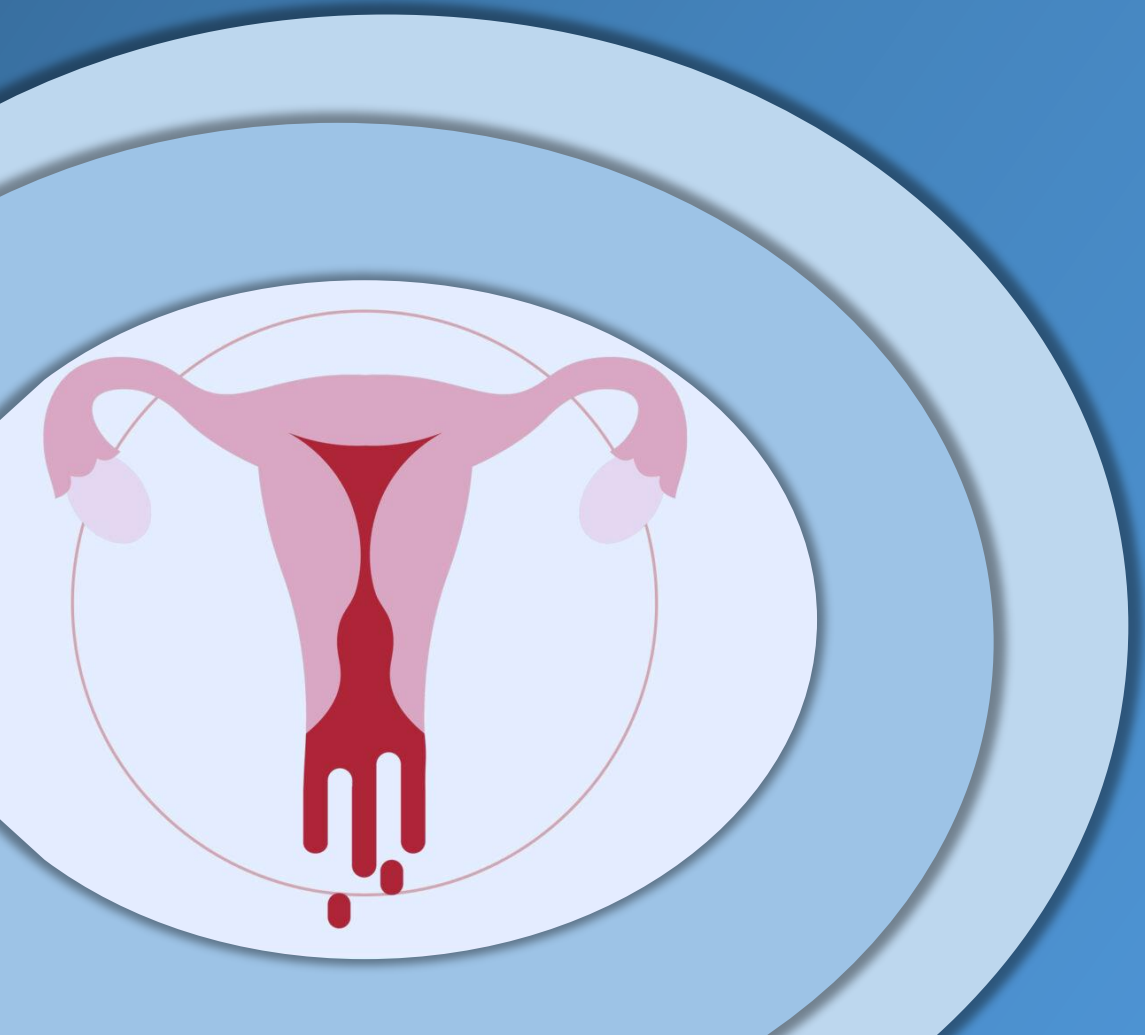
Understanding the Use of FCM in IDA due to Heavy Menstrual Bleeding



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Background and Objective of the Survey

Ferric carboxymaltose (FCM) has emerged as a valuable treatment option for iron deficiency anemia (IDA) resulting from heavy menstrual bleeding (HMB), offering several advantages in terms of efficacy, safety, and convenience.

Heavy menstrual bleeding is a common cause of iron deficiency anemia in women of reproductive age, characterized by excessive menstrual blood loss that leads to depleted iron stores and subsequent anemia. FCM addresses this underlying cause by rapidly replenishing iron stores, improving hemoglobin levels, and alleviating symptoms of anemia such as fatigue, weakness, and pallor.

One of the key advantages of FCM in the treatment of IDA due to HMB is its high-dose, single-infusion regimen, which allows for the administration of large doses of elemental iron in a short period of time. This is particularly beneficial for women with severe iron deficiency or intolerance to oral iron supplements, as it provides rapid correction of iron deficiency without the need for prolonged treatment courses.

Furthermore, FCM offers excellent tolerability and a low risk of adverse effects compared to traditional iron formulations such as ferrous sulfate or ferrous gluconate. Its iron-carbohydrate complex is well-tolerated by the body, minimizing gastrointestinal side effects such as nausea, constipation, and abdominal discomfort commonly associated with oral iron supplementation.

The objective of the survey is:

To understand the use of FCM in IDA due to heavy menstrual bleeding

Methodology of the Survey

A survey was conducted to understand the use of FCM in IDA due to heavy menstrual bleeding. A total of 50 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- Causes of menorrhagia
- Diagnostic approach to menorrhagia
- Guideline Recommendations for Diagnosis and Management of ID/IDA
- Management of Anemia/IDA: Iron Therapy
- Non-Iron-Based Correction of ID/IDA
- Treatments to Reduce Blood Loss from HMB
- Ferric carboxymaltose
- Clinical studies evaluating the efficacy of FCM
- Clinical and experimental information on the safety profile of FCM
- Quality of life in patients treated with FCM
- Abstract - Iron Deficiency Anemia with Menorrhagia: Ferric Carboxymaltose a Safer Alternative to Blood Transfusion

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Introduction[1]

Menorrhagia is subjectively defined as a ‘complaint of heavy cyclical menstrual bleeding occurring over several consecutive cycles’. Objectively it is a total menstrual blood loss (MBL) equal to or greater than 80 ml per menstruation. This degree of blood loss can cause disturbances of the woman's social, occupational or sexual life, concern about possible underlying serious disease (especially cancer), as well as medical risks such as chronic iron deficiency anemia. It is estimated that approximately 30% of women complain of menorrhagia. Excessive bleeding is the main presenting complaint in women referred to gynecologists and it accounts for two-thirds of all hysterectomies, and most of endoscopic endometrial destructive surgery. Thus, menorrhagia is an important healthcare problem.

Causes of menorrhagia[1]

Menorrhagia may be the result of systemic or pelvic pathology, or iatrogenic causes. The classic causes of menorrhagia are detailed in Table 1, however, there has been little confirmation with objective MBL measurement.

Table I. Causes of menorrhagia

(a) Uterine causes: organic, functional (dysfunctional uterine bleeding)
(b) Systemic causes: endocrinologic disorders, hematological disorders
(c) Iatrogenic causes: IUDs', use of anticoagulants

Occasionally it may be the result of systemic disease such as hypothyroidism or hematological disorders like bleeding diatheses such as von Willebrand's disease, deficiencies of factors V, VII, X and XI, or idiopathic thrombocytopenic purpura.

Although various pathologies have been implicated in menorrhagia, in 50% of cases of objective menorrhagia no pathology is found at hysterectomy. Although 'unexplained' menorrhagia is a very appropriate term this state is often labeled less clearly as dysfunctional uterine bleeding, which implies endocrine abnormalities.

Anovulation might be associated with menorrhagia close to menarche and to menopause. In ovulatory cycles excessive menstrual loss has been ascribed to abnormal uterine levels of prostaglandins. During menstruation higher levels of prostaglandin E2 and prostaglandin F2α in menstrual fluid are found in menorrhagic women when compared with those with normal menses. Furthermore release of prostaglandin E2, prostaglandin F2α and prostacyclin by endometrium and myometrium during menstruation is elevated from tissues obtained from menorrhagic women. Moreover increased concentrations of prostaglandin E receptors are found in myometrium collected from menorrhagic women. In addition, fibrinolytic activity is significantly elevated in the endometrium of most women with ovulatory dysfunctional uterine bleeding.

Diagnostic approach to menorrhagia[1]

Menstrual history

Evaluation begins with a detailed menstrual history focusing on length and subjective assessment of blood flow, intermenstrual intervals, and changes from previous bleeding patterns. Women presenting with ovulatory bleeding are likely to have heavy regular menstruation over several consecutive cycles without any intermenstrual or postcoital bleeding. They may also have dysmenorrhea with passage of clots. Presumptive evidence of ovulation can be gained from a history of premenstrual symptoms. Anovulatory bleeding is frequently not associated with any of these symptoms and occurs unpredictably.

Assessment of menstrual blood loss

Women seeking treatment for menorrhagia often do not have greater blood losses than average. It has been estimated in hospital practice that only 40% of women complaining of menorrhagia have measured losses greater than 80 ml. Therefore, objective verification of menstrual blood loss is essential, which is difficult in routine clinical practice. The number of sanitary pads or tampons used or the duration of bleeding has little or no correlation with blood loss. Women with true menorrhagia may not necessarily drop their hemoglobin concentration, as losses of 800–1000 ml can occur without anemia. Furthermore, assessment of menstrual blood loss should be undertaken over two menstruations because of cycle to cycle variation.

Although not available routinely, MBL can be quantified using the noninvasive 'alkaline hematin method', where sanitary devices are soaked in 5% sodium hydroxide to convert the blood to alkaline hematin and optical density is measured.

In order to obtain a semiquantitative measurement of the menstrual blood loss, better suited to general practice or nonresearch gynecologic out-patient settings, a pictorial blood loss assessment chart (PBAC) has been developed. The charts indicate not only the number but also the degree of soiling of items of sanitary wear. The patient scores the daily number of lightly, moderately, or heavily soiled tampons or sanitary towels used. Although in wide general use, results of studies correlating PBAC scores and menstrual blood loss are conflicting.

More recently, the measurement of total menstrual fluid using a weighing technique was described as sufficiently accurate for clinical purposes. This simple inexpensive technique might have considerable clinical potential but certainly needs further evaluation.

Clinical assessment

An abdominal and pelvic examination is recommended in all women complaining of menorrhagia. Cervical cytology should be up to date in accordance with local screening programs. A full blood count is needed to determine the degree of anemia. Ferritin is not recommended as a routine test in women complaining of menorrhagia. Testing for bleeding disorders should only be undertaken if clinically indicated, e.g. menorrhagia since the menarche and a history of bleeding after dental extractions and childbirth. Thyroid function tests should only be undertaken if clinically indicated. No other endocrine investigations are warranted.

Transvaginal ultrasound scanning

Transvaginal ultrasound scanning has become a routine procedure. Its use should be implemented as a first-step investigation in patients with abnormal uterine bleeding to select those in need of further diagnostic evaluation. Transvaginal ultrasound scan is a noninvasive, nonpainful method and represents a very good test for the diagnosis of endometrial pathologies including polyps, submucous fibroids and hyperplasia. Transvaginal sonography enables to assess endometrial thickness and detects polyps and myomata with a sensitivity of 80% and specificity of 69%.

There is evidence that endometrial thickness may be indicative of pathology in postmenopausal women. A meta-analysis of 35 studies showed that in menopausal women, endometrial thickness (endometrial double layer) of 5 mm at ultrasound has a sensitivity of more than 92% for detecting endometrial disease (polyp, atypical hyperplasia or cancer) and 96% for detecting endometrial cancer. This was independent from hormonal therapy.

No such correlations are firmly established in the premenopausal patient. The British 'RCOG Guideline Development Group' reviewed a number of studies involving premenopausal women and concluded that 10–12 mm represented a reasonable cut-off when using transvaginal ultrasound scanning as the method prior to more invasive procedures of endometrial assessment.

Ideally, transvaginal ultrasound scanning should be performed after menstruation in the follicular phase of the menstrual cycle. Ultrasound can sometimes miss small polyps particularly when performed in the late secretory phase when the endometrium is thicker.

Detection of benign lesions such as endometrial polyps and submucous fibroids can be enhanced by sonohysterography. By instillation of saline into the uterine cavity an interface between the fluid and an endometrial mass can be defined more clearly.

Some studies suggest that transvaginal ultrasound scanning in combination with color flow Doppler may assist in the diagnosis of endometrial cancer, as blood flow is increased in malignancies). However, increased blood flow has also been reported in benign conditions and results are conflicting whether Doppler sonography improves diagnosis of premalignant and malignant endometrial lesions).

Although transvaginal ultrasound may be a useful screening procedure, it is insufficient on its own to establish a histological diagnosis: this requires endometrial sampling.

Endometrial sampling

The principal purpose of endometrial sampling in women with menorrhagia is to obtain a histological diagnosis to exclude malignant and premalignant disease.

Endometrial sampling should be considered in all women with abnormal bleeding aged more than 40 years and in women who are at increased risk of endometrial cancer. Risk factors include nulliparity with a history of infertility, obesity (≥90 kg), a family history of endometrial or colonic cancer, abnormal PAP-smear and tamoxifen therapy).

Younger women may also need endometrial sampling if abnormal bleeding does not resolve with medical treatment. In certain conditions, such as polycystic ovary syndrome in which endometrial hyperplasia is more common, endometrial assessment may be necessary if abnormal bleeding is a presenting feature, or unusual sonographic endometrial appearances are discovered

The most common methods of endometrial sampling in current clinical use are:

- (a) Dilatation and curettage (D & C)
- (b) Endometrial biopsy
- (c) Hysteroscopy

In a meta-analysis Spencer et al. reviewed 142 studies to determine the value of endometrial sampling methods in women with menorrhagia. However, the results do not support a uniform recommendation for which method to choose for endometrial evaluation. Nevertheless, although the choice of sampling device may affect accuracy, no existing method will sample the entire uterine cavity. Therefore in most cases endometrial sampling methods have to be complementary to other techniques to increase sensitivity. Hysteroscopically directed sampling, for example, detects a higher percentage of abnormalities when compared with ‘blind’ D & C and if no pathology is observed during diagnostic hysteroscopy, the endometrium should be sampled, as hysteroscopy alone is insufficient to exclude endometrial neoplasia.

Dilatation and curettage (D & C)

The classic method of obtaining endometrium is by D & C. Despite having been considered as the 'gold standard', D & C does not sample the whole uterine cavity. As D & C is essentially a blind procedure it can miss lesions such as polyps, submucous fibroids, hyperplasia and carcinoma. It is estimated that in more than 50% of cases D & C does not uncover endometrial pathology.

For many years D & C has erroneously been considered to be a therapeutic as well as a diagnostic procedure. The reason is that traditionally follow up after any gynecologic procedure is at 6 weeks when most women will have only had one postoperative period. Objective menstrual blood loss measurement has shown that while the first period after D & C is lighter, subsequent ones are no different.

D & C requires general anesthesia and is associated with surgical complications including perforation in 0.6–1.3% of cases, hemorrhage in 0.4% of cases, infection in 0.3–0.5% of cases and cervical damage. Extensive curettage may cause intrauterine synechiae. D & C is therefore being increasingly replaced by outpatient procedures which avoid general anesthesia and are also less costly.

Available evidence suggests that, traditional D & C no longer has a place in either the treatment or the investigation of abnormal uterine bleeding. D & C should be reserved for those cases where office biopsy or directed hysteroscopic biopsy are not feasible.

Endometrial biopsy

The advantage of endometrial biopsy is that it avoids general anesthesia and has fewer complications than D & C. The technical skills required for outpatient endometrial biopsy are similar to those needed to fit an intrauterine contraceptive device and there is an argument in favor of its use in primary care.

The Pipelle sampler is a flexible polypropylene suction catheter that has an outer sheath of 23.5 cm in length and 3.1 mm in diameter. The device is inserted through the cervical canal to the uterine fundus and a piston within the sheath is withdrawn to create a vacuum inside the uterus. The tissue sample is obtained by twirling the catheter while moving it up and down within the uterine cavity.

The Vabra curette is a stainless-steel cannula of 24 cm in length and 3 mm in diameter with a chamber for collecting of the specimens at one end. The attached plastic chamber is connected to an electrically powered vacuum pump.

The Pipelle device obtains an adequate endometrial specimen in up to 99% of women in studies with large numbers of premenopausal patients. The Vabra aspirator is reliable in detecting endometrial pathology in 95% of cases.

A recent meta-analysis of Dijkhuizen et al. including 39 studies with 7914 patients reported the 'Pipelle' endometrial biopsy device with detection rates of 91% for endometrial carcinoma and atypical hyperplasia in premenopausal women to be superior to D & C and hysteroscopy.

The 'RCOG Guideline Development Group' also cited studies comparing the Pipelle sampler with formal D & C and with other endometrial sampling devices including Vabra. The group concluded that Pipelle was the preferable device in terms of diagnostic ability, patient acceptability and cost

However, a dilemma exists if there is a negative initial biopsy and menorrhagia persists. One study followed up 263 patients with a negative initial endometrial biopsy or D & C (either benign histology or insufficient sample). One-third underwent further sampling of which 2% were diagnosed with uterine malignancy and 2% were found to have complex hyperplasia. As a result of the high risk (more than 10%) of an existing lesion having been overlooked the authors recommended a repeated biopsy or a transvaginal ultrasound scan in patients with persistent symptoms after a negative initial biopsy.

While endometrial biopsy represents the method of choice for diagnosis or exclusion of malignancy and premalignancy, it is also acknowledged that blind endometrial biopsy is insensitive in diagnosing benign and organic causes of menorrhagia. The two principal techniques of investigating the uterine cavity to detect pathologies such as polyps and fibroids are transvaginal ultrasound and hysteroscopy.

Hysteroscopy

Hysteroscopy allows direct visualization of the uterine cavity. It is known to be a superior method for the detection of endometrial polyps and submucosal myomas, which can be easily missed by endometrial biopsy procedures, ultrasonography or 'blind' curettage. Diagnostic

hysteroscopy can be performed either as an outpatient procedure without anesthetic or as a formal theater procedure.

Hysteroscopy has been advocated by many as the standard for the diagnosis of abnormal uterine bleeding. However, results of various studies are conflicting whether this method improves upon the sensitivity of D & C in the detection of endometrial hyperplasia or carcinoma.

In addition, caution is advised in the uncritical use of hysteroscopy in patients suspected of having endometrial cancer. It has been shown that hysteroscopy can cause dissemination of malignant cells into the abdominal cavity from uteri containing endometrial carcinoma and that these cells are functionally viable. Consequently, hysteroscopy seems to affect prevalence of positive peritoneal cytology, especially in those patients with high-risk cell types. At least four case reports have described the hysteroscopic dissemination of endometrial cancer cells and it was suggested that hysteroscopy should be reserved for patients in whom prior endometrial sampling failed to demonstrate malignancy.

Guideline Recommendations for Diagnosis and Management of ID/IDA

Figure 1: Guideline recommendations for iron screening.

There is high heterogeneity among the guidelines with recommendations for screening iron levels in women with HMB, varying from those that recommend it routinely, those that specifically advise against this practice, and those that recommend iron testing as a second-line investigation. *HMB* heavy menstrual bleeding, *ID* iron deficiency. Guidelines referred to: red circle, blue circle, turquoise circle

In contrast, four guidelines explicitly advised against routine initial assessment of iron levels, citing the limitations of serum ferritin testing. One of these guidelines noted that iron therapy for IDA can be initiated on the basis of Hb levels from a full blood count, without the need for ferritin measurement.

Six guidelines, including two that explicitly advised against routine assessment of iron levels, recommended assessment of iron levels as part of second-line or supplementary investigations in cases where anemia had been confirmed or in non-anemic patients with overt symptoms of ID. Three guidelines recommended testing all patients with confirmed anemia for the presence of ID, while another recommended testing for ID when anemia did not respond to oral iron therapy. Two guidelines mention tests for serum iron in an additional battery of tests to be considered, but did not specify criteria for conducting them.

Finally, four guidelines recommended specific serum ferritin thresholds for diagnosis of ID/IDA, with both < 15 μg/L and < 30 μg/L given as levels consistent with ID.

Ferritin is an intracellular glycoprotein that binds iron, and low serum ferritin levels indicate diminished iron stores and thus ID. Serum ferritin tests are easily available, inexpensive to conduct, and an accurate measure of iron levels in women of reproductive age with no concomitant disease. However, as noted in one of the guidelines, while low ferritin always indicates low iron stores, serum ferritin may be normal in patients with inflammatory disorders; thus a normal serum ferritin result does not fully rule out ID. While multiple guidelines referred to this limitation of serum ferritin measurement, there was no consensus on which parameters other than serum ferritin to use instead. Suggestions included total iron-binding capacity (TIBC), hypochromic blood film, and serum soluble transferrin receptor (sTfR) if ferritin levels are normal, or transferrin saturation (TSAT) if ferritin levels are elevated. Other recommendations included the use of TSAT if Hb levels are < 12 g/dL, or to assess erythrocyte morphology and consider a microcytic hypochromic phenotype to be indicative of IDA. The guidelines from Saudi Arabia also recognize that RBCs with a low mean corpuscular volume (microcytosis) or mean corpuscular Hb concentration (hypochromic) may be indicative of ID, and these guidelines recommend testing serum ferritin levels in women suspected of having I.

Management of Iron Deficiency

Only six of the 22 included guidelines recommended treating patients with ID irrespective of the presence or absence of anemia, with two also recommending prophylactic oral iron therapy for patients who are asymptomatic but at high risk of developing ID or IDA. Two of the guidelines specifically recommended continuing iron treatment until iron stores are replete.

Management of Anemia/IDA: Iron Therapy

Ten guidelines included recommendations for managing anemia/IDA, all stating that women with IDA should receive iron therapy. Strikingly, one of these guidelines provided no guidance on screening for anemia/IDA. Eight of these guidelines gave guidance on providing iron therapy. Five guidelines recommended oral iron administration as the preferred route of treatment if permitted by the patient's health and circumstances, not only for patients with confirmed ID/IDA but also for those at high risk of developing ID/IDA. If there is sufficient time prior to surgery, oral iron administration can be used to normalize a patient's Hb. However, both the American College of Obstetricians and Gynecologists and Health Quality Ontario specified that oral iron therapy is only appropriate in cases of non-severe anemia.

Table 2. Guideline recommendations on the use of iron therapy

Citation	**First-line oral iron therapy?**	**Patient group/circumstance**	**IV iron therapy?**	**Patient group/circumstance/first or second line**	**Threshold Hb level for IV iron therapy**
Munro MG et al.	Y	In confirmed IDA (Hb < 12 g/dL and MCV low or normal < 100)	Y	First line: if there is a relatively short interval to surgery and SF < 30 ng/mL and/or TSAT < 20%	N/S

		Prior to surgery if time interval allows		Second line: if Hb does not increase > 1 g/dL with oral iron therapy, and SF < 30 ng/mL and/or TSAT is < 20%	
ACOG Opinion #785	Y	If Hb ≥ 8 g/dL or hematocrit ≥ 25%	Y	Second line: in patients with poor compliance to oral iron therapy	N/S
Health Quality Ontario	Y	In ID or any confirmed anemia (with Hb > 9 g/dL), including prior to surgery	Y	First line: to correct severe anemia, including before and after surgery First line: prior to surgery, particularly if in need of rapid correction, to increase Hb > 12 g/dL Second line: if unresponsive or intolerant to oral iron therapy	Hb ≤ 9 g/dL
Arab HA et al.	Y	In confirmed ID or IDA In women who are asymptomatic but at high risk of ID or IDA	Y	First line: prior to surgery/after GI or bariatric surgery First line: in those who express a preference for IV iron therapy, at the treating physician's discretion	Hb < 8 g/dL

				Second line: in poor/non-responders[a] or those intolerant to oral iron therapy Second line: if Hb does not increase by 2 g/dL and/or SF remains < 30 ng/mL after 3 months of oral iron therapy	
ACOG Opinion #136	Y	In confirmed ID or IDA	Y	Second line: in non-responders to oral iron therapy	N/S
American College of Nurse-Midwives	N/S[b]	In anemia			
Demers C et al.	N/S[b]	In confirmed ID or anemia			
Vilos GA et al.	N/S[b]	Preoperatively in patients with anemia undergoing surgery for uterine fibroids			

Eight out of 22 guidelines provided recommendations on the use of iron therapy in women presenting with HMB. Oral iron therapy is recommended as first-line treatment if patient health and circumstances permit. Intravenous iron therapy is recommended in preference to, or subsequent to, oral iron therapy depending on circumstances

ACOG American College of Obstetricians and Gynecologists, *GI* gastrointestinal, *Hb* hemoglobin, *HMB* heavy menstrual bleeding, *ID* iron deficiency, *IDA* iron-deficiency anemia, *IV* intravenous, *MCV* mean corpuscular volume, *N/S* not stated, *SF* serum ferritin, *TSAT* transferrin saturation

[a]Women with a 1% increase in reticulocyte count and an improvement in Hb by 0.5 g/dL after 30 days are considered responders and should continue on oral iron therapy for 2 further months

[b]Guidelines do not specify whether iron therapy should be oral or intravenous

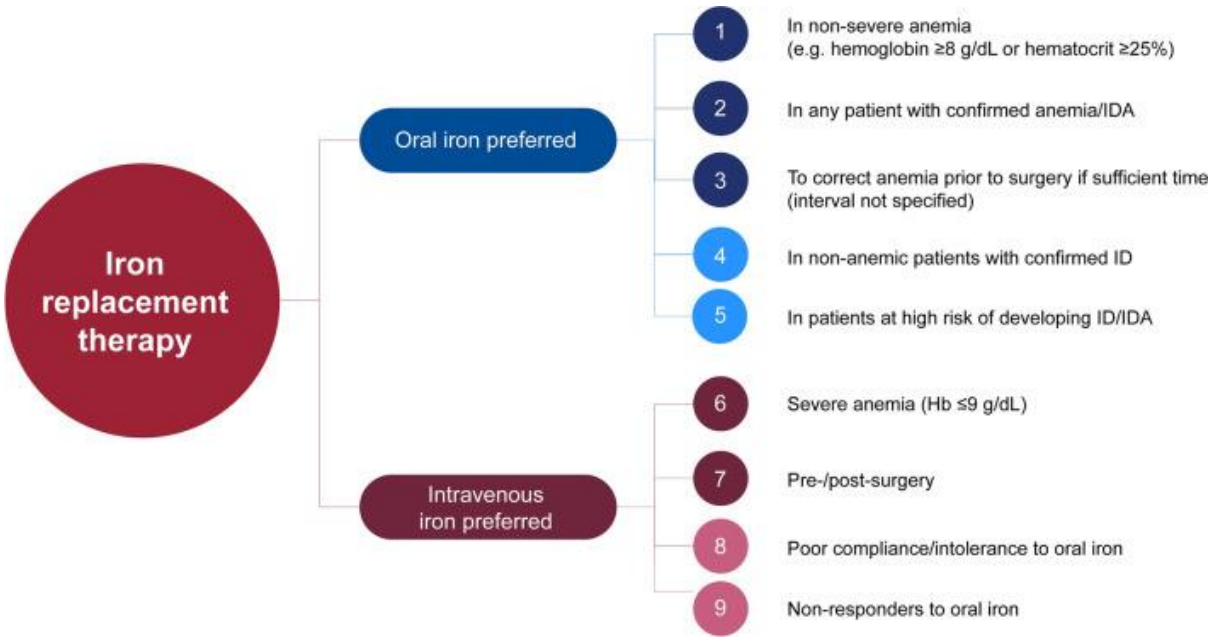

Figure 2: Patient populations in which iron replacement therapy is recommended by guidelines.

Oral iron administration is the preferred route of treatment if permitted by the patient's health and circumstances, both for patients with confirmed ID/IDA and patients classified at risk of developing ID/IDA. IV iron therapy is most commonly recommended in patients who do not respond, cannot tolerate, or do not comply with oral iron administration, before and after surgery and in patients with severe anemia. *ID* iron deficiency, *IDA* iron-deficiency anemia.

Similarly, only five guidelines provide recommendations on the use of IV iron therapy in preference to oral iron therapy, and this was advised as a first-line strategy under certain circumstances—including clinical scenarios warranting immediate correction of anemia, such as imminent surgery, or following gastrointestinal or bariatric surgery. IV iron treatment was also recommended for patients with severe anemia and a Hb level ≤ 9 g/dL. Guidelines also

recommended IV iron therapy as a second-line treatment in patients with poor compliance and/or intolerance to oral iron therapy, as well as in those who did not respond to oral iron therapy.

There was a notable lack of guidance around how to select patients for oral versus IV iron therapies, with only Health Quality Ontario recommending a specific threshold of 9 g/dL for use of IV iron administration. In several instances, guidelines did not specify whether iron should be given orally or IV in women diagnosed with ID/IDA.

Non-Iron-Based Correction of ID/IDA

Four guidelines recommended blood transfusion for severe anemia, and all recommended basing the treatment decision on the severity of anemia and/or patient symptoms. Specifically, one guideline stated that transfusion should only be used in cases of acute hemorrhage or hemodynamic instability; one recommended basing the decision to transfuse on the severity of symptoms (with transfusion recommended in patients with hypotension, chest pain, syncope or tachycardia), and two recommended that Hb levels should be examined in addition to symptoms. The recommended Hb threshold varied, with one guideline advising consideration of transfusion as a first approach to treatment if Hb levels are < 6 g/dL in symptomatic patients or < 5 g/dL in those who are asymptomatic, while a second guideline noted that otherwise healthy adolescents may tolerate Hb levels < 7 g/dL, and stated that the decision to transfuse should not be based solely on Hb levels but should also consider hemodynamic status.

Table 3. Guideline recommendations regarding non-iron-based management of HMB

Citation	Transfusion	Dietary interventions
ACOG Opinion #785	If Hb < 7 g/dL In hemodynamically unstable patients/presence of active bleeding	First-line therapy and long-term management: oral iron administration plus dietary optimization
Arab HA et al	In asymptomatic patients if Hb < 5 g/dL	Increasing consumption of foods rich in heme iron

	In symptomatic patients if Hb < 6 g/dL	
Health Quality Ontario	With severe symptoms of anemia	N/S
Munro MG et al.	In acute hemorrhage/hemodynamic instability	N/S
American College of Nurse-Midwives	N/S	Nutrition counseling and iron replacement

Five out of 22 guidelines provided recommendations on the use of non-iron-based management of ID/IDA in women presenting with HMB. Transfusion is sometimes recommended in cases of severe anemia, especially in the event of hemodynamic instability. Dietary interventions may be considered alongside other approaches.

ACOG American College of Obstetricians and Gynecologists, *Hb* hemoglobin, *HMB* heavy menstrual bleeding, *ID* iron deficiency, *IDA* iron-deficiency anemia, *N/S* not stated

Iron intake may also be boosted through dietary interventions such as increasing consumption of foods rich in heme iron (clams, oysters, shrimp, sardines, liver, red meat), and reducing consumption of foodstuffs that can block iron absorption, including tea and coffee. However, dietary intervention was only recommended in conjunction with iron therapy.

Treatments to Reduce Blood Loss from HMB

Several guidelines included recommendations for medical treatments to reduce blood loss from HMB by addressing the underlying cause. Hormonal treatments were commonly recommended. The 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS) was the most consistently recommended hormonal treatment approach with the UK-based NICE recommending to consider an LNG-IUS as first-line treatment for women with HMB but no identified pathology, uterine fibroids < 3 cm in diameter, or suspected or diagnosed adenomyosis. Other progestogen-only methods, such as depot medroxyprogesterone acetate,

and combined oral contraceptive pills (estrogens plus progestogen), can also markedly reduce HMB, including in adolescent. Gonadotropin-releasing hormone (GnRH) analogues may be used as a short-term solution to boost iron stores in women due to undergo surgery or in those who are experiencing HMB as a result of uterine fibroids. One set of guidelines also recommended considering the use of GnRH analogues to reduce HMB in women in whom other medical or surgical treatment options had failed or were contraindicated. Selective progesterone receptor modulators (SPRM) may also be used in the short term to correct anemia in patients with fibroids. However, ulipristal, the only licensed SPRM in the USA and the European Union, had its European license withdrawn in March 2020 because of safety issues.

Table 4. Guideline recommendations regarding pharmacological treatment of HMB

Citation	**Medications**				
	LNG-IUS	**GnRH**	**SPRM**	**Combined oral contraceptives/progestogens[a]**	**Non-hormonal[b]**
ACOG Opinion #785	Y	N/S	N/S	Y	N/S
Health Quality Ontario	Y	N/S	N/S	Y	Y
Munro MG et al.	Y	Pre-surgery	N/S	Y	Y
Munro MG et al.	N/S	Pre-surgery	N/S	Y	In cyclical HMB
Singh S et al.	Y	Pre-surgery	N/S	Y	In cyclical HMB
Vilos GA et al.	Y	Pre-surgery	Short-term use	Y	N/S

AAGL practice report	N/S	Pre-surgery	N/S	N/S	N/S
NICE guideline [NG88]	Y	N/S	N/S	Y	If women are unsuitable for LNG-IUS
Perez-Lopez FR et al.	Y	Pre-surgery	Short-term use	Y	Y
ACOG Practice Bulletin #136	Y	N/S	N/S	Y	N/S

Ten out of 22 guidelines provided recommendations on the use of medications (hormonal and/or non-hormonal) to minimize or reduce the bleeding in women presenting with HMB

AAGL American Association of Gynecologic Laparascopists, *ACOG* American College of Obstetricians and Gynecologists, *GnRH* gonadotropin-releasing hormone agonist, *HMB* heavy menstrual bleeding, *LNG-IUS* levonorgestrel-releasing intrauterine system, *N/S* not stated, *NICE* National Institute for Health and Care Excellence, *SPRM* selective progesterone receptor modulator

[a]Progestogens include medroxyprogesterone acetate

[b]Non-hormonal treatments include non-steroidal anti-inflammatory drugs (NSAIDs) or anti-fibrinolytic agents

Non-hormonal treatments are recommended for reducing blood loss from HMB in patients in whom hormonal treatment is not appropriate or desirable, as a second-line option after hormonal treatmen, or as first-line treatment in patients with abnormal uterine function or fibroids. The most frequently recommended options were non-steroidal anti-inflammatory drugs (NSAIDs) and antifibrinolytic agents such as tranexamic acid. Non-hormonal treatments were considered particularly effective in controlling HMB for women with more predictable periods and in those who are planning a pregnancy.

Ferric carboxymaltose[3]

Ferric carboxymaltose (FCM) is a new iv iron formulation. It is a polynuclear iron(III)–hydroxide carbohydrate complex designed to mimic physiologic ferritin. FCM is a water-soluble, brown, amorphous powder with a relative molecular weight of 150,000 Da, containing approximately 1,000 iron atoms, which corresponds to an iron content of 24%–32%, together with 25%–50% dextrin, ≤10% water, and <6% NaCl. It is pH neutral (5–7) and has physiologic osmolarity. FCM does not contain dextran or modified dextran and does not react with dextran antibodies. After iv FCM administration, the carbohydrate shell is incompletely broken down in the blood by α-amylase.

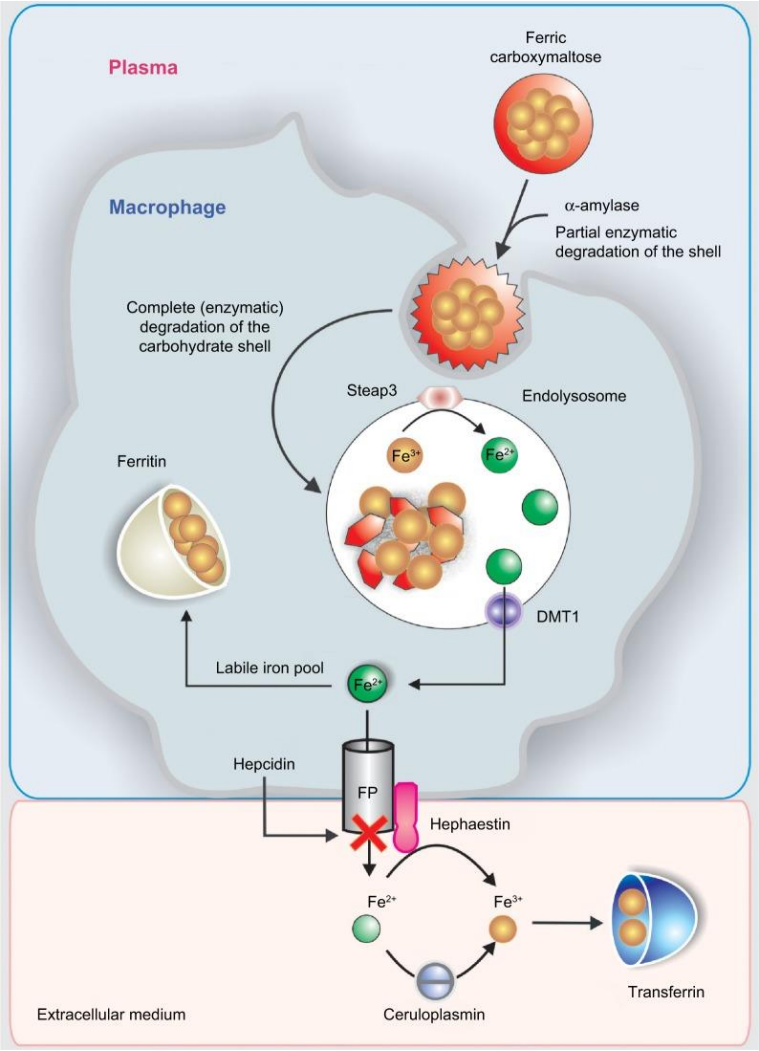

Figure 3. Schematic sequence illustrating the metabolic pathway of ferric carboxymaltose in the macrophage.

Abbreviations: DMT1, divalent metal transporter 1; FP, ferroportin.

Then, macrophages take the FCM by an endocytic mechanism by which the carbohydrate shell and the polynuclear iron core may be completely broken down in the endolysosomes to release Fe^{3+}. Then, six-transmembrane epithelial antigen of the prostate 3 (Steap3) is likely to reduce the released Fe^{3+} into Fe^{2}

Fe^{2+} is extruded from the endolysosomes to the cytosolic labile iron pool by the activity of DMT1 and from the cytosol to the plasma by FPN. Finally, it is transported by TF to the liver, bone marrow, and other tissues.

Four ascending doses were investigated in a total of 24 patients with mild IDA: 100 mg iron as FCM given as an iv bolus injection, and 500 mg, 800 mg, and 1,000 mg iron as FCM given as an iv infusion over 15 minutes. Assessments were made of pharmacokinetic iron status parameters up to 168 hours post dose. In comparison with placebo, a rapid, dose-dependent rise in total serum iron was observed across all dose groups. Peak serum iron levels occurred within 0.3–1.2 hours. Mean maximum total serum iron levels were 36.9 μg/mL following a 100-mg iv dose, 154.1 μg/mL following a 500-mg iv dose, and 306.4–317.9 μg/mL following a 1,000-mg iv dose.

Iron supplied as FCM is quickly provided to different tissues, mainly to the bone marrow, liver, and spleen, the volume of distribution being approximately 3 L. Following the administration of an i.v. dose of FCM, the level of total serum iron presents a reduction between 24 hours and 72 hours. After 60–96 hours post FCM infusion, most patients show total serum iron levels under the limit of quantification. Concerning serum ferritin, a dose-dependent, but not dose-linear, increase maybe observed within 48–120 hours post FCM dose, with maximum levels of a 23–210-fold increase above baseline level.

In an uncontrolled multidose study in patients with moderate IDA secondary to gastrointestinal disorders, a 15-min infusion of either FCM (500 mg iron) weekly for up to 4 weeks or FCM (1,000 mg iron) weekly for up to 2 weeks resulted in maximum serum iron levels of 154 μg/mL and 306 μg/mL at 1 hour post dose, respectively, and returned to baseline values at 4–7 days. Before the following dose, serum iron levels stayed within the normal level, and no change was observed with repeated infusions. Following a single infusion of FCM 100 mg labeled with $^{52}Fe/^{59}Fe$ as a tracer in patients with IDA or anemia related to chronic kidney disease (CKD), a rapid increase of radiolabeled iron incorporation from FCM into red blood cells was observed by the first 6–9 days. Additionally, after 24 days, iron incorporation was greater (91%–99%) in IDA patients than in those with renal anemia (61%–84%). iron was quickly

removed from plasma and mostly delivered to the liver, spleen, and bone marrow, but bone marrow showed a much higher iron uptake.

Most iron administered as FCM is utilized or eliminated within 24 hours (100-mg dose) or 72 hours (500–1,000-mg dose). The clearance for FCM appears to be essentially mono-exponential, suggesting that iron as FCM is not deposited in a body store from where it could diffuse back to the serum. FCM has a terminal elimination half-life of 7.4–12.1 hours. Less than 0.01% of the administered dose is excreted in urine. Concerning breastfed infants, there were no adverse effects reported.

Clinical studies evaluating the efficacy of FCM[3]

Studies with FCM in patients with anemia related to gynecological and obstetrics disorders

Van Wyck et al conducted a randomized, controlled trial to assess the efficacy of iv FCM versus oral FS in the management of anemia in more than 400 women with anemia, ID, and heavy uterine bleeding (HUB). The patients received either iv FCM (≤1,000 mg over 15 minutes, repeated weekly to obtain a full calculated supplement dose) or 325 mg of FS (65 mg elemental iron) orally thrice daily for 6 weeks. Compared to those assigned to FS, more patients in the FCM group presented an increase in Hb of 2.0 g/dL or more (82% vs 62%, $P<0.001$), obtained an increase in Hb of 3.0 g/dL or more (53% vs 36%, $P<0.001$), and achieved anemia correction (73% vs 50%, $P<0.001$). More vitality and less fatigue ($P<0.05$) were reported by patients treated with FCM in comparison with those receiving FS. No severe AEs were reported, and it was concluded that FCM was more effective than FS in resolving anemia, refilled iron deposits, and enhancing QoL in patients with IDA due to HUB.

Recently, Herfs et al performed a multicenter, prospective, noninterventional study on the efficacy and tolerance of FCM use in ordinary gynecological practice. The data from ~300 patients with iron deficiency or IDA were evaluated.

The etiologies of iron deficiency/IDA were hypermenorrhea, postpartum condition, or other causes. FCM was most frequently (92 %) administered by infusion (average 21 minutes), and in 7% of the patients by bolus injections.

The average total iron dosage was 788.7 mg (range: 50–3,000 mg)/patient and the median individual dosage was 500 mg (range: 50–1,000 mg)/patient. In most cases, the total dosage

was given as single application. The increase in Hb value was 2.5 g/dL in the whole group. However, in the IDA group, the value increase was 3.4 g/dL, with 80 % of women reaching normal Hb values. TSAT values and serum ferritin were also increased (16.3 %–22.8 % and 17.2–88.8 μg/L, respectively). No severe AEs were reported.

The role of FCM in pregnancy has been evaluated in some studies. There is general consensus in considering IS as a safe ICC to be used in the treatment of pregnant women with IDA. However, since the total iron dose usually requires numerous applications, the Hb target for an individual patient is not always achieved. Hence, in a retrospective analysis of 206 pregnant women who received either FCM or IS for IDA due to intolerance to oral iron substitution or insufficient Hb increase after oral iron treatment, Christoph et al evaluated comparatively the side effects and tolerance of these two ICCs. Mild AEs were reported in 7.8% for FCM and 10.7% for IS. The mean rise of Hb value was 1.5 g/dL for FCM and 1.1 g/dL for IS. FCM had a similar safety profile to IS, with the advantage of a higher iron dosage at a time, this diminishing the requirement of multiple administrations.

On this background, a recent prospective observational study was performed to test the safety and effectiveness of FCM in treating pregnant women with mild, moderate, and severe IDA in the second and third trimester. A total of 65 anemic pregnant women were treated with FCM between 24 weeks and 40 weeks of pregnancy. The FCM efficacy was tested by changes in Hb and by a report of the patients' well-being in the postpartum period. The fetal heart rate and occurrence of AEs were recorded during the infusion as a safety evaluation. A significant (P<0.01) rise in Hb was observed after FCM administration in all women. This positive Hb change was found at 3 weeks and 6 weeks post FCM application and in some cases up to 8 weeks. Moreover, serum ferritin also increased after FCM administration. No negative impact of the drug on the fetus was observed. Two-thirds of the interviewed women reported an improvement in their well-being, and one-third did not perceive any substantial modifications following FCM application. The rate of mild AEs was 20%.

There are some studies with FCM in postpartum anemia. In three of them, FCM was compared to oral iron– and in one versus IS. In a randomized, open label, controlled trial, Van Wyck et al estimated the efficacy of FCM (≤1,000 mg over 15 minutes, repeated weekly to achieve a total calculated replacement dose) compared with oral iron therapy (FS, 325 mg orally tid for 6 weeks) in anemic women (Hb ≤10.0 g/dL) within 10 days postpartum. One-hundred and seventy-four patients received 350 iv doses of FCM (mean total dose 1,403.1 mg) in three, two,

or one injection (10.9%, 79.3%, or 9.8% of patients, respectively); 178 received FS. Although an equivalent proportion of patients in both groups obtained an increase in Hb ≥2.0 g/dL, the therapeutic response was earlier with FCM (7.0 days vs 14.0 days, $P<0.001$). Additionally, the FCM group was more likely to normalize Hb (90.5% vs 68.6%, $P<0.001$). There were no serious AEs. In conclusion, FCM was an effective therapy for postpartum anemia. Moreover, in comparison with FS, FCM showed a quicker response and was better tolerated.

Another study was a multicenter, randomized, controlled one, including 291 women with <10 days after delivery with Hb ≤10 g/dL. The patients received FCM (n=143) ≤1,000 mg over 15 minutes or less, repeated weekly to a calculated replacement dose (maximum 2,500 mg) or FS (n=148) 325 mg orally tid for 6 weeks. FCM-treated subjects were significantly more likely to achieve an Hb >12 g/dL in a shorter time period with a sustained Hb >12 g/dL at day 42. Additionally, these patients achieved an Hb rise of 3 g/dL faster than those with FS, together with higher TSAT and ferritin levels. Drug-related AEs occurred less frequently with FCM.

Breymann et al conducted a multicenter (20 centers in three countries), open-label, randomized, and controlled Phase III study in women with postpartum IDA (Hb ≤10.5 g/dL). The patients were randomized to receive FCM (up to three weekly doses of 1,000 mg maximum, applied in 15 minutes; n=227) or FS (100 mg bid, 12 weeks; n=117). Both therapeutic regimens were equally effective in changing the Hb value. However, in the case of FCM, there was a shorter treatment period (2 weeks vs 12 weeks) and the ferritin levels were significantly higher. Except for the burning at the injection site, FCM was better tolerated than FS, mostly regarding gastrointestinal AEs. There were no safety concerns identified in breastfed infants.

A retrospective comparative study between FCM and IS in postpartum anemia was carried out in a cohort 210 of anemic inpatient women who received FCM (15 mg/kg; maximum, 1,000 mg) or IS (2 times 200 mg), respectively, in the postpartum period.

Both treatments were tolerated with overall AEs of 5% (FCM) versus 6% (IS); the most common complaint was burning and pain at the injection site. FCM was as effective as IS in changing Hb levels from the baseline. There was no difference in the mean daily Hb increase between the groups. Both drugs were effective and offered a rapid normalization of Hb after delivery. However, women with severe anemia showed the most effective responsiveness with FCM.

Clinical and experimental information on the safety profile of FCM[3]

Since iv iron may cause a variable degree of toxicity, a number of experimental studies in basic science have been performed in order to evaluate the safety profile of FCM.– In this sense, a comparative study of FCM versus other iv iron preparations (FG, IS, HMWID, and LMWID) demonstrated that after a similar dose of iv iron (weekly administration for 4 weeks) to nonanemic rats, FCM presents a better profile with respect to FG, HMWID, and LMWID on oxidative stress and inflammatory markers in tissue (liver, heart and kidney). Furthermore, in another study in rodents, FCM administration did not result in detectable levels of nitrotyrosine (marker of nitrosative stress) or significant levels of caspase 3 (apoptosis) in liver, heart, or kidney, versus control.

In clinical investigation, a direct comparison study on the safety of FCM versus iron dextran in patients with IDA was conducted by Hussain et al. Most of the patients were women, whose principal cause of anemia was HUB, IBD, or other gastrointestinal pathologies. FCM increased Hb levels, replenished iron stores, and had a low incidence of AEs. In this study, there was also a lower rate of allergic reactions in the FCM group with respect to the iron dextran group. The trial confirmed the safety profile of FCM in comparison with another frequently administered iv iron, iron dextran. Moreover, Onken et al have recently evaluated the efficacy and safety of FCM versus oral iron and versus standard care iv therapy in IDA patients who had presented inadequate response to oral iron after a 2-week treatment. Safety endpoints occurred in 3.4% in the FCM group versus 3.2% in the comparator groups. In conclusion, two 750 mg FCM infusions were safe and superior to oral iron in improving Hb in this cohort of patients.

Although the mechanism remains unknown, potential negative consequences on bone metabolism (hypophosphatemia and alterations in fibroblast growth factor 23 (FGF23) plasma level) have been attributed to iv iron therapies, including FCM. Some recent clinical and experimental data have contributed to clarify this controversial topic. In a post hoc analysis of a prospective study carried out in 47 NDD-CKD patients with IDA who had received a single 1,000-mg injection of FCM, Prats et al examined the effect of FCM on phosphate metabolism and FGF23 levels in patients with CKD using markers of mineral metabolism. They concluded that in NDD-CKD patients, FCM induced a reduction in serum phosphate levels that persisted for 3 months. Moreover, FCM produced a substantial reduction in FGF23 levels without modifications in other bone metabolism markers. Furthermore, in non-iron-depleted normal

and uremic rats, a single high dose of FCM had no effect on the plasma levels of FGF23 and phosphate for up to 7 days.

It has been suggested for years that iv iron may simpair host defense and promote bacterial growth, although the risk of infection associated with iron supplementation is controversial. Fell et al assessed the "in vitro" effect of different concentrations of ICCs including FCM on stimulated mature monocytes and hematopoietic $CD34^+$ stem cells during their differentiation into monocytes and phagocytosis and antigen presentation capacity. The authors reported no substantial specific immunologic effects after FMC stimulation, with no significant alterations in the differentiation of monocytes from hematopoietic $CD34^+$ stem cells. Moreover, FCM did not affect the expression of CD14, CD16, or CD86 in human monocyte subsets collected from control subjects without overt CKD.

Notably, using a standard experimental model of malarial anemia, Maretty et al studied the effect of FCM treatment on erythropoiesis, parasitemia, and weight as a marker of disease severity. They reported that FCM did not have a negative effect on parasitemia and disease progression. FCM resulted in significantly higher animal weights, enhanced reticulocytosis, and faster recovery in comparison with controls.

Concerning the safety of FCM administration during pregnancy, the transplacental passage of FCM (radio-labeled with ^{59}Fe) was evaluated in an "in vitro" perfusion model of human placenta. FCM was added to the maternal circuit in order to obtain a final iron concentration of 11 mM, which represents a 10 times higher iron concentration than the maximum predicted level in blood after an administration of 200 mg iron as FCM. No transferred iron radioactivity was detected in the fetal circuit. Importantly, there were no effects of FCM on placental permeability and other placental functions. In conclusion, FCM did not cross the placenta.

Quality of life in patients treated with FCM[3]

Various studies with FCM have included diverse evaluations on the changes in QoL. All of them have reported an improvement in QoL. Just to mention some of them, in the field of cardiovascular medicine, Comin-Colet et al performed a subanalysis of the previously published FAIR-HF study. They assessed baseline QoL in iron deficiency patients with CHF and the outcome of FCM on QoL. FCM remarkably improved QoL after 4 weeks and during the remaining study period. The favorable effects of FCM were independent of the anemia

status. In line with this, another subanalysis on the FAIR-HF study was conducted by Gutzwiller et al in which a multivariate analysis was carried out with various clinical variables as independent variables and QoL measures as dependent variables. They concluded that the treatment with FCM positively influenced the measures of QoL in patients with HF and ID.

Chronic fatigue is a regrettable condition affecting QoL. A randomized, placebo-controlled, single-blinded study tested the effectiveness and tolerability of a single dose of iv FCM in iron-deficient premenopausal women with symptomatic unexplained fatigue. Fatigued women with iron deficiency (ferritin <50 μg/L and TSAT <20%, or fer-ritin <15 μg/L) and normal or borderline Hb (≥11.5 g/dL) were enrolled in 21 sites in Europe, blinded to the study drug and randomized (computer-generated randomization sequence) to a single FCM (1,000 mg iron) or saline (placebo) infusion. FCM enhanced fatigue, mental QoL, cognitive function, and erythropoiesis in iron-deficient women with normal or borderline Hb.

Abstract - Iron Deficiency Anemia with Menorrhagia: Ferric Carboxymaltose a Safer Alternative to Blood Transfusion

Background:

Menstrual disorder accounts for 5%–10% of the women presenting with iron deficiency anemia (IDA) in the perimenopausal age group. Heavy menstrual bleeding in this age group leads to severe anemia and frequently requires blood transfusion which has its own adverse effects. We today have ferric carboxymaltose (FCM) as a safer alternative to blood transfusion.

Objective:

The objective of the study is to evaluate the safety and efficacy of FCM in treating anemia in patients of menorrhagia. Thus avoiding blood transfusion.

Materials and Methods:

It was an open, single arm observational study including 90 women of age more than 30 years with definitive diagnosis of menorrhagia with IDA and hemoglobin (Hb) levels between 4 gm% and 11 gm%. Intravenous FCM (500–1500 mg) was administered, and the improvement in blood indices was assessed after 3 weeks of total dose infusion. Menorrhagia was controlled by medical treatment till Hb improvement was achieved and definitive surgical intervention was done.

Result:

Most of the women were in the age group of 40–50 years. Blood indices measured pre-FCM and 3 weeks post-FCM showed a mean increase in Hb from 8.33 ± 1.10 to 10.89 ± 1.02 with a statistically significant $P < 0.01$. There was a statistically significant rise of packed cell volume, serum ferritin, and serum iron in the post-FCM blood levels after 3 weeks. No serious life-threatening adverse events were observed after FCM administration.

Conclusion:

Intravenous FCM is an effective and a safe treatment option for IDA with a single administration of high dose without serious adverse effects obviating the need for blood transfusion before surgery.

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3. Toblli JE, Angerosa M. Optimizing iron delivery in the management of anemia: patient considerations and the role of ferric carboxymaltose. *Drug Des Devel Ther*. 2014;8:2475-2491.
4. Mishra V, Verneker R, Gandhi K, Choudhary S, Lamba S. Iron Deficiency Anemia with Menorrhagia: Ferric Carboxymaltose a Safer Alternative to Blood Transfusion. *J Midlife Health*. 2018;9(2):92-96.

Survey Form

1) In your clinical practice how frequently the patients suffering from abnormal uterine bleeding visit at hospital?

a. Once a year
b. 2-3 times a year
c. 3-6 times a year
d. >6 times a year

2) In your clinical practice how do you diagnose Heavy Menstrual Bleeding?

a. Bleeding longer than one week
b. Need to change sanitary products during the night
c. Passing blood clots larger than a quarter
d. All of the above

3) In your clinical practice how many patients come with anemia and a history of abnormal uterine bleeding / heavy menstrual bleeding?

a. 2 in 10
b. 4 in 10
c. 5 in 10
d. 6 in 10

4) In your clinical practice how much blood loss you have noticed in patients of AUB?

a. 80-100 milliliters
b. 100-150 milliliters
c. 150-200 milliliters
d. > 200 milliliters

5) In your clinical practice in how many patients of AUB present with severe anemia?

a. 10-20%
b. 20-40%
c. 40-60%
d. 60-80%

6) In your clinical practice how frequently you see adolescent patients with IDA due to Heavy Menstrual Bleeding?

a. < Less than 25%
b. 25-50%
c. 50–60%
d. 60–70%
e. More than 70%

7) In your clinical practice, what dose of FCM you use frequently for the treatment of anemia in AUB?

a. 500 mg single dose
b. 500 mg 2 doses
c. 750 mg single dose
d. 1000 mg single dose

8) How is your experience with FCM in correcting IDA due to HMB?

a. Satisfactory
b. Good
c. Very good
d. Excellent

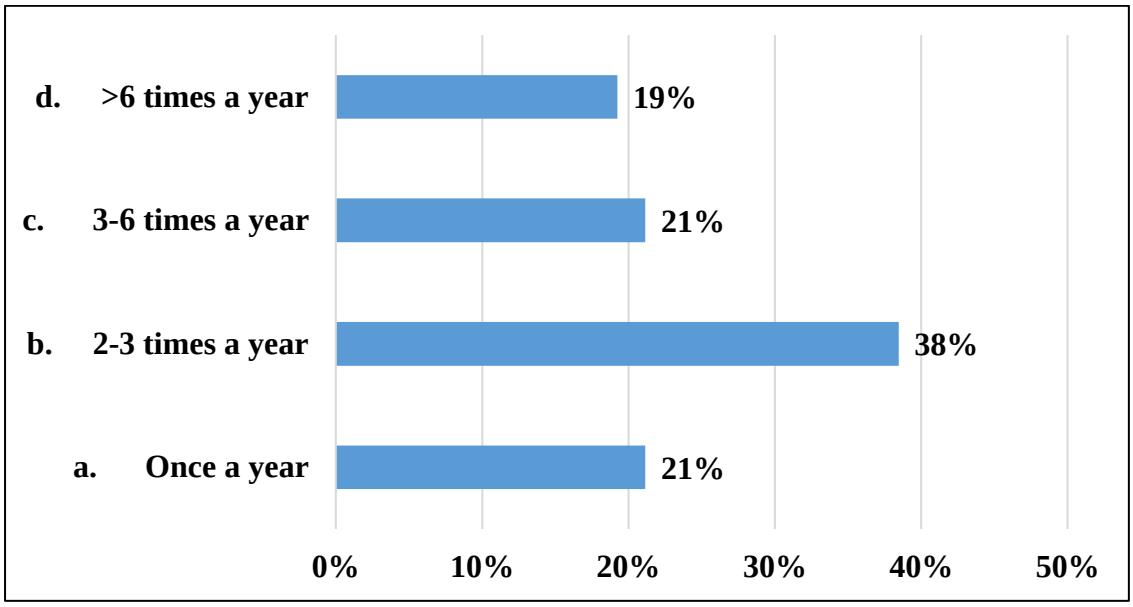
9) In your clinical practice heavy menstrual bleeding is most commonly associated with which condition?

a. PCOS
b. Fibroids
c. Miscarriage
d. All of the above
e. Other

Survey Findings

1) In your clinical practice how frequently the patients suffering from abnormal uterine bleeding visit at hospital?

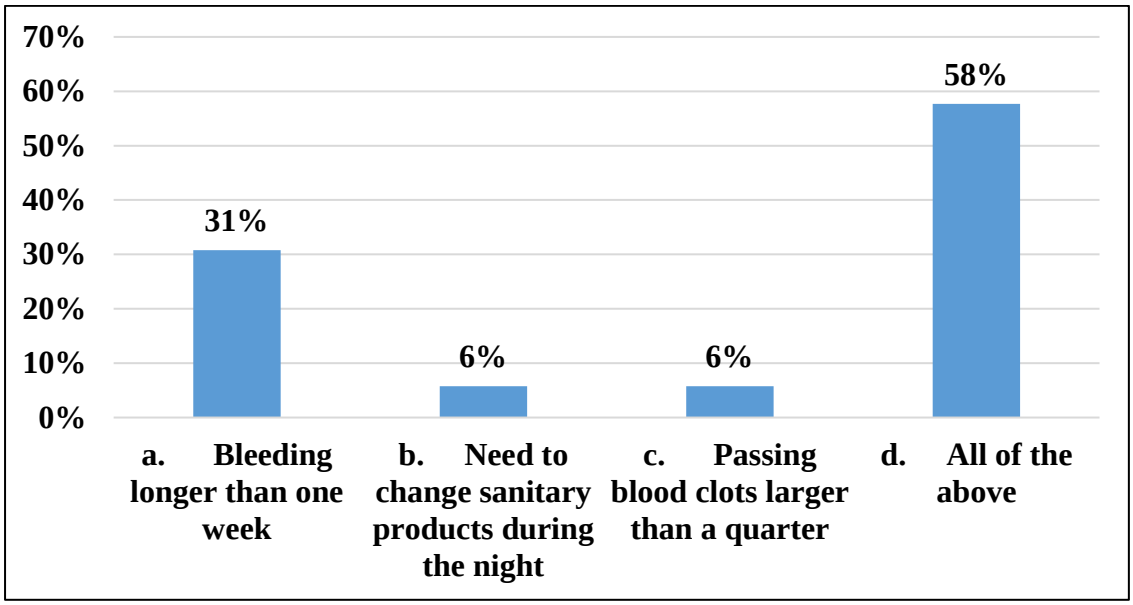
a. Once a year
b. 2-3 times a year
c. 3-6 times a year
d. > 6 times a year



In the clinical practice of 38% of doctors, the patients suffering from abnormal uterine bleeding visit the hospital 2 – 3 times a year.

2) In your clinical practice how do you diagnose Heavy Menstrual Bleeding?

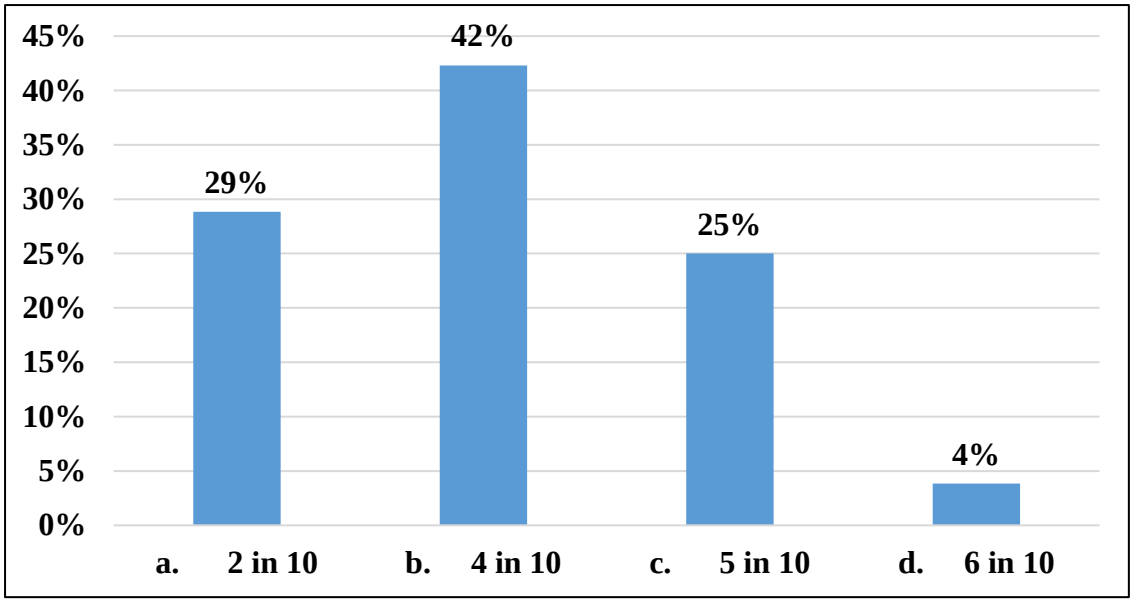
a. Bleeding longer than one week
b. Need to change sanitary products during the night
c. Passing blood clots larger than a quarter
d. All of the above



According to 58% of doctors, they diagnose Heavy Menstrual Bleeding through the indications of bleeding longer than one week, need to change sanitary products during the night and passing blood clots larger than a quarter.

3) In your clinical practice how many patients come with anemia and a history of abnormal uterine bleeding / heavy menstrual bleeding?

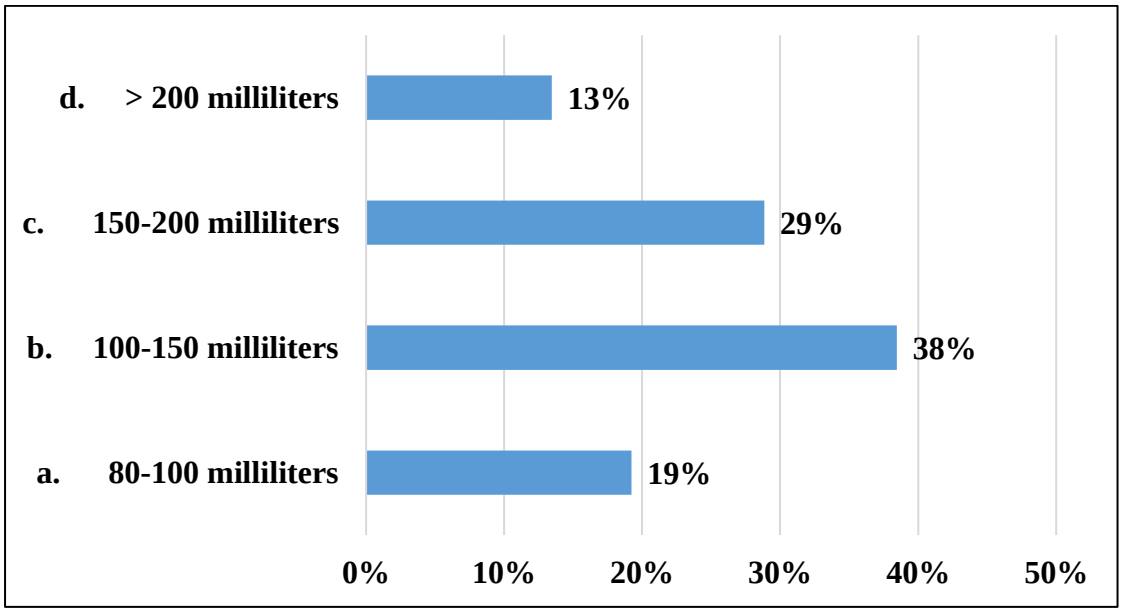
a. 2 in 10
b. 4 in 10
c. 5 in 10
d. 6 in 10



As per 42% of doctors, 4 in 10 patients come with anemia and a history of abnormal uterine bleeding / heavy menstrual bleeding.

4) In your clinical practice how much blood loss you have noticed in patients of AUB?

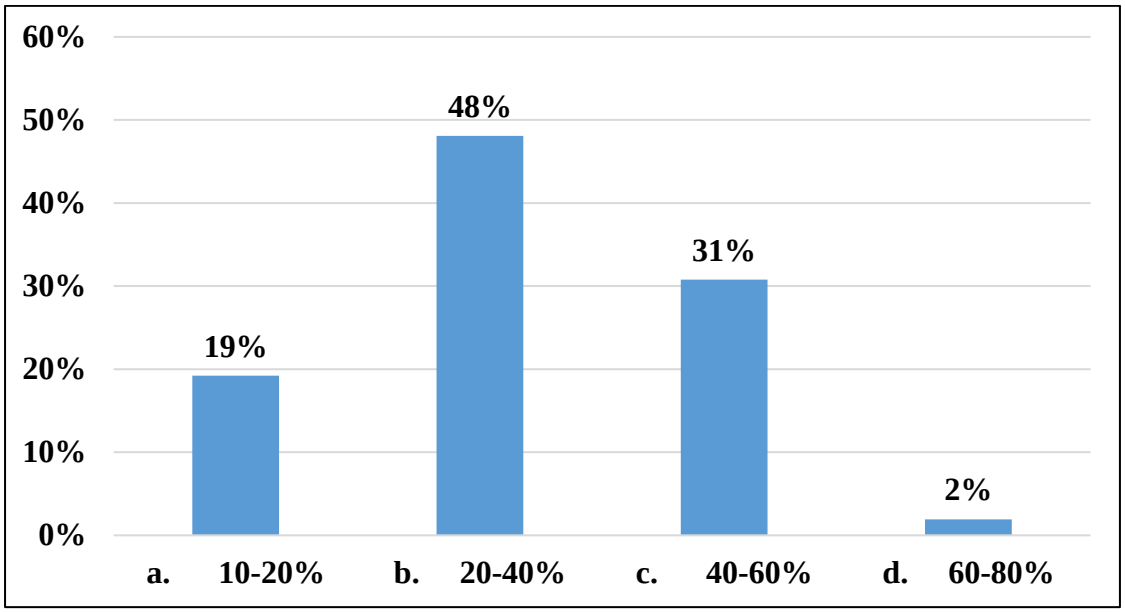
a. 80-100 milliliters
b. 100-150 milliliters
c. 150-200 milliliters
d. > 200 milliliters



38% of doctors have noticed 100-150 millilitres of blood loss in patients of AUB.

5) In your clinical practice in how many patients of AUB present with severe anemia?

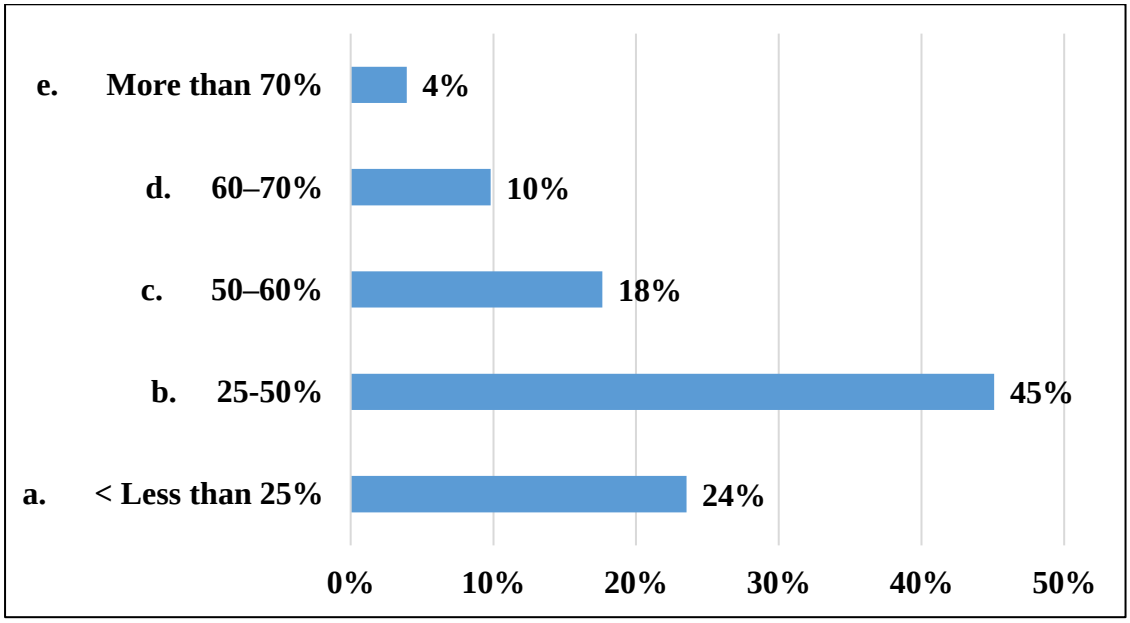
a. 10-20%
b. 20-40%
c. 40-60%
d. 60-80%



In the clinical practice of 48% of doctors, 20 – 40% patients of AUB present with severe anemia.

6) In your clinical practice how frequently you see adolescent patients with IDA due to Heavy Menstrual Bleeding?

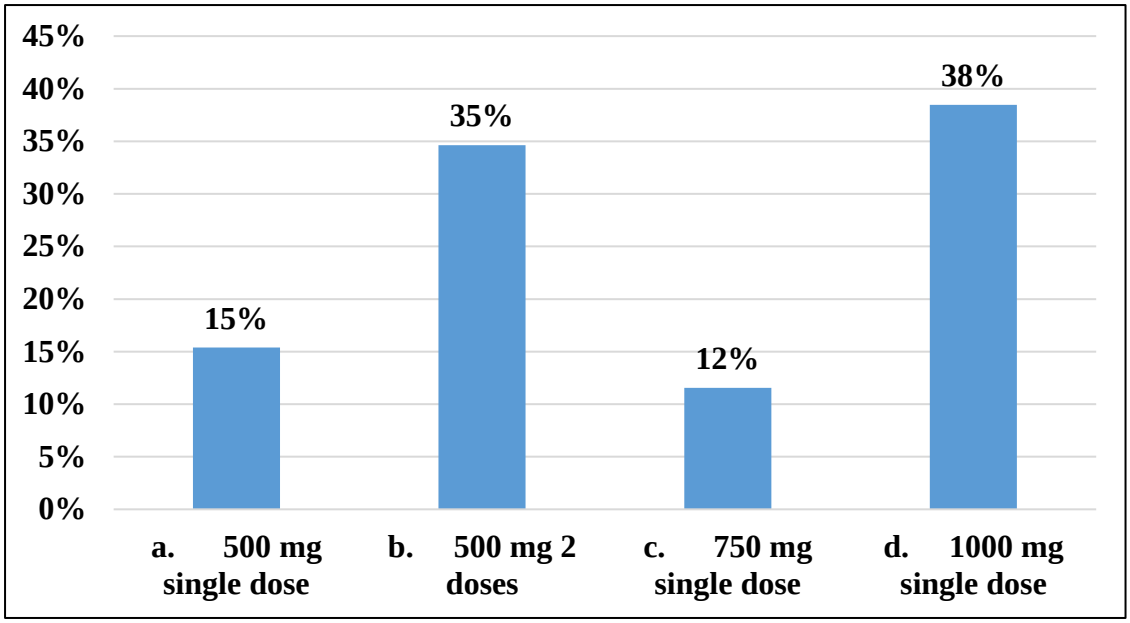
a. < Less than 25%
b. 25-50%
c. 50–60%
d. 60–70%
e. More than 70%



45% of doctors see 25 – 50% adolescent patients with IDA due to Heavy Menstrual Bleeding.

7) In your clinical practice, what dose of FCM you use frequently for the treatment of anemia in AUB?

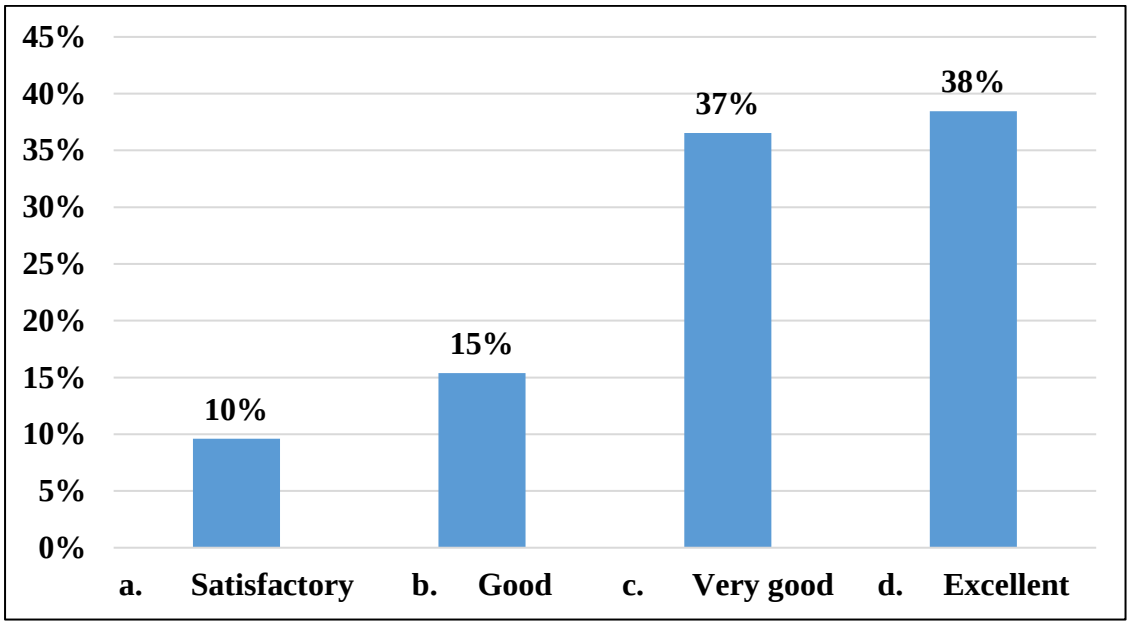
a. 500 mg single dose
b. 500 mg 2 doses
c. 750 mg single dose
d. 1000 mg single dose



38% of doctors frequently use 1000mg single dose of FCM for the treatment of anemia in AUB.

8) How is your experience with FCM in correcting IDA due to HMB?

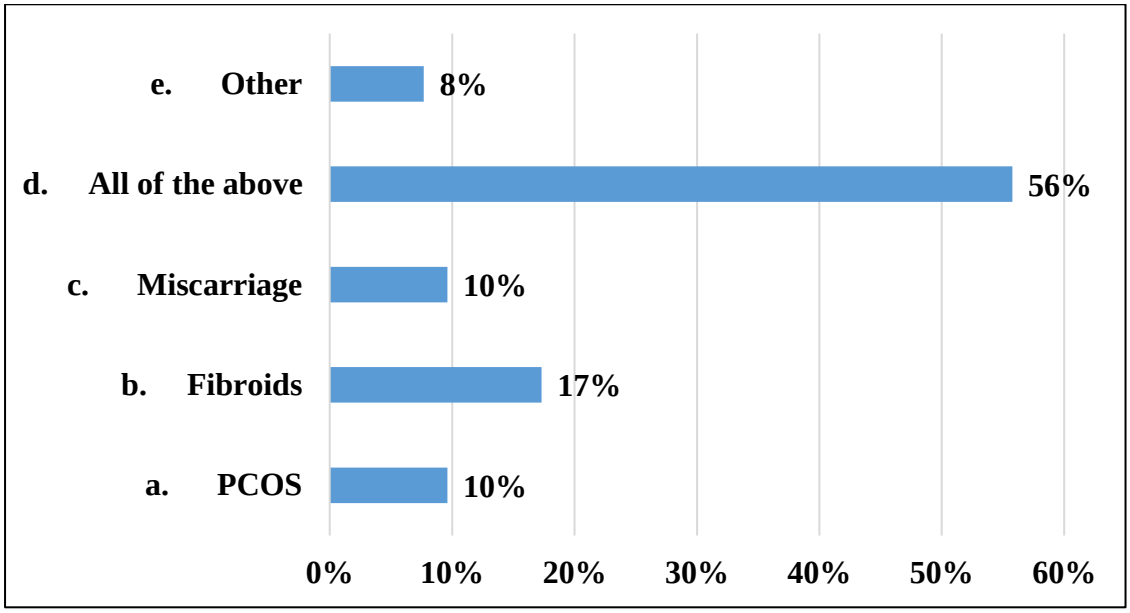
a. Satisfactory
b. Good
c. Very good
d. Excellent



As per 38% of doctors, their experience with FCM in correcting IDA due to HMB is excellent.

9) In your clinical practice heavy menstrual bleeding is most commonly associated with which condition?

a. PCOS
b. Fibroids
c. Miscarriage
d. All of the above
e. Other



In the clinical practice of 56% of doctors, heavy menstrual bleeding is most commonly associated with the conditions of PCOS, fibroids and miscarriage.

Summary

- In the clinical practice of 38% of doctors, the patients suffering from abnormal uterine bleeding visit the hospital 2 – 3 times a year.
- According to 58% of doctors, they diagnose Heavy Menstrual Bleeding through the indications of bleeding longer than one week, need to change sanitary products during the night and passing blood clots larger than a quarter.
- As per 42% of doctors, 4 in 10 patients come with anemia and a history of abnormal uterine bleeding / heavy menstrual bleeding.
- 38% of doctors have noticed 100-150 millilitres of blood loss in patients of AUB.
- In the clinical practice of 48% of doctors, 20 – 40% patients of AUB present with severe anemia.
- 45% of doctors see 25 – 50% adolescent patients with IDA due to Heavy Menstrual Bleeding.
- 38% of doctors frequently use 1000mg single dose of FCM for the treatment of anemia in AUB.
- As per 38% of doctors, their experience with FCM in correcting IDA due to HMB is excellent.
- In the clinical practice of 56% of doctors, heavy menstrual bleeding is most commonly associated with the conditions of PCOS, fibroids and miscarriage.

Consultant Opinion

Market Opportunities:

There is a market opportunity for pharmaceutical companies to develop targeted treatments for AUB and HMB that address the underlying causes of these conditions, such as polycystic ovary syndrome (PCOS), fibroids, and miscarriage. Therapies that specifically target the hormonal imbalances or structural abnormalities contributing to AUB/HMB could provide significant value to patients and healthcare providers.

Value for Healthcare Professionals:

Healthcare professionals should receive education and training on the latest diagnostic criteria and treatment options for AUB and HMB. Continuing medical education programs can help ensure that providers are up-to-date with best practices in managing these conditions, ultimately improving patient outcomes.

Adverse Effect Management:

Transplant teams should closely monitor patients for potential adverse effects associated with treatments for AUB and HMB, such as iron deficiency anemia (IDA) and side effects of medications. Regular monitoring and proactive management of adverse effects can help improve patient tolerability and adherence to treatment regimens.

Withdrawal Management:

Clear guidelines should be established for the diagnosis and management of AUB and HMB, including criteria for diagnosing HMB and recommended treatment algorithms based on patient characteristics and underlying conditions. Standardized protocols can help ensure consistent and evidence-based care for patients with AUB and HMB.

Market Positioning:

Pharmaceutical companies can differentiate their products for treating AUB and HMB by highlighting their efficacy, safety profile, and ease of administration. Marketing strategies should emphasize the unique features and benefits of each treatment option, positioning them as preferred choices for healthcare professionals managing these conditions.

Personalized Treatment Decisions:

Healthcare providers should take into account individual patient factors, such as age, reproductive goals, and comorbidities, when making treatment decisions for AUB and HMB. Personalized treatment plans tailored to each patient's needs and preferences can optimize outcomes and improve patient satisfaction.

Improving Patient Outcomes:

Patient education and support are essential for improving outcomes in AUB and HMB. Healthcare providers should educate patients about their condition, treatment options, and self-management strategies to empower them to make informed decisions about their care. Additionally, support services, such as counseling and peer support groups, can help patients cope with the physical and emotional challenges of living with AUB and HMB.

NOTES

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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