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Research Article

Milking Versus Delayed Cord Clamping in Full Term Neonates Delivered by Elective Caesarean Section a Randomized Controlled Trial

Abstract

Background: Preterm birth is a major health concern. It is the leading cause of perinatal mortality and morbidity. Besides varied etiology, it may be due to alteration in basic biochemical function of the body at cellular level stating emphasis to trace elements of which magnesium, being one of them. Pregnancy is marked by a state of hypomagnesaemia and varied hypomagnesaemia observed in preterm labor cases.

Aim of the work: The study conducted to find out the relationship between low serum magnesium concentrations with preterm labor.

Methods: It is a cross-sectional case-control study in which eligible participants were 200 pregnant women attended to El Galaa Teaching Maternity Hospital 100 of them admitted in preterm labor (*Case*), while the other 100 had normal antenatal care and completed their pregnancy till 37 weeks at least (*control*), relevant data were extracted from the case records of these women and blood samples were obtained from all participants and serum magnesium levels measured.

Results: The study showed that 36% of the study patients had varying degrees of hypomagnesaemia. The relative risk indicates that preterm labor is 1.83 times higher among the patients with low serum magnesium (less than 1.6mg/dL). The mean difference in serum magnesium levels in both groups was statistically significant ($P < 0.05$).

Conclusion: Low serum magnesium (hypomagnesaemia) is associated with preterm onset of labor. We can, also from this finding, formulate a proposition that would help in preventing preterm labor and birth with the use of prophylactic oral magnesium supplementation among patients with higher risk for development of preterm labor

Introduction

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation (between 20 and 37 completed weeks) [1].

Risk factors for preterm birth include demographic characteristics, behavioral factors, and aspects of obstetric history such as previous preterm birth. Demographic factors for preterm labor include non-white race, extremes of maternal age (< 17 y or >35 y), low socioeconomic status, and low pre-pregnancy weight [1].

Many risk factors may manifest in the same gravida. Methods used for predicting preterm birth include home

uterine activity monitoring (HUAM), assessments of salivary estriol, fetal fibronectin (FFN), the presence of BV, and cervical length assessment [2].

Among high-risk women with a history of one or more spontaneous preterm births (excluding those with multiple gestation, uterine anomalies, and prior cervical surgeries), 20% of patients demonstrated a cervical length shorter than 25 mm by transvaginal ultrasonography at 22–25 weeks. In October 2008, the American college of obstetricians and Gynecologists issued a Committee Opinion stating that progesterone supplementation for the prevention of recurrent preterm birth should be offered to women with a singleton pregnancy and a prior spontaneous preterm birth due to spontaneous preterm labor or premature rupture of membranes, Progesterone

supplementation for asymptomatic women with incidentally identified very short cervical length (< 15 mm) [3].

The risk of neonatal mortality and morbidity is low after 34 completed weeks of gestation; although a trial of acute tocolysis may be initiated; aggressive tocolytic therapy is generally not recommended beyond 34 weeks, due to potential maternal complications. Between 24 and 33 weeks' gestation, benefits of tocolytic therapy are generally accepted to outweigh the risk of maternal and/or fetal complications and these agents should be initiated provided no contraindications exist. Although aggressive tocolysis is not typically used beyond 34 weeks, gestation, clinicians are advised not to deliver patients at this gestation without indication because of a higher risk of neonatal morbidity in infants born at 34-36 weeks' gestation compared with deliveries at 37-40 weeks' gestation [4].

The administration of steroids is recommended in the absence of clinical infection whenever the gestational age is between 24 and 34 weeks' an attempt should be made to delay delivery for a minimum of 12 hours to obtain the maximum benefits of antenatal steroids. However, a randomized clinical trial by Porto et al showed that treatment with corticosteroids at 34-36 weeks of pregnancy does not reduce the incidence of respiratory disorders in newborn infants [5].

Hypomagnesaemia during pregnancy decrease the magnesium level in myometrium and a low magnesium concentration in pregnant human myometrium could be a cause of preterm labor, so magnesium sulfate is widely used as the primary tocolytic agent; Common maternal side effects include flushing, nausea, headache, drowsiness, and blurred vision. The mother should be monitored for toxic effects, such as respiratory depression or even cardiac arrest that can occur at supra therapeutic levels. In addition, magnesium sulfate readily crosses the placenta and may lead to respiratory and motor depression of the neonate [6].

Several observational studies have reported an association antenatal treatment with magnesium sulfate for preterm labor or preeclampsia with a decreased risk of cerebral palsy in low birth weight or preterm infants [7].

Materials and Methods

Sample size

This study was held in the period from March 2013 to July 2015 on 200 pregnant women attended and admitted from the obstetrics department in El Galaa Teaching Maternity Hospital. It was a cross sectional case-control study.

Study design

Sample size grouped as follows:

Group 1 (case): 100 case with preterm labor occurred after 28 weeks and before 37 completed weeks of gestation (3 uterine contraction in 10 minutes or 8 in 1 hour and documented cervical change), Women who had labor pain stopped and pregnancy continued discarded and excluded.

Group 2 (control): 100 women attended to ante natal care outpatient with the same gestational age & parity for achieving prenatal care, Samples were obtained and only women whose birth occurred after 37 weeks consider as (control group).

Venous blood samples were obtained by venipuncture and drawn into plain tube and sent to laboratory prior to every intervention for both group and serum magnesium was assayed.

The reference value for normal serum magnesium is 1.6-2.6 mg/dl, thus low maternal serum magnesium pregnancies are defined as those in which maternal serum magnesium level was below 1.6 mg/dL.

Inclusion criteria

Pregnant women aged 16 to 40 years, singleton pregnancy, gestation age not before 28 weeks best determined according to last menstrual period and/or early fetal ultrasonography.

Exclusion criteria

Evidence of fetal anomalies, intra uterine growth retardation, abruptio placenta, rupture of membranes, tocolytic therapy, severe maternal disease, any uterine or cervical malformation.

Ethical considerations

All the regulations of the ethical committee of El Galaa Teaching Hospital. The reference value for normal serum magnesium is 1.6-2.6mg/dL. Thus, low maternal serum magnesium pregnancies are defined as those in which maternal serum magnesium level was below 1.6mg/dL. The coefficient of variation within and between assays of <5% was used, All quantitative data were entered into a computer and analyzed using SPSS [8], version 17 for windows.

Descriptive statistics were then computed for all relevant data. The association of low maternal serum magnesium with preterm labor was tested using chi-square to determine the difference.

All significances were reported at $p < 0.05$

Results

Table 1 shows that the mean and standard deviation of age in the case and control groups were 29.75 ± 5.24 and 28.63 ± 5.93 , respectively, there was no statistically significant difference between the two groups ($P = 0.098$).

Table 1: comparison between the studied Groups as regard age.

Age	Case(preterm) N%	Control(term) N%	P-value
16-20	7(7)	13(13)	
21-25	15(15)	17(17)	
26-30	33(33)	30(30)	
31-35	27(27)	25(25)	
36-40	18(18)	15(15)	0.098
meanSD (years)	29.75±5.24	28.63±5.93	

Table 2 shows that there was no statistically significant difference between the two groups

In table 3, 36% of the study patients have varying degrees of hypomagnesaemia. It was also revealed that 47% of the case patients had serum magnesium level less than 1.6mg/dL, whereas only 25% of the control patients had this low serum magnesium level.

The relative risk (RR) indicates that the risk of preterm labor is 1.83 times higher among the patients with low serum magnesium (less than 1.6mg/dL). The mean difference in serum magnesium level in both groups was statistically significant ($p = 0.024$).

In table 4 there is no significant difference in the gestational age distribution of women who delivered preterm in the low and normal serum magnesium levels groups, respectively.

In table 5 shows that the occurrence of leg cramps was 44% higher in the hypomagnesaemia group than in patients who had normal serum magnesium levels but no significant difference.

Table 2: comparison between the studied Groups as body mass index.

Body mass index	case(preterm)	Control(term)	P Value
	N%	N%	
overweight	17(17)	14 (14)	0.139
normal	50(50)	57 (57)	
obese	33 (33)	29 (29)	

Table 3: relation between serum magnesium and preterm labor.

Serum magnesium	Case (preterm labor) Labor N (%)	Control(term) N (%)	Total N (%)
<1.6 mg/dL	47(47)	25(25)	72(36)
≥1.6 mg/dL	53(53)	75(75)	128(64)
Total	100	100	200
Mean ± SD(mg/dL)	1.73 ± 0.4	1.93 ± 0.4	1.83 ± 0.4

Table 4: Relationship between serum magnesium and gestational age for women with preterm delivery.

G.A. at delivery(wks)	Serum magnesium levels		p value
	<1.6mg/dL N(%)	≥1.6mg/dL N (%)	
28-29	1 (2.1)	3 (5.7)	0.098
30-31	3 (6.4)	4 (7.5)	
32-33	6 (12.8)	8 (15.1)	
34-35	12 (25.5)	12 (22.6)	
36-37	25(53.2)	26 (49.1)	
Total 47 (100.0)	53 (100.0)		

Table 5: Relationship between serum magnesium and leg cramps.

	Serum magnesium levels		P value
	<1.6mg/dL N (%)	≥1.6mg/dL N (%)	
Leg cramps	131 (131)	69(69)	0.716
Mean± SD	1.88± 0.4	1.80 ± 0.4	

Discussion

While preterm labor is defined as labor that occurs with regular and frequent uterine contractions causing progressive cervical changes before 37 completed weeks of gestation, it accounts for 10– 15% of all pregnancies. The incidence also varies with population studied [2].

The exact cause of preterm labor and delivery remains elusive and is likely to be multifactorial; in 50% of cases it is spontaneous and idiopathic, although several potential risk factors have been identified. The main one among them is premature rupture of membrane (PROM), and others are multiple pregnancy, polyhydramnios, Hypertensive disorders of pregnancy, infections, cervical incompetence, ante partum haemorrhage, fetal and uterine anomalies, anemia, heavy work, smoking, and so forth. It is also related to socioeconomic status and geographic location [9].

Prevention of viable spontaneous preterm birth through screening is one of the key aims of antenatal care as these have implications for child, mother, and society. If women can be identified to be at high risk in early pregnancy, they can be targeted for more intensive antenatal surveillance and prophylactic interventions (primary prevention). However, the disease mechanisms behind these problems are not well understood. Consequently, tests for their prediction and treatments for their prevention are not well developed.

Clinically, it would be useful to be able to predict who will deliver preterm. The predictors may be used in the management of women at high risk for preterm labor such as women with previous preterm labor and also can be used as a part of a management protocol to individualize patient care. Several markers more directly related to preterm labor have recently been proposed, some of which relate to direct causes of preterm labor such as cervical ultrasound measurement, fetal fibronectin (FFN), salivary estriol, serum CRH, and bacterial vaginosis. Several of these have predictive values, which are potentially useful for clinical practice but are at present still subjects of research interests [10].

Besides varied etiology, preterm labor may be due to alteration in basic biochemical functions of the body at cellular level. This supports the need to investigate the association between trace elements and preterm labor. In this regard, magnesium, one of the trace elements, has become the subject of interest.

Hypomagnesaemia during pregnancy decreases the magnesium level in myometrium and a low magnesium concentration in pregnant human myometrium could be a cause of preterm labor.

Rising serum magnesium level serves to relax the uterine smooth muscle, thereby providing the basis for the previous use of magnesium sulphate as a tocolytic agent in pregnancy, although a *Cochrane systematic review* has now concluded that it is ineffective as a tocolytic agent and may even be harmful to the unborn baby [11].

Our aim to investigate whether low maternal serum magnesium during pregnancy may be associated with preterm labor and delivery and there after describe a generic framework for combining this screening information with designing a prophylactic intervention. Several studies have examined the association between maternal serum magnesium levels and preterm labor but . Since we are trying to introduce a predictive test, all women within the usual age range of the Egyptian pregnant population (16–40 years) were included in our analyses, our study found no significant difference in age, parity, and body mass index between the case and control groups which confirmed similarities in the two groups used in the study. The incidence of hypomagnesaemia among the healthy parturient used in the study after excluding most of the major risk factors was found to be 36%. This is slightly lower than the incidence of 46% found among similar number of patients studied by [12].

This difference may be explained by the cut off points for magnesium (1.6 versus 1.9 mg/dL, resp.) used in the two studies.

The main focus of this study is the role of serum magnesium level in preterm labor and its relation with preterm labor.

Past studies and reports have shown a decreased level of serum magnesium in preterm labor. These were corroborated by our study where a reduction in mean serum magnesium level was found in cases of preterm labor (1.73 ± 0.4 versus 1.93 ± 0.4 mg/dL).

This result is also found to be similar to and supported by other investigators. In a study carried out by, the serum magnesium level in preterm labor was found to be 1.67 ± 0.23 mg/dL [13].

Patients with preterm labor had significantly depressed serum magnesium level and the mean was 1.60 ± 0.466 and 1.87 ± 0.3 mg/dL, respectively [14].

The finding from this study is also similar to the result obtained by [6], who found that the mean serum magnesium level in preterm labor cases was 1.4 mg/dL ± 0.22 SD and therefore suggested that the estimation of serum magnesium may prove to be a valuable tool in predicting the preterm onset of labor. A study by [15], also observed that there was significant reduction of serum magnesium (mean 1.77 ± 0.36) in women with preterm labor.

A relative risk of preterm labor was 1.83 among the patients with serum magnesium level less than 1.6 mg/dL compared to those who had a higher magnesium level and the difference was statistically significant ($p = 0.024$) which confirmed the study hypothesis.

There are, however, other studies that found no relationship between maternal serum magnesium level and preterm labor [16].

These studies were supported by systematic reviews and other studies that revealed that the use of oral or parenteral magnesium had no recommended for routine use as tocolysis.

However, reports from various studies showed significantly low serum magnesium levels in women with preterm labor indicating that hypomagnesaemia may in fact be a risk factor for preterm labor.

Conclusion

Low serum magnesium (hypomagnesaemia) is associated with preterm onset of labor, we can then suggest that maternal hypomagnesaemia may be used as a predictor of preterm labor. Further studies are however required to find out the other etiologies of irritability of uterus due to low level of serum magnesium, to evaluate the role of magnesium in preterm labor and the probability of use of low serum magnesium as a marker or predictor of idiopathic group of preterm labor.

This can then form the basis for formulating a proposition in the future for the use of prophylactic oral magnesium supplementation (not parenteral magnesium sulphate) among patients with higher risk for development of preterm labor.

Thus we according to our study we recommend use of oral or parenteral magnesium for delaying or prevent preterm labor and decrease leg cramp.

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