J Obstet Gynecol India Vol. 56, No. 4 : July/August 2006 Pg 311-314

ORIGINAL ARTICLE

The Journal of Obstetrics and Gynecology of India

Selenium levels and glutathione peroxidase activity in spontaneous inevitable abortion

***Panka*j Desai [1], *Purvi* Patel [1], *SP* Rathod [2], *Shailaja* Mahajan [2]**

Deparments of [1] Obstetrics and Gynecology, and [2] Pharmacology, Medical College and Faculty of Technology and Engineering, M.S. University of Baroda.

OBJECTIVE(S) : To determine changes in selenium levels and the glutathione peroxidase activity in the red cells and plasma in women having miscarriage as compared to those in women with normal pregnancy and in nonpregnant women.

METHOD(S) : Blood selenium levels and glutathione peroxidase activity were measured in 30 women presenting consecutively with a miscarriage, in 30 women having a normal pregnancy and in 30 nonpregnant women. In women presenting with miscarriage, the values were repeated after 48 hours of miscarriage. The mean values of each group were compared statistically.

RESULTS : The selenium concentrations in red cells and plasma in women with miscarriage were significantly lower as compared to those in women with normal pregnancy and in nonpregnant women. The glutathione peroxidase activity was also reduced significantly in women with miscarriage. Student t test was employed for statistical evaluation.

CONCLUSION(S) : The reduced selenium concentration and the decreased blood glutathione peroxidase activity may play an important role in the occurrence of spontaneous abortion.

Key words : selenium, glutathione peroxidase, miscarriage

Introduction

The trace mineral selenium is an essential component of the selenoproteins, especially glutathione peroxidase, required for normal health and reproduction. Selenium deficiency in humans can result in an increased susceptibility to viral infections, cancer, cardiovascular disease, miscarriage and impaired male fertility [1].

Various studies have demonstrated that during pregnancy, the whole blood and plasma selenium concentrations, and the activity of glutathione peroxidase in red cells and plasma decline in a linear fashion from the first trimester to parturition, with the lowest levels at delivery [2]. It has also been demonstrated that the requirement of selenium is increased during pregnancy as a result of transport to the growing fetus.

In veterinary practice, idiopathic miscarriage has been shown to be associated with selenium deficiency. In the last few years some studies suggested that miscarriages in women might be related to selenium deficiency [3-5].

We carried out this study to determine the selenium levels in red cells and plasma glutathione peroxidase activity in red cells and plasma, and the concentration of reduced glutathione in red cells in women presenting with spontaneous abortion.

Methods

The subjects were recruited from the department of obstetrics and gynecology between 1st April 2004 and 31st March, 2005. The analysis of blood samples was carried out in the department of pharmacology. Thirty women presenting consequently for spontaneous abortion, 30 normal

Paper received on 14/10/2005 ; accepted on 02/03/2006

Correspondence :
Dr. Pankaj Desai
Guru Krupa
Opp. Alankar Apartments, Dandia Bazaar
Baroda - 390 001.
Tel. 0265 412848 email : meera@wilnetonline.net

pregnant women and 30 nonpregnant healthy women were included in the study. All the 90 women were examined clinically before recruiting in the study. None had any medical or pregnancy related complications.

Group I (n=30) included women presenting with spontaneous inevitable abortion with mean gestational age 12.8 weeks (range 8 to 18 weeks). Fourteen were in the first trimester and 16 in the second trimester of pregnancy. Maternal age ranged from 20 to 28 years (mean 23.5 years). Seventeen were primigravidas, eight second gravidas and five third gravidas. None of the multigravidas had any abortion previously. None of the subjects were having missed abortion. No medications were given to these women before the collection of blood samples. From this group, blood samples were collected twice, first time at presentation with the spontaneous inevitable abortion and second time 48 hours after the spontaneous abortion.

Group II (n=30) included women with normal singleton pregnancy between 8 – 20 weeks (mean 13.2 weeks). Maternal age ranged from 18 to 26 years (mean 23.2 years). Fifteen were primigravidas, 10 second gravidas and five third gravidas. None of the multigravidas had any abortion previously.

Group III (n=30) comprised of healthy nonpregnant women of childbearing age between 20-32 years (mean 23.9 years) who served as controls. Nineteen were primigravidas, eight second gravidas and three third gravidas. None of them had history of miscarriage.

Blood samples (5mL) were collected in EDTA bulb with all aseptic precautions. They were centrifuged at 3000 rpm for 15 minutes. The plasma was extracted and the red cells were washed thrice with an excess of 0.9% prechilled sodium chloride solution. The selenium concentrations in the red cells and plasma were measured spectrophotometrically (SHIMADZU 1601/UV) at room temperature by using 3.3 diaminobenzedene hydrochloride dye. Glutahione peroxidase (GSI-Px) in red cells and plasma were measured by the method of Paglia and Valentine [6]. Reduced glutathione (GSH) was measured by the method of Moron et al [7].

The mean values with standard deviation were calculated for each group. Student t test was used to determine statistical significance which was set at $P<0.001$.

Results

Table 1 shows the demographic parameters of the women in the three groups. The groups were comparable as regards all the variables.

Table 2 shows the mean ± SD values of selenium, glutathione peroxidase activity and reduced glutathione in the three groups under study.

Table 3 shows the statistical comparison (P value) when the various groups were compared with each other with respect to all the parameters under study.

Table 1. Demographic variables.

	Group I	Group II	Group III
Mean maternal age (years)	23.5	23.2	23.9
Mean gestational age (weeks)	12.8	13.2	-
Primigravidas	17	15	19
Multigravidas	13	15	11
Mean weight (kg)	52.5	53.2	51.4

Table 2. Selenium levels and glutathione peroxidase activity.

Groups	Selenium levels ng/mL		Glutathione peroxidase activities		Reduced glutathione µg/mg of protein
	Red cells	Plasma	U/g Hb	U/L Plasma	
Group I (during abortion)	88,69 ± 11.15	70.84 ± 10.34	17.85 ± 2.6	187.89 ± 12.63	28.84 ± 2.17
Group I (48 hours after abortion)	91.81 ± 10.2	69.34 ± 12.57	19.75 ± 2.25	188.15 ± 9.2	33.36 ± 3.29
Group II	96.96 ± 8.87	68.27 ± 8.7	20.93 ± 2.6	234.08 ± 8.5	35.55 ± 2.94
Group III	115.33±9.5	85.62±11.27	21.17±3.45	237.81±9.15	49.46±3.42

All values are given as mean ± SD

Table 3. Statistical comparison between the groups.

Parameter	Group I during abortion compared with after abortion	Group I during abortion compared with Group II	Group I during abortion compared with Group III	Group I after abortion compared with Group II	Group I after abortion compared with Group III	Group II compared with Group III
Red cell selenium	0.0004	<0.0001	<0.0001	0.009	<0.0001	<0.0001
Plasma selenium	0.09	0.002	<0.0001	0.20	<0.0001	<0.0001
Red cell glutathione peroxidase	<0.0001	<0.0001	<0.0001	0.0046	0.001	0.594
Plasma glutathione peroxidase	0.7615	<0.0001	<0.0001	0.0001	<0.0001	<0.0001
Reduced glutathione	<0.0001	<0.0001	<0.0001	0.0001	<0.0001	<0.0001

Discussion

Selenium concentrations in blood are generally diet dependant [8]. The ultimate source of selenium is soil and its geographical distribution varies considerably. The recommended intake of selenium is 60 µg / day for women and its reference range in red cells in healthy adults is 75-240 ng /mL [9,10].

In our study, the mean red cell selenium level in all the groups was within the acceptable range. The red cell selenium levels were significantly lower in women at presentation for inevitable abortion as compared to the levels 48 hours after abortion and to those of the healthy pregnant women as well as the nonpregnant women. Women with a healthy pregnancy also had a significantly lower level of red cell selenium than that in the nonpregnant group (Table 3).

The plasma selenium levels in women with an abortion as well as normal pregnancy were significantly lower than those in the nonpregnant women. Women with an abortion had significantly lower plasma selenium as compared to that in women with normal pregnancy. However, the values at the time of abortion and after 48 hours of abortion did not show a significant decrease.

In farm animals, selenium deficiency has been associated with infertility, abortion, and placental retention [11]. There was a dramatic reduction in the incidence of barren ewes and an increase in the lamb crop when selenium was administered before mating and throughout the pregnancy [12].

Barrington et al [3] suggested that low selenium levels were found in a significant number of women with a single miscarriage. This study was followed by another study by Barrington et al [4] which demonstrated that in women with recurrent miscarriage, serum selenium concentration is significantly lower compared to that in nonpregnant women but significantly higher than that in nonrecurrent miscarriage. Kocak et al [5] also showed similar results.

Theoretically, two mechanisms have been proposed to explain the cause of miscarriage related to selenium deficiency – the loss of antioxidant qualities attributed to selenium leading to damage to the biological membranes and DNA [3] and reduced antithrombin III activity due to selenium deficiency [13].

Over the past few years, interest has been generated in the antioxidant status in normal pregnancy and pregnancy related diseases. Studies have documented a significant rise of antioxidant activity during normal pregnancy [14]. The antioxidant status acts as a physiological barrier against free radical attack. Free radicals have been shown to be associated with DNA changes, which may lead to mutagenesis, cell death and even tumor formation. Selenium is incorporated into the active site of glutathione peroxidase. Glutathione peroxidase catalyses the reduction of hydrogen peroxide and organic hydroperoxides, thus preventing lipid peroxidation of cell membranes and acting as free radical scavenger. Impairment of the antioxidant activity results in oxidative stress of the tissues. During pregnancy, this can lead to pathological conditions like preeclampsia [15,16]. Whether this leads to miscarriage is not yet clear.

In our study, the red cell glutathione peroxidase levels were found to be significantly lower in normal pregnancy when compared to those in the nonpregnant women. At abortion and after abortion, the red cell glutathione peroxidase levels as well as the plasma glutathione peroxidase levels were found to be significantly lower when compared with those in the normal pregnant women as well as in the nonpregnant women. The reduced glutathione levels were also significantly reduced in normal pregnancy as compared to those in nonpregnant women. During abortion the values further reduced and the difference was statistically significant.

A study by Sane et al [17] showed a rise in serum lipid peroxide levels before the onset of abortion and significantly lower values after abortion. A study by

Zachara et al [18] showed lower activities of glutathione peroxidase in women who had miscarriage compared to those in women with viable pregnancy but they found unchanged selenium concentrations. Zachara et al [2] showed that red cell glutathione activity was only nonsignificantly lower. Thus the information available about the antioxidant activity in women having a miscarriage is unclear as of now.

Conclusion

Our study shows that blood selenium concentrations as well as the glutathione peroxidase activity in red cells and plasma were significantly lower in women having abortion as compared to those in normal pregnant women as well as nonpregnant women. However, in view of conflicting results available on the blood selenium concentrations and the glutathione peroxidase activity of pregnant women, further studies are required to investigate the role of selenium deficiency in miscarriage.

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