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To Evaluate the Efficacy of Intravenous Iron Therapy in Optimizing Anemia in Colorectal Cancer Patients and Closed Loop Audit of this Pilot Programme

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Abstract

Background: Treatment of preoperative anemia is recommended aiming to minimize perioperative allogenic red blood cell transfusion. This study aims to analyses and evaluate the efficacy of administration Intravenous iron infusion (IV Iron) in preoperative optimization of anemic patients with colorectal cancer in a Pilot Programme. A close loop Audit of the programme is also conducted.

Methods: A Multidisciplinary Team was formed. Colorectal cancer patients with anemia and met the inclusion criteria were included. IV Iron was given at least 4 weeks before operation. Hemoglobin (Hb) and iron profile were collected as baseline, preoperation, postop Day 1, before discharge and 26 weeks after IV Iron give. Primary Outcome was need for blood transfusion, change in Hb and Fe profile level. Secondary Outcome was 2 Audit Cycles of this programme, postoperative morbidity, 30 Days mortality, hospital stay, safety profile and change in Hb level and anemic symptom 26 weeks after IV Iron.

Results: 214 patients were included with 183 patients proceeded to operation (1 Jan 2017-1 Feb 2021). 3.27%, 4.92% and 3.27% required preop, intraop and postoperation blood transfusion respectively. 94.9% had raised in Hb, the median increase in Hb was 2.35 g/dL. There was also raised in Fe and ferritin of 3 and 332 respectively. This showed that IV Iron had the effect of reduction of preoperative blood transfusion from 20% to 3.27% (when compared with our retrospective review of cases 2014-16). When compared with pre IV Iron Hb, there was an increase in 4 g/dL in Hb 26 weeks after IV Iron. The percentage of patients with anemic symptom also dropped from 55.1% to 0%.

Audit cycles were conducted with improvement in recruitment rate from 49% to 100% and compliance rate.

Conclusion: Our data demonstrates that preoperative IV Iron can help reduction of blood transfusion preoperatively. It can also raise the Hb and Iron profile. It also demonstrates the sustainability in terms of Hb level and improvement in anemic symptom. A close loop audit also demonstrates the feasibility of implementing this programme in optimizing anemia in colorectal cancer patients.

Keywords: Colorectal cancer; Anemia; Intravenous iron; Blood transfusion; Audit

Introduction

The overall prevalence of anemia in colon cancer is around 48% with moderate to severe anemia found in more than 20% of cases [1]. The type of anemia manifests in colorectal cancer patients is typically assumed to be Iron Deficiency Anemia (IDA) caused by tumor bleeding, poor oral intake or impaired iron absorption. It is also common for them to present with inflammatory related anemia of chronic disease [2]. Untreated anemia would lead to increase in surgical morbidity and mortality. Two large prospective observational studies showed IV Iron could correct iron deficiency anemia in cancer patients mainly with mild anemia with baseline hemoglobin levels of 10-11 g/dL. The evidence for IV Iron in cancer patients with moderate (Hb 8-9.9 g/dL) or severe (≤ 9 g/dL) anemia was limited [3]. Data on the rate of Hb response following IV Iron were also lacking. Blood transfusion though can correct anemia quickly, it may be associated with poorer oncological outcomes and transfusion risks. Avoiding blood transfusions and erythropoiesis-stimulating agents in oncological patients seems important because of its association with an increased risk of cancer recurrence and increased mortality. Blood products were of limited supply too [4].

Oral iron has been shown to correct anemia but is slow in absorption rate. It is also poorly tolerated and constipation is the most common side effect. IV Iron provides an alternative in optimizing patients with iron deficiency anemia preoperatively. Iron (III) isomaltoside (Monofer) is a form of IV Iron which is more effective than oral iron in treating anemia [4].

Retrospective review of our cases (2014-2016), up to 20% colorectal cancer patients required preoperative blood transfusion. In view of this our unit initiated the quality improvement pilot programme of anemia screening and optimisation in all colorectal cancer patients on 1 Feb 2017. Our aim was to optimize Hb and reduce blood transfusion preoperation. We would also like to see a longer term effect of IV Iron on anemic symptom and Hb level in 26 weeks after IV Iron given.

The quality improvement team consisted of colorectal surgeons, anaesthetists, hematologists, colorectal cancer and ward nurses. We aim at screening all newly diagnosed colorectal cancer patients for iron deficiency anemia and IV Iron will be given for optimization. For those preoperative patients, IV Iron will be given to them at least 4 weeks before operation. Blood tests will be repeated 2 weeks after IV Iron given and 2nd dose of IV Iron will be given for those with suboptimal increase in Hb and Fe profile. Hb and Fe profile will be repeated preoperation, 1 day after operation, day before discharge and 26 weeks after diagnosis. Patient's anemic symptom will also be screened. 2 Audit cycles were conducted to assess the efficacy and compliance to the Pilot Programme.

There is no publication on Audit on IV Iron therapy in optimizing colorectal cancer patients only so far. In our paper, we would also compare the patient's characteristic of those IV iron responder with those non-responder in terms of Hb change. The patient's characteristics of those who received 1 dose versus more than 1 dose of IV iron were also compared.

In this paper, we AIM at: To evaluate the efficacy of intravenous iron therapy in optimizing anemia in colorectal cancer patients in terms:

- Need for Blood Transfusion (preop, intraoperation and postoperation)
- Hemoglobin change (up to 26 weeks after IV Iron given)
- Iron profile change
- Postoperation morbidity and mortality
- Hospital stay
- Safety profile
- Improvement in anemic symptom

Closed loop audits of this Pilot Programme.

Materials and Methods

Multidisciplinary team

A multidisciplinary team consisting of surgeons, anaesthetist, colorectal cancer nurses, hematologist were formed and the Pilot Programme started on 1 Feb 2017.

The inclusion criteria

- Patients with colorectal cancer planning for surgery
- Hb<11 g/dL and Ferritin<100 ug/L
- Age>18 years old

The exclusion criteria

- Anaemia NOT caused by iron deficiency (e.g. Ferritin>200 ug/L and/or saturation>20%)
- Allergic to the product or any of the ingredients of this medicine
- History of serious allergic reactions to other injectable iron preparations
- Iron overload
- Haemachromatosis, Haemosiderosis, myelodysplastic syndrome, need of regular blood transfusion other than iron deficiency anaemia.
- ALT>3x upper limit of normal or a diagnostic label of cirrhosis
- History of Rheumatoid arthritis, Ankylosing spondylitis, Psoriatic arthropathy, Still's Disease, SLE, Mixed connective tissue disease
- Acute gouty arthritis. Can be used later when gouty attack subsided
- Incompletely treated infection still taking antibiotic
- History of anaphylaxis or angioedema to any drug
- History of Steven Johnson Syndrome
- History of asthma that require intubation or BIPAP. Sub-optimally controlled asthma that require ad hoc medical or AED attendance for the past 12 months.
- Pregnancy or lactation

Dose and administration

Single dose infusion of Monofer 500 mg (Amended in 2nd Audit cycle: dosage determined according to body weight: 1000 mg Monofer for >50 kg from 1 Jan 2019).

Infusion rate: 60 minutes

Infusion to be given can be repeated 2 week later if clinically indicated (Hb<8 g/dL or anemic symptoms clinically).

Blood tests

CBP D/C reticulocyte, LRFT CaPO4 LDH, Fe TIBC Ferritin as baseline and repeat 2 weeks after IV Iron given and before operation. Haemoglobin level was monitored on postoperation Day 1, before discharge and 26 weeks after IV Iron therapy.

Caution a nd give steroid prophylaxis i f t he patient has the following

History of asthma, allergic eczema or urticarial and any history of drug allergy.

Steroid prophylaxis

Oral Prednisolone 40 mg 12 hours and 2 hours before iron infusion (If oral route not feasible, then give hydrocortisone 200 mg ivi 12 hours and 2 hours before iron infusion).

Nursing observation

Check blood pressure/pulse/SpO_2 before infusion and at 0 min, 5 min, 15 min, 60 min from start of infusion.

Check symptoms and signs of allergic drug reaction 30 minutes after completion of infusion.

Possible side effects common (may affect up to 1 in 10 people)

- Nausea
- Skin reactions at or near injection site including redness of the skin, swelling, burning, pain, bruising, discolouration, leakage to the tissue around the site of infusion, irritation

Workflow

Patient recruitment in Colorectal Cancer Clinic

Blood taking (CBP D/C reticulocyte, LRFT $CaPO_4$ LDH, Fe TIBC Ferritin)+screening of inclusion and exclusion criteria+fill in Day Centre referral form → IV Iron infusion appointment within 1 week of referral.

On day of infusion in day centre

Patient admitted to day centre → identity and inclusion and exclusion criteria double checked → correct dosage of IV Iron +/- steroid cover prescribed → Vital signs monitoring before, throughout and after the infusion → Monitor for adverse reaction.

2 weeks a ter IV Iron therapy

Repeat blood taking (CBP D/C reticulocyte, LRFT $CaPO_4$ LDH, Fe TIBC Ferritin) → arrange 2nd dose of IV Iron therapy if Hb<8 or presence of anemic symptom. 26 weeks after IV Iron therapy (to assess sustainability of hemoglobin response):

- Repeat blood taking for Hb level
- Monitor for any blood transfusion in between xz
- Monitor for anemic symptom

Primary outcome measures

- Change in hemoglobin concentration (g/dL) after IV Iron therapy
- Change in serum ferritin (ug/L) after IV Iron therapy
- Need for Blood Transfusion (preop, intraop and postoperation)

Secondary outcome measures

- A closed loop Audit of this Pilot Programme (Patient recruitment rate, compliance)
- Postoperation morbidity (Graded according to the Clavien Dindo Classification of Surgical Complication)
- Postoperation 30 day mortality
- Hospital stays (days)
- Safety profile (Incidence of adverse reactions to IV iron therapy)
- Change in Hb level and anemic symptom 26 weeks after IV Iron

2 Audit cycles were conducted

1st Audit cycle (1 Feb 2017-31 Dec 2018)

2nd Audit cycle (1 Jan 2019–1 Feb 2021)

After formation of the multidisciplinary team, the protocol, checklist for day centre and checklist for doctors were drafted. Team members had regular meeting and case discussion mainly through email due to COVID 19. Data entry was done in a weekly basis. Blood taking was arranged by colorectal surgeons and nurses. An update on the protocol and checklist for day center was done after the 1st Audit cycle. Recruitment rate, compliance rate in terms of IV Iron time given and blood taking, feedback from doctors, nurses and patients were all collected to help programme improvement.

Statistical analysis

Categorical data were summarized as number and percentage. Continuous variables were presented as mean, median +/- standard deviation. Independent-samples t tests were used to assess the changes in Hb level and Iron profile. Patients with missing data for any of the primary or secondary outcomes were excluded from analysis. A significance level of 0.05 was considered to be significant.

Results

214 patients were included with IV iron given preoperation. The median age is 72 years old (29-93). 108 Male and 106 Female were included. The mean ASA was 2. Median Body Mass Index was 20.58. Median number of comorbidities was 1 (0-4). 10.75%, 5.61% and 3.27% were taking aspirin, non-vitamin K antagonist oral anticoagulant (NOAC) and warfarin respectively. 42.1% (90/214) presented with gastrointestinal bleeding and 55.1% (118/214) presented with anemic symptom (Table 1a).

Majority of tumors were located over right colon (37.9%), rectum (33%), left colon (22.4%) respectively. 15/214 (7%) had neoadjuvant therapy (Table 1a).

Concerning the severity of anemia, 118 (55.1%), 74 (34.6%), 21 (9.8%) had severe (Hb<8), moderate (Hb 8-9.9) and mild anemia (Hb 10-11) respectively. Concerning pre iv iron blood results (Median), Hb: 7.65 g/dl, Ferritin: 30, Fe: 3.85, TIBC: 58, Iron saturation: 6, phosphate: 1.14. Post IV iron blood results (Median) showed Hb: 10.3, 94.9% had raised in Hb, the median increase in Hb was 2.35. Post IV Iron Fe: 7.2, there was increased in Fe: +3, ferritin: 431, there was increase in ferritin +332, (Table 1b).

The median days from IV iron to OT was 18 days. 27 (12.6%) and 187 (87.4%) patients had 500 mg and 1000 mg Monofer respectively. 9 (4.2%) had 2 doses of Monofer preoperation. (Table 1d).

183 patients proceeded to operation whereas 31 patients could not proceed to surgery due to metastatic, progressive disease or multiple comorbidities. 41.5% had right hemicolectomy, 12.6% had total mesorectal excision and sigmoidectomy, 8.74% had anterior resection, 7.7% had transanal total mesorectal excision respectively.

Concerning the approach, 86.9% had laparoscopic surgery whereas 9.29% were converted to open surgery. Nil of them had intraoperation complication.

The median OT time was 190 mins (0-740) and median blood loss was 20 ml (0-250). 47.5% has blood loss<50 ml (Table 1e).

18% (33/183) required preoperative blood transfusion as preoperative optimization. All 33 of them had severe anemia with Hb<8. 3.27% (6/183) required blood transfusion after IV iron. 4.92% (9/183) had intraoperation blood or blood products transfusion. 8 had packed cell whereas 1 had fresh frozen plasma transfusion. 4 and 5 of them had moderate and severe anemia respectively (Table 1c).

Postoperation blood (Median) Day 1 Hb 9.5, Hb before discharge 10, Hb 26 weeks posteropation 11.65. 3.27% (6/183) required postoperation blood transfusion. 3 of them moderate and severe anemia respectively (Table 1b,g).

5.6% had postoperation morbidity. 4.2% were Grade III of Clavien Dindo Classification. 0 had neither readmission nor 30 day mortality. The median hospital stay was 10 days. 59.3% was AJCC stage III. None had postoperation anemic symptom (Table 1f).

Table 1a: Patient's demographics (N=214).

		N=214
Age	72	Median (29-93)
Sex	Male	108
	Female	106
ASA	2	Mean (1-4)
BMI	20.58	Median
No of comorbidities	1	Median (0-4)
Anticoagulants	Aspirin	23 (10.75%)
	Warfarin	7 (3.27%)
	Plavix	1 (0.47%)
	NOAC	12(5.61%)
	Combined Drug	2 (0.93%)
Proton pump inhibitor	Yes	64 (29.9%)
	No	150 (70.1%)
Oral Iron	Yes	52 (24.3%)
	No	162 (75.7%)
GIB symptom	Yes	90 (42.1%)
	No	124 (57.9%)
Anemic symptom	Yes	118 (55.1%)
	No	96 (44.9%)
Tumor location	Right colon	86 (37.9%)
	Transverse colon	3 (1.3%)
	Left colon	48 (22.4%)
	Rectum	75 (33%)
	2 locations	2 (0.9%)
Neoadjuvant therapy	Yes	15 (7%)
	No	199 (93%)
Neoadjuvant type	RT	1 (6.67%)
	Chemo+RT	14 (93.3%)

Table 1b: Blood results (Hb, Iron profile, Phosphate).

Hemoglobin		
Pre IV Iron Hb	7.65 g/dL	Median
Severity of anemia	mild (10-11)	21 (9.8%)
	mod (8-9.9)	74 (34.6%)
	severe (</=7.9)	118 (55.1%)
	Jehovah's witness	1 (0.5%)
Preop Hb (After IV Iron)	10.3	Median
Change in Hb ?	Increase	203 (94.9%)
	Decrease	5 (2.3%)
	No change	6 (2.8%)
Change in Hb	2.35	Median
Postop D1 Hb	9.5	Median
Postop Hb before discharge	10	Median
Iron profile		
Pre IV Iron ferritin	30 ug/L	Median
Post IV Iron ferritin	431	Median
Change in ferritin	332	Median
Pre IV Iron Fe	3.85	Median
Post IV Iron Fe	7.2	Median
Change in Fe	3	Median
Pre IV Iron TIBC	58	Median
Post IV Iron TIBC	44	Median
Pre IV Iron saturation	6	Median
Post IV Iron saturation	17	Median
Preop phosphate	1.14	Median

Table 1c: Need of blood transfusion (preop, intraop, postoperation).

Preop blood transfusion before iv iron	Yes No	33 (18%) 150 (82%)
No. of rbc transfused	1u	11.00 (25%)
	2u	32.00 (72.73%)
	3u	1.00 (2.27%)
Preop blood transfusion after iv iron	6	3.27%
Intraop blood/blood product transfusion	Yes No	9 (4.92%) 174 (95.1%)
Intraop transfusion	Packed cell	8
	Fresh frozen plasma	1
No. of unit transfused	1 unit	1
	2 units	5
	3 units	2
	4 units	1
Postop blood transfusion	Yes No	6(3.27%) 177 (96.73%)
Postop unit of blood transfused	1u 2u	2 4

Table 1d: IV Iron therapy details.

Year	**Total No. of colorectal cancer patients screened**	**No. of patients with IV Iron given**
Days from IV Iron to OT	18 days	Median
IV Iron dosage	500mg	27 (12.6%)
	1000mg	187 (87.4%)
Adverse reaction after IV Iron infusion	0	0%
No. of times IV Iron given	1 time	205 (95.8%)
	2 times	9 (4.2%)

Table 1e: Operative details.

Operation done	Yes No	183 31
Type of operation	Right hemicolectomy	76 (41.5%)
	Total mesorectal excision (TME)	23 (12.6%)
	Sigmoidectomy	23 (12.6%)
	Anterior resection	16 (8.74%)
	Transanal TME	14 (7.7%)
	Left hemicolectomy	11 (6%)
	Total colectomy	8 (4.37%)
	Colostomy	8 (4.37%)
	Abdominoperineal Resection	4 (2.2%)
	Hartmann's operation	2 (1.09%)
	Transanal Endoscopic Operation	1 (0.55%)
	Pelvic exenteration	1(0.55%)
Approach	Lap	159 (86.9%)
	Open	9 (4.92%)
	Lap converted open	17 (9.29%)
	Endoanal	1 (0.55%)
OT time	190 mins	Median (0-740)
Blood loss	20 ml	Median (0-250)
Blood loss level	Low<50	87(47.5%)
	Mod50-250	74 (40.4%)
	High>250	19 (10.4%)
Intraoperation complication	Yes	0 (0%)
	No	183 (100%)

Table 1f: Postoperative details and pathology.

Hospital stay	10 days	Median
Postop morbidity	Yes No	12 (5.6%) 202 (94.4%)
Clavien Dindo Classification	GII GIII	2 (0.9%) 9 (4.2%)
Readmission	0	0%
30-Day Mortality	0	0%
AJCC staging	0 1 2 3 4	41 (19.2%) 2 (0.9%) 42 (19.6%) 127 (5.3%) 2 (0.9%)

Table 1g: Hb and symptom 26 weeks postoperation.

Hb 26 wks post IV Iron	11.65 g/dL	Median
Preop anemic symptom	Yes	118 (55.1%)
Anemic symptom 26 wks post IV Iron	Yes	0 (0%)
post IV Iron		

Change Hb *vs.* no change Hb

When compared those patients with increase in Hb level (203) *vs.* no change in Hb level after IV iron, both groups were comparable in terms of demographics, tumor location, operation, OT time, blood loss, approach, intraoperation complication, preop, intraop and postoperation blood or blood product transfusion and hospital stay. The pre and post iv iron Hb, Fe, ferritin, Iron saturation and postop Hb before discharge were all significantly higher in no Hb change group than raised in Hb group (Table 2).

Table 2: Change Hb *vs.* no change Hb after IV Iron.

	Raised Hb (203)	No change/Decrease Hb (11)	Sig 2 tailed
IV Iron dosage	500 mg 22	5	0.006
	1000 mg 181	6	
Severity of anemia	mild 10-11 17	4	0.001
	mod 8-9.9 68	6	
	severe</=7.9 118	0	
	Jehovah's witness 0	1	
Pre IV Iron Hb	7.69	10.05	0.001
Pre IV Iron Fe	4.9	9.06	0.027

Pre IV Iron sat	8.9	17.4	0.008
Pre IV Iron ferritin	75.8	162.6	0.033
Preop Hb after IV Iron	10.31	17.65	<0.05
Change in Hb	2.63	-0.22	0.002
Postop Hb before discharge	9.13	11.13	0.049
AJCC	0:41	0	0.04
	I: 2	0	
	II: 36	6	
	III: 122	5	
	IV: 2	0	
26 weeks post IV Iron Anemic symptom	0	0	

1 *vs.* 2 doses of IV Iron given

When compared those patient with one vs. two doses of Monofer given, the pre iv iron Hb was significantly lower in the two doses group. The demographics, operative details, pre and post iv iron Fe profile, post iv iron Hb, preoperation, intraoperation and postoperation blood transfusion, hospital stay, morbidity and mortality were all statistically insignificant (Table 3).

Table 3: 1 *vs.* 2 doses of IV Iron given.

	1 dose (205)	**2 doses (9)**	**Sig 2 tailed**
ASA	I 2	0	0.003
	II 86	1	
	III 97	6	
	IV 4	2	
Anticoagulant	No 164	5	0.023
	aspirin 21	2	
	warfarin 7	0	
	plavix 1	0	
	NOAC 11	1	
	combined drugs 1	1	
Pre IV Iron Hb	7.86	6.64	0.034
Anemic symptom	0	0	

Close loop Audit

Set Standards

- The aim of our Pilot programme is to optimize anemia in colorectal cancer patients with IV Iron

- We aim at screening all newly diagnosed colorectal cancer patients
- IV Iron should be given within 1 week after referral done
- Blood taking as baseline, 2 weeks after iv iron given, preoperation, D1 postoperation, before discharge and 26 weeks after iv iron given should be taken
- IV Iron to be given as day case if possible

Measure current practice

- Retrospective review of cases of our unit (2014-16) showed 20% patients required preoperative blood transfusion
- Only oral iron or blood transfusion is given to colorectal cancer patients with anemia during preoperation workup

Compare results and standards

- Can help raised Hb, reduce blood transfusion and relieve anemic symptom with IV Iron

Audit cycle 1: (1 Feb 2017-31 Dec 2018)

Low recruitment rate: Colorectal surgeons forgot to recruit patients. Also many patients were excluded due to Allergy. Patients with history of asthma, allergic eczema or urticaria, drug allergy were excluded in the first audit cycle. No active screening of patients, many patients were missed.

- Change: Amendment of the protocol and updated inclusion and exclusion criteria was done Dec 2018: Those with history of asthma, allergic eczema or urticaria, drug allergy were not excluded and were included in Caution group with steroid prophylaxis given before iron infusion.
- Reminded colorectal surgeons to recruit patients according to protocol.

Monofer dosage not given according to weight

Change: Adjustment of Monofer according to body weight with dosage increased to 1000 mg for those>50 kg.

Forgot blood taking after IV iron given

Change: Colorectal cancer nurses reminded doctors and nurses for baseline and post IV iron blood taking.

No 2nd dose given for those failed Hb top up, just proceed to blood transfusion

Change: 2nd dose will be given if rechecked Hb<8 or presence of anemic symptom.

Only preliminary checklist is available

Change: A finalized form for I.V iron infusion for doctors, a booking form and checklist were available in Apr 2019.

I.V Iron was not given within 1 week as planned

Change: Reminded day care centre for arrangement of IV Iron infusion within 1 week.

I.V Iron not referred to be given as day case

Change: Reminded colorectal surgeons and nurses to fill in the referral form and referred cases as day case.

Re-audit audit cycle 2 (1 Jan 2019 – 1 Feb 2021)

- Recruitment rate raised from 49.5% and 67.1% to 100%) (Table 4)
- 100% patients with Adjustment of Monofer according to body weight with dosage increased to 1000 mg for those>50 kg
- 99% patients with baseline and post IV iron blood taking
- 9 patients with 2 dose iv iron given due to rechecked Hb<8 or presence of anemic symptom
- 100% referral of suitable cases to day case for IV Iron infusion
- Increase in Hb level after IV Iron given: 2.35 g/dL
- Reduction of blood transfusion rate from 20% to 3.27%
- Median Hb was up to 11.65 g/dL and 0 patient had anemic symptom 26 weeks after IV Iron given

Table 4: Recruitment of patients for IV Iron therapy.

Year	Total no. of colorectal cancer patients	No. of colorectal cancer patients screened	No. of patients with IV Iron given	Recruitment rate
2017	303	150	15 (10%)	49.50%
2018	298	200	37 (18.5%)	67.10%
2019	314	314	53 (16.88%)	100%
2020	310	310	68 (21.94%)	100%
2021	226	226	41 (18.14%)	100%

Discussion

Anemia is one of the most frequent extraintestinal manifestations of colorectal cancer, and may be present in 30-75% of patients. A study on 358 patients with colorectal cancer reported a 25% prevalence of moderate to severe anemia [5-11]. There is also evidence that iron deficiency is associated with poor performance and more advanced disease.

This study demonstrates that preoperative IV Iron is both feasible and efficacious in optimizing anemia in colorectal cancer patients. In our result, 214 patients had IV Iron and 183 proceeded to surgery at the end. 3.27%, 4.92% and 3.27%

required preop, intraop and postoperation blood transfusion respectively. 94.9% had raised in Hb, the median increase in Hb was 2.35 g/dL. There was also raised in Fe and ferritin of 3 and 332 respectively. This showed that IV Iron had the effect of reduction of preoperative blood transfusion from 20% to 3.27% (when compared with our retrospective review of cases 2014-16). The improvement in Hb and Iron profile also contributed to the reduction in blood transfusion. Besides, all blood transfusion preoperation were for patients presented with severe anemia (Hb<8 g/dL) which was also shown in previous studies [3,8].

We also noticed a sustainability in the maintenance of Hb level 26 weeks and improvement in anemic symptoms after IV Iron therapy. When compared with pre IV Iron Hb, there was an increase in 4 g/dL in Hb 26 weeks after IV Iron. The percentage of patients with anemic symptom also dropped from 55.1% to 0%. A recent retrospective review [10,13] also showed a better outcome after administering IV Iron which resulted in continuous increase in Hb level during early post-operative period after colorectal cancer surgery. Our results add to a growing body of evidence in the literature demonstrating the efficacy of preoperative IV Iron therapy in colorectal cancer patients [12].

Concerning the safety profile, no adverse reaction was noticed in all patients. When compared the group with Hb change *vs.* no Hb change, it was noted that the pre and post IV Iron Hb, Fe, ferritin, Iron saturation and postop Hb before discharge were all significantly higher in no Hb change group than raised in Hb group. This showed that those with mild anemia were expected to have less Hb change than those with moderate or severe anemia.

When compared the group with 1 dose *vs.* 2 doses of IV Iron given, it was noted that Hb in 2 doses group were significantly lower than 1 dose group. This showed that repeat blood tests 2 weeks after 1st dose of IV Iron was important especially in those with severe anemia as a 2nd dose could be given to them if the improvement in Hb level was suboptimal.

This study also included a close loop audit of the Pilot Quality Improvement Programme of our unit. We initiated this programme with the aim of optimizing anemia in colorectal cancer patients. The Multidisciplinary team set the goals at the beginning and 2 Audit cycles was carried out to evaluate the results. We noticed several issues after initiation of the programme especially low recruitment rate, low compliance rate to protocol in terms of blood taking and the time of IV Iron given after referral. The issues were identified after the 1st Audit cycle and changes were implemented accordingly. Also, timing and dosing are crucial for IV Iron therapy. Maximal Hb response usually takes 4-6 weeks and sometimes more than 1 dose is required with a maximum of 1 g weekly [5]. Thus we adjusted our protocol according to the evidence with 2nd doses given to patients with repeated Hb<8 or with anemic symptom.

After the 2nd Audit cycle the recruitment rate reached 100%. Though 3 patients had missing post IV Iron blood, the compliance rate to protocol much improved to 99% in terms of blood taking. 100% patients had IV Iron within 1 week of referral.

As strength of our study, the results suggest that IV Iron could be a viable treatment option for anemic colorectal cancer patients who may otherwise require blood transfusion. This is meaningful especially when there is a shortage of blood products worldwide and the demand is rising due to aging population [3,12]. The sustainability of the Hb level and marked reduction in anaemic symptom as shown in the study result can set a direction for future management of colorectal cancer patients postoperation.

Besides, it is the 1st Audit report on the IV Iron therapy as a Pilot programme in a surgical unit for optimization of anemia on Colorectal Cancer patients only. Previous Audit reports were on all surgical patients, not just specifically on Colorectal Cancer patients. This Audit showed that implementation of this programme was feasible and improvement of the programme could be attained throughout the Audit cycles. Also, all patients in our study were selected based on our protocol's pre-specified eligibility criteria. This reduces variability and can be more informative to other departments which would also like to implement similar programme in the future.

The present study has several limitations that warrant acknowledgement. This study is a non-randomized study and is only a retrospective review with no comparison group. This will limit the interpretation of the results. Also the retrospective data from 2014-16 were not included for comparison due to lots of missing data. However these patients represent "real-life" clinical practice [1]. Although a recent Randomised controlled trial [9]. Showed preoperative IV Iron was not superior to placebo to reduce the need for blood transfusion when administered to patients with anemia 10-42 days before major abdominal surgery, included patients were not specific for colorectal cancer (operation for abdominal aortic aneurysm, gynaecological, upper gastrointestinal, urological and general surgeries were included. Future randomized controlled trial recruited for Colorectal Cancer only should be considered to aid to confirm our findings.

Besides, the assessment of anemic symptoms was performed by colorectal cancer surgeons only. It should be best performed by a validated patient-reported outcome instrument e.g. 36-item Short Form Health Survey to make the results more reliable [13-14].

Conclusion

In conclusion, our data demonstrates that preoperative IV Iron can help reduction of blood transfusion preoperatively. It can also raise the Hb and Iron profile. It also demonstrates the sustainability in terms of Hb level and improvement in anemic symptom. A close loop audit also demonstrates the feasibility of implementing this programme in optimizing anemia in colorectal cancer patients.

Reference

1. Jose LC, Salvadora D, Adolfo de V, Antonio H, Jose L L, et al. (2016) Ferric carboxymaltose reduces transfusion and hospital stay in patients with colon cancer and anemia. Int J Colorecal Dis 31:543-551
2. JAD Simspon, SL Ng, MJ Brookes, A G Acheson (2005) Single Dose Preoperative Administration of Intravenous Iron corrects Iron Deficiency Anemia in Colorectal Cancer. J blood disord transfuse 1: 1000101
3. W Chan, FAS Lee, WWY Tin, SF Yip, FCS Wong (2020) Efficacy of Intravenous Iron in cancer patients with moderate to severe iron deficiency anemia. Hong Kong J Radiol 23:261-274
4. Michael JW, Jan WD, Emma B, Wernard B, Johannes J, et al. (2018) Short-term effect of preoperative intravenous iron therapy in colorectal cancer patients with anemia: results of a cohort study. Blood Management 58:795-803
5. MJ Wilson, JWT Dekker, JJ Harlaar, J Jeekel, M Schipperus, et al. (2017) The role of preoperative iron deficiency in colorectal cancer patients: prevalence and treatment. Int J Colorectal 32:1617-1624
6. Manuel Munoz, Susana Gomez-Ramirez, Elisa Martin-Montanez, Michael Auerbach (2014) Perioperative anemia management in colorectal cancer patients A pragmatic approach. World J Gastroenterol 20:1972-1985
7. M Munoz, AG Acheson, E Bisbe, A Butcher, S Gomez-Ramirez, et al. (2019) An international consensus statement on the management of postoperative anemia after major surgical procedures. Anaesthesia 73:1418-1431
8. F Lebrun, J Klastersky, D Levacq, Y Wissam, M Paesmans (2017) Intravenous iron therapy for anemic cancer patients: a review of recently published clinical studies. Support Care Cancer 25:2313-2319
9. Toby Richards, Ravishankar Rao Baikady, Ben Clevenger, Anna Butcher, Sandy Abery et al. (2020) Preoperative intravenous iron to treat anemia before major abdominal surgery (PREVENT) a randomized double-blind controlled trial. The lancet 396:1353-61
10. Young Ju Oh, Dae Hee Pyo, Jung Kyong Shin, Yoon Ah Park, Jung Wook Huh, et al. (2020) Efficacy of intravenous ferric carboxymaltose in patients with acute post-operative anemia after colorectal cancer surgery. J Nutr Metab 11:61-65
11. Jose Carlos Titos-Arcos, Victoriano Soria-Aledo, Enrique Pellicer-Franco (2012) Is intravenous iron useful for reducing transfusion in surgically treated colorectal cancer patients? World J Surg 36:1893-1897
12. YF Chow, Benny CP Cheng, HK Cheng, Betty Ho, CK Lee, et al. (2020) Hong Kong Society of Clinical Blood Management recommendations for implementation of patient blood management. Hong Kong Med J 26: 331-338
13. Maria Jesus Laso-Morales, Roser Vives, Caridad Pontes (2018) Intravenous iron administration for post-operative anemia management after colorectal cancer surgery in clinical practice a single-centre retrospective study. Blood Transfus 16:338–342
14. BD Keeler, JA Simpson, O Ng, H Padmanabhan, MJ Brookes, et al. (2017) Randomised clinical trial of preoperative oral versus intravenous iron in anemic patients with colorectal cancer. Br J Surg 104:214-221