Skrb za bolnikovo kri: kje smo in kako naprej

Patient Blood Management: Where Are We Now and What Should We Do?

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Izvleček

Program »Skrb za bolnikovo kri« (angl. Patient Blood Management, PBM) temelji na interdisciplinarnem pristopu, osredotočenem na pacienta in je zasnovan kot niz ukrepov, ki temeljijo na treh stebrih: 1. celovito obvladovanje anemije; 2. zmanjšanje izgube krvi in optimizacija koagulacije perioperativno; 3. izkoristek in optimizacija bolnikove specifične fiziološke tolerance anemije. Zaradi učinkovitosti in varnosti tega pristopa ter dejstva, da zaradi anemije trpi več kot 30 % celotnega svetovnega prebivalstva, kar uničujoče vpliva na zdravje in gospodarstvo, je Svetovna zdravstvena organizacija leta 2021 izdala priporočilo o nujnosti uvedbe PBM programa.

Stopnja izvajanja programa PBM se po evropskih državah razlikuje.

Abstract

Patient blood management (PBM) is an interdisciplinary, patient-centred approach based on three pillars: 1) comprehensive anaemia management; 2) minimization of blood loss and optimization of coagulation perioperatively; and 3) leverage and optimization of patient-specific physiological tolerance of anaemia. The effectiveness and safety of PBM, together with the fact that >30% of the world population is anaemic with detrimental health and economic consequences, led the World Health Organisation to issue a policy brief in 2021 on the urgent need to implement PBM. Implementation of the PBM programme, differs among European countries. On the basis of the current guidelines, the Central Eastern European Patient Blood Management Steering Com-

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Usmerjevalni odbor PBM programa za države Srednje in Vzhodne Evrope je letos dosegel soglasje v skladu s trenutnimi smernicami, ki naj bi zagotovilo minimalne bolnišnične standarde izvajanja PBM v teh državah. Prispevek definira trenutno stanje programa PBM in možnosti za perioperativno izvajanje glede na tri stebre PBM v UKC Maribor, kot drugi največji bolnišnici v Republiki Sloveniji skozi perspektivo anesteziologa in kliničnega farmakologa. Njegov namen je obvestiti bralce, zakaj je izvajanje PBM ključnega pomena, skupaj z dvigovanjem zavesti o nujnem ukrepanju zdravstvenih delavcev in oblasti v dobro naših bolnikov.

mittee reached a consensus in 2024 to ensure minimal hospital standards of PBM implementation in Central and Eastern European countries. This article describes the PBM programme, its current status, and the possibilities for its perioperative implementation, according to the three pillars of PBM, at the University Medical Centre Maribor, as the second largest hospital in the Republic of Slovenia, from the point of view of an anaesthesiologist and a clinical pharmacologist. Its purpose is to inform readers about the importance of PBM implementation and raise awareness of the need for urgent action by healthcare providers and authorities to ensure optimal patient care.

INTRODUCTION

An expert group representing the International Foundation for Patient Blood Management (IFPBM), the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA), the Society for the Advancement of Patient Blood Management (SABM), the Western Australia Patient Blood Management (WAPBM) Group, and OnTrac (Ontario Nurse Transfusion Coordinators) have defined patient blood management (PBM) as "a patient-centred, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment." [1] In 2017, the Directorate-General for Health and Food Safety of the European Commission issued a practical implementation guide for hospitals to put PBM into clinical practice. [2] The World Health Organisation (WHO) recognised PBM as an overall framework to address the risks of iron deficiency, anaemia, blood loss, and coagulopathy, which led them to issue a policy brief entitled "The urgent need to implement patient blood management" in 2021. [3]

The National Blood Authority (Australia) reinforced the three pillars of PBM in their definition: "PBM aims to improve clinical outcomes by avoiding unnecessary exposure to blood components. It includes the three pillars: optimisation of blood volume and red cell mass; minimisation of blood loss; and optimisation of the patient's tolerance of anaemia." [1] In Slovenia, the three pillars of PBM were presented as early as 2015 through modern approaches to optimize blood transfusion. [4] Despite much debate, however, only one (private) medical institution in the Republic of Slovenia has a written plan for implementation of the PBM program in everyday perioperative clinical practice. [5] It is therefore still necessary to introduce PBM in Central Eastern European (CEE) countries.

This article describes the PBM program, its current status, and the possibilities for its perioperative implementation, according to the three pillars of PBM, in the University Medical Centre Maribor, as the second largest hospital in the Republic of Slovenia, from the point of view of an anaesthesiologist and a clinical pharmacologist. Its purpose is to inform readers about the importance of PBM implementation and to raise awareness of the need for urgent action by healthcare providers and authorities to ensure optimal patient care.

FIRST PILLAR OF PBM

WHO defines anaemia as a haemoglobin (Hb) level <130 g/L in men, <120 g/L in non-pregnant women, and <110 g/L in pregnant women and children <5 years old. [6] Anaemia is a clinical condition with important consequences, including increased morbidity and mortality, poor functional outcomes, higher risk of blood transfusion, and prolonged hospital stay and resulting increased costs. [7] It is estimated that anaemia affects 1.95–2.36 billion people, including 1.24–1.46 billon with iron-deficiency anaemia. Isolated micronutrient deficiency, caused by a lack of iron (iron deficiency without anaemia), can also lead to anaemia and is found in another 0.98–1.18 billion people. [3] Anaemia caused by a lack of iron is the most frequent form of anaemia during the perioperative period. [8] Iron deficiency can be either absolute, with low iron stores in the body (microcytic anaemia), or functional, with sufficient iron body stores. [9] Chronic inflammation in autoimmune and chronic diseases, chronic infections, and malignancy all block iron absorption from the gastrointestinal system and prevent its transfer from supplies in the liver and macrophages, which influence the concentration of hepcidin and can reduce bone marrow erythropoiesis. [10]

Anaemia is a significant global healthcare problem and a major predictor of the need for perioperative allogenic blood transfusion. Furthermore, it is estimated that >600 million people with acute or chronic loss and coagulopathies add to the population at risk for anaemia. [3] The treatment of perioperative anaemia is based on laboratory results. Older patients are more prone to anaemia than younger ones; however, anaemia may be more difficult to determine and treat in the elderly population because it is usually caused by a combination of several risk factors. [10,11]

Iron-deficiency anaemia should be treated with iron solutions, and oral iron-replacement therapy (IRT) can be prescribed if there is enough time before surgery (≥6 weeks before the planned surgery), if there is no chronic inflammation, and if there is sufficient iron absorption from the gastrointestinal system. Oral IRT with iron salts is the standard first-line treatment in otherwise healthy and asymptomatic patients. Recent results indicated that lower doses and every-other-day regimens resulted in equivalent or even better iron absorption than daily dosing, with fewer adverse events and increased tolerability. [12,13,14] It is recommended to initiate oral ferrous salts once daily, changing to once every other day if this is not tolerated. Oral IRT formulations include ferrous ascorbate, fumarate, gluconate, or sulphate, while other oral IRTs are carbonyl iron, iron protein succinylate, and iron amino acid chelates (ferrous bisglycinate and ferric trisglycinate). Oral iron salts are inexpensive and thus good for use in under-resourced areas. They are generally effective but have tolerability problems due to gastrointestinal side effects, especially for ferrous sulphate formulations and among the elderly population. Administration not more than once daily and even once every other day may thus be preferable in older adults, to decrease gastrointestinal effects, and intravenous (IV) IRT may be considered earlier.

Other oral formulations include heme iron polypeptide (HIP), polysaccharide iron complex (PIC), and ferric citrate, which should be taken with meals. Of these, heme iron polypeptide and polysaccharide iron complex are more expensive but have better tolerability. [15] Unpredictable absorption means that enteric-coated or sustained-release formulations are usually not recommended. [16] It should also be considered if the duration of therapy could be extended to 6 months to replenish iron stores. [16] Oral IRT is the first-line treatment for patients with uncomplicated iron deficiency. In patients with moderate to severe anaemia with a poor response or intolerant to oral iron, however, or when a rapid response to iron is required, parenteral iron may be administered, which is more efficient for improving Hb values. [17]

IV IRT formulations include low molecular weight-iron dextran [requires 2–6 hours infusion time (IT)], iron sucrose (60–90 min IT), ferrous gluconate (10 min IT), ferumoxytol (15 min IT), ferric carboxymaltose (15 min IT), and iron isomaltoside with variable IT, depending on the brand. These formulations have a lower risk of allergic reactions,

Table 1. PBM in some CEE countries

Question / Country	1. Are there PBM guidelines or a specific law for the country?	2. How is the situation monitored?	3.What is the rate of implementation?	4. Who is the PBM champion(s) in the country?	5. Are there anaemia clinics?
AUSTRIA	+	-	No data	ÖGARI, the Austrian society of Anaesthesiology	-
CZECH Republic	Local hospitals guidelines only	A national survey among anaesthesiologists and related specialties	Less than 10% of hospitals	The VFN Prague Hospital	-
HUNGARY	+	+	Pillar I: 10%, Pillar II: 80%, Pillar III: 70% at Anaesth/ICU	Anaesthesiologists	-
SLOVAKIA	+	Reporting of adverse effects only	No data	The Slovak Society of Anaesthesiology and Intensive Medicine	-
ROMANIA	+	-	Unofficialy 75%	The Romanian multidisciplinary group for PBM implementation	-
SLOVENIA	-	administration of blood and blood product is controlled by hospital, and by MoH	No data	Anaesthesiologists	-
CROATIA	+	+	No data	CRO-PBM organization	+
SERBIA	-	transfusion clinic and MoH monitor the consumption of blood products	No data	-	-
GERMANY	+	PBM certificate	0-93%	German PBM network	+
POLAND	+	+	All public hospitals	Polish Society of Anaesthesiology	+

MoH, Ministry of Health

anaphylaxis, and shock. IV iron, particularly, should only be administered by staff trained to evaluate and manage anaphylactic and anaphylactoid reactions, in a suitable location with rapid access to resuscitation facilities. Iron infusions should always be slow, especially in the first minutes of administration, and the patient should be monitored carefully. Because of a lack of safety data, women in the first trimester of pregnancy should be excluded from IV treatment. [16] Evaluating the risk of thromboembolic complications, erythropoietin therapy should be considered as an addition to iron supplementation in severe cases. [18,19]

Anaemia has a global prevalence of 33% [3] and about 100 million surgeries are performed in anaemic patients. [20] In some countries, anaemia outpatient clinics exist as healthcare centres, specialised for treating anaemia patients, while other countries have hospitals with preoperative anaesthesia outpatient departments. Neither of these facilities is standard in the Republic of Slovenia, but hospitals have protocols to avoid preoperative anaemia and improve Hb and iron levels. Table 1 shows the situations in some CEE countries based on answers by their representatives to five different questions.

SECOND PILLAR OF PBM

The second pillar refers to the perioperative minimization of blood loss and optimization of coagulation. The cornerstone of the second pillar of PBM is accurate anamnesis, which supports the systematic and timely management of risk factors for bleeding and blood loss and the impact of coagulopathies that may lead to bleeding through further anaesthesiologic, haemostatic, surgical, and other appropriate measures and interventions. [3]
Preoperative management of patients who receive anticoagulants must be considered before pausing anticoagulants or, in patients at severe risk of ischemic events, replacing them with low molecular weight heparins. Patients with family members who suffer from blood coagulation disorders or women with strong menstrual bleeding should be identified.
Operative management includes blood-sparing surgical techniques (such as thoracoscopy and laparoscopy), maintaining normothermia, permissive hypotension, and preventing venal stasis, perioperative autologous blood collection and retransfusion (cell salvage is only justified when the expected blood loss is >1 L and in non-malignant disease), [21] the use of pharmacological/haemostatic agents (antifibrinolytics, such as ε-aminocaproic acid and tranexamic acid, use of clotting factor concentrates or the application of topical skin adhesives by surgeons during bleeding), and/or haemostasis management (point-of-care diagnosis). [22] The evaluation of platelet function instead of the liberal transfusion of numerous platelet concentrates is recommended.
Postoperative management includes patient safety techniques for maintaining normothermia, normotension (after permissive hypotension during surgery), and colloid and crystalloid management, to prevent blood coagulation disorders caused by haemodilution.

THIRD PILLAR OF PBM

The third pillar of PBM involves the use of all appropriate measures to leverage and optimize patient-specific physiological tolerance of anaemia. [3] To achieve this goal, phlebotomy blood loss as a result of daily laboratory analyses should be reduced by the early management of preoperative anaemia and by restricting blood sampling using the smallest appropriate blood-collection tubes and only carrying out necessary laboratory analyses. It is also important to reduce unnecessary blood culture draws and redundant blood volume when obtaining samples from indwelling lines, and to reduce blood wastage by using closed in-line flush blood sampling devices for arterial and central venous lines. [5,23]
The cornerstone of this pillar is to restrict blood transfusion by complying with the guidelines for transfusion triggers, which recommend a Hb threshold for red blood cell transfusion of 70 g/L in patients without reduced tissue oxygenation and without cardiovascular pathology. Theoretically, this threshold could be almost half lower (~35 g/L) regarding the compensatory limits of Hb oxygen-carrying capacity. [24] Notably, both anaemia and transfusion have detrimental effects on the patient's health, particularly when they occur in the same patient. [25]

PBM PROGRAM IMPLEMENTATION

The fourth CEE PBM meeting was held on the 16th of May 2024 in Bran Castle, Romania. The Steering Committee aiming to ensure minimum hospital standards of PBM implementation. Six statements based on scientific data from the last 10 years (PubMed) and several guidelines derived from available evidence were accepted which reflected the opinion of experts from CEE countries (Table 2).
In our medical centre, anaemia is detected and treated according to the current guidelines; however, not all elective-surgery patients receive ambulatory preoperative anaesthesia evaluation early enough. This could be solved by implementing anaemia

Table 2. BM CEE Steering Committee statements

Recommendations for PBM implementation in CEE countries based on the current guidelines [26,27,28]	
1.	It is recommended to measure haemoglobin and treat anaemia in advance preoperatively in patients scheduled for intermediate- to high-risk non-cardiac surgery to reduce the need for red blood cell transfusion.
2.	It is recommended to measure haemoglobin and treat anaemia in advance preoperatively in patients with high bleeding risk to reduce the need for RBC transfusion.
3.	In patients undergoing surgery with high risk of bleeding, the use of washed cell salvage is recommended.
4.	It is recommended to use point-of-care diagnostics to guide blood component therapy.
5.	It is recommended to reduce the frequency of laboratory testing and to implement blood-collecting tube systems with reduced diagnostic volumes.
6.	It is recommended to implement a massive bleeding protocol / algorithm into any hospital for haemorrhage control and correction of coagulopathy.

RBC, red blood cell

outpatient clinics as part of anaesthesia's ambulatory services, where surgical patients could be treated in collaboration by haematologists. This would optimize the Hb concentration preoperatively in all our patients, given that we could meet them at least 6 weeks before the planned surgery. Given the relevance of anaesthesiologists to this issue, the Slovenian Society of Anaesthesiologists could be involved in the implementation of PBM in many CEE countries and in the Republic of Slovenia, especially by setting platforms for collecting and analyzing data for the whole country. The University Medical Centre Maribor is equipped with modern cell saver machines (Elite+, Haemonetic®) and point-of-care diagnostic appliances (e.g., ROTEM Sigma, EDAN i15, I-STAT Abbott Alinity, US GE Venue), which require blood-collecting tube systems with reduced diagnostic volumes. All of the above are used in our daily practice, in accordance with the current guidelines, including a diagnostic anaemia algorithm, transfusion decision algorithm, postsurgical anaemia diagnosis, and massive bleeding protocol, to obtain haemorrhage control and the correction of coagulopathy.

CONCLUSION

PBM has proven life-saving benefits, leading to questions about why there are difficulties with its implementation. According to Hofmann et al., [29] two of the main factors preventing PBM implementation are low awareness and education gaps, indicating the need for further discussions; however, further measure may also be needed. Regarding the first pillar, establishing anaemia outpatient clinics, as an extension of preoperative assessment facilities, would allow more time for the assessment itself and to ensure patient safety in general. Regarding the second and the third pillars, most of the PMB elements have already been implemented as part of standard patient care, but further prospective data collection and evaluation are needed to improve patient safety. The situation in CEE countries suggests that PBM requires a multidisciplinary approach (surgeons, haematologists, and others), but with a leading role for anaesthesiologists, who are particularly keen to implement the PBM programme into clinical pathways. Given that PBM improves patient safety, WHO urges the medical world to implement this programme promptly. [30]

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