

The Role of a Parenteral Multivitamin Preparation (Eldervit-12[®]) in the Prevention of Anaemia in Pregnancy

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Abstract

Context: Over half of all women in developing countries develop anaemia during pregnancy. It is a significant contributory factor to maternal morbidity and mortality.

Objective: To determine if the administration of a parenteral multivitamin preparation (Eldervit 12 R) in pregnancy is effective in reducing the prevalence of anaemia in pregnancy.

Materials and Methods: A prospective, randomized controlled trial using patients pooled into study and control groups receiving Eldervit-12 injections and oral multivitamin preparations respectively. One hundred patients were recruited into each group. Baseline Haemoglobin concentration and reticulocyte count were done at the time of recruitment and repeated at 36 weeks gestation.

Results: The changes from baseline to final value in the Haemoglobin concentration (9.7 - 11.7g/dl) and reticulocyte count (2.1 - 3 %) were higher in the study than in the control group (9.8 - 10g/dl and 2.2-3 % respectively). The final Haemoglobin concentration and reticulocyte count of the study group (11.7 g/dl and 5.3 % respectively) were significantly higher than in the control group (10.0 g/dl and 3.0 % respectively). In the study group 9.7% of patients were anaemic (WHO Definition) while in the control group 75% remained anaemic at 36 weeks gestation. Overall the drug was well tolerated.

Conclusion: This study suggests that the use of Eldervit-12 in pregnancy can significantly reduce the prevalence of anaemia in the later stages of pregnancy.

Key Words: Anaemia, Pregnancy, Eldervit-12 injection, Haemoglobin, Reticulocytes.

Introduction

It is estimated that over half of all women in developing countries develop anaemia during the course of their pregnancy¹. It is the most common nutritional problem among pregnant or lactating women². Anaemia has also remained a significant contributing factor to maternal morbidity and mortality. It is said to be one of the four major causes of maternal deaths in Nigeria and is associated with high fetal wastage³. The main causes of anaemia in pregnancy in Nigeria have been identified as haemolysis of red blood cells by malaria infection, and folic acid and iron deficiency⁴.

The World Health Organisation defined anaemia in pregnancy as a level of haemoglobin of 11g/dl or less⁵. Globally it has been shown that 30-60% of pregnant women go into labour anaemic with a haemoglobin of less than 11g/dl or packed cell volume (PCV) of less than 33%⁶. In the West African sub region (which includes Nigeria), most hospitals regard a level of 10 g/dl or less as representing anaemia^{7,8} hence reducing further an internationally accepted level. The justification is based on studies in Nigeria which showed that the number of low birth weight babies and perinatal mortality increase as Haemoglobin concentration drops from 10 g/dl⁸. Despite this reduced value, the incidence of anaemia in pregnancy is still high in these areas with the unacceptable negative impact on fetal outcome which includes miscarriage, low birth weight babies and high infant mortality⁶.

The iron demand on the mother and fetus in pregnancy is quite high. The reason behind the failure of women to achieve an erythropoietin response sufficient to compensate for anaemia that develops in pregnancy is not fully understood. To prevent this, most clinicians advocate prophylactic iron supplements in pregnancy. In economically deprived communities the cost of the supplements may be prohibitive. Ignorance and inadequate ingestion may also contribute to slow response to medication. A major pitfall in the prevention of anaemia in pregnancy in our environment is that our patients cannot be relied upon to take their drugs according to prescription, once outside medical supervision⁴.

Most studies and reports on anaemia in pregnancy in Nigeria have utilized preventive and therapeutic measures based on oral iron and multivitamin supplements. This route of administration has not shown a regular and consistent improvement in anaemia in pregnancy, probably due to poor patient compliance. A recent report⁹ on parenteral administration of Eldervit-12 (provided by Elbe Pharma. Ltd) has been suggestive of enhanced erythropoietic response. This

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pilot study was therefore conducted to determine its acceptability and efficacy in reducing the prevalence of anaemia in pregnancy compared to the traditional oral haematinics used in pregnancy.

Aims and Objectives

(1) To determine the mean Haemoglobin concentration {Hb} and the mean reticulocyte count during the study period. This would determine if the administration of Eldervit-12 would reduce the number of pregnant women going into labour anaemic.

(2) To compare the fetal outcome in the two groups.

Materials and Methods

This was a prospective, randomized controlled trial conducted between 2nd October 2004 and 30th April 2004. This study was approved by the ethical committee of the Abia State University Teaching Hospital (ABSUTH). Informed consent was obtained from each patient after the treatment was explained to her. All drugs used had the National Agency for Food and Drug Administration (NAFDAC) approval.

ABSUTH is a tertiary teaching hospital situated in the commercial city of Aba in Abia State. Aba has a population of approximately 1.5 million. The hospital offers treatment to all classes of patient without any restrictions. The annual delivery rate in the hospital is about 1,000 and most of the patients are women who booked with us for antenatal care.

All the patients involved in this study were booked for antenatal care. Certain inclusion and exclusion criteria were strictly adhered to in patient selection.

Inclusion criteria included:

- (1) Pregnancy of 20 or more weeks of gestation
- (2) Ability to understand and sign informed consent
- (3) Willingness to consent to laboratory investigations and blood transfusion if indicated
- (4) Acceptance of parenteral route of drug administration
- (5) Ability to tolerate oral iron tablets.

The exclusion criteria included:

- (1) Proven case of human immune deficiency virus (HIV)
- (2) Psychiatric illness
- (3) Sickle cell disease (DSD) or any other form of haemoglobinopathy
- (4) Refusal to give informed consent.

Patients who qualified for the study were randomized using a ballot system and classified into two groups. A total of 100 patients were recruited into each group. The study group patients had injectable multivitamin (Eldervit -12). Eldervit-12 contains vitamin C (150mg), Vitamin B12 (2500 mg), folic acid (0.7mg) and Niacinamide (12mg). This drug comes in two different ampoules which are withdrawn and mixed in one

syringe and administered intramuscularly. Each patient received one injection, at two weekly intervals, while the second group which served as controls, were treated orally with multivitamin tablets, one eight hourly and folic acid tablets 5mg daily for the duration of the pregnancy. Both groups of patients received oral Iron in a routine daily dose of 200mg three times daily. Patients in both groups were seen at fortnightly intervals for the duration of the study. No attempt was made as matching the patients for age and parity since these variables were not necessary in evaluating the individual response to the different modalities of treatment.

Out of 100 patients recruited in each group, 82 and 56 were followed up to 36 weeks in the study and control groups respectively. The data collected from the patients included baseline Haemoglobin concentration, reticulocyte count at the time of recruitment, Haemoglobin concentration and reticulocyte count at 36 weeks gestation, mode of delivery, maternal/fetal outcome and patients reaction to Eldervit-12 injection. The data were subjected to statistical analysis using SPSS software package where relevant and the t-test was used to test for significance at 5% level.

Results

The mean of the baseline haemoglobin for the study and control groups were 9.7g/dl \pm 0.37 and 9.8g/dl \pm 0.77 respectively; with no marked difference. Similar observations were made for the baseline reticulocyte count for the study and control groups of 2.1 \pm 0.17 and 2.2 \pm 0.24 respectively. Table 1 shows the percentage increase in Haemoglobin concentration from the baseline mean to the mean at 36 weeks gestation in the study and control groups. There was a 20.6% increase in Haemoglobin concentration from baseline value in the study group compared to 2% increase in the control group.

Paired t-test was used to compare the difference between the baseline and the final values. There was a significant increase in Haemoglobin concentration. ($t = 14.2, P < 0.05$)

The increase in haemoglobin concentration baseline to final value was greater in the Eldervit-12 (study) group (9.7 to 11.7 \pm SD 0.52 g/dl) than in the control group (9.8 to 10.0 \pm SD 0.78 g/dl). An analysis of the distribution of anaemic patients according to WHO (= 11 g/dl) and African standard (= 10g/dl) definitions of anaemia in the study and control groups at the point of enrolment and at 36 weeks gestation. In the study group 8(9.7%) were regarded as anaemic by WHO standard and none (0%) by African standard at 36 weeks gestation; while in the control group 42(75%) remained anaemic by WHO classification and 30 (56%) by the African standard at 36 weeks gestation.

Table 2 shows the statistical analysis of the mean of the reticulocyte count during the trial at 36 weekly gestation. The change in percentage of reticulocytes from the baseline to the final value was also greater in the Eldervit (study) group (2.1 to 5.3% SD \pm 0.42) than in the control group (2.2 to 3.0% SD \pm 1.97). The final reticulocyte count of the study group was significantly higher than that of the control group (t = 8.2; p<0.05). Fifty four patients in the study group had delivered at Abia State University Teaching Hospital while 29 in the control group had also delivered there. In the study

group, six patients (11.1%) were delivered by Caesarean section while 48 (88.9%) had vaginal delivery. In the control group two women (6.9%) were delivered by Caesarean section while 27 (93%) delivered vaginally. Table 3 shows the pregnancy and fetal outcome in both groups. Z test was used to compare the birth weight of the study and the control group. There was no significant difference. (Z = 1.49, P<0.05) Table 4 shows the reaction to Eldervit-12 injection. Only one patient complained of discomfort at the injection site while the other responses are as shown in the table.

Table 1:
Percentage increase in haemoglobin concentration at 36 weeks gestation from baseline value.

Group	Baseline Value	Value at 36 weeks	% Increase	t- Value	P< 0.05
Study	9.7	11.7	20.6	14.2	1.833
Control	9.8	10.0	2.0		

Table 2:
Statistical analysis of the mean of the reticulocyte count at 36 weeks gestation.

Group	Reticulocyte count (%)		t -value	P < 0.05
	MEAN	*SD		
Study	5.3	\pm 0.42		
Control	3.0	\pm 1.97	8.2	1.833

Table 3:
Pregnancy & Fetal outcome

Outcome	Study group n=54	Control n=29 group	Z- value	P < 0.05
Preterm delivery	-	3 (10.3%)		
Fresh stillbirth	-	2 (9.5%)		
Transfer to special care baby unit	8 (14.8%)	9 (33.33%)		
Congenital abnormality	-	1 (3.5%)		
Birth weight (Mean \pm SD)	3.19 \pm 1.5	3.03 \pm 0.4	1.49	1.96
APGAR Score@ 1 min. (mean \pm SD)	7.04 \pm 1.5	6.93 \pm 1.6	0.31	1.96
APGAR Score@ 5 mins. (mean \pm SD)	8.91 \pm 0.4	8.59 \pm 1.2	1.40	1.96

Table 4:
Patients reaction to Eldervit 12 injection.

	RESPONSES	
	YES	NO
Injection preferred to oral medication	90 (90%)	10 (10%)
Would prefer injection irrespective of cost	80 (80%)	20(20%)
Increase in appetite.	80 (80%)	20(20%)

Discussion

Eldervit-12 injection not only improved the haemoglobin level at 36 weeks gestation compared to the control group, there also seemed to be a superior fetal outcome. Eldervit-12 injection resulted in a remarkable 20.6% increase in Haemoglobin concentration in the study group compared to 2.0% in the control group. The use of the routine combination of oral Iron preparation and multivite tablets instead of placebo was done for comparative purposes. The marked erythropoietic response to pharmacological doses of Eldervit-12 injection is comparable to that obtained from recombinant human erythropoietin administration¹⁰.

The prevalence rate of anaemia in pregnancy by African standard in this study of 59.5% is similar to a report of 58.6% observed by Olodeoku¹¹ and 55.3% observed by Lamina and Sorumnu⁹. In this study a, remarkable difference exists between final Haemoglobin concentration of those receiving Eldervit-12 injection and the control group, (11.7 and 10.0 g/dl respectively). This finding may have been influenced by the patient's acceptability of the drug and its route of administration, which ensured compliance as both groups received essentially the same components but through different routes¹². Eldervit-12 injection, once given is available in the body tissues, thus providing for dietary inadequacy, avoids malabsorption and thus increases iron utilization by the bone marrow. Compliance with oral medication is usually less than that of the parenteral route. This may partly explain the lower Hb in the control group.

The baseline reticulocyte count of 2.1% and 2.2% respectively for the study and control groups is consistent with normal values (0.5-1%) in non pregnant women and 1-2% in pregnant women. This variation may be related to increased pregnancy demand¹³. A significant increase in reticulocyte count in the study group (5.3%) compared with the control group (3%) is a reflection of the erythropoietic function of Eldervit injection since the increase in reticulocyte count with an ongoing treatment is an index of the effectiveness of the treatment.

In view of the fact that both groups received the same dose and frequency of oral iron, it implies that iron alone is not sufficient to increase Hb levels of pregnant women and there is in fact a mineral deficiency anaemia. This is not surprising as vitamins are known to play a vital role in affecting the metabolism of amino acid, carbohydrate and fats and as such are involved in anemias¹⁴. It further proves the effectiveness of Eldervit-12 injection in the stimulation of

erythropoiesis since iron supplementation is not enhanced by intravenous iron^{15, 16}. In the formation of red cells, an active bone marrow requires not only iron and incidental traces of copper for Haemoglobin formation but also folic acid, Vitamin-B12, Vitamin C and Nucleoprotein¹⁷ which Eldervit-12 injection contains.

Only fifty four women in the study group and 29 of the control group delivered in the labour ward of Abia State University Teaching Hospital. The timing of the study encompassed the festive season of Christmas and New Year when the patients might have delivered in their villages. Others might also have gone into labour and delivered in other centres. Although the caesarean section rate in the study group of 11.1% was higher than the 6.9% rate of the control group the numbers involved were too few to draw a meaningful conclusion. Also, the difference cannot be directly attributed to an effect of Eldervit 12 injection, since these rates were even lower than the prevailing caesarean section rate of the hospital (14.4%) during the study period. The preterm delivery rate, fresh stillbirth rate and transfers to the special care baby unit were higher in the control than in the study group. Poor compliance in the control group might have resulted in the relatively low {Hb} of mothers in this group, with resultant poor fetal outcome. The study shows that the drug was well accepted by the participants. Traditional African populations prefer injectable medication hence the high (90%) acceptance rate in the study and most (80%) would prefer the injection irrespective of the cost.

In conclusion, although the study population is relatively small, this study strongly indicates that there is merit for advocating the case for Eldervit 12 injection treatment in pregnancy combined with other aspects of good antenatal care to prevent anaemia in pregnancy. This study has opened up an opportunity for a multicentre trial to have a larger pool and emphatically validate this finding.

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