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DIAGNOSIS OF ANEMIA AND THE PROPER MEDICATION FOR ITS MANAGEMENT IN POPULATION OF ALSAMAWAH CITY, IRAQ

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Abstract

Anemia is a blood disorder in which there is a reduction in the hemoglobin Hb concentration of the peripheral blood below the normal level, People of all ages, races and ethnicities can develop anemia at some point in their lives, the World Health Organization WHO stated that anemia in men is <13 gm/ dL, in women is <12 gm/ dL. Iron deficiency is recognized as the most common cause of anemias as estimated it affect about 35% of the population in the world. IDA defined as both low iron and low hemoglobin levels, which can be a result of the following reasons: insufficient iron intake from daily nutrition, increased iron demand, decreased iron absorption or due to blood loss which accounts for one-half or the recorded anemia cases worldwide. It is very important to determine the ferritin levels (iron stores) before the initiation of the treatment because it will provide a diagnosis of iron deficiency. The oral iron replacement therapy was chosen to be evaluated for its impact on anemia because it is more preffered by patients for being available, noninvasive, convenient, inexpensive and effective but unfortunately possible gastric side effects due to long term treatment. 133 were confirmed as anemic as the blood tests results obtained. Exclusion criteria were age below 18, pregnant woman or patient with current or previous cancers. From our experimental work in this study the treatment was successful in decreasing and management of anemia in the participants compared to the initial anemia status in patients according to their tests result. patients were asked for their opinion whether if they prefer to switch to IV iron therapy and the majority answered with No justifying their answer due to painful route of administration and difficulty to self-administration which will need the help of proficiently health care provider.

Keywords: Anemia, IDA Iron Deficiency Anemia, Hemoglobin, Ferritin

Aim:

The aim of our research is to identify the most effective oral treatment to restore the hemoglobin and iron level of the patients to be in a level that works best for their bodies in which the decision is made by the prescribing physician and administered by pharmacists to provide the best health care in order to keep any patient from needing blood transfusions and being more energetic, less tired and safer from any further complications due to anemic status.

INTRODUCTION

Anemia is a blood disorder in which there is a reduction in the hemoglobin Hb concentration of the peripheral blood below the normal level that is documented according to the age and sex. blood carries oxygen and nutrients, regulating the body temperature, fights infections and get rid of waste products, so when anemia occurs it will have a huge impact on the whole body and the quality of life. [1]

People of all ages, races and ethnicities can develop anemia at some point in their lives, the World Health Organization WHO stated that anemia in men is <13 gm/ dL, in women is <12 gm/ dL, which is affected by age, sex, pregnancy status and chronic diseases such as kidney diseases, liver diseases, HIV, AIDS, systemic lupus or cancer.[2,3]

Anemia occur in a result to a malfunction in either the production, destruction of red blood cells rate, sometimes due to acute or chronic blood loss.[4] Sometimes in some

elderly patient anemia is known as unexplained anemia when a precise etiology was unable to be determined.[5]

Iron deficiency is recognized as the most common cause of anemias as estimated it affect about 35% of the population in the world, where the lack of iron in the body leads to a reduction in the number of the red blood cells, normally iron is stored in the liver and it is essential to red blood cell production. Some cases present a low body iron stores with normal hemoglobin levels which will considered as iron deficiency without anemia. [6]

IDA defined as both low iron and low hemoglobin levels, which can be a result of the following reasons: insufficient iron intake from daily nutrition, increased iron demand, decreased iron absorption or due to blood loss which accounts for one-half or the recorded anemia cases worldwide. [7]

A data supported by laboratory evidences should be done to confirm the presence of anemia, small red blood cell size and low iron storage. [8]

For the determination of MCV (mean corpuscular volume), a complete blood count is very useful. The major cause of microcytic anemia is iron diffeciency, but up to 40% of anemic cases showed normocytic erythrocytes. It is very important to determine the ferritin levels (iron stores) before the initiation of the treatment because it will provide a diagnosis of iron deficiency whether anemia is present or not, the target normal ferritin >100 µg/L. Low MCV level with normal ferritin may indicate hemoglobinopathies such as thalassemia. Long term iron therapy is harmful for these patients. [9]

On general physical examination there will be some signs that help to indicate anemic patient including: pallor in mucus membrane especially in lower palpebral conjunctiva, nail changes where there might be thining, flattening in nails or koilonychias, pale tounge, excessıve bruising, restless leg syndrom, irritability, depression, cold intolerance, fatigue, hair loss, pagophagia (ice craving), headaches. [10]

The oral iron replacement therapy was chosen to be evaluated for its impact on anemia because it is more preffered by patients for being available, noninvasive, convenient, inexpensive and effective but unfortunately possible gastric side effects due to long term treatment. [11]

Inspite of the good safety profiles for IV preparations but they might be painful to patients, require monitoring, may have a risk of anaphylaxis and injection site discoloration. [12]

Iron supplements when taken orally, its absorption might be affected in the GIT after administration so in the presence of gastric acid the iron will conjugated with amino acids, sugars or vitamin C it is more likely to be protected from the pancreatic alkaline secretion in the GIT. Iron is advised to be taken on empty stomach in this case the iron will bound more easily and be available as an absorbable form, otherwise it might convert to ferric hydroxide which is unabsorbable form. [13]

Sometimes preexisting diseases may cause alteration in iron absorption which lead to iron deficiency such as Helicobacter pylori infection which leads to reduced soluble iron for absorption likely cause chronic gastritis, peptic ulcer, dyspepsia as stated by patients who were the subjects of a study that focused on the treatment of H.pylori infected individuals (103 patients) to evaluate the best approach for their treatment in alsamawah city. [14]

Patients with celiac disease CD frequently suffer from IDA and may benefit from iron supplementation which is proved after 90 days follow up in a study that showed improvement in Hb levels and significant improvement in all iron parameter with oral liposomal iron. [15]

The clinicians are familiar with available options for iron therapy including oral and IV preperations, their selection of the route for iron supplement administration is based on hemoglobin level and anemia severity, the tolerance to oral iron medications with persistent IDA after the oral course of treatment, low adherence to oral iron therapy, presence of concomitant disease that affect the iron absorption, bariatric surgery patients. [16]

METHODS AND MATERIALS

This study was only possible when the communicated people who were reached by the researchers kindly confirmed their acceptance to participate in our study. Once the permissions were granted from the patients, the researchers started to interview each patient separately by asking the questions included in a questionnaire prepared earlier, which consisted of personal information: sex, age, marital status, BMI, current smoking status, medical history: ulcer, diabetes, hypertension, heart failure, renal or respiratory insufficiency, health care life style and daily dietary habits: fruits/vegetables intake, food variation, meal planning, dietary supplements use , daily vitamin tablets . Also each patient was asked to evaluate their physical activity in which inactive were the patients who had the lowest level of activity, minimally active who had 20 minutes of vigorous activity 2-3 days per week or 30 minutes of moderate activity five or more days per week, active who has 7 days per week with intensive of or moderate combination of activity. The questions were filled out within 20 minutes in average.

After finishing the questionnaire, the researchers collected blood and stool samples in order to be sent to the laboratory for investigation. The blood was tested to obtain "Hb value" complete blood count, serum ferritin. Stool was analyzed to indicate the presence red blood cells, parasites, bacteria especially H.pylori.

Our field work extended over a four months period of time, November 2021-end of February 2022. All the participants were informed that they can withdraw from the study at any time they want and their participation was completely optional. 142 individuals who already suspected to be anemic after initial physical examination were involved in this study, 137 were confirmed as anemic as the blood tests results obtained and 133 included in our study. Exclusion criteria were age below 18, pregnant woman or patient with current or previous cancers.

Our research end point was to diagnose people with anemia and evaluate the efficacy of administered medications and dietary modification of the treated individuals.

The treatment regimen was chosen by the physicians according to the patient's blood tests result. For each patient a blood collected in the first day for diagnosis and prescribing the proper medications then a second blood test done after one month to determine the suitability of the administered medications whether the regimen is making any progress or failing to fulfill the required aim and a third blood test was taken after 3 months from the beginning of the treatment to detect the impact of treatment on the anemic patients, during this time patients were asked for any side effects to set the records.

The patients were divided into 2 groups: group A (n=65) treated with iron proteinsuccinylate 800mg equivalent to 40mg of elemental iron oral solution and B12 oral solution containing 25 µg, group B (n=68) treated with iron proteinsuccinylate 800mg equivalent to 40mg of elemental iron oral solution, B12 oral solution containing 25 µg,folic acid 400 µg and vitamin C chewable tablets.

All the patients were instructed by the pharmacist to take their oral medications on empty stomach to enhance the iron absorption unless (nausea, vomiting, constipation, diarrhea or dyspepsia) appeared as a side effects from the therapy then it should be taken with meals to minimize such events and increase both adherence and tolerance to the oral iron dosage forms. To maximize the iron absorption they have been told to take the medications in the morning when hepcidin levels are low and avoid the consumption of calcium or high oxalate containing products such as tea, coffee spinach etc. unless there is a 2 hour window between the drug intake and those products. Also they were notified that iron might be toxic to children which should be stored properly away from children reach. [17]

Each one of our volunteers was asked if they were taking antacid as an OTC medication or any other PPI which affect the absorption of iron.

Table 1: demographic data of the 2 groups

Demographic data	Groups	Group A (n=65)	Group B (n=68)	P value
Sex	Female Male	49 (75.4) 16 (24.6)	54 (79.4) 14 (20.6)	0.579
Age	20-30 31-40 41-50 51-60 61-70	20 (38.8) 14 (21.5) 14 (21.5) 8 (12.3) 9 (13.8)	22 (32.4) 14 (20.6) 13 (19.1) 11 (16.2) 8 (11.8)	0.963
Marital state	Single Married	7 (10.8) 58 (89.2)	8 (11.8) 60 (88.2)	0.856
BMI	Underweight < 18. Normal weight 18.5-24.9 Overweight 25-29.9 Obesity BMI ≥30	6 (9.2) 24 (36.9) 29 (44.6) 6 (9.2)	8 (11.8) 17 (25) 34 (50) 9 (13.2)	0.492
Smoking status	Smokers Non-smoker	9 (13.8) 56 (86.2)	6 (8.8) 62 (91.2)	0.360

* represents a significant difference at $p<0.05$

The pharmacists investigated every subject about their medical history and current ongoing medical conditions to set the records as shown in table 2.

Table 2: the medical history of the patients

Medical condition	Group A (n=65)	Group B (n=68)	P value
Ulcer	3 (12.5)	2 (10)	0.712
DM	11 (45.8)	8 (40)	
Hypertension	9 (37.5)	10 (50)	
Renal disease	1 (4.2)	0 (0)	
Respiratory failure	0 (0)	0 (0)	

* represents a significant difference at $p<0.05$

During the questionnaire some of the etiologies of the anemia and IDA was established such as being with poor nutrition due to decreased appetite or unhealthy

diet, lactation in some woman, already taking some prescribed medications such as epilepsy or antipsychotics, aspirin, diagnosed ulcers, female with heavy menstrual bleeding, gastric bypass surgeries. Other conditions were established after the urine, blood, stool, ultrasound examinations such as H.pylori infection, hematuria, thyroid dysfunction, polycystic ovaries, uterine fibrosis.

Table 3: etiologies of anemia and IDA

Etiology	(n) no. of cases	Prevalence %
menorrhagia	23	25.0
Polycystic ovary syndrome	16	17.4
Uterine fibrosis	5	5.4
Thyroid disease	4	4.3
Decreased appetite	13	14.1
H.pylori infection	3	3.3
Peptic ulcer	5	5.4
gastrectomy	1	1.1
lactation	7	7.6
hematuria	2	2.2
Long term use of aspirin or other NSAID	10	10.9
Use of antiepileptic or antipsychotic drug	3	3.3
Total	92	100
P value	<0.001*	

* represents a significant difference at p<0.05

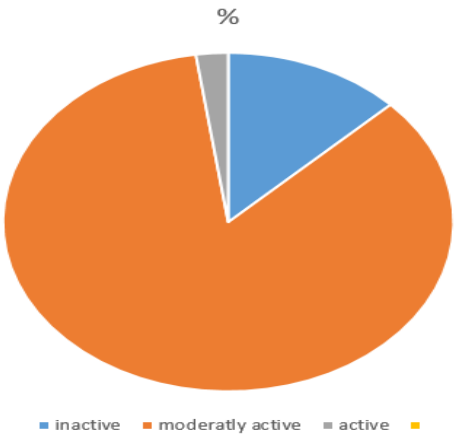

Figure 1: the physical activity of the patients

Our patients were 12.8% inactive, 84.9% moderately active and 2.3% highly active depending on their answers about how much activity and exercise they are doing on daily basis.

Each group were given a list of high iron containing foods that can enhance the anemia status by improving the dietary intake and changing the quality of nutritional items to be eaten through the period of treatment, which definitely beneficial adjacent to the medications prescribed. Recommending a sufficient amount of sleep, trying to exercise more for those with sedentary life style, and the most important giving the instructions about the timing of the medication to be best taken with or before meals. Depending on the patients drug records, they were advised to take the iron supplements with certain time gap if they already taking antacids, PPI, antipsychotics, antiepileptics or NSAID.

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RESULTS

A total of 142 patients accepted the request to participate in our research, all of them were investigated to diagnose anemia and after laboratory test results only 137 were confirmed anemic, one female patient was confirmed pregnant and one male patient informed us he is a cancer survivor which were cases that are part of the research exclusion criteria, 2 patients were unresponsive to orally treatment and they been switch to IV treatment, so only 133 involved and they enrolled into 2 groups (group A: 65 patients, group B 68 patients).

The researchers tried to make no difference between the two groups by distributing the patients almost evenly as the number of participants, age, sex, marital status, BMI and smoking habits.

From our experimental work in this study the treatment was successful in decreasing and management of anemia in the participants compared to the initial anemia status in patients according to their tests results as shown in table 4 and 5.

Table 4: laboratory test results before and after drug intervention group A(65 patients)

Test		Female	Male	P value
Hb	Before the intervention Mean±SD	8.1±0.53	9.1±0.54	<0.001*
	After 3 months Mean±SD	12.4 ±0.55	13.2±0.52	<0.001*
P value		<0.001*	<0.001*	
Ferritin	Before the intervention Mean±SD	19±2.5	28± 2	<0.001*
	After 3 months Mean±SD	66±5	81±3.3	<0.001*
P value		<0.001*	<0.001*	

* represents a significant difference at p<0.05

Table 5: laboratory test results before and after drug intervention group B (68 patients)

Test		Female	Male	P value
Hb	Before the intervention Mean±SD	8.3±0.64	8.8±0.50	0.009*
	After 3 months Mean±SD	12.07±0.61	12.69±0.512	0.001*
P value		<0.001*	<0.001*	
Ferritin	Before the intervention Mean±SD	12±2.39	16±3.23	<0.001*
	After 3 months Mean±SD	63±4.93	87±4.13	<0.001*
P value		<0.001*	<0.001*	

* represents a significant difference at p<0.05

Table 6: laboratory test results before and after drug intervention group A

MCV	Before the intervention	After 3 months
	Mean : females 69 Femtoliter males 77 Femtoliter	Mean: females 85 femtoliter males 88 femtoliter

Table 7: laboratory test results before and after drug intervention group B

MCV	Before the intervention	After 3 months
	Mean: females 73 Femtoliter males 78 Femtoliter	Mean: females 79 femtoliter males 83 femtoliter

Table 8: complains of patients due to oral iron treatment

Adverse effect	Prevalence % in group A	Prevalence % in group B	P value
Epigastric pain	20 %	23.5%	0.519
nausea	29.2%	30.8%	0.758
diarrhea	10.7%	8.8%	0.637
constipation	29.3 %	32.3%	0.645
Metallic taste	61.5%	75%	0.038*
vomiting	1.5%	4.4%	0.400
Dyspepsia	44.6%	39.7	0.474
Black stool	55.4%	60.3%	0.474
	<0.001*	<0.001*	

* represents a significant difference at p<0.05

DISCUSSION

For over a century, iron absorption and metabolism investigated by researchers widely because it is considered as the most important heavy metal in the body of human. Despite that investigations are still of great interest because the iron deficiency and anemia problems has not yet been totally solved worldwide.

After questioning our participant most cases showed poor nutrition due to lack of meal planning and inadequate amount of fruits and vegetables that can ensure the minimal daily required amount of nutrients (like iron, folic acid & vitamin B12) which keep them from being anemic, low consumption of animal protein, poor nutritional knowledge. One female participant was a vegetarian has anemia who admitted of her poor nutrition and not taking any multivitamins supplements that might support her general health. 6 patient confirmed recent surgical operation (blood lost) around the time of our study, also one patient confirmed doing gastric bypass surgery 2 years ago for obesity related reasons which in most times can lead to poor GI absorption that give rise to anemia due to reduced iron absorption.

2 patients said that they are on herbal remedies of unknown source (no label for ingredients and content) that is thought to help with arthritis pain, so they were advised to cut it immediately because most of these remedies might cause disturbances in food digestion and nutrients absorption.

3 women were breastfeeding expressed that they are with decreased appetite and lack of sleep due to new born child and new responsibilities making them fatigued and exhausted most the time plus the high iron demand required during lactation, which directly explaining the reasons of anemia.

2 of our initial participants they were unresponsive to oral treatment which was confirmed by their laboratory test results after one month of treatment so they have been switched to intravenous treatment by the prescribing physician and their data were excluded from our results and calculations.

Considering that 27% of our participants are (50-70 years old),therefore due to age related physiological changes and already existing chronic diseases such as diabetes, hypertension and cardiac diseases which contribute in decreased RBCs production and decreased RBCs life span.

Blood in stool was a compliant of few patients, who had been asked for a stool analysis which confirmed H.pylori infection in 3 of them which cause GI bleeding that present

in stool. Some previous trials showed the relation between H.pylori infection and depleted iron storage and it was proven through field work on patients that its eradication resulted in beneficial increase in ferritin levels. [18]

As pharmacist; we asked the patients about current drug profile to avoid any drug-drug interaction, patient who were using PPI and antacids occasionally or continuously were advised by our team to make sure there is a two-hour gap between the medications to avoid any alteration of iron absorption. Also patients who were taking antipsychotic or antiepileptics were warned that iron might impair absorption or bioavailability of these agents.

Iron complexing agents such as phosphates, phytates and oxalates contained in some vegetables, milk, coffee and tea inhibit the absorption of iron so there must be a gap between iron supplement the consumption of such foods.

The real challenge was to identify the underlying cause to choose the best treatment for simple and complex cases of anemia, according to literature many cases counts about 24% were with no precise cause and categorized as unexplained anemia.[19]

The determination of physical activity was a good parameter to identify the overall effect of fatigue, tiredness and exhaustion that might be caused by anemia.

After obtaining the data about the side effects each patient suffered from oral iron therapy, they were asked for their opinion whether if they prefer to switch to IV iron therapy and the majority answered with No justifying their answer due to painful route of administration and difficulty to self-administration which will need the help of proficiently health care provider.

CONCLUSION

In clinical practice, the diagnosis and management of anemia poses great challenge, Because it can be due to nutritional bad habits which can be only controlled by the patients themselves, also can be related to various underlying pathologies. The outcomes of our used treatment highly depended on the commitments of our patients to our advice about daily nutrition, daily food intake and adherence to oral iron therapy for 3 months long. After thorough work and follow up by the pharmacists we obtained a good results regarding the correction of existing anemia by making a necessary dietary modification and iron oral medication to improve the quality of life and protect the health of people in our community by proper education about the importance of healthy diet and iron supplement in specific and multivitamin supplements in general.

References

1. King, TC. Hematopoietic pathology. In: Elsevier's integrated pathology.Philadelphia (PA):MosbyElsevier; 2007.pp. 263-289.
2. WHO. Prevalence and diagnosis of iron deficiency anemia: a guide for program manager. Vol. 52. Geneva: WHO, UNICEF; 2001. pp. 447-501.
3. World Health Organization. Iron deficiency anaemia: assessment, prevention and control: a guide for programme managers. Vol. 36. Geneva: WHO, UNICEF, UNU
4. British Columbia Ministry of Health. Iron deficiency—investigation and management. http://www.bcguidelines.ca/guideline_iron_deficiency. html. Accessed November 13, 2012.
5. Guralnik JM et al (2004) Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood 104(8):2263–2268

6. Bailey R, West K, Black R. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab. 2015; 66:22-33.

7. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. Therap Adv Gastroenterol. 2011;4(3):177-184.

8. U.S. Preventive Services Task Force. Screening for iron deficiency anemia, including iron supplementations for children and pregnant women: recommendation statement. Am Fam Physician. 2006;74(3):461-464.

9. Goddard AF, James MW, McIntyre AS, Scott BB, British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. Gut. 2011 Oct;60(10):1309–16.

10. Cook JD. Diagnosis and management of iron-deficiency anaemia. Best Pract Res Clin Haematol. 2005 Jun;18(2):319–32.

11. Camaschella C. Iron-deficiency anemia. N Engl J Med. 2015;372(19):1832-1843.

12. Jonathan BC, Jonathan B. Correcting iron deficiency. Aust Prescr 2016 Dec;39(6):193-199.

13. Camaschella C. New insights into iron deficiency and iron deficiency anemia. Blood Reviews. 2017;31:225-233.

14. NTA Alsaadi, MTA Alsaadi, ZT. Ali Comparison between levofloxacin based therapy and clarithromycin based therapy through 14 days period for *H-pylori* eradication Sys Rev Pharm, 11 (2020), pp. 593-598.

15. Elli L, Ferretti F, Branchi F, Tomba C, Lombardo V, Scricciolo A, Doneda L, Roncoroni L. Sucrosomial iron supplementation in anemic patients with celiac disease not tolerating oral ferrous sulfate: a prospective study. Nutrients 2018 Mar;10(3):E330.

16. Bencaiova G, Mandach U, Zimmermann R. Iron prophylaxis in pregnancy: Intravenous route versus oral route. Eur J Obstet Gynecol Reprod Biol 2009;144:135-39

17. Muñoz M, Gómez-Ramírez S & Bhandari S. The safety of available treatment options for iron-deficiency anemia, Expert Opinion on Drug Safety, 2018;17:2, 149-159,
DOI: 10.1080/14740338.2018.1400009

18. Hudak L, Jaraisy A, Haj S, Muhsen K. An updated systematic review and meta-analysis on the association between helicobacter pylori infection and iron deficiency anemia. Helicobacter. 2017;22(1):e12330

19. Tettamanti M et al (2010) Prevalence, incidence and types of mild anemia in the elderly: the ‘‘health and anemia’’ populationbased study. Haematologica 95(11):1849–1856