Daily Versus Weekly Oral Iron Supplementation in Pregnant Women
(A Randomized Controlled Clinical Trial)

Thesis

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By

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List of Contents

List of Abbreviations

Abbr.	Full term
CBC	Complete blood count
DCT	Divalent cation transporter
DMT-1	Divalent metal transporter-1
DNA	Deoxyribonucleic acid
ED	Emergency department
EDTA	Ethylene diamine tetraacetic acid
GDS	Gastric delivery system
Hb	Hemoglobin
HIV	Human immunodeficiency virus
HUS	Hemolytic-Uremic Syndrome
IDA	Iron deficiency anemia
IMP	Integrin-mobilferrin pathway
LBW	Low birth weight
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
PDR	Physicians' Desk Reference
RBC	Red blood cell
RDW	Red cell distribution width
SFT	Stimulators of iron transport
STRs	Serum Transferrin receptors
TIBC	Total iron-binding capacity
TRs	Transferrin receptors
TTP	Thrombotic thrombocytopenic purpura
UNICEF	United Nations Children's Emergency Fund
WBC	White blood Cells
ZPP	Zinc protoporphyrin

List of Tables

List of Figures

INTRODUCTION

It is estimated that 38.2% of pregnant women are anemic worldwide ***(WHO, 2015)***, which translates to 32.4 million pregnant women. Half of the global anemia prevalence is assumed to be due to iron deficiency in non-malaria areas ***(Stevens et al., 2013).***

Anemia during pregnancy is diagnosed if a woman's hemoglobin (Hb) concentration at sea level is lower than 11 g/dL, although it is recognised that during the second trimester of pregnancy, Hb concentrations diminish by approximately 0.5 g/dL ***(WHO, 2011).*** This is due to iron deficit intake of diet that could not meet the increased iron demand for the developing fetus. Regulation of iron is a highly sophisticated phenomenon where its imbalance could result into significant morbidity and mortality. The disturbed intricate balance during iron regulation may either result in iron deficiency or iron overload, out of which iron deficiency is most commonly observed ***(Zimmermann and Hurrell, 2007).***

The most common strategy for the management of this staggering situation is to start oral iron supplementation during pregnancy . Iron consumption for pregnant women is

undesirable, because of the side effects. The probable cause is the effect of oxidative stress of high doses of Iron, which leads to gastrointestinal intolerance ***(Schaefer et al., 2007).*** Exposing intestinal cells to supplemental iron less frequently, (e.g. every week in synchrony with the human mucosal turnover that occurs every five to six days) may improve the efficiency of absorption since the mucosal cells are not "blocked" by large amounts of iron as may occur with daily iron intake ***(Anderson et al., 2005).***

Significant equality and reduced side effects have been reported in several epidemiological studies in comparing the weekly prescription of iron with daily supplementation ***(Schaefer et al., 2007).*** Thus, weekly rather than daily administration of iron has been proposed as a safe, beneficent, and cost-effective method to prevent and alleviate anemia in pregnant women ***(Arch med Res, 2006).***

Intermittent oral iron supplementation (i.e. one, two or three times a week on non-consecutive days) is recommended as an alternative to daily iron supplementation in pregnant women ***(WHO, 2012).*** So this study was designed to compare between the hemoglobin levels, side effects and compliance in pregnant women receiving weekly versus daily oral iron supplementation.

Research question:

In pregnant women, Is weekly oral supplementation equally effective to daily oral iron supplementation?

Research Hypothesis:

In pregnant women, weekly oral iron supplementation may be equally effective as daily oral iron supplementation with less side effects and more tolerability!

Aim of The Work

Primary aim:

This study aims to assess the efficacy and tolerability of weekly versus daily oral iron supplementation in pregnant women.

Secondary objectives :

1- Comparison between the hemoglobin levels in pregnant women receiving weekly versus daily iron supplementation.

2- Comparison between both groups regarding side effects and compliance.

Anemia

Anemia is strictly defined as a decrease in red blood cell (RBC) mass. The function of the RBC is to deliver oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs. This is accomplished by using hemoglobin (Hb), a tetramer protein composed of heme and globin. Anemia impairs the body's ability for gas exchange by decreasing the number of RBCs transporting oxygen and carbon dioxide. Anemia, like a fever, is a symptom that requires investigation to determine the underlying etiology. Often, practicing physicians overlook mild anemia. RBCs are lipid membranes encasing Hb and are supported by a cytoskeleton. Abnormalities of the membrane, the chemical composition of the Hb, or certain glycolytic enzymes can reduce the life span of RBCs to cause anemia ***(Maakaron et al., 2018).***

Anemia in pregnancy is a major public health problem, especially in developing countries. It affects 41.8% of pregnant women globally, with the highest prevalence in Africa (57.1%) which corresponds to 17.2 million. Different studies have shown different prevalence of anemia during pregnancy ranging from 16.6–95.0% ***(Gedefaw et al., 2015).***

Anemia in pregnant women has severe consequences on health, social, and economic development ***(Tadesse et al., 2017)***.

Anemic pregnant women will be at risk of low physical activity, increased maternal morbidity and mortality, especially those with severe anemia ***(Gedefaw et al., 2015)***.

In addition, both pregnant women and their neonates encounter negative consequence including fetal anemia, low birth weight (LBW), preterm delivery, intrauterine growth restriction and perinatal Mortality ***(Tadesse et al., 2017)***.

Classification of anemias:

A. Morphological classification:

Based on appearance of RBCs under the microscope of red blood cell indices.

Normochromic, normocytic anemia (normal MCHC, normal MCV) (Kulkarni and Srinivas, 2018):

These include:

1. Anemias of chronic disease
2. Hemolytic anemias (those characterized by accelerated destruction of RBC'S).
3. Anemia of acute hemorrhage.

4. Aplastic anemias (those characterized by disappearance of RBC precursors from the marrow).

Hypochromic, microcytic anemia (low MCHC, low MCV) (Chaudhry and Kasarla, 2019):

These include:

1. Iron deficiency anemia
2. Thalassemias.
3. Lead poisoning anemia.
4. Sideroblastic anemia.
5. Anemia of chronic disease (rare cases)

Normochromic, macrocytic anemia (normal MCHC, high MCV):

These include: vitamin B12 deficiency and folate deficiency ***(Aslinia et al., 2006)***.

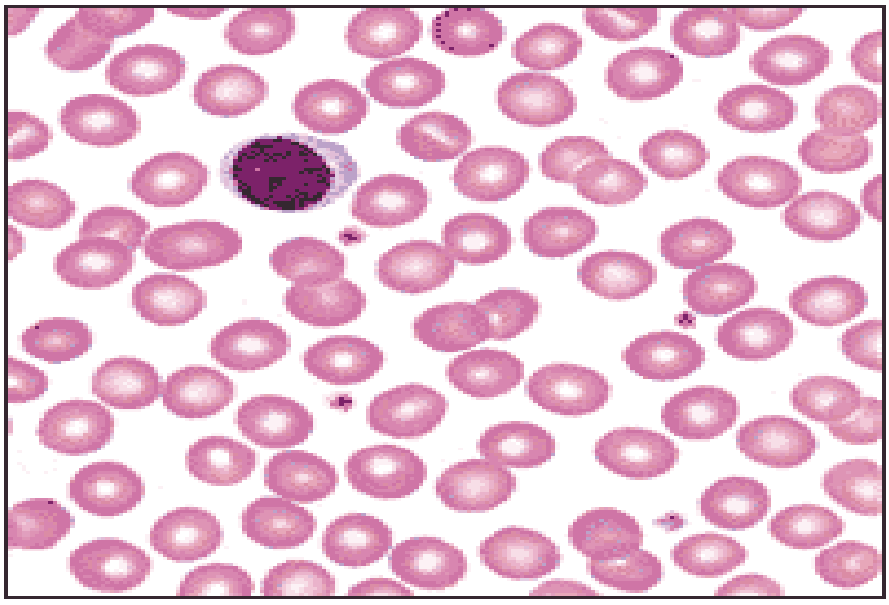

Figure (1): Normocytic normochromic anaemia
(Kulkarni and Srinivas, 2018)

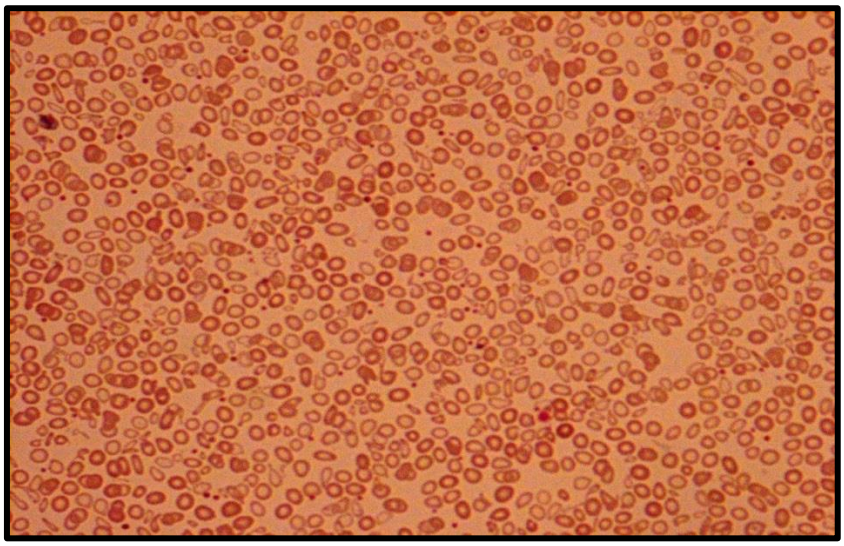

Figure (2): Hypochromic Microcytic Anaemia
(Chaudhry and Kasarla, 2019)