TITLE: Prescribed Iron Supplements, Natural Products, and Intravenous Iron for the Treatment of Iron Deficiency Anemia: Comparative Clinical Effectiveness and Guidelines

DATE: 29 June 2010

RESEARCH QUESTIONS:

1. What is the comparative clinical effectiveness of prescribed iron supplements, natural products, and intravenous iron for the treatment of iron deficiency anemia?

2. What are the guidelines for the prevention and treatment of iron deficiency anemia?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 6, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2005 and June 21, 2010. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and guidelines. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and evidence-based guidelines.

One systematic review and eleven randomized controlled trials were identified pertaining to prescribed iron supplements, natural products, and intravenous iron for the treatment of iron

deficiency anemia. Two evidence-based guidelines were identified regarding the prevention and treatment of iron deficiency anemia in children and pregnant women. Additional information that may be of interest has been included in the appendix.

OVERALL SUMMARY OF FINDINGS:

Overall, data from one systematic review[1] and from randomized controlled trials indicate that intravenous or intramuscular iron supplementation seems to be more effective than oral iron supplementation in treating iron deficiency anemia in pregnant women,[1,2,4,10,11] women post-partum,[7-9] and children younger than 12 years of age.[3] Intravenous iron supplementation is likely also more effective than oral supplementation in preventing iron deficiency anemia in pregnant women.[4] Natural supplementation with oral bovine lactoferrin was found to have similar effectiveness as oral ferrous sulphate in treating pregnant women with iron deficiency anemia.[5] Table 1 contains further details pertaining to the included randomized controlled trials.

The identified guidelines do not specify the type of iron supplementation that should be used, but indicate that iron supplementation should be given to pregnant women with iron deficiency anemia[12] and that there is insufficient evidence to recommend for or against iron supplementation in pregnant women without anemia.[13] Routine iron supplementation is indicated for asymptomatic children between the ages of six and twelve months who are at higher risk for iron deficiency anemia, but not for those at average risk.[13]

Table 1: Details of Included Randomized Controlled Trials

Participants	Type of iron supplements, dose	Duration of treatment	Effect on Iron levels	Clinical outcomes
Pregnant women with moderate iron deficiency anemia[2]	Oral ferrous sulphate, 250 mg (80 mg elemental iron) Oral ferrous sulphate (same dose) + IV iron polymaltose (single infusion, delivered prior to oral supplementation)	NR	Patients in the IV iron polymaltose group had increased hemoglobin levels, increased serum ferritin levels, and fewer patients with ferritin levels lower than 30 mug/L (ng/L).	No safety concerns.
Children younger than 12 years of age with iron deficiency anemia[3]	Oral sodium iron edetate Oral iron polymaltose complex IM iron sorbitol (all according to "recommended	Oral groups: 12 weeks IM group: 2 weeks	After 2 weeks, patients in the IM group had increased mean hemoglobin %, mean corpuscular volume, and mean corpuscular hemoglobin concentration. A persistent rise occurred in the oral supplementation group	Adverse effects were more common in patients taking sodium iron edetate.

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	dosage")			
Pregnant women (enrolled between 21st and 24th gestational week, prophylaxis of iron deficiency)[4]	IV iron sucrose (either 2 or 3, 200 mg doses) Oral ferrous sulphate (80 mg daily)	From time of study enrollment to birth of infant	Higher frequency of increased hemoglobin response in the IV group. IV group had a higher frequency of repleted iron stores by delivery.	No clinically significant maternal or fetal differences between the two groups.
Pregnant women with iron deficiency anemia[5]	Oral bovine lactoferrin (100 mg twice a day) Oral ferrous sulphate (520 mg once a day)	30 days	Serum ferritin and iron levels significantly increased in both groups.	Fewer gastrointestinal adverse events in the bovine lactoferrin group.
Women with iron deficiency anemia in heavy uterine bleeding[6]	IV ferric caboxymaltose (1000 mg or less over 15 minutes, weekly) Oral ferrous sulphate (325 mg, 80 mg elemental iron)	6 weeks	More patients in the IV group had a significant increase in hemoglobin levels and more achieved a correction in anemia.	Quality of life increases were more prominent in the IV group. No serious adverse events in either group.
Women with post-partum iron deficiency anemia[7]	IV iron carboxymaltose (1000 mg or less over 15 minutes, weekly) Oral ferrous sulphate (100 mg, twice daily)	IV group: 3 weeks Oral group: 12 weeks	Hemoglobin increases in the IV group at 2 weeks were similar to the increases in the oral group at 12 weeks.	Gastrointestinal adverse events were more common in the oral supplement group.
Women with post-partum iron deficiency anemia[8]	IV iron carboxymaltose (1000 mg or less over 15 minutes, weekly) Oral ferrous sulphate (325 mg, three times daily)	IV group: 3 weeks Oral group: 6 weeks	Patients in the IV group achieved the desired hemoglobin levels in a shorter time period than patients in the oral group. Serum ferritin saturation and ferritin levels were higher in the IV group.	Adverse events were less frequent in the IV group.
Women with post-partum iron deficiency anemia[9]	IV ferrous sucrose (200 mg, given on days 2 and 4) Oral ferrous	IV group: 4 days Oral group: 6 weeks	Increase in hemoglobin levels seen on day 5 in IV group but not in oral group. Hemoglobin levels on day 14	No safety data available.

Table 1: Details of Included Randomized Controlled Trials				
Participants	**Type of iron supplements, dose**	**Duration of treatment**	**Effect on Iron levels**	**Clinical outcomes**
	sulphate (200 mg, twice daily)		were higher in the IV group than t he oral group, and remained higher throughout the study.	
Pregnant women with iron deficiency anemia[10]	IV iron sucrose (dose based on a weight calculation) Oral iron polymaltose complex (300 mg elemental iron, daily)	Not clear in the information provided in the abstract.	Change from baseline in hemoglobin level was higher in the IV group than the oral group at 14 days, 28 days, and on the 1st post-partum day. Ferritin values were higher in the IV group.	No serious adverse reactions in either group.
Pregnant women with iron deficiency anemia[11]	IM iron sorbitol (250 mg, every 4-6 weeks) Oral elemental iron (100 mg, daily)	36 weeks	Improvement in hematocrit, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, serum iron, and total iron binding capacity were similar in both groups.	Obstetric outcomes were similar in both groups.

IM = intramuscular; IV = intravenous; L = litre; mg = milligram; mL = milliliter; ng = nanogram; NR = not reported

REFERENCES SUMMARIZED:

Health technology assessments
No literature identified.

Systematic reviews and meta-analyses

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Randomized controlled trials

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11. Kumar A, Jain S, Singh NP, Singh T. Oral versus high dose parenteral iron supplementation in pregnancy. Int J Gynaecol Obstet. 2005 Apr;89(1):7-13. PubMed: PM15777891

Guidelines and recommendations

12. National Guideline Clearinghouse [Internet]. Rockville (MD): National Guideline Clearinghouse; c2009 -. Anemia in pregnancy; 2008 Jul [cited 2010 Jun 28]. Available from: http://www.guideline.gov/summary/summary.aspx?doc_id=13320&nbr=006764&string=006764

13. U.S. Preventive Services Task Force (USPSTF). Screening for iron deficiency anemia - including iron supplementation for children and pregnant women [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2006 May. [cited 2010 Jun 28]. Available from: http://www.ahrq.gov/clinic/uspstf/uspsiron.htm
Summary available: http://www.guideline.gov/summary/summary.aspx?doc_id=9274

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APPENDIX – FURTHER INFORMATION:

Randomized controlled trials

14. Bopche AV, Dwivedi R, Mishra R, Patel GS. Ferrous sulfate versus iron polymaltose complex for treatment of iron deficiency anemia in children. Indian Pediatr. 2009 Oct;46(10):883-5. PubMed: PM19430060

Review articles

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Additional references

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