Preoperative intravenous iron in general surgical patients with iron deficiency anaemia: an observational, retrospective study

Neil Brown (ngbrown@outlook.com)
Queen Elizabeth University Hospital https://orcid.org/0000-0003-0538-5205

Ruoling Yan
Queen Elizabeth University Hospital

Jenniffer Henderson
Queen Elizabeth University Hospital

Genevieve Lowe
Queen Elizabeth University Hospital

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Abstract

Background: Preoperative iron deficiency anaemia (IDA) is common in the surgical population. Our institution has implemented a pathway for the treatment of IDA using intravenous iron. The impact of this pathway on patient outcomes is assessed in this observational, retrospective cohort study.

Methods: Data were collected on patients undergoing elective general or colorectal surgery during 2020 at a tertiary referral centre in the west of Scotland, United Kingdom. Analysis was undertaken to assess the change in haemoglobin level in response to iron administration and any associated impact on blood transfusion requirements, hospital length of stay and readmission rates.

Results: A total of 178 patients were included in the analysis, 43% of whom were anaemic preoperatively. Intravenous iron was administered to 26 patients, 92% of whom were iron deficient. An average haemoglobin increment of 22 g/l was observed in patients who received intravenous iron by the time they attended for surgery, and those patients had better recovery of their haemoglobin postoperatively. No statistically significant differences were observed in the rates of postoperative blood transfusion, hospital length of stay or readmission to hospital within 30 days.

Conclusions: Although administration of intravenous iron preoperatively was associated with an improvement in haemoglobin levels, it did not appear to be associated with improved hospital outcomes. Further evaluation is required to refine our preoperative anaemia pathway.

Introduction

Preoperative anaemia is common within the surgical population, with prevalence ranging between 8–64% depending on surgical speciality.[1] The majority of anaemic patients have iron deficiency anaemia (IDA). There are multiple well known associations between IDA and negative outcomes, such as surgical complications, infection and major adverse cardiovascular events. The use of blood transfusion to treat preoperative anaemia is an expensive intervention with rare, but serious, risks. Over the past decade, significant efforts have been made to address preoperative iron deficiency anaemia with the development of local, national[2], and international[3] guidelines for the detection and treatment of iron deficiency.

Our perioperative iron pathway was established in January 2020 but its clinical effectiveness has not been evaluated. We conducted a retrospective, observational cohort study to assess our study objectives. The primary objective of our work was to assess how effective intravenous iron administration is in increasing preoperative haemoglobin levels in anaemic patients. Our secondary objectives were to assess how this treatment impacts patient outcomes including blood transfusion rates, hospital length of stay and hospital readmission rates.

Materials And Methods

Participants and data collection

All adults aged 18 years or older listed for elective general or colorectal surgery with anticipated blood loss exceeding 500 ml planned between 1 January 2020 and 31 December 2020 at the Queen Elizabeth University Hospital, Glasgow, United Kingdom were included.

Anonymised data were collected with Caldicott guardian approval. Demographic data, American Society of Anaesthesiologists (ASA) physical status classification, type of surgery, laboratory haemoglobin (Hb), ferritin, C-reactive protein (CRP) and transferrin saturation (TSAT) were recorded where available. Baseline Hb levels were collected at the preoperative assessment clinic visit, with repeat haemoglobin measurements made post-iron infusion (pre-surgery), at hospital discharge and again at 6 months postoperatively. Data relating to blood transfusions, hospital length of stay (LOS), unplanned critical care admission and re-admission to hospital within 30 days of discharge were obtained by cross-referencing other hospital datasets.

The patients were divided into separate cohorts. Comparisons were made between patients who were diagnosed with preoperative anaemia with those who were not anaemic. Within the anaemic patient group, they were further divided into those who received intravenous iron and those who did not.

Definitions

Anaemia was defined according to consensus guidelines as a haemoglobin of less than 130 g/l, regardless of gender[2]. Iron deficiency anaemia was defined as haemoglobin of less than 130 g/l with either (i) ferritin < 30 µg/l; (ii) ferritin 30–100 µg/l and C-reactive protein (CRP) > 5 mg/l; or (iii) ferritin 30–100 µg/l and transferrin saturation (TSAT) < 20%.

Surgery was classified as laparoscopic if the recorded procedure name referred to any portion of the surgery being laparoscopic or laparoscopic-assisted.

Intervention

Where iron deficiency was identified, oral or intravenous iron may be prescribed. Decisions around whether to offer patients intravenous iron and blood transfusion were at the discretion of the treating clinician. Intravenous iron was administered as ferric carboxymaltose infusion (Ferinject, Vifor pharma), with dosing calculated using weight and initial haemoglobin. Based on dosing, some patients required a course of two infusions.

Surgery was scheduled following iron administration at the judgement and convenience of the treating clinician, taking account of surgical urgency.

Data analysis

We assessed the change in haemoglobin levels experienced by both the anaemic and non-anaemic cohort after their surgical procedure. They were also assessed for the absolute risk of blood transfusion, hospital length of stay and 30-day hospital readmission rates. Continuous data is presented with the mean and standard deviation when normally distributed, otherwise the median and interquartile range is

used. For categorical data, counts and percentages are used. Records with missing information were excluded from analysis. Comparisons between groups was done with a Student's t-test or a Wilcoxon rank-sum test and a p-value of less than 0.05 was taken as statistical significance. All statistical analysis was undertaken in R (version 4.0.3).

Results

Data from a total of 183 patients were reviewed. For analysis, five patients were removed due to incomplete data. Some patients were lost to follow up at 6 months and did not have post discharge haemoglobin levels evaluated, therefore the number of analysed patients is represented in brackets.

Baseline characteristics

The two anaemic groups contained similar proportions of female patients and of patients undergoing laparoscopic surgery (Table 1). Most patients in the group who received intravenous iron were iron deficient and were ASA 1 or 2. A high proportion of anaemic patients who didn't receive intravenous iron were also iron deficient.

Table 1
Baseline characteristics and haemoglobin (Hb) concentrations. N/A = not applicable; * = percentage of patients with full haematinic data who were classified as iron deficiency anaemia; patients without full haematinics were excluded from this metric

	Anaemic: IV iron	Anaemic: No IV iron	Non-anaemic
n	26	50	102
Female, %	50.0	58.0	29.4
Age, median [IQR]	67 [19.5]	67 [19]	65.5 [17]
Laparoscopic surgery, %	69.2	72.0	66.7
ASA 1, %	4	6	5
ASA 2, %	77	56	74
ASA 3, %	19	34	22
ASA 4, %	0	4	0
Iron deficiency anaemia, % *	92.3	54.8	N/A

Intravenous iron infusions

Of the 26 patients who received intravenous iron, 15 (58%) were given a single infusion of intravenous iron. The median [IQR] interval between a patient's final infusion of intravenous iron and surgery was 6 [5] days in the group who received one infusion and 13 [20] days in the group who received multiple

infusions. Similar Hb increments were observed regardless of whether a single or multiple infusions were given.

Haemoglobin trend over perioperative course

Haemoglobin response, defined as the difference in Hb measured at preassessment clinic and the latest Hb measured prior to surgery, was greatest in patients with the lowest initial haemoglobin (Fig. 1).

On average, a haemoglobin increment of 22 g/l was observed in patients who received intravenous iron (Table 2). All groups demonstrated a drop in haemoglobin between the preoperative period (either preassessment or post-intervention) and discharge home. Better recovery of haemoglobin concentration at 6 months was observed in patients who had received intravenous iron.

Table 2
Haemoglobin response and perioperative outcomes

	Anaemic: IV iron	**Anaemic: No IV iron**	**Non-anaemic**
Haemoglobin measurements			
Preassessment Hb, g/l (SD)	103 (14.0)	119 (9.7)	143 (10.0)
Mean post-intervention Hb, g/l (SD)	122 (18.3)	N/A	N/A
Mean Hb at discharge, g/l (SD)	107 (11.2)	108 (10.5)	122 (16.6)
Mean Hb at 6 months post-op, g/l (SD)	127 (15.2)	124 (18.8)	136 (16.5)
Blood transfusion			
Patients transfused, n	5	9	5
Absolute risk of blood transfusion	0.20	0.18	0.05
Hospital course			
Median length of stay (LOS), days [IQR]	5.5 [4]	7 [4]	6 [5]
Unplanned critical care admissions, n (%)	0 (0)	2 (4)	4 (4)
Hospital readmission within 30 days, n (%)	4 (15)	4 (8)	13 (13)

Perioperative outcomes

The rate of postoperative blood transfusion was similar between patients who did and did not receive intravenous iron infusion. Significantly fewer patients received blood transfusion if they were not anaemic preoperatively. Median hospital length of stay was longest in anaemic patients who did not receive intravenous iron.

Discussion

This article presents a contemporary snapshot of preoperative intravenous iron use in our hospital and data about associated patient outcomes. In this series of elective general surgical and colorectal patients, 43% of patients presenting for surgery were anaemic preoperatively. This is in line with prevalence reported elsewhere. Just over one third of our anaemic patients received a course of intravenous iron. This study is not restricted to tightly vetted trial participants, exclusion criteria or study protocols. While the 'real world' nature of this data may be considered beneficial, it also presents several challenges in drawing meaningful conclusions.

In our data, there is a marked difference in the male-to-female ratios of patients between the anaemic and non-anaemic groups, with females being over-represented in the anaemic group. This may be explained by the universal Hb threshold of 130 g/l used to define anaemia. This threshold is based on the AAGBI consensus statement – a change from more traditional practice of accepting a lower threshold in female patients, considering that women are just as likely to bleed similar amounts as their male counterparts and may even start with a lower circulating volume. This difference in male-to-female split observed here, however, may affect outcomes between the groups studied.

When comparing anaemic patients who received intravenous iron and those who did not, it is important to note that those who received intravenous iron had a lower mean starting haemoglobin. This may indicate differing characteristics between the groups such as comorbidity or frailty, and suggests that those who received intravenous iron were starting from a worse baseline health status. This, however, was not reflected in their ASA classification as there was a higher proportion of ASA 3 patients within the cohort who did not receive intravenous iron. Other differing characteristics, not captured within this data, may also have influenced decision making. While this makes it difficult to assess the impact of the intervention, it is reassuring to see that the outcomes between cohorts are similar.

Decision making around offering intravenous iron was at the discretion of the treating clinician. Where intravenous iron was not offered to a patient with IDA, the reason for this was not recorded. In addition to this, the CoVID-19 pandemic has presented significant challenges to maintaining services, with limited access to theatres and the redeployment of preoperative nurses to wards. This likely will have affected patient selection for surgery, decision making and prioritisation. Details regarding such external factors have not been recorded but will almost certainly have influenced outcomes. No immediately pre-surgery haemoglobin data are available for the group who didn't receive intravenous iron, and so an assumption was made that their haemoglobin had remained stable in between the preoperative assessment clinic and the day of surgery – this of course may not have been the case, particularly in those with colorectal cancer.

The recently published PREVENTT trial[4] suggested that administering a standard dose of intravenous iron in the 10 days prior to major open surgery had no effect on risk of blood transfusion or mortality, although there was an indication that it may reduce readmissions to hospital. The PREVENTT study protocol poorly reflects our local practice. In the PREVENTT trial, laparoscopic surgery was excluded, the

dose of iron was limited to a single standardised dose; severely anaemic patients were excluded and in many cases the participant's iron status was unknown.

Locally, our pathway offers individualised doses of intravenous iron to patients with proven iron deficiency anaemia of any severity presenting for open or laparoscopic surgery. This may mean that our intervention is better targeted to those patients who stand to receive the most benefit. Despite this, we did not observe any difference in the rates of blood transfusion, hospital length of stay, unplanned critical care admission or readmission to hospital following discharge in patients with IDA who received intravenous iron.

The use of intravenous iron was associated with a Hb increment in our patients. While we have failed to demonstrate significant outcome benefits of using preoperative intravenous iron in our analysis, there are too many potential confounders in our data to say why this was the case. It may also be that our threshold haemoglobin of 130 g/l is too high for this intervention. It is clear from Fig. 1 that those with a lower starting haemoglobin showed the best Hb response to intravenous iron.

Despite this, we strongly believe that we should continue to identify and treat IDA preoperatively, unless significant high quality evidence to the contrary is presented. As with any other medical comorbidity, our aim is to optimise our patients preoperatively. Investigating and treating IDA is considered an example of good medicine – indeed, in our centre we have referred several patients for investigation of IDA aetiology, with some revealing new diagnoses which have significantly altered their management. When compared with blood transfusion, intravenous iron is a safe and relatively cheap intervention. Aside from outcomes relating to blood transfusion, intravenous iron has been shown to improve quality of life indicators, which probably reflects the ubiquitous role of iron in physiology. In a recently published follow-up of the IVICA trial examining IDA in colorectal cancer, clinically significant improvements in multiple quality of life domains were observed following iron administration.[5] It would be interesting to know if similar improvements were experienced by our patients.

Conclusions

Intravenous iron administration was associated with an improvement in haemoglobin concentration, but was not associated with blood transfusion rate, length of stay or readmission rates. Further work is required to optimise our perioperative pathway for patients with iron deficiency anaemia. Efforts are currently ongoing to improve referral pathways, enabling identification of IDA earlier in a patient's journey – thus providing a longer period for intravenous iron to take effect prior to surgery.

Declarations

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Conflicts of interest: There are no conflicts of interest to declare.

Ethics approval: Approval was obtained from the Caldicott guardian to allow collection, analysis and publication of anonymised patient data.

Consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: Available on request

Code availability: Not applicable

Authors' contributions: All authors contributed to the study conception and design, and in drafting and approving this manuscript.

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Figures

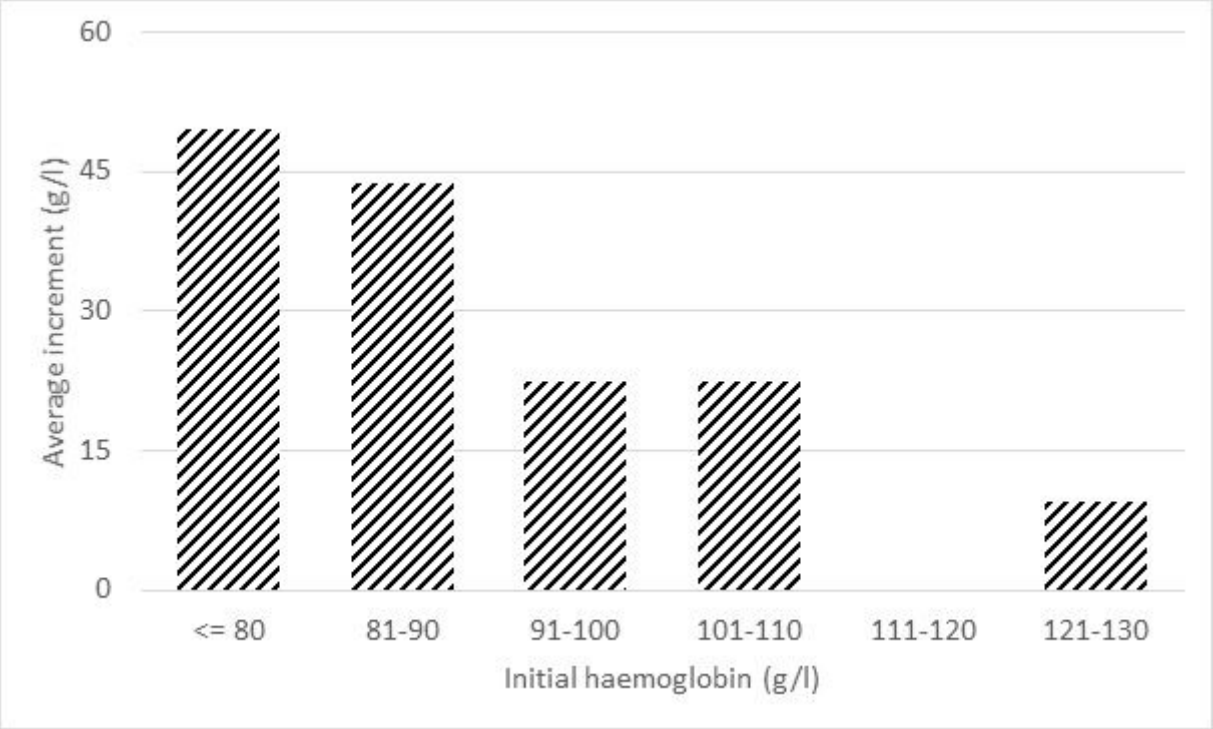

Figure 1

Average haemoglobin increments (g/l) following intravenous iron, grouped by initial preassessment haemoglobin

Supplementary Files

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- STROBEchecklist.pdf