WEEKLY VERSUS DAILY ORAL IRON SUPPLEMENTATION IN NONANEMIC PREGNANT WOMEN

Protocol of a Thesis
Submitted for Partial Fulfillment of Master Degree in obstetrics & Gynecology

By

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Introduction

Pregnant women are at particular risk of developing anemia because of the added iron requirement during pregnancy. Increasing the effectiveness of iron supplementation program is the most practical short-term approach to alleviating the problem (**Mukhopadhyay et al., 2004**).

The main hazards of routine iron supplements are a high incidence of undesirable side-effects, leading to poor compliance. High doses of iron lead to gastrointestinal intolerance suggesting some toxic effect on the gut mucosa that is probably mediated by iron-related oxidative stress. Recent study have shown that both iron deficiency and daily iron supplements increase lipid peroxidation in rats, and studies are being conducted to document similar effects in humans **(Knutson et al., 2000)** . Large doses of iron are also associated with a reduction in the absorption of other elements, such as zinc **(Solonomos et al., 1983)**. Study in humans indicate that administration of oral iron impairs the absorption of a subsequent iron dose **(O'Neil-Cutting et al.,1987)**.These results have motivated a few experimental studies that have searched for alternative efficacious iron supplementation schemes that will minimize undesirable side-effect **(Beard JL 2000)** .

In the rat model, administration of iron supplements is synchrony with gut mucosal turnover rates (every 3 days) have been shown to be equally effective at correcting IDA as daily supplementation. **(Viteri et al., 1995)** Furthermore, intermittent supplementation reduces the constant gut mucosal iron load that accompanies daily supplementation and improves the efficiency of iron absorption 2.6-fold. **(Viteri et al., 1995)** In humans, gut mucosal turnover occurs every 5-6 days. Based on these results, weekly rather than daily administration of iron has been proposed as a safe, efficacious and cost-effective method with which to prevent and alleviate anemia in pregnant women **(Casanueva et al., 2006 & Ridwan et al.,1996)** .

Aim of the work

The purpose of this study was to compare the hemoglobin level in non anemic pregnant women receiving weekly versus daily iron supplementation.

Material & Methods

- This study will be conducted in Ain-Shams University Maternity hospital at the antenatal clinic.
- **Type of study :**
  A prospective randomized controlled clinical trial.

Inclusion criteria :

1- Pregnant women before 20 weeks of gestation .
2- No prior intake of iron supplements in the current pregnancy.
3- Hemoglobin level ≥ 11 g/dL.

Exclusion criteria: were:

1. Hemoglobin level < 11 g/dL.
2. History of chronic renal disease .
3. History of chronic liver disease.
4. Chronic peptic ulcer.
5. Bleeding piles.
6. Known Thalassamia and other hemoglobinopathies.
7. Multiple pregnancy.
8. History of prior blood transfusion in the current pregnancy.
9. History of obstetric hemorrhage in the present or past pregnancies.
10. Pregnant women who cannot tolerate oral iron intake.

- **Sample size calculation :**

  A sample size of 70 patient in each group would have 80% power to detect a difference in a mean of 2g / dL in hemoglobin (The difference between the anticipated daily supplementation mean 12 g / dL and the weekly supplementation mean 10 g / dL). (**Mukhopadhyay et al., 2004& Casanueva et al.,2006**)

- After taking an informed consent , all participants will be randomly assigned to either group by computer – generated selection using consecutively numbered sealed envelops :
  - **Group A :** (weekly group) will receive 2 capsules of 100 mg elemental iron (from 305mg ferrous fumarate) plus 2 mg of folic acid (Ferro – 6 – Pharco – Egypt) once weekly .
  - **Group B :** (daily group) will receive one capsule of 100 mg elemental iron (from 305mg ferrous fumarate) plus 2 mg of folic acid (Ferro – 6 – Pharco – Egypt) once daily .

- All participants will be subjected to the following :

1-Full history taking particularly regarding the intake of iron containing foods.

2-Confirmation of gestational age using the date of the last menstrual period (LMP) and to be confirmed by U / S .

3-Routine antenatal investigation at the first visit (14–20 weeks) including complete blood count (CBC).

4-Follow up visit will be arranged in the same antenatal clinic every month till 32weeks then every 2weeks till 36 weeks then weekly till delivery.

5- Iron supplementation will be started between 14 and 20 weeks of gestation and will be continued until delivery.

6- CBC will be done after one and three months from starting supplementation and a final one will be done at 36 weeks of gestation.

7- The participants will be instructed to bring back their empty packets at each antenatal visit and the total number of tablets consumed during pregnancy will be calculated.

8- Symptoms related to iron intake e.g ; nausea , vomiting and bowel disturbances …….. etc, will be recorded (in the weekly supplementation group related to iron intake during the 24 hours after the intake will be recorded) .

9-The results will be tabulated and statistically analyzed.

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الملخص العربي

يعتبر فقر الدم الناتج عن نقص الحديد في الدم من أكثر أمراض سوء التغذية انتشارا في العالم وخصوصا في الحوامل نظرا لزيادة احتياج الجسم للحديد في أثناء فترة الحمل .
ولذلك يتم إعطاء الحديد يوميا للحوامل كبرنامج لمنع حدوث فقر الدم الناتج عن نقص الحديد ولكن هذا البرنامج يقابل العديد من الصعوبات نتيجة لعوامل عدة ومنها الأعراض الجانبية للحديد المتمثلة في اضطرابات الجهاز الهضمي والغثيان وقلة وعى المرضى مما يؤدى إلى عدم انتظام المريضة في تعاطى الحديد بانتظام يوميا .
وقد أجريت بعض الدراسات العملية لاستخدام الحديد مرة واحدة أسبوعيا . مما حدا بنا إلى اختبار مدى فاعلية استخدام الحديد مرة واحدة اسبوعياً ومقارنة ذلك باستخدامه يوميا في منع حدوث فقر الدم الناتج عن نقص الحديد.
وفى هذه الدراسة سوف يتم إعطاء مجموعة من المرضى الحديد مرة واحدة أسبوعيا .
وإعطاء مجموعة أخرى الحديد يوميا بداية من ١٤-٢٠ أسبوع من بدء الحمل وحتى نهاية الحمل ولذلك سوف يتم تقسيم المرضى عشوائيا إلى مجموعتين:

١- مجموعة (ا)
يتم إعطاء ٢٠٠مجم من الحديد أسبوعيا مرة واحدة .

٢- مجموعة (ب)
يتم إعطاء ١٠٠مجم من الحديد يوميا مرة واحدة.

وسوف يتم عمل صورة دم كاملة في بداية الدراسة لكل الحالات المشاركة في الدراسة قبل البدء ، ثم بعد شهر وبعد ثلاثة اشهر من بدء تعاطى الحديد وأخيرا عند إتمام ٣٦اسبوعا من بدء الحمل.
وسوف يتم مقارنة نتائج المجموعتين لمعرفة ما إذا كان نظام إعطاء الحديد أسبوعيا كافي لحماية الحوامل من التعرض لفقر الدم الناتج عن نقص الحديد وتجنب الآثار الجانبية للجرعات الكبيرة للحديد نتيجة التعاطي للعقار يوميا.

المقارنة بين إعطاء الحديد بالفم مرة واحدة أسبوعياً وإعطاءه يومياً أثناء الحمل

خطة رسالة توطئة للحصول على درجة
الماجستير في أمراض النساء والتوليد

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List of Abbreviations

Anti-PLA .....Anti-platelets anti-bodies

ATP .....Adenosine tri-Phosphate

BFU .....Burst forming units

CFC .....Colony forming cells

CFU .....Colony forming Unit

2.3 – DPG 2,3-diphosphoglycerate

DMT1 .....Divalent metal transporter 1

DNA .....Deoxyribonucleic acid

DRIs .....Dietary reference intakes

EDTA .....Ethylenediamenetetraacetic acid

Fe2+ .....Ferrous ion

Fe3+ .....Ferric ion

FEP .....Free erythrocyte Protoporphyrin

Fl .....Femtolitre

GDS .....Gastric delivery system

HFE .....Human hemochromatosis protien

HIV .....Human immunodeficiency virus

HLA .....Human leucocytic antigen

IDA .....Iron deficiency anemia