IMPROVING UTILISATION OF PARENTERAL IRON THERAPY FOR TREATMENT OF IRON DEFICIENCY ANAEMIA IN MEDICAL WARDS OF *HOSPITAL KUALA LUMPUR*

Gan Shiau Shuang[1], Sharifah Suryani Syed Rahim Shah[2], Adelin Yong Sue Wen[1], Marilyn Tan May Yeen[1], Chang Cheok Ee[1], Lee Hooi Peng[1].

[1] Pharmacy Department, Hospital Kuala Lumpur,
Ministry of Health Malaysia

[2] General Medicine Department, Hospital Kuala Lumpur,
Ministry of Health Malaysia

Corresponding Author: Gan Shiau Shuang
Email: gan.shiau@moh.gov.my

Abstract

Parenteral iron, despite being the recommended treatment for iron deficiency anaemia (IDA) in hospitalised patients, was underutilised in medical wards of *Hospital Kuala Lumpur* (HKL), where excessive use of blood transfusions for treating IDA was observed. A verification study in 2020, showed only 9.3% of IDA patients in HKL received parenteral iron. The indicator used was the percentage of IDA patients who received parenteral iron. The standard is 40% based on haematologist consensus and as practiced in tertiary hospitals abroad. This quality improvement study was conducted using universal sampling in selected medical wards from September 2020 until July 2022 in two consecutive phases. All IDA patients with traceable records were included, giving a total of 182 subjects throughout the study. A survey was conducted among healthcare providers to identify contributing factors to the underutilisation. Main contributing factors include a lack of confidence in using parenteral iron (52.8%), cost concerns (20.2%), lack of trained staff for monitoring (15.7%), and no protocol to guide its use (15.7%). Parenteral Iron Infusion Protocol (PREFER) was developed. Several continuous medical and nursing education sessions were conducted for training and to introduce PREFER. More strategies included were building a website with the feature of a smart dose calculator, poster displays in the wards, and adding iron derisomaltose to the hospital formulary. Implementation led to an increase in parenteral iron utilisation from 9.3% to 33.3%, conserving 100 pints of blood and saving MYR 8000.00 monthly. We plan to expand the study to other disciplines and promote PREFER at the state and national levels.

KEYWORDS: Iron deficiency anaemia, Parenteral iron, Quality improvement study

Problem

Iron deficiency anaemia (IDA) is a significant public health concern. Recent findings from the Global Burden of Disease project indicated that an estimated 1.24 billion individuals, comprising a substantial sixth of the global population, are affected by IDA (1). Beyond its well-known impact on specific cohorts such as paediatric and pregnant populations, IDA is increasingly acknowledged as a clinical concern in various medical specialities, particularly among individuals with chronic diseases and the elderly (2).

Hospital Kuala Lumpur (HKL) is the biggest government hospital under the Ministry of Health of Malaysia. It serves as the flagship hospital of the Malaysian public healthcare system and acts both as a tertiary and referral hospital, particularly for cases from government health clinics within the Wilayah Persekutuan Kuala Lumpur (WPKL) area where Kuala Lumpur, the capital of Malaysia is located. HKL has 83 wards and 2,300 beds, with 22 medical wards consisting of 495 beds. The medical wards at HKL are staffed by approximately 300 doctors including medical officers, specialists, and consultants, alongside 680 staff nurses, and 50 clinical pharmacists.

In WPKL, the anaemia prevalence was reported as high as 27.6% in 2015 (3). Although institutional data on the types of anaemia is not available, local data suggests IDA is predominant among patients in Malaysia (4). As HKL is the main government hospital within WPKL, most of the anaemia cases are likely to be referred to or treated here. At HKL, blood transfusions have been observed being used excessively for the treatment of IDA over the years. During several clinical ward rounds, a recently transferred haematologist in HKL raised this concern, which was then discussed with the pharmacists. Parenteral iron, which should be the primary choice for treating IDA among hospitalised patients, was not fully utilised by doctors practising in medical wards. Many IDA patients who were hemodynamically stable were still transfused instead of being administered parenteral iron.

A verification study conducted in five medical wards of HKL in September 2020 showed that only 9.3% of IDA patients were treated with parenteral iron. This figure contrasts sharply with findings from hospitals in New York and Mexico, where utilisation rates reach as high as 40% (5,6). The underutilisation of parenteral iron, paired with the use of blood transfusions to treat IDA, led to unnecessary consumption of the blood bank stock, which was already critical during the COVID-19 pandemic (7) and putting the patients at risk of getting transfusion-related adverse effects (8).

Therefore, this study aimed to improve the utilisation of parenteral iron for the treatment of IDA from 9.3% to 40% within two years.

Background

Anaemia is characterized by reduced levels of haemoglobin concentration, haematocrit, or red blood cell counts. Causes may include iron, folate or vitamin B12 deficiencies, chronic diseases, haemolysis, or bone marrow suppression (8). IDA is diagnosed when haemoglobin concentration falls below 12 g/dL in non-pregnant females or below 13 g/dL in males, mean corpuscular volume (MCV) is below 75 fL, and serum ferritin concentration is below 30 µg/L, or transferrin saturation (TSAT) is below 20% (9–11).

Patients with IDA should be treated with iron supplementation either orally or parenterally, while blood transfusions are reserved for severe cases. Oral iron is the preferred initial treatment (12), but many patients struggle with it due to intolerance and absorption issues (13,14). Parenteral iron, administered directly into the bloodstream, is more effective (15) and has shown comparable efficacy to blood transfusions in situations requiring rapid haemoglobin elevation (16,17). Furthermore, using parenteral iron also leads to cost savings as it preserves the blood bank stock. On average, 500 mg of parenteral iron, which costs MYR 82 (~USD 17) for iron dextran and MYR 44 (~USD 9) for iron sucrose, contains an equivalent amount of iron in two pints of blood, which costs MYR 240 (~USD 51) (18), making it a more cost-effective treatment option.

In Malaysia, three parenteral iron formulations are available: iron dextran, iron sucrose, and iron derisomaltose (19). Iron dextran and iron sucrose are available at HKL, while iron derisomaltose was

introduced during the study. In HKL, iron dextran can be prescribed by any physician, while iron sucrose requires authorisation by nephrologists or haematologists (20). Both iron dextran and iron derisomaltose allow total dose infusion, with the latter offering shorter infusion times and smaller fluid volume (21,22). Conversely, iron sucrose necessitates divided doses over several days (23). Due to convenience and accessibility, iron dextran is predominantly used at HKL.

Parenteral iron administration requires careful monitoring due to the rare but serious risk of allergic reactions, including life-threatening anaphylaxis (24). Healthcare personnel administering parenteral iron should be capable of monitoring and managing these adverse reactions (25). The recommended monitoring parameters include vital signs and signs of hypersensitivity reactions during the test dose, for one hour after the test dose, and during and after the infusion (21–23). Nurses, responsible for medication administration and patient monitoring in medical wards are best suited to oversee parenteral iron infusion, ensuring its safe administration (26).

Parenteral iron remains underutilised and less favoured by medical practitioners, as noted in various studies (27,28). Auerbach and Macdougall (28) attributed this trend to concerns about adverse effects and misinterpretation of minor infusion reactions. Mayson et al. (29) found that lack of knowledge, cost concerns, and fear of adverse reactions were key factors in parenteral iron's underuse. They also identified potential facilitators, such as trained staff, streamlined referral systems, and newer preparations with shorter infusion times.

Many promising methods appear to be under investigation, according to research on ways to enhance the usage of parenteral iron. A quality improvement study conducted at Sunnybrook Health Sciences Centre in Canada demonstrated that the implementation of the "Pumping Iron Bundle" comprised of an IDA screening tool, treatment algorithm, order set, and patient information handout significantly improved the utilization of parenteral iron from 17% to 90.3% among heart failure patients with IDA (30). Similarly, a study protocol published in BMC Pregnancy and Childbirth outlines a continuous quality improvement strategy to strengthen screening practices and facilitate the routine use of intravenous iron for treating anaemia in pregnant and postpartum women in Nigeria. The multifaceted intervention involves training healthcare providers, strengthening supply chains, and conducting evaluations to increase the uptake of IV iron and improve maternal-neonatal outcomes (31).

These studies highlight the potential of quality improvement methods to optimize the utilization of parenteral iron in various patient populations. By implementing targeted strategies tailored to the local context, healthcare institutions can work to ensure that patients with IDA receive appropriate and timely treatment, ultimately leading to improved clinical outcomes.

Measurement

A quality improvement study was initiated by a team comprising a haematologist who strongly advocated for improving Patient Blood Management (PBM) and five clinical pharmacists dedicated to optimising treatment options for patients with IDA. The study was conducted using universal sampling in five selected medical wards in HKL between September 2020 and December 2021 and expanded to two additional wards in Cycle 2 between January and July 2022. These wards were selected as they were non-COVID wards, and the ward consultants were not haematologists, removing any bias in prescribing preference. All patients diagnosed with IDA were included, except those without traceable medical records.

The indicator used was the percentage of IDA patients treated with parenteral iron. The standard was set at 40% based on haematologists consensus and as found practiced in tertiary hospitals in the United States and Mexico (5,6).

Indicator:

$$\textit{Percentage of IDA patients treated with parenteral iron} = \frac{\textit{Number of IDA patients treated with parenteral iron}}{\textit{Number of IDA patients}} \times 100$$

A verification study was carried out in September 2020 to measure the percentage of IDA patients treated with parenteral iron. All iron studies blood tests taken in the selected wards during the specified period were traced by five pharmacists in the team through the HKL online laboratory investigation system to identify IDA patients. Their medical records were retrieved with permission from the record department and reviewed by the same team members. A unique identifier was assigned to each reviewed record for data tracking and verification. A data collection form was used to document: (i) patients' socio-demographics, (ii) results of iron studies blood tests (including ferritin level and TSAT), (iii) any treatment given (parenteral or oral iron, blood transfusion, or no treatment), (iv) the dilution and administration rate of parenteral iron, and (v) the adherence to documentation of necessary monitoring parameters. Additionally, pharmacy records were cross-referenced for parenteral iron usage. All the collected data was entered and compiled into a Google Sheet.

Remedial measures for Cycle 1 were implemented from October 2020 to November 2021, with data collected in December 2021. Further remedial measures were implemented from January to June 2022, followed by data collection in July 2022. Using consistent sampling and data collection methods, the study included 43, 58, and 81 IDA cases in the verification study, Cycle 1, and Cycle 2, respectively.

Results from the verification study showed that out of 43 IDA patients, only four (9.3%) received parenteral iron. Additionally, it was also found that the monitoring of patients' parameters every 15 to 30 minutes during infusion was not recorded for all cases of parenteral iron therapy. This implied that monitoring for infusion-related reactions and other adverse events might not have been done.

Initial Assessment of the Problem

The contributing factors to this problem were analysed using a problem analysis chart as illustrated in Figure 1.

An online survey via Google Form (refer to Appendix 1) was conducted using purposive sampling among 102 healthcare providers (HCPs), which comprised of doctors and pharmacists working in all the medical wards in the hospital. Their confidence and awareness in using parenteral iron, as well as the perceived contributing factors to its underutilisation were assessed.

The main perceived contributing factors included lack of confidence in use (43.1%, n=44), concern about its cost (16.7%, n=17), no available facility or trained staff to do close monitoring (12.7%, n=13), and no local guideline or protocol to guide its use (12.7%, n=13) (Figure 2).

In the same survey, 15 questions to assess level of knowledge of IDA and parenteral iron were included. The questions and answers were reviewed by a haematologist for their relevance. A respondent is considered to have good knowledge when achieving a score of 60% or higher, as agreed by the haematologist and senior clinical pharmacists. Results from the survey showed that 79.7% of doctors and 96.8% of pharmacists were aware of parenteral iron as the treatment option for IDA. However, only 24.6% of doctors and 35% of pharmacists had good knowledge on the use of IDA and parenteral iron (Table 1).

The process of care for the treatment of IDA with parenteral iron therapy was reviewed, and the critical steps for improvement were identified, as shown in Figure 3. Four critical steps were identified; (i) Doctors prescribe parenteral iron, (ii) Pharmacists intervene (iii) Nurses administer parenteral iron therapy, and (iv) Nurses monitor the patient's parameters. During the pre-remedial study, 100% of parenteral iron was administered correctly by nurses, however, none of the cases had complete documentation, test dose monitoring and full dose monitoring. Due to the limitation of the study, the first two critical steps were not objectively measured.

Strategy

Firstly, a parenteral iron infusion protocol was developed to address the two main contributing factors, including a lack of confidence and knowledge among HCPs and the lack of standardised protocol. Before the protocol, there was inconsistency in parenteral iron prescription across specialties. The protocol, serving as both a reference and an educational tool, outlines



Figure 1: Problem analysis chart for underutilisation of parenteral iron therapy for the treatment of IDA in medical wards, HKL

indications, contraindications, precautions, dosage, and specially designed charts for dilution, administration, and monitoring. Reviewed by the only haematologist in HKL, the head of the national haematology service, and the chief clinical pharmacist for its content, the protocol led to more precise prescriptions and reduced the need for pharmacist clarification with prescribers.

The protocol was distributed in both printed and electronic forms to ensure accessibility among HCPs. However, during an observation conducted by two pharmacists in the team on a working day in January 2021, it was found that while physical copies were present in the wards, many staff were unaware of them. In contrast, HCPs provided positive feedback on the e-protocol to the team members. Yet, a survey conducted later revealed that only 50% of HCPs read the protocol, indicating a weakness in the strategy, though the reasons were not explored. Overall, while the electronic format proved to be more accessible, there was insufficient awareness and uptake among staff.

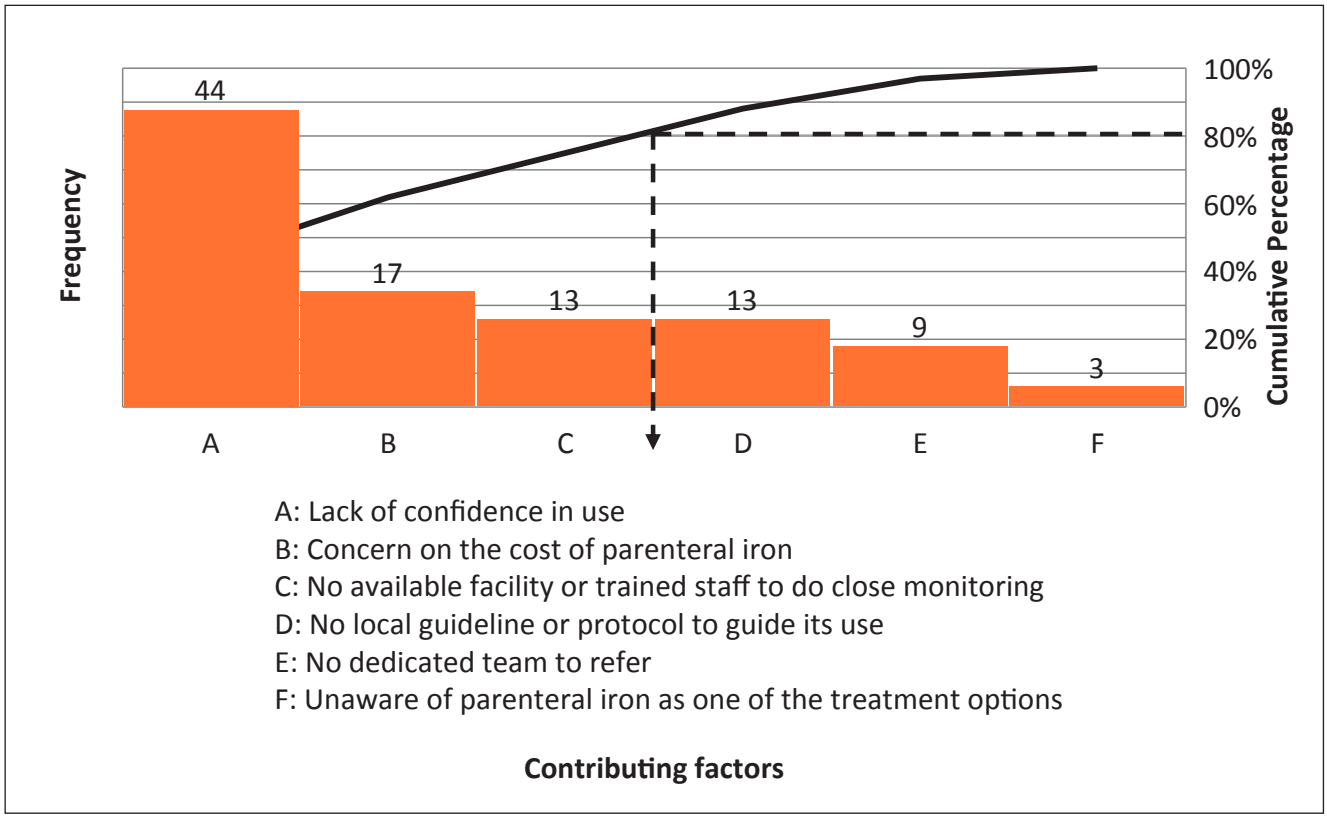


Figure 2: Pareto chart - Contributing factors to underutilisation of parenteral iron therapy based on a survey among doctors and pharmacists (n = 102)

Table 1: Results from the online survey among 102 HCPs and improvement from verification phase to Cycle 1 and Cycle 2

		Verification	Cycle 1	Cycle 2
Awareness	Doctors	79.7%	98.1%	100%
	Pharmacists	96.8%	100%	100%
Knowledge	Doctors	24.6%	67.9%	81.3%
	Pharmacists	35%	85%	81.8%

Thirdly, to enhance HCPs' confidence and knowledge as well as to correct misconceptions about the cost of parenteral iron, two virtual CME sessions were conducted by the haematologist and pharmacists via Zoom. Invitations to the CME sessions were shared through group chats with consultants, specialists, medical officers, and pharmacists. The response was positive, with consultants expressing strong support and assuring that their ward medical officers would attend the sessions. The CME had achieved 102 participants, constituting 29% of the targeted HCPs working in the related medical wards. Pre-tests and post-tests were performed to assess knowledge improvement, and participants achieving the highest score were recognized with tokens of appreciation at the end of the session to enhance participation. Comparison between pre-test and post-test results demonstrated improvement in HCPs' knowledge and confidence. Despite challenges posed by the COVID-19 pandemic, 29% of attendance at

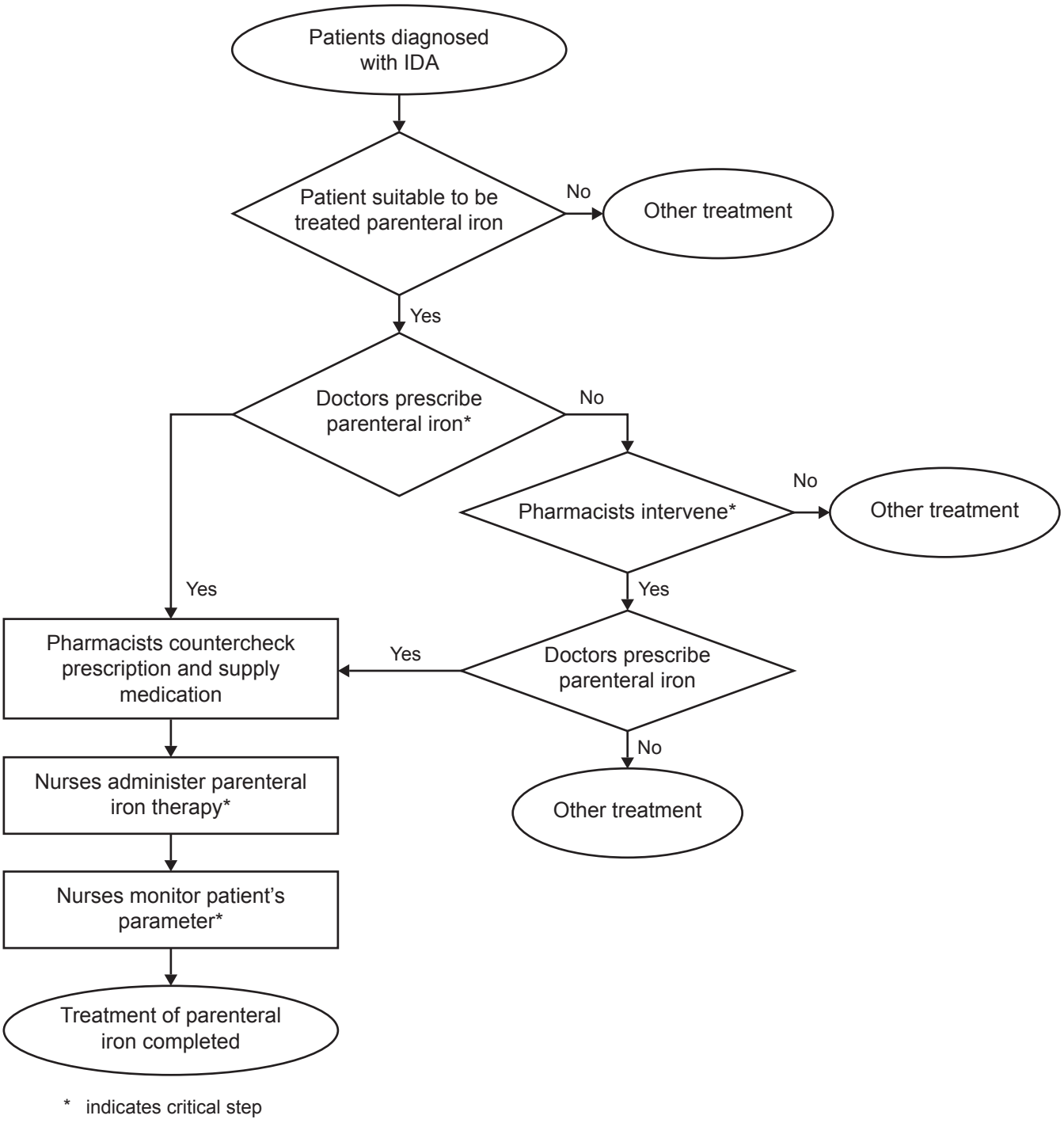


Figure 3: Process of care for the treatment of IDA with parenteral iron therapy in medical wards, HKL

the CME surpassed our expectations, which may be attributed to the virtual format and influential consultants involved. Additionally, the recognition of top scorers effectively encouraged participation and sustained engagement throughout the event.

The fourth remedial action targeted the lack of training and awareness for nurses to do close monitoring. Two sessions of continuous nurse education sessions (CNE) were conducted to educate nurses on the basic knowledge of IDA and parenteral iron, monitoring parameters, and to introduce the monitoring charts from the protocol. The charts are to be printed and used by the nurses for monitoring the vital signs of patients and to check for any signs of adverse reactions during the infusion. The CNE achieved 63 attendees, comprising about 10% of all medical ward nurses, with two to three nurses from each of the selected wards attending the CNE. Despite the limited attendance, the strategy improved compliance with monitoring requirements,

as evident in post-cycle 1. This highlights the value of training ward representatives and the practicality of the monitoring chart.

Cycle 2 implemented further strategies to bridge gaps identified in Cycle 1 results. After Cycle 1, only 67.9% of doctors had good knowledge. Additionally, the CME in Cycle 1 covered only 29% of the targeted HCPs. Hence, a hybrid CME session was conducted as the movement control order was lifted, reaching 145 additional attendees. In comparison to the previous CME, the hybrid mode achieved a higher attendance with a single session accommodating 145 attendees. The quiz questions in Cycle 2 included another three questions to assess the knowledge of the updated content of the protocol.

The sixth strategy was the rebranding and redesign of the protocol to gain more awareness and uptake among staff. Consultations to explore ways for protocol improvement took place with the quality assurance and improvement experts. The protocol was rebranded with the name PREFER and redesigned with a more attractive colour theme and layout. The content of PREFER was also revised based on users' feedback, particularly the recommendation to incorporate a summary table comparing different parenteral iron formulations. Additionally, the recent addition of iron derisomaltose to the hospital formulary necessitates the inclusion of its dosage, method of administration, and monitoring parameters in the protocol. The electronic version of PREFER was broadcasted to HCPs through messaging applications as this method had shown better uptake during Cycle 1. It was observed that PREFER had attracted greater attention than the preceding protocol, sparking discussions among HCPs since its introduction.

Taking a step further, the team members developed a website to publish PREFER online (Appendix 2) as the seventh strategy. The website was built using Google Sites which is free, does not require advanced technical skills, and is complemented with Google Analytics for visitor statistics. As the eighth strategy, a smart dose calculator (Appendix 3) was invented by using Google Sheets to ease calculation for different formulations of parenteral iron, embedded on the website. The ninth strategy involved promoting the website to HCPs through messaging applications and placing posters with QR codes (Appendix 4) linked to the website in the wards. The website attracts over 1300 visitors per annum, with the calculator section receiving 100 monthly visits. It was observed by team members that HCPs have been utilising the calculator in their daily practice, based on the alteration history recorded on the Google Sheet.

The tenth strategy aimed to improve nurses' compliance with the monitoring requirements by providing physical folders with monitoring chart copies in the wards. This was because Cycle 1 revealed an unsatisfactory level of compliance with the monitoring requirements: 66.7% for documentation, 66.7% for test dose monitoring, and 33.3% for full dose monitoring. The responsibilities of replenishing the monitoring chart copies were assigned to ward pharmacists and nurses. Positive feedback was received from ward pharmacists and nurses as the charts are readily available when needed, facilitating parenteral iron administration.

Following Cycle 1, team members received verbal feedback from HCPs about the challenge of treating IDA patients with heart failure or severe kidney impairment with fluid restriction. As 500mL of fluid needs to be given for the total dose infusion of iron dextran, this takes up the majority of the amount of fluid allowed daily for these patients. Hence, iron derisomaltose was added to the hospital formulary and introduced to HCPs during CME. Nevertheless, due to its high cost (approximately MYR 1218 (~USD 258) for 1 course of treatment), iron derisomaltose is listed as a controlled item and can only be prescribed by haematologists for selected patients. During cycle 2, no patient received it, resulting in minimal impact on parenteral iron usage.

Results

Upon implementation of the above strategies, the percentage of IDA patients treated with parenteral iron increased from 9.3% (n=4) to 20.6% (n=12) in Cycle 1. In Cycle 2, the result further increased to 33.3% (n=27). Achievable benefit not achieved (ABNA) improved from 30.7% to 19.4% and 6.7% in Cycle 1 and Cycle 2 respectively (Figure 4).

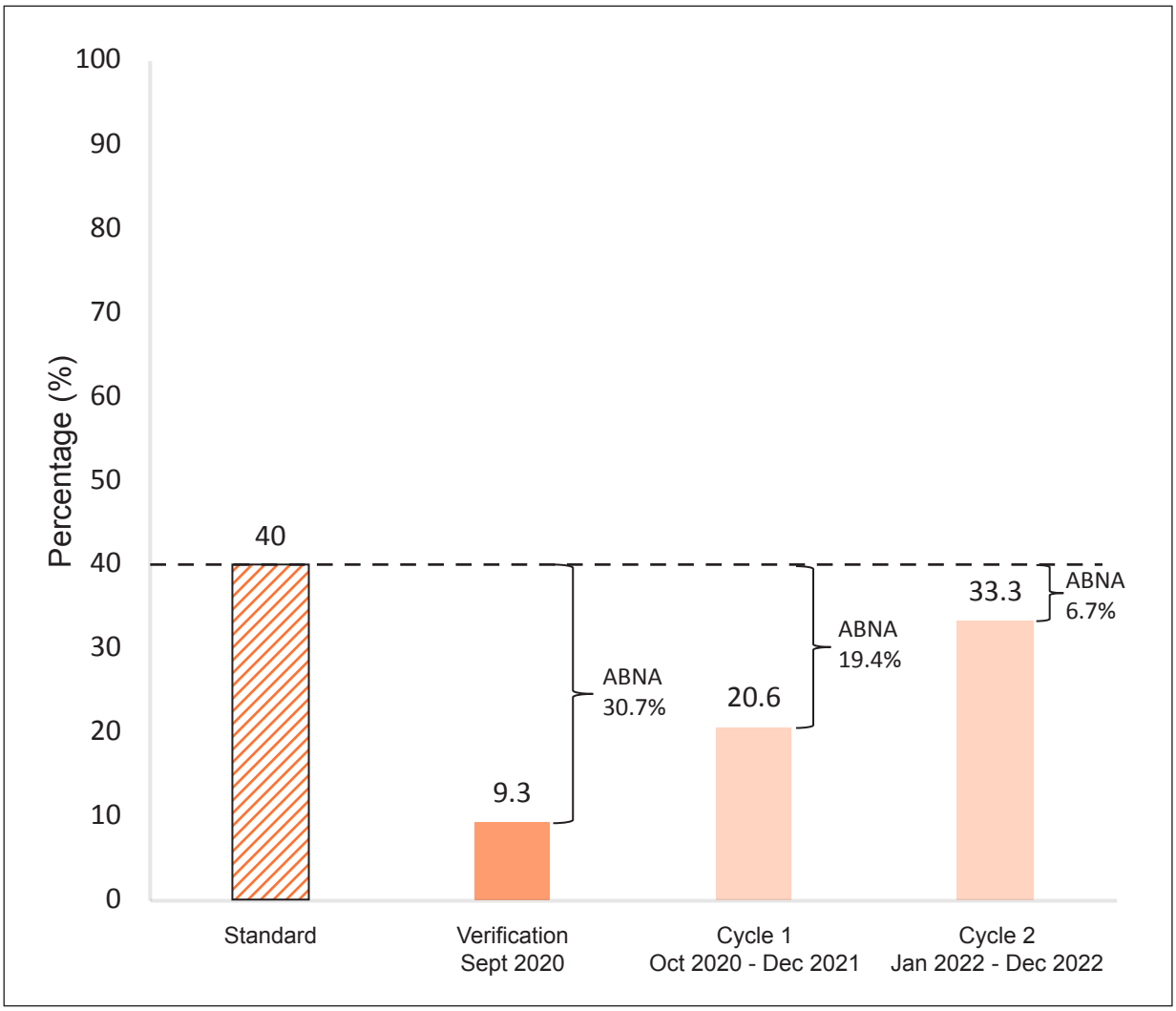


Figure 4: Percentage of IDA patients treated with parenteral iron from Sept 2020 - July 2022

A total of 10,000 mg (100 ampoules) of iron dextran, costing approximately MYR 1600 (~USD 338), was given over a month in Cycle 1, and 25,175 mg (252 ampoules) of iron dextran costing approximately MYR 4,000 (~USD 845) was given over a month during Cycle 2. As mentioned earlier, 500 mg of parenteral iron contains an equivalent amount of iron in two pints of blood as in transfusion therapy. Hence, we had successfully conserved 40 pints of blood costing MYR 4800 (~USD 1000) in Cycle 1, and 100 pints of blood costing MYR 12,000 (~USD 2537) in Cycle 2 and saved approximately MYR 3200 (~USD 700) per month in Cycle 1 and MYR 8000 (~USD 1700) per month in Cycle 2 after the implementation of our quality improvement project.

From this study, we managed to improve the knowledge among HCPs (247 doctors and pharmacists, 70% of medical ward staff) in using parenteral iron from 24.6% to 67.9% in Cycle 1 and 81.3% in Cycle 2 (doctors) and from 35% to 85% in Cycle 1 (pharmacists). The marked improvement in knowledge is proven to be sustainable albeit there is a slight drop in the pharmacist group from Cycle 1 (85%) to Cycle 2 (81.8%) due to a slight variation in the quiz questions for Cycle 2. The self-perceived level of confidence in using parenteral iron among the HCPs involved in the survey increased from 43.1% to 100% in Cycle 1 and 2. The awareness also improved from 79.7% (doctors) and 96.8% (pharmacists) to 100% for both parties (Table 1). We also successfully established a routine for nurses to do close monitoring during the administration of parenteral iron. The compliance with monitoring requirements improved from 0% to 100% on documentation, 0% to 88% on test dose monitoring, and 0% to 76% on

full dose monitoring. Increased compliance with monitoring requirements also implies improvement in patient safety as adverse drug reactions can be detected and managed early (32).

Lessons and limitations

The objective of promoting the usage of parenteral iron is in line with the aims of the first pillar of PBM, which is to optimise erythropoiesis (8), and to improve patient outcomes while conserving the blood bank reserves. This study is the first initiative done in HKL to assess the usage of parenteral iron among IDA patients in medical wards. The study's strength lies in its execution in wards where consultants lacked expertise in haematology. This approach eliminates potential biases related to specialist knowledge and prescribing preferences.

This study underscores the importance of thorough problem analysis in identifying contributing factors and practice gaps. Multidisciplinary collaboration between doctors, pharmacists, and nurses is crucial for safe and effective parenteral iron treatment. The strategies used are applicable in Malaysian specialist hospitals to optimize IDA treatment, potentially reducing blood transfusion needs and enhancing PBM practices nationwide.

Despite the success, this study has several limitations and challenges. Firstly, the first two criteria of MOGC (doctors prescribe parenteral iron and pharmacist intervene) were not developed, hence full assessment of MOGC was not conducted. Therefore, future cycles should identify criteria for the two critical steps and collect data to assess whether patients with IDA are prescribed the correct dosage of parenteral iron and to assess the interventions made by pharmacists in cases of inappropriate treatment or incorrect prescriptions. Additionally, data on the impact on patients' anaemia status and haemoglobin levels were not collected, which could provide further insights into the effectiveness of parenteral iron therapy. An overlooked factor affecting the prescription of parenteral iron is the presence of concomitant infections, as therapeutic iron doses may pose an increased risk due to bacteria utilising iron as a growth factor. Recommendations from experts suggest delaying parenteral iron administration during active infections (12). This is consistent with the findings from observations by the team members and feedback received from ward pharmacists, where most prescribers generally avoided parenteral iron when patients had acute infections, leading to its underutilisation. Therefore, the presence of active infections should be considered in the exclusion criteria of the study.

In Cycle 2, the introduction of iron derisomaltose enables the total dose infusion to be given in smaller amounts of fluid and is suitable for patients with fluid restriction. However, accessibility to the new drug was limited by its cost and prescribing restriction, hence, the effect of its addition could not be elucidated in this study.

Another limitation of this study is the potential need for refinement in the problem analysis chart and the data collection process. While the lack of a standardised protocol was identified as a primary contributing factor through the online survey and as illustrated in the Pareto Chart (Figure 2), it could also be viewed as a secondary factor related to lack of confidence in use. To remain aligned with the collected data, the results were presented based on the original categorisation. However, future studies may need to revisit this issue, improving the data collection form to allow for clearer distinctions between primary and secondary factors. This step could enhance the accuracy and reliability of the problem analysis process.

Conclusion and the Next Steps

In conclusion, the strategies employed have brought us closer to the study goals. The verification study revealed an underutilisation of parenteral iron, in which only 9.3% of IDA patients were treated with parenteral iron, compared to the standard of 40%. The main contributing factors were identified, which included the lack of confidence in using parenteral iron, concerns about its cost, lack of facilities and trained staff for monitoring, and absence of a standardised protocol. Strategies formulated include the development of PREFER protocol, website, and dose calculator, the use of standardised dilution worksheets and monitoring charts, the display of posters in wards, and the implementation of continuous staff training. After two cycles of

remedial measures, the percentage of IDA patients treated with parenteral iron therapy increased from 9.3% to 33.3%.

To address the challenge of administering parenteral iron to patients with acute infections, a daycare service for parenteral iron infusion was implemented at the Medical Admission Unit (MAU) after discussions between our team haematologist and the specialist in charge of MAU. Upon discharge from the ward, patients eligible for parenteral iron may receive a referral letter to be admitted to MAU later for administration.

To date, this study has already been expanded to all other medical wards. According to data from the pharmacy inventory system, the annual usage of iron dextran in HKL increased by 34% from 9,515 ampoules in 2022 to 12,780 ampoules in 2023. By applying this increment to the study indicator, the utilisation of parenteral iron is estimated to reach 44.6%, surpassing the standard of 40%. This suggests the positive impact of expanding the study to all medical wards and also the sustainability of our project outcomes. We also plan to expand the study to other disciplines to magnify its impact. In the future, we plan to promote the usage of the PREFER protocol and website at the national level so that beneficial outcomes in terms of patients' clinical improvement and saving on blood and the costs of treatment can be achieved nationwide.

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Conflict of Interest

The authors declare that there was no conflict of interest.

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Appendix 1: Questionnaires to assess awareness, perceived contributing factors, and knowledge among HCPs

Questionnaires: Management of IDA and Parenteral Iron Therapy

This set of quizzes consists of 15 multiple-choice questions to be answered by physicians and pharmacists. Please answer all the questions in 10 minutes and thanks for your participation.
* Indicates a required question

A. Email*

_____

B. Mobile number (to follow up on post-test)*

_____

C. Designation*
Mark only one oval.
- o Consultant
- o Specialist
- o Medical officer
- o House officer
- o Pharmacist

D. Current place of practice*
**Mark only one oval.*
- o Medical ward
- o Non-medical ward
- o Other:_____

E. Years of working in the current place of practice*
Mark only one oval.
- o < 1 year
- o 2-5 years
- o 6-10 years
- o 10 years

F. Are you aware of the availability of parenteral iron therapy as one of the treatment options for iron deficiency anaemia?*
Mark only one oval.
- o Yes
- o No

G. Which of the following parenteral iron formulations are currently available in HKL?
I. Iron Sucrose
II. Iron Polymaltose
III. Iron Dextran
IV. Sodium Ferric Gluconate

Choose the correct answer
**Mark only one oval.*
- o I and II
- o I and III
- o II and III
- o I and IV
- o Not sure

H. How often do you prescribe/recommend parenteral iron therapy for the treatment of iron deficiency anaemia in your daily practice?
Mark only one oval.
- o Always (100% of IDA cases)
- o Often (>70% of IDA cases)
- o Sometimes (30-70% of IDA cases)
- o Rarely (<30% of IDA cases)
- o Never prescribe/ recommend before

I. What is the main reason you choose not to prescribe/ recommend parenteral iron therapy for patients with IDA?
Mark only one oval.
- o Unaware of parenteral iron as one of the treatment options
- o Not confident to use (unsure dosage, doubt on efficacy or concern on side effects)
- o No dedicated team to refer
- o Concern about the cost of parenteral iron
- o No available facility or trained staff to do close monitoring
- o No local guideline or protocol to guide its use

Quiz Questions

1. Below are the indications of parenteral iron except:
*1 point
Mark only one oval.
- o Iron deficiency anaemia with intolerance of oral iron, especially in inflammatory bowel disease, or where oral iron is ineffective
- o As an alternative to blood transfusion when a rapid increase in haemoglobin is required for example perioperative anaemia
- o Non-ransfusion dependant thalassemia
- o To support the use of erythropoiesis-stimulating agents

2. Below are the contraindications to the use of parenteral iron except:
*1 point
Mark only one oval.
- o Anaemia with iron overload
- o Drug hypersensitivity including mono- or di-, saccharide complexes, and dextran
- o Macrocytic anaemia
- o Second and third trimester of pregnancy

3. Below are the differences between Iron Dextran (CosmoFer ®) and Iron Sucrose (Venofer ®) except:
*1 point
Mark only one oval.
- o Iron Sucrose (Venofer ®) is a vesicant agent while Iron Dextran (CosmoFer ®)is a non-vesicant agent
- o There has been less incidence of anaphylactic reactions with Iron Sucrose (Venofer ®) versus Iron Dextran (CosmoFer ®) in recent years
- o Iron Dextran (CosmoFer ®) can be given as a total dose infusion while Iron Sucrose (Venofer ®) cannot be given as a total dose infusion
- o The efficacy of both Iron Dextran (CosmoFer ®) and Iron Sucrose (Venofer ®)are similar

4. Which of the following are not the contraindications of parenteral iron preparation?
   I. Patient with a history of hypersensitivity to iron preparation
   II. Patient with underlying stage 3 CKD
   III. Patient with transfusion-dependent thalassemia
   IV. Patients with underlying hepatitis B

   Choose 2 options from the question above.
   *1 point
   Mark only one oval.
   - o I and IV
   - o II and IV
   - o III and IV
   - o I and II

5. Parenteral iron should be given cautiously in the following patients except:
   *1 point
   Mark only one oval.
   - o Patient with a history of drug allergies
   - o Patients with severe atopy or systemic inflammatory diseases
   - o A patient in her second trimester of pregnancy
   - o Patient with a history of blood transfusion in the past 1 year

6. What are the possible allergic reactions to parenteral iron preparation?
   I. Angioedema
   II. Kounis syndrome
   III. Bronchospasm
   IV. Dyspnea

   Choose the correct answer.
   *1 point
   Mark only one oval.
   - o All of the above
   - o II and III
   - o I and IV
   - o I, II, and III

Dosage calculation for parenteral iron based on the Ganzoni formula: (Body weight (kg) x 10 X (target Hb - actual Hb) (g/dL) x 0.24) + mg iron for iron stores

Body weight:
- Actual Weight if BMI < 30kg/m^2
- Ideal Body Weight if BMI > 30kg/m^2
- Pre-pregnant weight for pregnant women

Iron Stores:
- <35 kg body weight = 15 mg/kg body weight
- >35 kg body weight = 500 mg

7. A patient was admitted to the hospital with the chief complaint of dizziness for 2 days. Her Full Blood Count shows Hb of 8 g/dL, MCV 105(Ref range 80 - 96 femtoliters), MCHC of 35 (Ref range: 33-36 g/dL). She was diagnosed with symptomatic anaemia and her anaemic workout is still pending. What is the dose of IV Cosmofer that should be given to this patient to reach the target Hb of 12 g/dL? Patient's details: Body weight: 50kg, 158cm, BMI 20.0 kg/m^2

*1 point

Mark only one oval.

- o 975mg
- o 850mg
- o 775mg
- o Wait for an anaemic workout before giving IV iron

8. A female patient in her third trimester of pregnancy was admitted to the hospital and was diagnosed with severe iron deficiency anaemia. She has an Hb of 6.1g/dL and has yet to receive a blood transfusion. What is the ideal dose of IV Venofer that can be given to her to increase her Hb level to 11g/dL? Patient's details: Body weight: 60kg, height 160cm, BMI 23.4kg/m^2

*1 point

Mark only one oval.

- o 1230mg given as a total dose infusion over 4 hours
- o 2 doses of 600mg as total dose infusion given in 2 different days
- o 200mg 3 times a week for 6 doses
- o Do not give IV Venofer

9. A patient was admitted and diagnosed with Iron deficiency anaemia. Her Full Blood Count shows Hb of 6.6 g/dL, and an iron study shows Iron of 3.4 and Transferrin saturation of 12%. What is the ideal dose of IV Cosmofer that should be given to this patient to reach the desired target Hb level of 12 g/dL? Patient's details: Body weight: 70kg, 160cm, BMI 27 kg/m^2

*1 point

Mark only one oval.

- o A total dose infusion of 1500mg over 4 hours
- o 200mg EOD x 5 doses
- o Split doses of 700mg + 700mg as total dose infusion over 2 days
- o Do not give IV Cosmofer

10. Which of the following statements regarding parenteral iron is incorrect?

*1 point

Mark only one oval.

- o A test dose of parenteral iron is required continuation of iron therapy
- o Flushing with 3ml heparinised saline is not required parenteral iron infusion
- o Stop infusion of parenteral iron if the patient develops allergic / intolerance reactions
- o Parenteral iron to be diluted in Sodium Chloride 0.9% before infusion

11. Below is the recommended dilution & infusion time for IV Cosmofer except:
*1 point
Mark only one oval.
- o IV Cosmofer 25mg in 100ml Sodium Chloride 0.9%, run over 30 min
- o IV Cosmofer 25mg in 20ml Sodium Chloride 0.9%, run over 20 min
- o IV Cosmofer 600mg in 500ml Sodium Chloride 0.9%, run over 1 hour
- o IV Cosmofer 200mg in 100ml Sodium Chloride 0.9%, run over 1 hour

12. Which of the following parenteral iron preparations is/are vesicant?
*1 point
Mark only one oval.
- o Iron Dextran (CosmoFer ®)
- o Iron Sucrose (Venofer ®)
- o Both of them
- o None of them

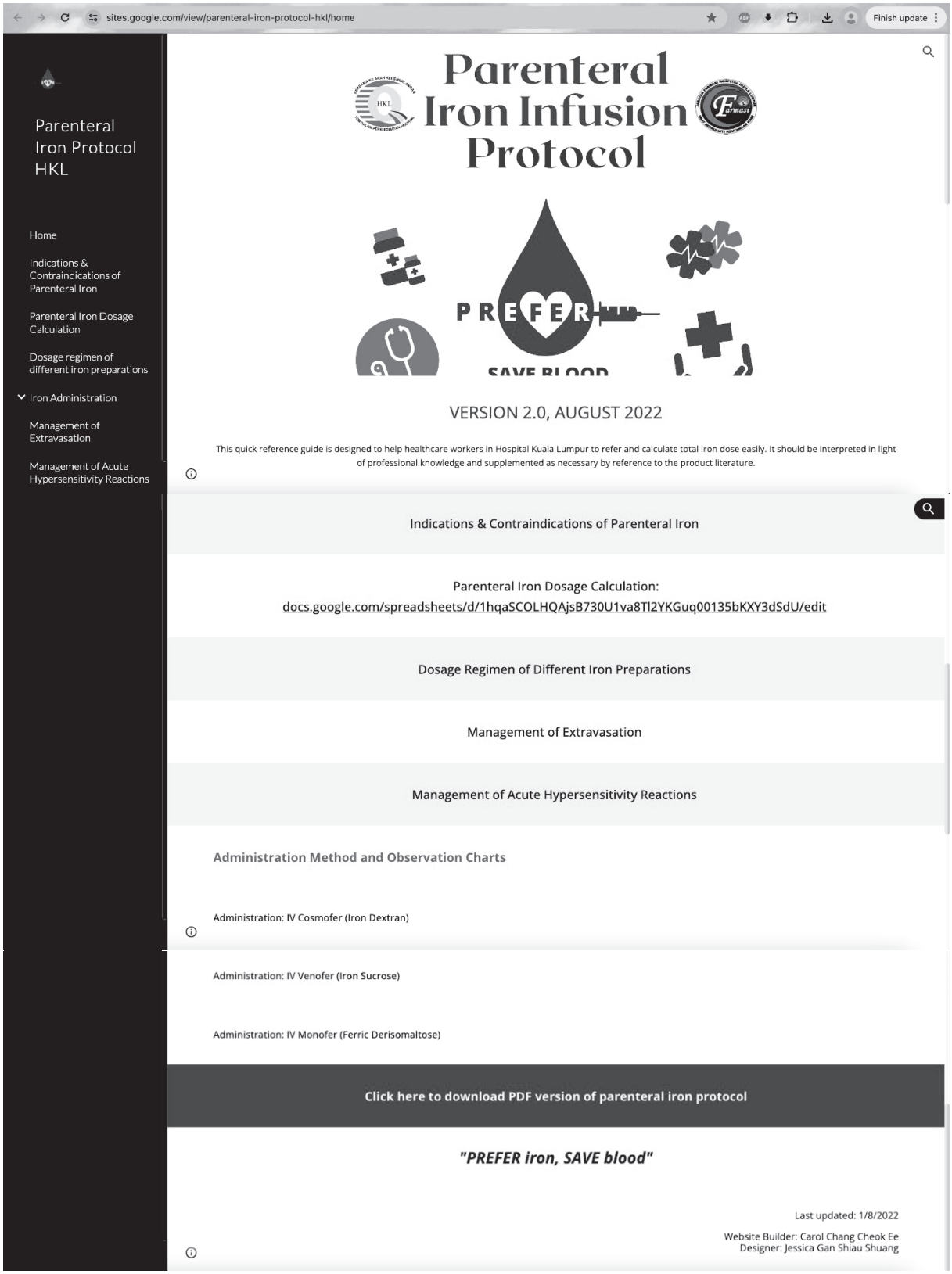
13. Which of the following regarding the management of extravasation of vesicant preparations is incorrect?
*1 point
Mark only one oval.
- o Stop and disconnect infusion immediately.
- o Remove the needle/ cannula immediately.
- o Aspirate as much extravasated solution as possible.
- o Apply dry cold compression.

14. Which of the following regarding the management of acute hypersensitivity reactions to parenteral iron infusions is incorrect?
*1 point
Mark only one oval.
- o If mild reactions such as itching, flushing, and slight chest tightness occur, an iron infusion can be withheld and then restarted at a reduced rate if the patient is well.
- o Patients who developed hypersensitivity reactions to Iron Dextran (CosmoFer ®) can be rechallenged with Iron Sucrose (Venofer ®) and vice versa.
- o If the patient does not develop any sign of hypersensitivity reactions after the test dose, the remaining dose can be safely given without the need for close monitoring.
- o For test dose monitoring, patients should be monitored every 15 minutes until 1 hour after the completion of infusion.

15. Which of the following are the monitoring parameters required for parenteral iron infusions?
I. BP
II. Body temperature
III. Signs and symptoms of allergy reaction such as itchiness, SOB, chest pain
IV. Infusion site reactions

Choose the correct answer.
* 1 point
Mark only one oval.
- o I, II, III
- o I, II, IV
- o I, III, IV
- o All of the above

Appendix 2: PREFER Website Interface via https://sites.google.com/view/parenteral-iron-protocol-hkl/home



Appendix 3: Smart dose calculator

Based on Ganzoni's formula: (Body weight (kg) x (target Hb - actual Hb) (g/dl) x 2.4) + mg iron for iron stores

	Kindly fill in:		Note:
	Body weight (kg)	50	Use Ideal Body weight if BMI > 30kg/m2; Use pre-pregnancy weight for pregnant women
	Current Hb or Initial Hb (g/dl)	9.3	
	Target Hb (g/dl)	12	12 for female, 13 for male
	Iron stores (mg)	**500**	< 35 kg body weight = 15 mg/kg body weight > 35 kg body weight = 500 mg
	Exact Iron dose Calculated (mg)	824	
	TOTAL IRON DOSE NEEDED (MG) (Rounded up/down to the nearest 100mg)	800	
	**Maximum Iron dose / day for this patient:	1000	(Maximum: 20mg/kg/day)

Iron preparations & dosage regimen (Choose 1)

a.	**IV Cosmofer**	**25**	mg test dose in 100ml NS over 30minutes infusion,then observe for 1 hour (200ml/H)				
	(Total Dose Infusion)	**775**	mg* in 1 pint Normal Saline infused over 4 hours (125ml/H)				
	*note: Maximum iron per DAY for this patient is	1000	mg/day (20mg/kg/DAY)				
	If total iron dose is > 20mg/kg, kindly split the dose and serve the remaining dose the next day.						
b.	**IV Cosmofer Split doses (Patient with ROF):**	**25**	mg test dose in 20cc NS over 20 minutes infusion (60ml/H) , then observe for 1 hour (for first dose only)				
		200mg	1 - 3 times per week for	**4**	doses	(First dose is 175mg after minus test dose 25mg)	
		Dilution: Withdraw 200mg & dilute in 100ml NS infused over 1 hour (100ml/H)					
c.	**IV Venofer**	**20**	mg test dose in 20cc NS over 15 minutes infusion (80ml/H), then observe for 1 hour (prior first dose only)				
	(JKUT Hematologi & Nephrologi)	**200mg**	1 - 3 times per week for	**4**	doses	(First dose is 180mg after minus test dose 20mg)	
		Dilution: withdraw 200mg & dilute in 100ml NS infused over 1 hour (100ml/H)					
	Maximum Venofer dose per week:	< 45kg: 7mg/kg/week > 45kg: 600mg/week					
d.	**IV Monofer**	**800**	mg (#) in 100 ml NS over 1 hour (100ml/H)				
	(JKUT Hematologi & Cardiology)						
	# note: Maximum iron PER WEEK for this patient is	1400	mg/Week (20mg/kg/WEEK)				
	If total iron dose is > 20mg/kg, kindly split dose and serve the remaining dose **after 1 week interval.**						

Note:

1. For details of various iron preparations and monitoring parameters, please refer to HKL PREFER protocol available at:
   https://sites.google.com/view/parenteral-iron-protocol-hkl/home
2. This iron calculation guide is designed to help healthcare workers in Hospital Kuala Lumpur to calculate total iron dose easily.
   It should be interpreted in light of professional knowledge and supplemented as necessary by reference to the product literature.
3. For any feedback or queries, kindly contact pharmacists in Parenteral Iron Team HKL (03-2615 5555 Ext: 5684)

"PREFER iron, save bloods"

Last updated: 20/7/2022

Appendix 4: Poster with QR code linked to PREFER website

Guidance on Prescribing Parenteral Iron Therapy

Indications

Iron deficiency anaemia

- Hb < 13g/dL (male), 12g/dL (female) with MCV < 75fL
- TSAT < 20% or < 30% (CKD)
- Serum ferritin < 30ng/mL (may be elevated in certain clinical conditions)

Support the use of **erythropoiesis-stimulating agents** (including patients on renal dialysis)

As an **alternative to blood transfusion** when a rapid increase in Hb is required

Formulations available

C — **Low molecular weight iron dextran (Cosmofer®)**
- Can be given as total dose infusion

V — **Iron sucrose (Venofer®)**
- To be given in divided doses

M — **Ferric derisomaltose (Monofer®)**
- Can be given as total dose infusion with smaller volume

Monitoring

- Vital signs
- Skin rashes
- Chest pain
- Angioedema
- O_2 Shortness of breath
- Infusion site reaction

Dosage

Calculate based on **Ganzoni formula**

(Body weight (kg) x (target Hb - actual Hb) (g/dL) x 2.4) + mg iron for iron stores

- Body weight: Actual Weight if BMI < 30kg/m2
- Ideal Body Weight if BMI > 30kg/m2
- Pre-pregnant weight for pregnant women

Iron Stores:
- <35 kg body weight = 15 mg/kg body weight
- >35 kg body weight = 500 mg

Target Hb level: 12g/dL (Female)

Body Weight (kg)	Actual hemoglobin (g/dL) 8	7	8	9	10	
35kg	1000	925	825	750	675	mg
40 kg	1075	975	875	800	700	mg
45 kg	1150	1050	925	825	725	mg
50 kg	1225	1100	975	875	750	mg
55 kg	1300	1150	1025	900	750	mg
60 kg	1375	1225	1075	925	775	mg
65 kg	1450	1275	1125	975	800	mg
70 kg	1500	1350	1175	1000	825	mg

Target Hb level: 13g/dL (Male)

Body Weight (kg)	Actual hemoglobin (g/dL) 6	7	8	9	10	
35kg	1100	1000	925	850	750	mg
40 kg	1175	1075	975	900	775	mg
45 kg	1250	1150	1050	950	825	mg
50 kg	1350	1225	1100	975	850	mg
55 kg	1425	1300	1150	1025	900	mg
60 kg	1500	1350	1225	1075	925	mg
65 kg	1600	1450	1275	1125	975	mg
70 kg	1675	1500	1350	1175	1000	mg

Kindly scan the **QR code** and refer to HKL **Parenteral Iron Infusion Protocol** for more information.

By HKL Parenteral Iron QA project team
(Pharmacy Department in collaboration with Hematology Unit of Medical Department)