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Research Article

Occult Blood in Iron Deficiency Anemia: The Key Diagnostic Approach to Treatment in Chronic Cases

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Received: August 16, 2017; **Published:** September 20, 2017

Abstract

Background: Globally, anemia due to iron deficiency or lack of iron is the commonest nutritional disorder. The incidence of Iron deficiency anemia (IDA) is 30% in developing countries whereas in America, 9% of children are estimated to have iron deficiency anemia. A lot of children are known to have anemia due to lack of iron for long periods (chronic), although they have treatment for their iron deficiency. Occult blood or unrecognized blood is the key approach for children with chronic IDA.

Objective: The goal of this research study is to focus on the occult blood as a main key etiology in children with chronic IDA based on history taking, clinical examination and serum ferritin level in the blood. Furthermore, this research was conducted to approve that occult blood in IDA is the key diagnostic and therapeutic tool to approach in children with IDA.

Design: This research study was conducted on sixty two children who suffered with chronic IDA, thirty nine (63%) out of them were boys, and twenty three of them were girls (37%), aged (1 - 5) years old, from in and outpatient clinic at Zakho/Duhok General Hospital in Kurdistan Region-Iraq. Patients were clinically diagnosed and followed up for three months. They were represented and adjusted by full history taking, clinical examination and laboratory screening. Among those 62 patients, all of them had chronic IDA with occult blood positive stool test.

Serum ferritin level as a main specific and sensitive guide was used in the investigation and follow up of the intervened children.

Results: There is a significant clinical and laboratory improvement in children with chronic IDA after dealing with their occult bleeding as a key approaching management. Among sixty two patients of both sexes, all of them clinically suffered from pallor, lethargy, poor appetite, and irritability. All children involved in this research study had received a frequent treatment for their IDA without clinical and laboratory benefit. Hence, parents were given advice to observe their children's stool for any discoloration. No one of the intervened patients had a recognized blood in their stool. Occult blood in the stool is considered in this study as a key for diagnosis and treatment of IDA.

In this research study, among all patients with chronic IDA, they showed very good clinical response with elevated serum ferritin levels in their blood. Patients had significant improvement of their clinical symptoms and signs, including pallor, poor appetite, lethargy and irritability based on clinical examination and history taking from their parents. This is achieved after exclusive treatment of their underlying anal fissures. Moreover, both sexes had an equal response to therapy.

Conclusion: All children with chronic IDA showed progressive clinical and laboratory improvement after treating their conditions based on occult blood as a key approach in patients between one and five years of age. However, for each child with chronic IDA,

occult blood must be clinically considered as treating the latter, this significant approach is greatly helpful to manage children with chronic IDA. The greatest clinical and laboratory improvement was significantly approved in almost all patients with chronic IDA after being managed clinically for their causative occult blood in their stools.

Keywords: *Children Under 5; Iron Deficiency Anemia; Occult Blood; Clinical Improvement; Serum Ferritin; In and Outpatient Clinic*

Introduction

Iron deficiency anemia is the most common nutritional disorder in the world [1]. In developing countries, thirty percent of estimated population has iron deficiency anemia, whereas, nine percent of children ages 12 - 36 months in the USA are iron deficient [1]. Breastfed infants have an advantage because they absorb iron 2 - 3 times more efficiently than infants fed cow's milk [1]. Absorption of 0.8 mg of iron daily is compulsory during the first 15 years of life; this is because of the change in quantity of iron from birth to adulthood. A full term newborn baby has about 0.5g of iron, as compared to 5g of iron in adult [1].

Causes of Iron Deficiency Anemia

Occult gastrointestinal (GI) bleeding may occur anywhere in the GI tract, from the oral cavity to the anorectic region [3,4]. A review of multiple studies has shown that lesions in the upper GI tract and small bowel are often the cause of iron deficiency anemia [5].

In term infants, iron stores are sufficient for blood formation in the first six to nine months of life, whereas in low birth weight infants or infants with perinatal blood loss, stores are depleted because their iron stores are smaller than those of term infants [1].

Another risk factor for iron deficiency anemia include an early clamping of the umbilical cord (< 30 Sec), whereas delayed clamping (1 - 3 min) can improve iron status and reduce the risk of iron deficiency anemia [1]. Furthermore, an excessive consumption of cow's milk (low iron content, blood loss from milk protein colitis) in an overweight child is the main etiology of nutritional iron deficiency anemia [1]. In older children, blood loss must be considered as a possible reason in almost every case of iron deficiency anemia [1].

Moreover, as shown in table 1, certain causes might precipitate to chronic iron deficiency anemia and result in occult bleeding, and these include: peptic ulcer, Meckel's diverticulum, polyp, hemangioma, or inflammatory bowel disease [1]. However, infants with occult bleeding, present with more severe and earlier anemia than those who do not have occult bleeding. Also, children with occult bleeding or unrecognized blood loss might present with chronic diarrhea and pulmonary hemosiderosis [1].

- *Infants with perinatal blood loss*
- *Early clamping of the umbilical cord < 30 Sec*
- *Cow's milk protein colitis*
- *Peptic ulcer, Meckel's diverticulum, polyp, hemangioma, or inflammatory bowel* disease
- *Infections with hookworm, Trichuris trichiura, Plasmodium and Helicobacter Pylori*
- *Celiac disease*
- *Giardiasis*

Table 1: *Possible causes of occult bleeding in children with Iron deficiency anaemia.*

In developing countries, infections with hookworm, *Trichuris trichiura, Plasmodium* and *Helicobacter Pylori*, in addition to Celiac disease and giardiasis are all contributing factors for iron deficiency anemia [1].

In addition, occult gastrointestinal bleeding is defined as gastrointestinal bleeding that is not visible to the patient or physician, resulting in either a positive fecal occult blood test, or iron deficiency anemia with or without a positive fecal occult blood test [2].

In general, gastrointestinal (GI) bleeding may be classified as overt, obscure, or occult [2]. Overt GI bleeding is visible, such as hematemesis (bloody or coffee-ground emesis), hematochezia (the presence of blood and blood clots in the feces), or melena (black tarry stools). Obscure GI bleeding refers to recurrent bleeding in which a source is not identified on upper endoscopy, colonoscopy, or small bowel radiography. Obscure bleeding may be either overt or occult, with the source of bleeding often found in the small bowel. Occult bleeding is not visible to the patient or physician [2]. This research article focuses on the value of occult blood as an indicator for the diagnosis and treatment of iron deficiency anemia manifested as iron deficiency anemia with a positive fecal occult blood test.

Methods

In this research study, consent was obtained from parents when this data was collected and entered into the dataset. This is a cross-sectional hospital and private clinic based study, carried at Zakho General Hospital-Kurdistan-Iraq in and outpatients in pediatric units for the period from May 2017-August 2017.

A total of sixty two children (aged 1 - 5) years old with chronic IDA (23 girls, 39 boys) were conducted. Data were collected from their parents about age, sex, main clinical presentation, and duration, color of the stool, perinatal history and type of feeding. They all had a complete clinical examination and laboratory screening (serum ferritin). Data were analyzed using percentage. Patients were treated for three months with iron replacement and they were represented and adjusted by full history taking, clinical examination and laboratory investigation.

Results

Significantly, as shown in table 2 in this study, all involved infants with chronic IDA had positive occult blood in their stool.

Children with chronic IDA	Children with +ve fecal occult stool test
62	62

Table 2: *Number of children with chronic IDA and positive occult stool test.*

In addition, table 3 illustrates the common clinical symptoms and signs of intervening children in this research study. Among intervening children with IDA, no one had a systolic flow murmur, tachycardia and heart failure (Table 3). However, 72% had pallor, 4% had irritability, 8% had anorexia and eight percent of them were lethargic (Table 3).

Clinical signs	No of intervening children	Total (%)
Pallor (Palmar creases, nail beds, conjunctivae)	45	72
Irritability	7	11
Anorexia	5	8
Lethargy	5	8
Systolic flow murmurs	Zero	Zero
Tachycardia	Zero	Zero
Heart failure	Zero	Zero

Table 3: *Clinical presentation of children with chronic IDA and +ve fecal occult stool test.*

Furthermore, all children with chronic IDA have been followed up clinically by history taking, physical examination and serum ferritin level after iron replacement therapy for three months.

A magnificent finding was obtained and great response of patients with chronic IDA after approaching and treating their occult bleeding was clinically identified as shown in table 4.

Clinical signs	No of intervening children		Occult blood After treatment For 3 months	Total (%)
	Before Mx	After Mx		
Pallor (Palmar creases, nail beds, conjunctivae)	45	45	Negative	72
Irritability	7	7		
Anorexia	5	5		
Lethargy	5	5		

Table 4: *Clinical improvement of children with chronic IDA before and after intervention.*

An approach and Treatment of the examined children with IDA were achieved by identifying the cause of their bleeding.

As a consequence, all children with chronic IDA must be evaluated for their occult bleeding based on clinical examination and laboratory investigation as a key approach to assess their conditions.

The presence of occult blood in stools was tested by benzidine test in 62 children aged (1 - 5) years, with iron-deficiency anemia. The test was done both before and after iron therapy for correction of anemia. Hemoglobin level ranged from 6 - 7 gm.

Almost all children with chronic IDA anemia showed evidence of occult blood in their feces. After iron therapy and the disappearance of anemia, the benzidine test was repeated in all children and was found to be negative in all patients. A group of 20 normal children served as controls. None of them had any evidence of occult blood in stools. The pathogenesis of occult bleeding in the gastrointestinal tract are discussed. It is suggested that such blood loss is one of the several manifestations of disturbed intestinal function in iron deficiency. See table 5.

Serum ferritin Before treatment	Serum ferritin after treatment	No of children	Total (%)
3	37	62	100

Table 5*: Evaluation of serum ferritin level of intervening children with IDA before and after treatment in this research study.*

Discussion

The findings in this research study revealed that the presence of occult blood in the stool of children with chronic IDA is the key approach in the diagnosis, treatment and follow up for their conditions. Iron deficiency anemia is the most common nutritional disorder in the world [1]. In developing countries, thirty percent of estimated population has iron deficiency anemia, whereas, nine percent of children ages 12 - 36 months in the USA are iron deficient [1].

Significantly, no one of the involved children in this research study had surgical intervention, and medication for IDA was given to the patients involved, and treatment was just restricted for their IDA due to occult bleeding as the main etiology.

Among all sixty two children with IDA, all had positive occult blood in their stool; they were treated with ferrous sulfate 3 - 6 mg\kg\ day. Also, parents were advised to give iron rich food for their children and avoid tea in their daily meals. All children were originally from Iraq and of Kurdish ethnicity, and the average age was one to five years.

Among intervened children with IDA, pallor was the commonest clinical signs among their 45 patients (72%), whereas seven children (11%) had irritability, five patients (8%) had anorexia and 8% of children were lethargic (Table 4).

In addition, the etiology of IDA was considered in this research study. Treatment of the underlying reasons of chronic IDA was significantly evaluated as a key approach in the management of IDA. Causes of IDA in infancy might be due to perinatal blood loss, early clamping

of the umbilical cord < 30 Sec, cow's milk protein colitis, peptic ulcer, Meckel's diverticulum, polyp, hemangioma, or inflammatory bowel disease, infections with hookworm, *Trichuris trichiura*, *Plasmodium* and *Helicobacter pylori*, Celiac disease and Giardiasis as shown in (Table 1).

However, in this research, various causes for chronic IDA were identified; children were treated and followed up for three months. Hence, each case of IDA was treated accordingly. For instance: in children with H. Pylori and IDA, triple therapy was administrated including amoxicillin, metronidazole and clarithromycin for 14 days; children with hookworms and IDA were treated with albendazole 100 mg suspension for 2 weeks, and those with peptic ulcer were treated with omeprazole tab 10mg daily for three months. Moreover, metronidazole was given to those with confirmed giardiasis for 10 days.

As investigated in table 4, almost all children had a clinical improvement in their symptoms and signs. As a consequence, serum ferritin level before treatment was 3 ng/dl and after treatment was 37 ng/dl as an average laboratory evaluation of children with IDA.

Serum ferritin is used as a guide investigation for the diagnosis and following up of children with chronic IDA. No further investigation was needed in this research study a part of serum ferritin and occult blood to assess children's response to treatment in chronic cases.

Moreover, most children with IDA are identified by recommending laboratory screening and are often asymptomatic till the age of 12 months [1]. Clinical manifestations of IDA are hemoglobin dependent, this means that the more hemoglobin falls, the more symptoms and signs of IDA clinically develop [1]. Therefore, pallor of the palms, Palmar creases, nail beds, or conjunctivae are the most important clinical sign of IDA, and it is unusual until the hemoglobin falls to 7 - 8 g/dl. In addition, when hemoglobin falls to 5 g/dl, irritability, anorexia, lethargy, systolic flow murmurs, tachycardia and high input heart failure might clinically appear [1].

Furthermore, IDA has non hematologic systemic effects, and this include decreased neurocognitive function in infancy or irreversible cognitive defects, increased risk of seizures, strokes, and breath holding spells in children [1]. Other non hematologic impacts of IDA are pica, which can result in ingestion of lead containing substances (plumbism), and the desire to ingest ice (pagophagia) [1].

A targeted history and physical examination should be performed. A history of GI bleeding, surgery, or pathology may reveal important diagnostic clues. Unintentional weight loss suggests a malignancy. Abdominal pain with aspirin or other no steroidal anti-inflammatory drug use suggests ulcerative mucosal injury. Anticoagulants or ant platelet medications may precipitate bleeding in an undiagnosed lesion. A family history of GI bleeding may suggest hereditary hemorrhagic telangiectasia (associated with vascular lesions on the lips, tongue, or palms) or blue rubber bleb nevus syndrome (a syndrome with venous malformations in the GI tract, soft tissues, and skin). A history of gastric bypass surgery may suggest impaired iron absorption [6]. A history of liver disease or stigmata of liver disease suggests portal hypertensive gastropathy or colopathy. Other helpful physical examination findings that could indicate the presence of an underlying condition include dermatitis herpetiformis (celiac disease); erythema nodosum (painful erythematous nodules seen in Crohn disease); an atrophic tongue and brittle, spoon-shaped nails (Plummer-Vinson syndrome); hyper extensible joints and ocular and dental abnormalities (Ehlers-Danlos syndrome); and freckles on the lips and in the mouth (Peutz-Jeghers syndrome) [7].

In addition, concerted efforts to prevent iron deficiency anemia largely result from its association with lower test scores of mental and motor development in young children, at least some of which are long-lasting [8-10]. Such deficits may result from reduced activity of key iron-containing enzymes in the brain. Less appreciated are the similar effects in older pediatric patients with IDA. For example, iron-deficient adolescent girls without anemia have improved verbal learning and memory after taking ferrous sulfate for 8 weeks compared with those receiving placebo [11].

On the other hand, a lot of children with chronic IDA have been misdiagnosed, therefore as a key approach, evaluation of children with IDA based on clinical examination and the presence of occult blood in their stool is of a great value in the management of children with chronic IDA.

Regarding IDA treatment, the most widely cited dosing range in children is 3 mg/kg/day to 6 mg/kg/day of elemental iron divided 1 to 3 times daily. Although no clinical trials have compared the efficacy of different dosing regimens, 3 mg/kg/day of elemental iron was effective in a well-designed clinical trial; may minimize adverse gastrointestinal effects; and is recommended by the Centers for Disease Control and Prevention [12,13].

Patients must be instructed about administering iron medication. Ideally, it is taken on an empty stomach or at least 1 to 2 hours before or after meals to maximize absorption. In young children, parents must be specifically instructed not to give milk with the iron medication because this will interfere with absorption [14]. Administering iron with vitamin C (e.g. juice) may improve absorption, but is not critical to successful therapy.

Adverse effects commonly associated with oral iron therapy include poor taste, stained teeth, dark stools, mild abdominal discomfort, and constipation. Iron may cause fewer adverse gastrointestinal effects if given in low dosages on an empty stomach at night, although this approach has not been validated by formal studies [14].

Duration of iron therapy is guided by the patient's response, measured by resolution of anemia and repletion of iron stores, typically requiring a minimum of 3 months [14].

After the planned 3-month treatment duration, it is reasonable to assess the serum ferritin level to confirm the apparent resolution of IDA based on improving blood count findings [14].

Conclusion

In summary, any child presents with IDA symptoms should be necessarily examined for their occult blood as a key approach in chronic cases. This research study revealed that occult blood is an important key approach to deal with children who have IDA. Further research is required and suggested for future studies to include a larger number of children in such study; therefore further evaluation of the results would be obtained.

Limitations

There are certain limitations of this study that should be acknowledged. A small number of infants participated in this research study; therefore it is not easy to generalize to a larger or broader population. More authors if included in this research study, we might get better results and further understandings of the findings. Also, a pediatric gastroenterologist might be of value and help to share in such study and better conception of the findings would have been achieved as compared to results obtained by an individual research author.

Also, the restriction to use Interventional tool for instance: endoscopy for the involved children to confirm the diagnosis of upper GI bleeding must be acknowledged as a limitation in this research study.

Despite of these limitations, the findings generated will have significant reference value for future studies.

Conflict of Interest

Nil.

Support and Funding

Nil.

Acknowledgment

This edition could have never been completed without the assistance and support of children and their parents. I also could not have accomplished this research article without department of pediatrics and child's nutrition at the Zakho General Hospital, Kurdistan, Iraq, whose prompting, organizing, and overseeing of the process helped us create this new edition.

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Volume 5 Issue 5 September 2017