

# Short time effect of Chemiron® (A combination iron preparation), single iron, and different magnesium salts on plasma. Magnesium concentration during early pregnancy in Nigerian women. A preliminary report

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## Summary

Maternal magnesium requirements increase during pregnancy because of the synthesis of new tissue – both fetal and maternal. Magnesium takes part in almost 300 enzymatic reactions in the human body and regulates membrane permeability and protein biosynthesis by promoting initiation and dissociation factors. The absorption velocity of magnesium differs from one tissue to another in animal experiments. It is highest in the liver, kidney, heart and is low in skeletal muscle, the brain and erythrocytes. It obeys and follows the Michaelis-Menten Kinetic law. 15 mmol of magnesium is consumed daily depending on the types of food taken in. The main sources of magnesium are vegetables and meats. Many Nigerian women are not able to afford enough of these. The amount of magnesium reabsorbed depends on the magnesium intake and not on magnesium needed which is about 10-40% of the intake. In this study, we examined the short-term effect of magnesium aspartate HCL (614.18 mg/MG), magnesium diasporal (magnesium citrate 610 mg + magnesium laevalitat 30 mg = 100 mg magnesium = 8.2 mval), ferrous gluconate (300 mg) plus folic acid and chemiron, a new combination hematonic agent (ferrous fumarate 300 mg, folic acid 5 mg, vitamin B12 10 mg, vitamin C 25 mg, magnesium sulfate 0.3 mg and zinc sulfate 0.3 mg) on plasma magnesium concentration during early pregnancy in Nigerian women.

Significant increases of plasma magnesium concentrations were found in these groups (magnesium aspartate HCL,  $0.83 \pm 0.12$  to  $0.96 \pm 0.14$  mmol/l, magnesium diasporal  $0.843 \pm 0.14$  to  $0.891 \pm 0.14$  mmol/l and chemiron  $0.848 \pm 0.16$  to  $0.866 \pm 0.16$  mmol/l after five days. The ferrous gluconate and folic acid treated group showed no significant changes. This study shows that a chemiron supplement leads to increased magnesium plasma levels whereas ferrous gluconate and folic acid do not. These results suggest that the low level of magnesium is a normal physiological adjustment of pregnancy and that iron supplementation does not influence this unless magnesium salt is given.

*Key Words:* Combined Iron (Chemiron®; Single Iron; Magnesium Oral Therapy; Magnesium Concentration; Early Pregnancy.

## Introduction

The subject of magnesium deficiency in pregnancy and its effects on the offspring has been reviewed in several publications [15, 22]. It is established that magnesium levels in blood plasma or serum are lower in pregnant than in non-pregnant women, but the physiological significance of this observation is still under clinical study worldwide [1-4, 11, 17, 19, 28].

The maternal magnesium requirement increases during pregnancy because of the synthesis of new tissue, both fetal and maternal. Balanced studies have suggested that there is an accumulation of magnesium in pregnant women of approximately 1 gram at the 10<sup>th</sup> lunar month. The needs of the foetus for magnesium are especially great during the third trimester because of its rapid rate of growth and the increasing concentration of magnesium in the tissue [15].

Experimental studies with rats have demonstrated that a diet deficient in magnesium, although adequate in all other nutrients, causes a variety of problems depending

on the severity of the deficiency. These include foetal death, malformation, foetal anaemia, difficulty of labour and neonatal abnormalities.

Although intensive care has resulted in an important increase in neonatal survival rates, preterm delivery is still the cause of most neonatal morbidity. Although magnesium has had its place in obstetrics in the management of eclampsia since the beginning of the century, a connection with preterm labour was only recognised in the 1960's [12].

The role of magnesium in obstetrics was reactivated by the observation that supplemental magnesium therapy allowed a considerable reduction in the dose of beta-mimetic agents used for tocolysis of preterm labour [23]. Based on this finding, Conradt in 1984 [10] showed in a retrospective study that in association with magnesium supplementation 30-50% of normally ingested magnesium is absorbed. Magnesium is efficiently absorbed in both the jejunum and the ileum, however, ileal uptake is slightly more required than jejunal uptake [18]. Intestinal absorption of magnesium appears to involve an active and passive transport system. The exact transport mechanism involved in intestinal magnesium absorption is contingent on vitamin D and its metabolite 1-25-hydrogen

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vitamin D which have been shown to eliminate magnesium absorption but to a lesser extent than calcium [5, 6, 7, 14, 21, 25, 27, 29]. It is known that magnesium absorption is impaired by a protein and calcium rich diet, and also by alcohol consumption or by excessive phosphate or fat intake in the diet. About 40-70% of orally taken magnesium is lost in the feces. A more sensitive degree of magnesium regulation occurs at the renal level. In a normal state, the kidney filters approximately 2.5 g of the magnesium and reclaims 95%, excreting some 100 mg/day in the urine to maintain homeostasis. Under conditions of deprivation, the kidney conserves magnesium and excretion can decrease to less than 12 mg/day.

In this study we report the effect of different hematonic therapy including Chemiron®, a new combination hematological agent, and oral magnesium salt therapy on plasma magnesium concentrations in the first 5 days of treatment during the first trimester.

### Method and Materials

A total of 30 patients were studied. Group I, consisted of 9 patients treated with Chemiron, one capsule daily. The ages of the patients varied between 21 and 35 years ( $27.4 \pm 6.3$  mean  $\pm$  SD years). Each capsule of Chemiron contained ferrous fumarate (300 mg), folic acid (5 mg), vitamin B12 (10 mg), vitamin C (25 mg), magnesium sulfate (0.3 mg) and zinc sulfate (0.3 mg). The gestational age in this Chemiron group ranged between 8-14 weeks. Group II consisted of 6 normal pregnant patients treated with ferrous gluconate (300 mg), one tablet twice daily and folic acid (0.5 mg), one tablet daily. The gestational age ranged between 9-15 weeks. The ages varied between 19-34 years ( $26.3 \pm 7.3$  mean  $\pm$  SD) years. Group III consisted of 7 normal pregnant patients treated with magnesium diasporal

(magnesium citrate, 610 mg + magnesium laevalinate 30 mg = 100 mg magnesium = 8.2 mval) one tablet daily. The gestational age ranged between 8-15 weeks. The ages varied between 19-35 years ( $25.3 \pm 6.8$  mean  $\pm$  SD years). Group IV consisted of 8 normal pregnant patients treated with Mg asphat HCL (Magnesiocard) one tablet daily (614, 18 mg Mg). The gestational age ranged between 9-15 weeks. The age varied between 22-32 years ( $23.9 \pm 4.9$  mean  $\pm$  SD years). All patients were invited to the Labour Ward of Lagos University Teaching Hospital, Lagos by the appointment clinic.

Venous blood samples were taken before, after 30 minutes, 90 minutes and 120 minutes during the various therapy regimens, centrifuged and stored at  $-20^{\circ}\text{C}$  before being assayed by atomic-absorption spectrometry.

### Results

As can be seen in Fig. 1 a significant increase ( $p < 0.05$ ,  $p < 0.01$ ) in the plasma concentration of magnesium was seen more under Mg-Asphat HCL, Magnesium Diasporal (magnesium citrate 610 mg + magnesium laevalinate 300 mg = 100 mg magnesium = 8.2 mval) than the Chemiron (ferrous fumarate 300 mg, folic acid 5 mg, vitamin B12 10 mg, vitamin C 25 mg, magnesium sulfate 0.3 mg, zinc sulfate 0.3 mg) treated group. The ferrous gluconate plus folic acid treated group showed no significant changes.

### Discussion

The concentration in plasma of an orally taken magnesium combination is through its reabsorption and limited laxatant effect [9, 13]. Animal experiments conducted by Wischnik (30) showed that the asphat HCL compound

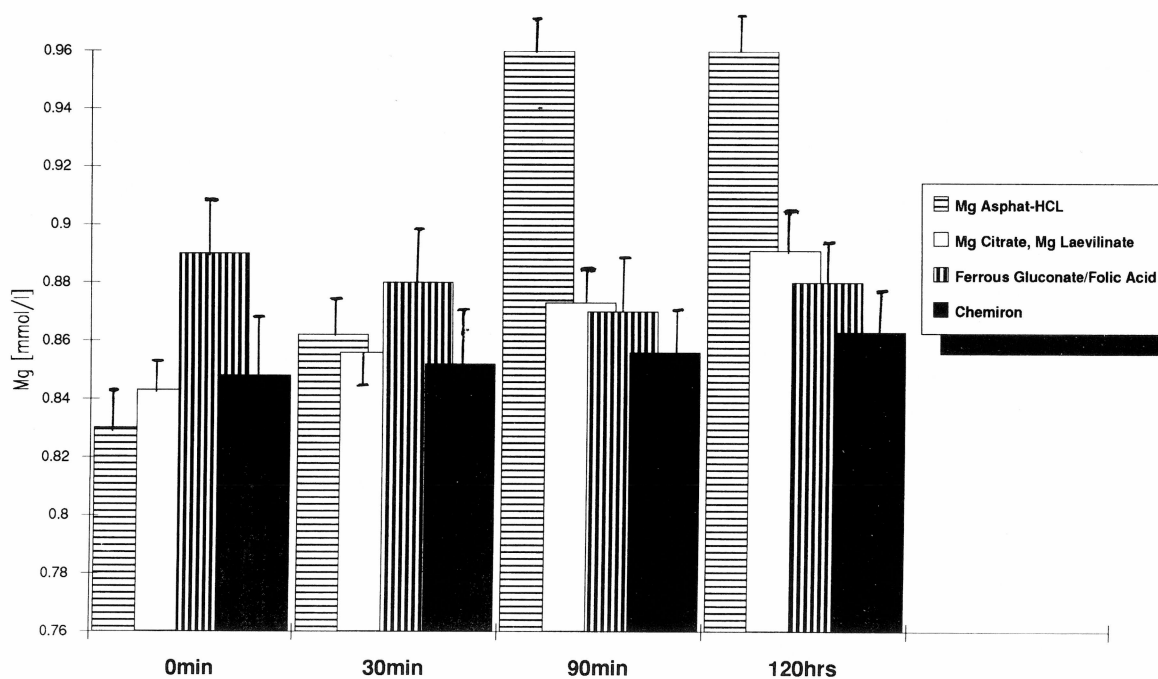


Figure 1. — Plasma Magnesium concentration under Mg-Asphat-HCL, Mg Laevalinate & Mg Citrate, Ferrous Gluconate/Folic-Acid, and Chemiron therapy.

was the best. Asphat acid has a high level in the intracellular space, where it is almost 200 times more concentrated than in plasma. Asphat acid permits an accelerated penetration through the cell membrane to the cations it binds to [20, 24].

In this study all the magnesium containing groups showed a significant increase in plasma magnesium levels, although there were differences in treatment before a significant change was noticed in the plasma. These could be explained through different concentrations of magnesium in the different compounds and the properties of the different salt components. More studies are needed to be able to explain the mechanism of magnesium absorption during early pregnancy using different magnesium salts with different magnesium concentrations in early human pregnancy.

The results suggest that a low level of magnesium is a normal physiological adjustment of pregnancy and that iron supplementation does not influence this except if magnesium salt is given.

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