

Expert Consensus on the Significance of Intravenous Iron using Ferric Carboxymaltose Perioperatively and in Elective Major Orthopedic Surgeries

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Abstract

Anemia has emerged as a significant healthcare crisis in India and often remains undiagnosed, with broad implications across all age groups. Iron deficiency remains the most important and correctable cause of anemia in our country. It often leads to significant morbidity during major operative procedures such as hip and knee arthroplasties, due to the substantial intraoperative bleeding associated with these procedures. To address this challenge and mitigate complications related to blood transfusions, peri-operative iron therapy, notably parenteral iron therapy, has become common practice. Nevertheless, there is a lack of consensus on managing peri-operative anemia and the role of ferric carboxymaltose (FCM) in pre-operative and post-operative orthopedic surgeries in India. A group of 14 experts, primarily orthopedic surgeons and an hematologist in India, convened an in-person expert group meeting. Their primary focus was on the approach of FCM in managing anemia in elective orthopedic surgeries within the diverse landscape of the Indian healthcare system. The consensus strongly advocated using FCM as a rapid and adequate source of iron replacement, especially in cases of significant pre-operative and post-operative anemia in patients undergoing elective orthopedic surgery.

Keywords: Pre-operative, post-operative, orthopedic surgery, anemia, ferric carboxymaltose.

Anemia has emerged as a significant healthcare crisis in India, affecting adolescent girl, and young child; yet it often goes unnoticed and unaddressed [1]. Despite several causes of anemia,

one of our country's most critical and correctable causes [2]. Multiple sociodemographic factors contribute to the increased risk of anemia among adults in India. These factors include poor economic and educational status, inadequate diet, and a lack of healthcare awareness.

In parallel, the burden of osteoarthritis has also continued to rise in our country, leading to an annual demand for emergency orthopedic surgery among approximately 50 out of every 100,000 people [3]. Nearly 100 out of every 100,000 individuals in India require elective orthopedic surgery each year, with the majority of these procedures focusing on arthroplasty of the knee and hip joints [4]. As per the

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- i. What is the burden of IDA on preoperative and postoperative orthopaedic surgery patients?
- ii. What number of monthly cases (or %) do you see with preoperative and postoperative anaemia?
- iii. What is your recommendation regarding screening patients for IDA?
- iv. What is the optimum time for evaluating a patient to check for anaemia before a planned surgery?
- v. What should the Hb cutoff be to go ahead for planned surgery?
- vi. Do you consider oral iron to manage IDA in pre-and postoperative anaemia cases?
- vii. What are the critical attributes in selecting IV iron in anaemic patients pre- and post-orthopaedic surgery?
- viii. In your routine practice, which parenteral iron do you prefer for preoperative and postoperative iron correction?
- ix. When do you consider parenteral iron therapy for managing IDA in patients with pre- and postoperative anaemia?
- x. In your clinical practice, do you prefer FCM to iron sucrose to manage IDA?
- xi. What are the appropriate patient profiles for FCM in elective orthopaedic surgeries?
- xii. As per your clinical practice, what are the limitations of blood transfusion?
- xiii. What are the indications for blood transfusion?
- xiv. Can FCM reduce the need for blood transfusion?

Figure 1: The questions discussed in the expert group meeting.

Indian data, about 2,00,000 knee arthroplasty surgeries were registered in 2020 [5]. Major orthopedic surgeries, especially hip and knee arthroplasties, result in significant peri-operative bleeding, often exceeding 1/3rd of the patient's blood volume [6].

Approximately 24% of patients who underwent total hip replacement and total knee replacement were found to have pre-operative anemia [7]. The prevalence of IDA is approximately 20% in patients screened and scheduled to undergo major orthopedic surgery (knee and hip prosthesis and back surgery) [8]. The adverse implications of peri-operative anemia include an increased risk of allogeneic blood transfusion (ABT), prolonged hospital stays, delayed functional recovery, and readmissions [9]. In addition, acute kidney injury and cardiovascular events secondary to anemia lead to significant post-operative morbidity and mortality. Pre-operative anemia affects 25–75% of patients, with an increasing prevalence in the elderly, whereas post-operative anemia is more common in up to 90% of patients following major surgery [10].

A hemoglobin (Hb) level of <13 g/decilitre (g/dL) is an independent predictive factor for the need for any peri-

operative ABT [11]. Pre-operative anemia, peri-operative bleeding, and a liberal transfusion policy are the main risk factors for rising ABT [6]. Patient blood management interventions aiming to decrease the need for ABTs and improve patient outcomes deserve increased medical attention in India [7].

Need for consensus

Pre-operative anemia impacts 30–40% of patients with major surgery, independently posing risks for ABT and increasing morbidity and mortality [11]. Post-operative anemia is more prevalent (up to 80–90%) due to surgery-related blood loss, inflammation impacting red

blood cell production, and existing anemia [10]. Orthopedic surgeries, especially major ones like hip and knee arthroplasty, commonly lead to peri-operative anemia due to substantial intraoperative bleeding [6]. To manage IDA and reduce its transfusion-related complications, peri-operative iron therapy is often used. Positive results are noted with parenteral iron therapy, elevating Hb levels and reducing transfusions in anemic patients [12]. Establishing a consensus is necessary for the optimal management of peri-operative anemia associated with IDA, specifically addressing the role of intravenous (IV) iron, such as ferric carboxymaltose (FCM), in Indian patients undergoing major orthopedic procedures.

Methodology

The consensus group included 14 experts, mainly orthopedic surgeons and an hematologist from India, who participated in an in-person expert group meeting conducted in July 2023 to discuss the role of IV iron FCM in preoperative and post-operative orthopedic surgery. The goals and issues related to anemia management in elective orthopedic surgery were the focus of a group discussion where experts shared their insights and opinions, resulting in a lively exchange of ideas. A leading

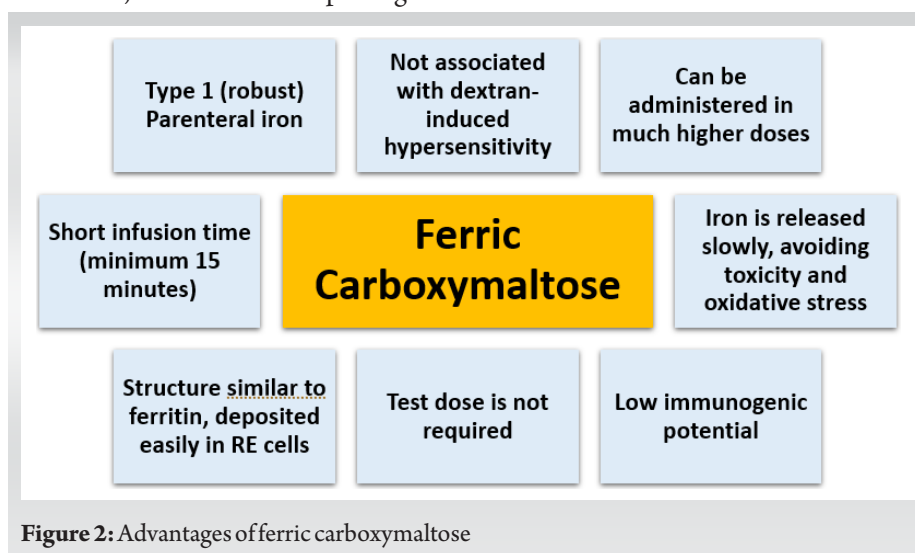


Figure 2: Advantages of ferric carboxymaltose

| Surgery | Intervention | Change from baseline Hb (g/dL) | | | Change from Baseline serum Ferritin (µg/L), mean (SD) | | | Change from baseline TSAT (%), mean (SD) | | |
|---|--|--------------------------------|------|------|---|------|----|--|-------|----|
| | | G1 | G2 | G3 | G1 | G2 | G3 | G1 | G2 | G3 |
| Orthopedic (post-operative) | G1: IV FCM 700–1000 mg single dose on post-operative day 1 | 1.7 | 1.3 | — | 571 | 60 | — | 7.2 | 0.7 | — |
| | G2: Oral ferrous glycine sulfate 100 mg/d from post-operative day 7–30 | | | | | | | | | |
| Hip fracture (pre-operative) | G1: EPO 40,000 IU/1 mL EPO SC + IV FCM 1000 mg infused over 20 min | 1.38 | 1.53 | 0.88 | 317 | 288 | -4 | — | — | — |
| | G2: placebo + IV FCM 1000 mg infused over 20 min | | | | | | | | | |
| | G3: Placebo | | | | | | | | | |
| Major orthopedic surgery, abdominal, and genitourinary surgery (post-operative) | G1: IV FCM single 15 mg/kg injection (maximum: 1000 mg) over 15 min | 3.2 | 2.81 | — | 114 | -133 | — | 20 | 13.3 | — |
| | G2: No intervention (standard care) | | | | | | | | | |
| Unilateral TKA or THA (Intra-operative) | G1: IV FCM 1000 mg diluted in 100 mL NS administered over 15 min. | 0.3 | -0.8 | — | 1157.5 | 83.8 | — | 8.7 | -19.5 | — |
| | G2: IV 100 mL NS placebo | | | | | | | | | |

Table 1: Summarized clinical evidence for the management of FCM in orthopedic elective surgery [44].

orthopedic surgeon moderated the expert group meeting and examined the existing literature and current practice with panel members to draft consensus statements. Fourteen questions were framed to be discussed, (Fig. 1), and consensus statements were prepared after more than 75% of the experts agreed on the information [13]. The questions aimed to gather insights from Indian orthopedic specialists and a hematologist, ensuring relevance in addressing specific challenges in the Indian healthcare landscape. Seeking input from these specialists is vital to tailoring approaches suited to the Indian context.

Expert Opinion

Prevalence and burden of IDA

Evidence

Pre-operative anemia is common among patients undergoing major orthopedic surgery and can be found in up to 20% of patients [11].

The occurrence of IDA among most patients scheduled for elective major orthopedic surgery varied between 15%

and 40% [14]. About 10% of female patients reported pre-operative Hb ranging from 12 to 13 g/dL, which is standard by the World Health Organization (WHO) [15].

Nevertheless, it is essential to note that these Hb levels may not be suitable for a major surgical procedure with the expected significant blood loss [16]. Approximately 90% of patients

undergoing these procedures develop post-operative anemia, which may be aggravated by inflammation-induced blunted erythropoiesis [6].

Screening and diagnosis

Evidence

Pre-operative investigations are essential for the planning, optimization,

stratification, and peri-operative management of patients undergoing surgical procedures, and for improving patient outcomes.

Pre-operative evaluation involves

Expert opinion:

As per the National Family Health Survey 2019–2021 data, the prevalence of anemia is very high in India [17]. Due to the patient-related economic and logistic constraints, the degree of the pre-surgical anemia measured may be missed in actual clinical practice. Thus, asymptomatic, and chronic anemic patients may not receive iron correction on time. This leads to a higher prevalence of anemia in post-operative cases. Many cases of mild and asymptomatic anemia often go undetected due to patient-related factors such as cost, logistics, follow-up challenges, and time constraints before scheduled surgeries. On the other hand, severe anemia tends to be reported more reliably.

In 2018, the Indian government initiated the Anemia Mukh Bharat [18] program with the aim of achieving the World Health Assembly's goal of reducing the prevalence of anemia among women of reproductive age by 50% by 2025. In addition, the government implemented the POSHAN Abhiyan initiative (2018–2022) to decrease the prevalence of anemia in young children, adolescents, and women of reproductive age groups by 3% each year.

detailed history-taking and all organ function assessments, particularly in elderly patients. Essential tests include a complete blood count (CBC), an iron profile encompassing ferritin, and an assessment of renal function. Additional tests may be required, such as screening for underlying hemoglobinopathy using Hb electrophoresis and examining serum Vitamin B12 levels on a case-by-case

| No. | Expert recommendations |
|-----|--|
| 1 | Untreated anemia in patients undergoing orthopedic surgery reduces the quality of life, increases morbidity and mortality, and increases the risk of transfusion. |
| 2 | Intravenous iron should preferentially be used in cases of: |
| | a. Moderate-to-severe iron deficiency anemia |
| | b. Short time to surgery |
| | c. Elective surgery |
| | d. Post-operative anemia management. |
| 3 | In patients undergoing elective orthopedic surgery, the pre-operative Hb should be ≥ 10 g/dL. |
| 4 | In patients with pre-operative anemia with Hb ≥ 10 g/dL and ≤ 13 g/dL, the surgery need not be delayed, but etiology of anemia should be evaluated. If the patient has confirmed IDA, then it must be corrected with parenteral iron like FCM. |
| 5 | In patients with post-operative anemia, the Hb levels must be corrected as per WHO recommendations of normal Hb values |
| 6 | Preoperative intravenous iron administration is safe and helps reduce transfusion requirements and hospital stays. |
| 7 | IV iron is generally preferable to oral iron in patients with IDA in the pre-operative setting. |
| 8 | Post-operative, high-dose, intravenous iron treatment may contribute to reduced transfusion rates, facilitate hemoglobin recovery after staggered bilateral TKA, and minimize the development of moderate to severe anemia. |
| 9 | Post-operative intravenous FCM administration facilitates recovery of surgery-related anemia by improving Hb and may reduce the need for transfusion in patients undergoing orthopedic surgery. |

Table 2: Final consensus recommendations from experts.

basis [17-19].

Pre-operative anemia is linked to increased post-operative morbidity, mortality, and an increased risk of peri-operative transfusion. The British Network for the Advancement of Transfusion Alternatives guidelines recommend screening for anemia 4 weeks before the scheduled elective orthopedic procedure [20]. According to a recent international consensus, correction of IDA should be considered at least 30 days before surgery in patients undergoing hip surgery. A decrease in serum ferritin (normal 15–200 nanogram/Milliliter [ng/mL] in males and 12–150 ng/mL in females) is a very sensitive laboratory test to determine

Expert opinion:

Experts suggest starting with a CBC alone. If the Hb is <13 g/dL in males and <12 g/dL in females, additional investigations such as serum vitamin B12, iron profile (Sr. Ferritin, total iron binding capacity, and transferrin saturation) can be recommended. Hb electrophoresis may be needed if sickle cell anemia or thalassemia is suspected. Serum ferritin, although a highly sensitive marker for IDA, is also an acute inflammatory marker and can rise in response to inflammation or infection despite coexisting deficiency. Although 28 days are sufficient for presurgical evaluation of the patient to check for anemia before planned surgery, there are several challenges in pre-operative screening for anemia in a developing country like India. These include the following:

- Patients' traveling long distances for elective surgery and unable to visit 1 month before surgery for detailed pre-surgical screening
- There is a high volume of surgeries conducted per day in India (planning of surgical dates is challenging) due to a partly concentrated health care system in India.

A practical decision based on available survey of practicing orthopedic surgeons is to at least maintain a Hb cutoff of ≥ 10 g/dL in men and women before the surgery after identification of the cause of anemia and every possible perioperative correction of the cause, e.g., with IV iron correction with drugs such as FCM for a confirmed IDA.

IDA [19]. Pre-operative investigation and practices are not uniform in India due to various factors, including socioeconomic, demographic, and medicolegal considerations [21].

Management

Evidence

Expert opinion:**Goals of therapy**

- To reduce the use of allogenic blood transfusion
- Better recovery
- Prevent long-term complications

All pre-operative patients detected as having anemia should undergo a physician review and involve a hematologist for evaluation of the cause of anemia. Oral iron replacement therapy is the first-line treatment for IDA, but its use is limited to stable patients only [22]. Oral supplementation is traditionally poorly tolerated due to the unpleasant gastrointestinal side effects, and parenteral iron may be more suitable for reducing non-compliance due to oral iron-related side effects. Parenteral iron is indicated as a first-line treatment for IDA, especially helpful in patients needing more rapid restoration of iron stores [23]. A European-based consensus recommends intravenous iron administration during the peri-operative period for patients undergoing elective and non-elective orthopedic surgery and expected to develop severe post-operative anemia [24].

Oral iron**Evidence**

Although Hb levels usually respond rapidly to oral iron therapy, repleting iron stores and normalizing ferritin levels may

require 3–6 months of treatment [22].

Parenteral iron therapy in orthopedic surgery**Evidence**

Intravenous iron therapy is better than oral iron in terms of the speed and absolute extent of the rise in Hb and replenishment of iron stores [25]. Based on the chronology of approvals, parenteral iron can be classified as first-generation, iron dextran, high molecular weight and low molecular weight (LMW), second-generation (ferric gluconate and iron sucrose), and third-generation (FCM, iron isomaltoside, and ferumoxytol) [26].

Indications of parenteral iron therapy include [25]

- Failure of oral iron therapy
- Non-compliance or intolerance to oral iron
- Rapid correction of anemia and repletion of iron stores are expected
- Malabsorption (e.g., bowel resection/celiac disease)
- Bleeding diathesis when hemorrhage is likely to continue.

Properties of an ideal parenteral iron:

First-generation, second-generation, and a few third-generation iron preparations have limitations.

i. The high molecular weight of iron dextran is correlated with an increased incidence of serious adverse events (SAE), anaphylaxis, and pain at the intramuscular (IM) site. In addition, it stains the buttocks and requires multiple injections. A test dose and long IV infusion time are necessary to administer LMW iron dextran. Furthermore, it is associated with a high risk of non-fatal SAEs, including anaphylactic reactions

ii. The use of ferric gluconate is limited by its approval for treating IDA in patients with chronic kidney disease (CKD) receiving hemodialysis who receive supplemental epoetin therapy

iii. Iron sucrose requires multiple hospital visits, considering the limitation of the maximum dose infused simultaneously

iv. Since high doses lead to high labile-free iron release, ferric gluconate, and iron sucrose can only be administered in low doses [27].

Ferumoxytol is limited to CKD patients with IDA. The maximum allowed single ferumoxytol dose was lower than that of other third-generation parenteral iron.

A higher risk of allergic or anaphylactic reactions is associated with more labile iron [27]. The physiochemical properties of iron isomaltoside were compared with those of the FCM. Third-generation iron isomaltoside 1000 contains a high amount of labile iron compared to FCM and ferumoxytol [28].

FCM, a Type 1 parenteral iron preparation, is best suited for clinical use because it is not associated with dextran-induced hypersensitivity, has a short infusion time, and can be administered in high doses. Fig. 2 depicts the advantages of the FCM [28].

For individuals undergoing orthopedic procedures with an expected likelihood of severe post-operative anemia, the

Expert opinion:

Oral iron therapy for maintenance is usually considered for post-operative anemia. Oral iron has certain limitations: The time needed for an optimum Hb rise is 5–6 months, gastrointestinal (GI) disturbances such as constipation and intolerance leading to a poor compliance. Limitations of using oral iron for post-operative anemia correction

- cost
- constipation
- compliance
- initial gastritis

Expert opinion:

Ferric carboxymaltose injection contains the equivalent of 50 mg of elemental iron per mL.

i. Selection of parenteral iron:

Experts rank the key attributes in the selection of IV iron in anaemic patients with pre- and post-orthopedics surgery as follows.

1. Both efficacy and safety
2. Short infusion time
3. Can be administered at higher doses in a single visit.

ii. Place of parenteral iron in elective and perioperative orthopedic surgeries

In patients undergoing elective orthopaedic surgery, the pre-operative Hb should be ≥ 10 g/dL. In patients with pre-operative Hb of 8-10 g/dL, patients must be administered parenteral iron like FCM (dose to be administered based on Hb and body weight) for anemia correction before surgery. In case of logistic challenges in the real-world setting, the patient can be administered IV FCM just before elective surgery, thus preventing delay in planned surgery.

Pre-operative: Hb ≥ 10 g/dL, and ≤ 13 g/dL, the surgery need not be delayed, but etiology of anemia should be evaluated and if the patient has confirmed iron deficiency anemia, then it must be corrected with parenteral iron like FCM.

Post-operative: The Hb levels must be corrected as per WHO recommendations of normal Hb values. The patient may be referred to a Haematologist for anaemia correction. Patients with Hb $> 8-10$ g/dL should be treated with parenteral iron like FCM whereas patients with Hb ≤ 8 g/dL must receive blood transfusion according to the experts.

iii. Dose and administration (Ferric carboxymaltose, Summary of Product Characteristics, Updated April 04, 2023)

The individual iron need for repletion using ferric carboxymaltose is determined based on the patient's body weight and hemoglobin (Hb) level.

The following table should be used to determine the cumulative iron dose:

| Hb (g/dl) | Patients with body weight < 35 kg | Patients with body weight ≥ 35 kg and < 70 kg | Patients with body weight ≥ 70 kg |
|-----------|-----------------------------------|--|--|
| < 10 | 30 mg/kg body weight | 1,500 mg | 2,000 mg |
| 10 to <14 | 15 mg/kg body weight | 1,000 mg | 1,500 mg |

A single ferric carboxymaltose administration should not exceed:

- 15 mg iron/kg body weight (for administration by intravenous injection) or 20 mg iron/kg body weight (for administration by intravenous infusion)
- 1,000 mg of iron.

The maximum recommended cumulative dose of ferric carboxymaltose is 1,000 mg of iron per week. All experts agreed that all strengths (500 mg, 750 mg, and 1000 mg) of FCM play vital role in management of IDA in pre- and post-operative anemia patients.

If the total iron need is higher, then the administration of an additional dose should be a minimum of 7 days apart from the first dose. Thus, 1-2 sittings are required to administer the cumulative iron dose.

iv. Monitoring

After FCM administration monitor the patient for 30 min.

panel recommends using IV iron therapy in the peri-operative phase after confirming the presence of iron deficiency as the etiology of anemia [24]. IV iron therapy notably lowered the risk of requiring red blood cell transfusions (risk ratio 0.74, 95% confidence interval 0.62-0.88) [29].

Advantages of FCM

FCM is a superior choice for iron supplementation compared with traditional alternatives. FCM allows a single infusion of 1000 mg of elemental iron, in contrast to 200 mg of iron sucrose [30]. Moreover, FCM reduces clinic visits and streamlined administration compared to iron sucrose. FCM's near-neutral pH and physiological osmolality lead to fewer injection site reactions, boosting patient comfort and compliance. FCM addresses the

limitations of low-dosage iron sucrose, offering robustness and effectiveness without dextran [30]. It is stable complex structure that prevents the release of non-transferrin-bound iron, thereby minimizing side effects, such as ferritin. FCM's structure aids deposition in the reticuloendothelial system, enhancing efficacy [31]. It has low antigenicity, reduces immune reactions, eliminates the need for a test dose, and expedites treatment [32].

Side-effect Profile of FCM

FCM is developed explicitly for fast intravenous administration at high doses, ensuring controlled iron delivery to target tissues [30]. FCM can be administered in amounts of up to 1000 mg of iron as a rapid infusion over 15 min, eliminating the need for a test dose [33]. FCM has demonstrated a strong safety

profile in various clinical trials and studies [34]. In a randomized trial involving 559 patients with IDA, the intravenous administration of FCM at specified doses showed a low incidence of adverse events (AEs), with none categorized as severe AEs [35]. Moreover, a comprehensive meta-analysis of 14 studies found minimal differences in AEs, including serious AEs, when comparing FCM to other iron therapies or oral iron alone [36]. Patients with hemodialysis CKD, non-dialysis, and FCM have proven to be well-tolerated, with low rates of AEs, even in high-dose regimens, and no reports of immediate hypersensitivity reactions or serious AEs [37]. These findings reaffirm the safety and tolerability of FCM, making it a suitable choice for iron deficiency treatment.

The most common adverse drug reaction

with this treatment is nausea (3.2%), followed by injection/infusion site reactions, fatigue secondary to hypophosphatemia a week after infusion, headache, flushing, dizziness, and hypertension.

Role of FCM in elective surgery

The effectiveness of intravenous FCM was assessed as a treatment for post-operative anemia following total knee arthroplasty (TKA) [38]. Patients treated with FCM achieved a Hb level of 12.0 g/dL or higher more frequently than those treated with oral ferrous sulfate (42.3% vs. 23.5%; $P = 0.04$). There was a trend toward an increase in Hb levels from day 4 to day 30 in the FCM group compared to the FS group (+1.7 [1.2] vs. +1.3 [1.0]; $P = 0.075$) [38].

A study evaluated the effectiveness of a single dose of FCM immediately after knee surgery in correcting anemia [39]. The FCM group showed a significant decrease in anemia rates at post-operative day 7 ($P = 0.021$) and post-operative week 5 ($P < 0.001$), along with a lower transfusion rate ($P = 0.008$). Severe anemia occurrence at week 5 was significantly lower in the FCM group ($P < 0.001$).

Studies including longer follow-up times after IV iron administration preoperatively in major orthopedic surgeries show consistent improvement in Hb [40].

The post-operative FCM administration aided in recovering from surgery-related anemia by enhancing Hb levels,

potentially lowering the need for blood transfusion in patients undergoing knee surgery [39].

Role of FCM in Indian patients

A study of 263 patients who underwent knee surgery analyzed the effect of intravenous FCM on Hb levels. Patients were divided into two groups: One given FCM and the other an alternative iron supplement after surgery. Results showed that the FCM group significantly increased Hb levels from 10.5 g/dL to 12.0 g/dL between the 3rd day and 5th week post-surgery ($P < 0.001$). The study concluded that FCM, given a day after surgery, is safe and consistently effective in raising Hb levels after knee surgery [41].

FCM versus iron sucrose

One study compared intravenous FCM and iron sucrose to correct pre-operative anemia in surgical patients. FCM was found to be more effective, achieving iron replenishment more frequently (82% vs. 62% for iron sucrose, $P = 0.007$) with fewer treatment sessions (2 sessions on average for FCM versus five sessions for iron sucrose, $P < 0.001$). The FCM group also showed higher final Hb levels, indicating a trend toward better anemia correction and reduced the need for blood transfusions during surgery or recovery. In addition, a cost analysis revealed that FCM could lead to cost savings per treatment compared with iron sucrose for these patients [15].

In a randomized trial with 118 patients

undergoing bilateral knee surgery, one group received FCM infusion, and the other received saline. The FCM group had significantly higher Hb levels than the control group (62.1% vs. 31.6%, $P < 0.001$). Their Hb levels remained consistently high for 12 weeks post-surgery, with statistically significant differences (all $P < 0.05$). In addition, the FCM group displayed significantly higher ferritin, iron, and transferrin saturation levels during this period (all $P < 0.05$) [42]. In another trial with 110 patients who experienced post-operative anemia after unilateral knee surgery, they were randomly given FCM or a placebo. FCM significantly improves Hb response and enhances various Hb and iron metabolism variables in post-operative anemia following knee surgery [43].

Evidence

The pre-operative Hb level stands out as a crucial predictor for the likelihood of requiring a transfusion after orthopedic surgery. Several studies have indicated that elective surgery can be safely performed in individuals with a pre-operative Hb level > 10 g/dL, particularly when estimated blood loss exceeds 500 mL [44,45]. In osteoporotic hip fracture cases where admission Hb < 10 g/dL, elevating pre-operative Hb levels to ≥ 10 g/dL can markedly decrease the risk of mortality [46]. For high-blood-loss surgery, pre-operative anemia is characterized by a Hb level < 13 g/dL for both genders [47].

Blood transfusion

Evidence

Peri-operative anemia and the need for ABT are well-recognized factors that increase the risk of adverse clinical outcomes [48]. In addition, blood components' quality, cost, and availability pose significant limitations in the context of ABT [49]. In an observational study, the impact of immediately administering a single, high-

Expert opinion:

Experts suggest incorporating post-operative FCM therapy on POD-2 or 3 for better outcomes including an improved wound healing if Hb levels are still low.

i. Limitations of blood transfusion:

A unit of red blood cells supplies between 150–200 mg of elemental iron but also Hb allowing, in principle, a more rapid correction of microvascular hypoxemia even one unit of ABT post-operative increases morbidity and leads to poor outcomes, attributed to increased susceptibility and transmission of infections, transfusion reactions, altered immune response, circulatory overload, and transfusion-related acute lung injury.

ii. Indications for blood transfusion

According to experts, blood transfusion is opted for only if the patient's Hb level < 8 g/dL.

dose intravenous iron supplement post-surgery was assessed to reduce transfusion needs and aid in anemia recovery for patients. Results revealed that the FCM group had higher Hb levels 5 weeks after surgery than the non-FCM group (12.25 ± 0.83 mg/dL vs. 11.48 ± 1.36 mg/dL, $P < 0.001$). Moreover, a significantly smaller proportion of patients in the non-FCM group experienced moderate-to-severe anemia at the 5-week post-surgery evaluation ($P < 0.001$). These findings suggest that immediate post-operative administration of a high-dose intravenous iron supplement, such as FCM, may effectively decrease the need for transfusions and expedite recovery from anemia in surgical patients [50].

Limitations

Although FCM is approved in India for use in IDA patients, there is a need for a multi-center real-world evidence study with a larger number of patients. The real-world data would help comprehensively assess the impact of FCM therapy in anemic patients undergoing elective, pre-orthopedic, and post-orthopedic surgeries, especially in developing countries with a diverse and patchy healthcare system like in India.

Conclusion

Untreated anemia in the pre-operative and post-operative period affects the quality of life, significantly increasing their morbidity and mortality. In the near future, ideally, every attempt should

be made to improve screening and to achieve the desirable Hb level of 12 g/dL in women and 13 g/dL in men according to the established WHO recommendations before any significant surgeries. Orthopedic surgeons can develop a standardized pre-surgery checklist, even during online consultations, to be shared a month before the operation. The consensus emphasizes that IV FCM should be the preferred approach, especially in the case of pre-operative and post-operative IDA in patients undergoing elective orthopedic surgery. The consensus also highlights the importance of FCM in improving patient outcomes and cutting the burden of blood transfusions to manage anemia in orthopedic surgery.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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