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Essentials of anaemia in the intensive care unit

# FOCUSING ON EFFECTIVE AND SUSTAINED PATIENT-CENTERED CARE

Prepared by: Dr. Jameela Sathar & Dr. Ananthi Krishamoorthy as part of MyPBM education program.

Approved by: MyPBM committee
Reviewed by: Dr. Aryeh Shander, Clinical Professor of Anaesthesiology

# Anaemia in Intensive Care~
## Focusing on effective and sustained Patient- centred care

## INTRODUCTION

Anaemia is a common medical condition in critically ill patients admitted into the intensive care unit (ICU). Studies have shown that two-thirds of these patients have a haemoglobin concentration (Hb) below 12 g/dL on admission and 95% become anaemic after 3 days in ICU.[1,2]

The World Health Organization (WHO) defines anaemia as:

- Hb <12 g/dL in women
- Hb <13 g/dL in men

The default treatment of anaemia in critically ill patients, namely transfusion of red cells, has shifted from liberal transfusions to restrictive transfusions in the past 2 decades. Although this is progress, it is crucial to shift focus from product to patient, true to the real intent of patient blood management (PBM).[3]

Management of anaemia involves identifying causes and targeting therapy to specific causes just as we do with other disease management. This will provide effective and sustained results and possible cure, with good outcome for patients, while reducing cost.[2,3,4]

- As common as anaemia is, and is something expected to be present in the critically ill, it should not be considered as acceptable, only to be acted upon when reaching the transfusion threshold.
- A proactive approach to prevention, detection and management of anaemia will save both the patient and healthcare cost.

# CAUSES OF ANAEMIA IN CRITICALLY ILL PATIENTS

The causes of anaemia are multifactorial **(Table 1).**[1,2,3,4,5]

**Table1: Causes of anaemia in critically ill patients in ICU**

| | Causes of anaemia | Mechanisms |
|---|---|---|
| 1. | Loss of red blood cells | ○ Frequent phlebotomies (average 40 – 70 mLs of blood loss daily; every 100 mLs blood loss decrease Hb by 0.7 g/dL)<br>○ Bleeding from:<br>  ○ surgical sites<br>  ○ trauma sites<br>  ○ venous access sites<br>  ○ gastrointestinal (GIT)<br>○ Bleeding due to coagulation abnormalities<br>  ○ Liver disease<br>  ○ Thrombocytopenia<br>  ○ Disseminated Intravascular Coagulation (DIC)<br>  ○ Hypothermia leading to acidosis |
| 2. | Decreased production of red blood cells | ○ Iron sequestration & reduced iron absorption from gut<br>  ○ Inflammation/ infection (anaemia of inflammation or chronic disease), critical illness<br>○ Erythropoeitin deficiency<br>  ○ Functional<br>  ○ Inflammation/ infection (anaemia of inflammation or chronic disease), critical illness<br>  ○ Absolute<br>  ○ Renal insufficiency<br>○ Bone marrow suppression<br>  ○ Infection, inflammation, drugs |
| 3. | Increased destruction of red blood cells | ○ Haemolysis<br>  ○ Drugs, infections, alloimmunization |
| 4. | Nutritional deficiency | ○ Iron, folate or B12 deficiency |
| 5. | Haemodilution | ○ Fluid resuscitation, massive transfusion |

## CONSEQUENCES OF ANAEMIA

Anaemia is associated with poor outcomes in all patients, with or without co-morbid conditions. The compensatory response of anaemia is an extra burden in critically ill patients especially those with cardiopulmonary failure.[2,3,4]

Anaemia also increases chances of patient's exposure to blood transfusion that may not only be unnecessary but largely avoidable in most circumstances.[3]

Blood transfusion has its risks such as: [1,3]

- transfusion-associated circulatory overload (TACO)
- transfusion-related acute lung injury (TRALI)
- transfusion-related immunomodulation (TRIM) predisposing to increase risk of nosocomial infections
- transfusion-transmitted infections (TTI)
- venous thromboembolism (VTE)
- red cell alloimmunisation and haemolysis
- diminished organ function
- increased mortality

## MANAGEMENT OF ANAEMIA IN THE ICU- INCORPORATING PRINCIPLES OF PBM [3]

Among the critically ill patients, PBM can be particularly effective given the extremely high prevalence of anaemia, variable and unjustified transfusion practices, high frequency of coagulation disorders and avoidable sources of blood loss such as unnecessary diagnostic blood draws. Incorporating PBM principles involves a multidisciplinary, multifaceted approach for patient-centred decision making.

The proper management of anaemia in the ICU is focused on the **prevention of anaemia** (taking into account coagulopathy and blood loss) and **harnessing tolerance to anaemia** . A restrictive transfusion strategy is only one among many treatment modalities that should be weighed based on its merits – potential risks and benefits – for the individual patient in the context of other alternatives.

## Prevention of anaemia

Clinicians must recognise that anaemia is a common problem in critically ill patients managed in the ICU and must have steps in place to prevent or reduce its occurrence **(Table 2).**[3] Iron deficiency and anaemia of inflammation are the most common causes. As ferritin is an acute phase reactant, it is not a reliable marker to diagnose iron deficiency in the critically ill.[1]

Intravenous iron and subcutaneous erythropoietin are 2 modalities of treatment that have been shown to be effective in the treatment of anaemia in these patients. In 3 randomised controlled studies in critically ill patients, erythropoietin increased haemoglobin levels while reducing allogeneic blood transfusion in the early 2 studies, improving patient outcomes and reducing mortality.[6,7,8]

A meta-analysis of randomised clinical trials showed that intravenous iron therapy is effective in increasing haemoglobin concentration and reducing the risk of allogeneic red blood cell transfusion in acute care settings.[9]

**Table 2: Prevention of anaemia in critically ill patients in ICU**

| | Causes of anaemia | Preventive measures |
|---|---|---|
| 1. | Loss of red blood cells | ○ Reducing blood loss from phlebotomies<br>○ Minimising blood tests<br>○ Using small-volume phlebotomy (paediatric) tubes<br>○ Continuous non-invasive Hb monitoring [10] tubes<br>○ Preventing peptic ulcer<br>○ Prophylaxis with proton-pump inhibitors<br>○ Early nutrition<br>○ Preventing / managing bleeding from coagulopathy<br>○ Vitamin K supplementation [11]<br>○ IV Vitamin K 10 mg 2x/week<br>○ Preventing hypothermia<br>○ Warming techniques<br>○ Point of care testing<br>○ Viscoelastic test for targeted haemotherapy |
| 2. | Decreased production of red blood cells | ○ Iron sequestration & reduced iron absorption<br>○ Intravenous (IV) iron therapy<br>○ After acute sepsis control<br>○ 100 mg EOD 3x/week<br>○ Erythropoietin deficiency [8]<br>○ S/C erythropoietin therapy<br>○ Indicated in patients with renal insufficiency (Creatinine Clearance <60ml/min)<br>○ 50-100 units/kg per dose 2-3x/week with supplemental IV iron<br>○ Anaemia of inflammation or chronic disease<br>○ 40,000 units once weekly or 300-600 units/kg/week with supplemental IV iron (to reduce the effect of functional iron deficiency) [6,7,8]<br>○ Avoiding bone marrow suppression<br>○ Treat infections promptly<br>○ Review drugs that can cause marrow suppression e.g. Bactrim, Cephalosporins |

| | | |
|---|---|---|
| 3. | Increased destruction of red blood cells | ○ Preventing haemolysis<br>○ Ensure patient is not Glucose-6-Phosphate Dehydrogenase (G6PD) deficient<br>○ Review drugs that can cause haemolysis e.g. Nitrates, Methyldopa, Dapsone, Cephalosporins<br>○ Treat infections promptly<br>○ Judicious use of blood transfusions to avoid alloimmunisation |
| 4 | Nutritional deficiency | ○ Early nutrition<br>○ Supplement with folic acid, S/C vitamin B12 and IV iron<br>○ Oral folic acid 5mg once daily (water-soluble, readily absorbed)<br>○ S/C or I/M Vitamin B12 1mg once a month<br>○ IV iron 100mg EOD 3x/week |
| 5. | Haemodilution | ○ To avoid unnecessary blood transfusions based on target Hb level, be aware that [5]<br>○ haematocrit decreases by 30% up to 3 hours following fluid resuscitation due to haemodilution or<br>○ 500 mLs of fluid reduces Hb by 1g/dL or about 8% |
| Note | EOD | Every other day |
| | S/C | Subcutaneous |
| | I/M | Intramuscular |
| | IV | Intravenous |

## Harnessing tolerance to anaemia

The 3rd pillar of PBM (harnessing tolerance to anaemia) plays an important role in anaemia management as well.[3] It is crucial to support patient while erythropoiesis is taking place, along with other measures such as:

- sepsis management
- temperature control
  - reduces shivering/rigors which consumes energy
- intubation, paralysis and ventilation
  - reduces energy requirements

## Looking beyond transfusion thresholds

- As demonstrated in transfusion practice in critically ill patients (the TRICC trial[12] and other large cohort studies), transfusion of RBC at haemoglobin level of less than 7 g/dL is as effective as, or possibly superior than using a more liberal threshold of Hb less than 10 g/dL, with the possible exception of patients with

acute myocardial infarction or unstable myocardial ischemia. (due to the paucity of data on these patients).

- Studies on the effect of blood transfusion on the indices of tissue hypoxia in critically ill patients did not show that blood transfusion improves tissue hypoxia in these patients with baseline Hb > 8g/dL.[13]
- The guidelines from the joint taskforce of Eastern Association for Surgery of Trauma (EAST) and the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM) emphasise that [14]
  - **use of haemoglobin as the only "trigger" for RBC transfusion should be avoided.**
  - transfusion decisions should be made based on other parameters
    - patient's volume status,
    - evidence of shock,
    - duration and severity of anaemia, and,
    - cardiopulmonary status of the patient.
- We should not limit ourselves to the dichotomy of accepting anaemia or ordering blood, when there are many treatment modalities available, just as it is for other diseases. [15]
- Hence, when all reasonable measures have been taken, and when absolutely necessary and unavoidable, then an individualised restrictive transfusion strategy is sought. When indicated and with exception of acute haemorrhage, RBC transfusion should be given as **a single unit at one time**, with **reevaluation** of the patient prior to giving the next unit. [14]

- In the event of bleeding, a good quick action would include identifying and arresting bleeding, while giving supportive management and optimising erythropoiesis (again incorporating the fundamental 3 pillars of PBM) as well as engaging the patient in decision making.

- As tempting as it may be to reach for the transfusion of RBC once a threshold is met, we must remember, we should never treat a number, but only the patient.

*" If blood is an organ, then anaemia is blood failure; and just like organ transplant which is the last resort for organ failure, blood transfusion (liquid transplant) should also be the last resort for anaemia after all necessary measures have been taken "*

*Sherri Ozawa,*

*President SABM*

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