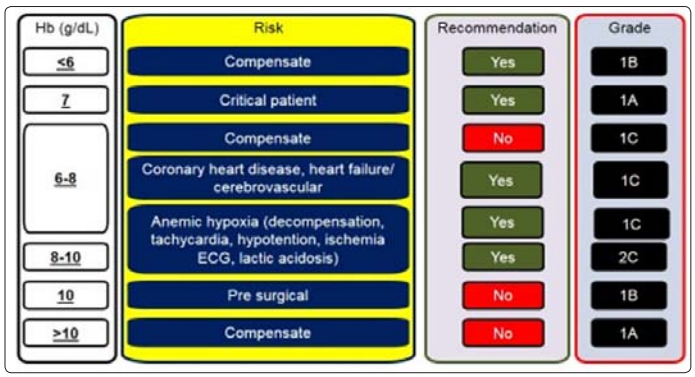

Figure 2 : RBC Transfusion
ECG: electrocardiogram

Even in critical patients, it seems that a restrictive RBC transfusion strategy is as effective (and possibly more effective) than the classic liberal strategy (Fig 3) [9-11].

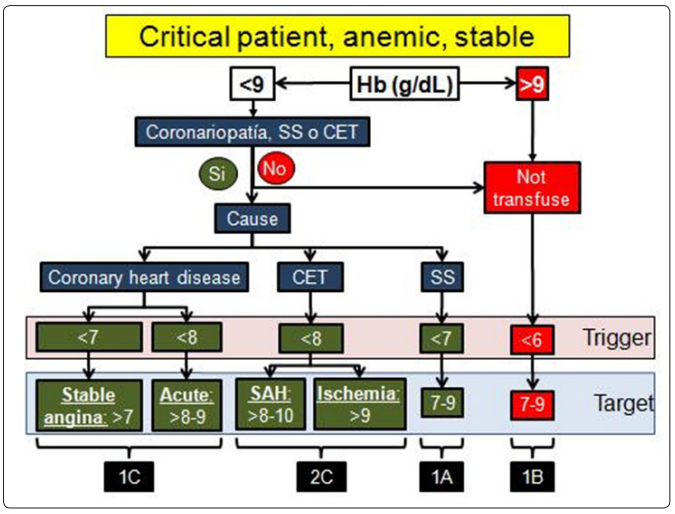

Figure 3: RBC Transfusion in critical care
CET: Cranioencephalic Traumatism
SAH: Subarachnoid hemorrhage
SS: severe sepsis

In post-chemotherapy cancer patients, it may be important to maintain a level of Hb between 8-9 g/dL, and those subjected to radiotherapy an Hb higher than 10g/dL.

RBC transfusion is not indicated in chronic anemia if it can be treated with specific medications (iron, vitamin B12, erythropoietin or folic acid) [12-15].

There is no indication to transfuse in:

- Asymptomatic Anemia or correctable with drugs.
- To normalize Hb/Ht, coagulogram, platelet count, to correct acid-base balance, hypoproteinemia or heal wounds (plasma).
- Improve the "general conditions of the patient" or as a "volume expander".
- To shorten the hospitalization time.
- Family presence.
- Blood availability (autologous).

Key Points

There is no definite and general degree of anemia that indicates the need to transfuse.

- It is the clinical situation of the patient and not the level of Hb that determines the transfusion.
- The only justified indication of transfusion is the need to improve the delivery of oxygen to the tissues in a short period of time.
- A surgical intervention is not in itself a transfusional indication.

Platelet Concentrates

The platelet concentrate is a platelet suspension in plasma prepared by centrifugation of a total blood unit, or a single donor by plateletpheresis.

The types of bleeding are classified, according to the World Health Organization (WHO), in grade 0, no bleeding; grade 1, petechiae, ecchymosis, occult blood in body secretions; grade 2, severe hemorrhage that does not require RBC transfusion (epistaxis, hematuria, hematemesis, for example); grade 3, haemorrhage that requires the transfusion of 1 or more units of red blood cells/day; and grade 4, potentially deadly hemorrhage, defined as massive haemorrhage which causes hemodynamic compromise or haemorrhage in a vital organ (such as intracranial, pericardial or pulmonary hemorrhage) [16].

Platelet transfusion is used therapeutically in patients with haemorrhage grade 2 or higher. The prophylactic use of platelet transfusion is indicated in grade 2 bleedings or lower and is directly related to the platelet count (postchemotherapy or postradiotherapy). In general, higher bleeding grades (2 o >) are more related to additional factors than with the platelet count, and although they are transfused, bleeding may persist if these factors such as fever, splenomegaly, drugs, disseminated intravascular coagulation (DIC), among other factors, are not detected and corrected [16].

Before deciding the platelet transfusion, the severity of the hemorrhage, the platelet count, their functionality and the cause of the thrombocytopenia should be assessed (Fig 4).

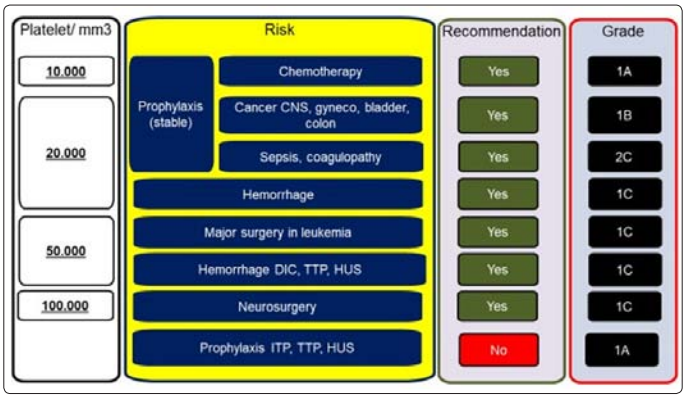

Figure 4: transfusion of platelet
DIC: disseminated intravascular coagulation
TTP: thrombocytopenic thrombotic purpura
HUS: hemolytic uremic syndrome
ITP: immune thrombocytopenic purpura:

The dose to be administered depends on the type of platelet concentrate (multiple or single donor - plateletpheresis) according to the following table:

		Count x 1010	Dose	Expected increase
	Multiple	5,5	1 U c/10 Kg weight	5.000 x U
Donor	Single (plateletpheresis)	31	1 U	17.000
		49		32.000

The assessment of the recovery and the clinical efficacy of the transfusion is based on the cessation of hemorrhage and the platelet counts one hour after the transfusion. If the recovery is not good, the patient may be refractory to platelet transfusion. Splenomegaly will decrease recovery in 20%.

Key Points

Cause of thrombocytopenia: ↓production, ↑destruction or dysfunction. Beware: drug-induced thrombocytopenia (DIT) due to heparin, hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP).

Evaluate:

- ✓ Active bleeding, fever, splenomegaly, anemia.
- ✓ Platelet count in the moment of indication and the state of hemostasis.
- ✓ Drugs (amphotericin, antiaggregants, e.g. acetylsalicylic acid).
- ✓ Previous response to platelet concentrates transfusion.
- ✓ Invasive procedures to perform.

It is the clinical situation of the patient and not the platelet count that determines the transfusion.

Plasma

It is obtained by centrifugation of a unit of blood. Each unit can increase most of the coagulation factors by 3-5%.

Its use should be limited to the treatment of the well-documented multiple coagulation factors deficits and associated with active bleeding (DIC, massive transfusion) or surgical intervention.

Although generally it is used to normalise the international normalized ratio (INR), there is not enough evidence to justify this practice (Fig 5).

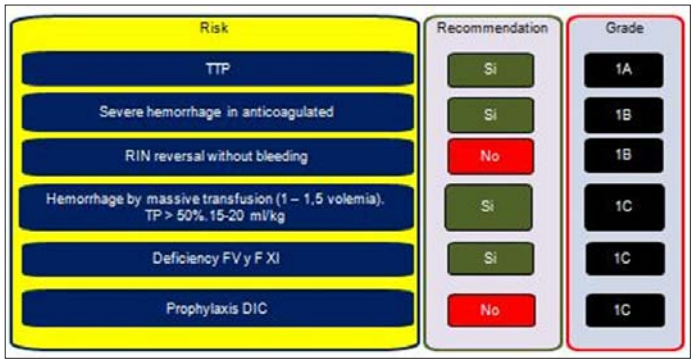

Figure 5: transfusion of plasma
TTP: thrombocytopenic thrombotic purpura

RIN: International normalized ratio
TP: time of prothrombin
DIC: disseminated intravascular coagulation

The dose usually effective is 15 - 25 ml/kg body weight, and later 10 ml/kg [17]. Although prothrombin time may provide useful information regarding the response to treatment, the need of additional treatment depends on the clinical response and not the laboratory tests.

Key Points

It is not indicated in the following situations:

1. Volume replacement (crystalloids are safer, more economical, and more available).
2. As a replacement liquid in therapeutic plasma exchange (except for PTT).
3. Alteration of coagulation tests without evidence of bleeding. No clinical trial has shown benefit of prophylactic transfusion of fresh plasma in patients without hemorrhage or before invasive procedures.
4. Contribution of plasma proteins (including immunoglobulins).

Cryoprecipitates

It is the insoluble in cold plasma fraction, obtained from a unit of fresh frozen plasma. The final product contains 60-85% of factor VIII, von Willebrand factor and factor XIII as well as fibrinogen in 10% of the original volume (10 - 15 ml of plasma) [14].

It should only be used in a demonstrated fibrinogen deficiency or in the absence of adequate therapeutic concentrate for von Willebrand disease (Fig 6).

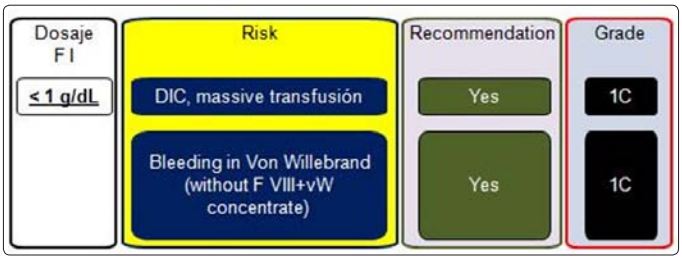

Figure 6: transfusion of cryoprecipitate

Leucoreduction

It is the processing of RBC or platelet concentrates prepared by a method that reduces the number of white blood cells in the final component to less than 5 x 10^8 (Fig 7 and Fig 8) [8].

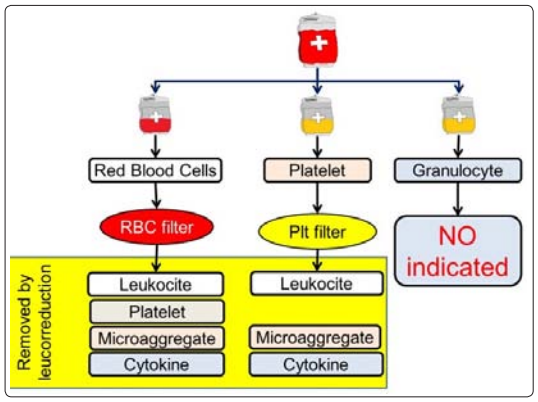

Figure 7: Leukorreducion

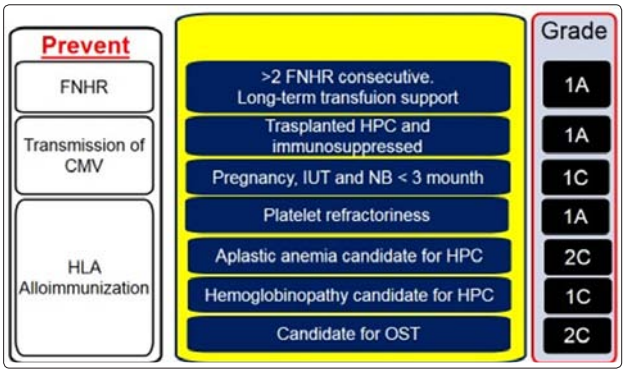

Figure 8: Indication of leukoreduction
FNHR: Febrile no hemolytic reaction
IUT: intrauterine transfusion
HPC: hematopoietic progenitor cells
CMV: cytomegalovirus
OST: organ solid transplant

It is indicated to prevent:

1. Febrile non-hemolytic transfusion reaction (FNHTR).
2. Cytomegalovirus transmission in CMV negative receptors and reinfection with other virus strains in CMV positive receptors.
3. HLA alloimmunization responsible of immunological refractoriness to platelet transfusions.

One of the risks associated with the use of leucoreduced units is the hypotensive transfusion reaction, frequent in leucoreduction decided at patient's bedside and in patients treated with angiotensin converting enzyme inhibitor (ACE inhibitor).

Irradiation

It is the inactivation (shortens survival and inhibits proliferation) by radiation of T lymphocytes present in the cellular component to prevent transfusion-associated graft-versus-host disease (TA-GVHD). The components involved in this complication are: RBC concentrates, platelet concentrates, leukocyte concentrates, fresh plasma not frozen [8].

The most important indications are (Fig 9):

- Patients with risk of developing TA-GVHD.
- Donations from family members of the receptor.
- Patients receiving HLA compatible components.

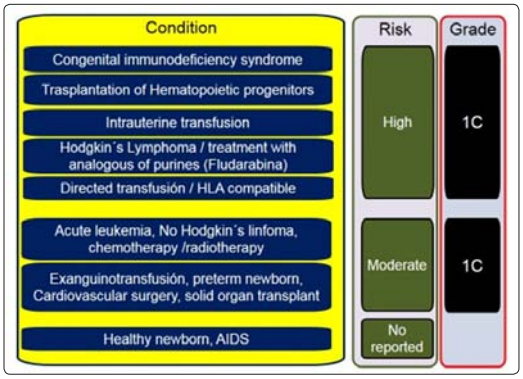

Figure 9: Irradiation of component

Transfusional Risk

Blood transfusions are a medical intervention that presents risks

inherent to the procedure and to the biological origin of the component, which is the human being itself [18].

The prevalence of adverse reactions varies: most cases are mild 1:100; severe 1:370 and fatal 1:117.000 [19-21].

Because many of these reactions **are inevitable**, transfusions in cancer patients must be monitored constantly to ensure their early detection and treatment [22,23].

Synthesis

The most relevant practical aspects from a clinical point of view are:

			RBC concentrate	Platelet concentrate/ plasma	Granulocytes concentrate
Needle calibre			18	23	>20
Filter			170-260 µm	170-260 µm	170-260 µm
Leucoreduction			Yes	Yes	No
Irradiation			Yes	Yes	Always
Microaggregate			Yes	No	No
Volume			300 ml	150-270 ml	200-300 ml
Infusion	Time	Average	1- 2 h	30 minutes – 1 hour	2-4 h
		< than	4 h	4 h	4 h
	Velocity		2-5 ml/ minutes	4-10 ml/ minutes (no < 2 ml/m)	1 ml/minute

Conclusion

Since transfusional support in cancer patients is essential in the context of their integral treatment, it is important to recognise the indications of transfusions. This publication aims to contribute to their updating.

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