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Original Article

Pharmaceutical and Biomedical Research

Copper and selenium levels in women with second-trimester induced abortion in Mazandaran, 2009: A case control study

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Received: Nov 8, 2014, Revised: Jan 14, 2015, Accepted: Jan 25, 2015

Abstract

Abortion is the termination of a pregnancy by the removal or expulsion of a fetus or embryo from the uterus, resulting in or caused by its death. Missed abortion is the most common dangerous condition in pregnancy. An abortion can occur due to maternal complications, chronic disease, endocrine disorders, abortificient drugs, radiation, heavy metals and toxins. The study population consisted of 43 aborted patients and 43 normal pregnant females, referred to Imam Khomeini hospital. 10 mL blood was taken and centrifuged to isolate the patients' serum. Then, the samples were analyzed to determine the copper and selenium levels, using atomic absorption spectrometry. All data were statistically analyzed by T-test and Mann-Whitney methods. As a result, we found a significant decrease in serum copper level in cases compared with controls. Also the results showed an insignificant decrease in serum selenium levels in the patients compared to the healthy women. According to the results, deficiency of the essential heavy metals may be a probable reason for missed abortion occurrence. These deficiencies can be related to malnutrition, decreased consumption of essential metals and supplementary compounds in pregnancy, lack of regular laboratory monitoring. Thus, consuming supplements in Iranian pregnant women can be helpful in completing a successful pregnancy.

Keywords: Abortion, copper, selenium, serum concentration

Pharm Biomed Res 2015; 1(1): 44-47 DOI: 10.18869/acadpub.pbr.1.1.44

Introduction

Abortion refers to spontaneous or induced termination pregnancy before fetus getting into sufficient evolution for survival. In fact, abortion is complete or incomplete discharge of fetus or membranes spontaneous abortion is the most common pregnancy complication. Recent studies showed that almost 10-20% of pregnancies are resulted in abortion in the first-trimester. Bleeding is Patho-physiologically seen during menstruation period and then tissue necrosis adjacent to bleeding volume along with abortion. In mature abortion faded state of ovum and in immature abortions, fetus mashed state and in case of amniotic fluid absorption, squeezed state of fetus is seen (1,2). Over 80% abortion occurs in the first 12 weeks of gestation and chromosomal disorders are at least in charge of half of the abortions. After the first-trimester, abortion occurrence and chromosomal disorders are decreased. So, abortion incidence in women in the first-trimester of pregnancy is increased. The abortion occurrence is increasingly, clinically diagnosed from 12% in women younger than 20-years to 26% in 40-years. In the first-trimester of gestation, fetus death almost occurs prior to automatic ovum discharge (3).

The abortion-induced factors include:

- Maternal factors, such as zygote abnormal evolution, aneuploid abortion and euploid abortion, etc;
- Immunological and auto-immunological factors, such as auto-

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immune factors, inherited thrombophilia, etc;

- Physical trauma and laparotomy (4).

Maternal factors in abortion can be classified as infections, disabling chronic diseases like tuberculosis or carcinomas, endocrine disorders such as hyperthyroidism, mellitus diabetes and progesterone deficiency, inappropriate diet, drugs, radiation, environmental toxins and chemicals including arsenic, lead, formaldehyde and benzene (5). It is obvious that uterus defects are the significant abortificient factors including uterus acquired defects and insufficiency. Thus, abortion incidence can be partially prevented by treatment of these defects (6). Some studies introduce a meaningful correlation between some essential micronutrients like selenium selenium, zinc and copper and reproductive risk (7). In some studies selenium presents as a part of a reproductive enzyme and there is an increase in its demand during pregnancy due to fetus uptake (8). Also copper is presented as an effective micronutrient during pregnancy (9). It presents in some tissues such as liver, kidney, spleen, heart, etc. It is also essential for some enzymes (10). Nutritional deficiencies are common during pregnancy. In developing countries it has been reported some deficits of minerals and vitamins in their diet (11).

In this study we want to evaluate two important trace elements copper and selenium (Cu and Se) among normal pregnant women compare to aborted women in the greatest gynecology centre in Mazandaran.

Materials and methods

This case-control study was performed at the Department of Obstetrics and Gynecology of Imam Khomeini educational hospital of Mazandaran University of Medical Sciences in 2009. The ethical research code was 87/88 that was approved in Mazandaran University of Medical Sciences. 43 pregnant women suffering from abortion at second-trimester were selected as cases. The control group (n = 43) consisted of women who were selected, based on the demographic information resulted from the questionnaire, among age-, gravidity-, and socio-economic status (SES)-matched women who had a normal triple-screen and targeted ultrasound during the second-trimester. Inclusion criteria: The subjects were between 20-40 years old were included; abortions must be occurred during 12^{th} to 14^{th} weeks of gestation; the subjects must have no limitation in their daily diet; also they were not taking any medication, and had no known-vitamin deficiency and prior significant medical illnesses. All volunteers gave their written informed consent before being included in our study.

Blood sampling

Overnight fasting venous blood specimens were drawn from the antecubital vein and collected into heparinized blood-collecting tubes according to standard hospital guidelines for venipuncture and sample collection. The serum separator tube specimens were allowed to clot and then were centrifuged for 2 min at 1500 rpm to separate the serum. Serum samples were stored at -20 ˚C until the analyses.

Measurement of serum Cu and Se levels

Serum Cu levels were analyzed in graphite furnace atomic absorption spectroscopy (AAS; Perkin Elmer Analyst 800). Samples and calibration standards for Cu and Se measurement were prepared in four concentrations with 5% and 10% glycerol. Commercial standard Cu and Se calibrators were used as standards (1 mg/l) by serial dilutions and samples were evaluated according to a standard curve (12-17). Our used AAS LOD was 0.01 µg/dl and its LOQ was 0.1 µg/dl.

Statistical analysis

The prism software ver.3 (USA) was used for the statistical analysis of the mean and standard deviation of the metals concentrations in aborted and healthy subjects. The data were analyzed based on statistical-comparative quantitative tests using one way-ANOVA, Mann-Whitney test and paired t-test for multiple comparisons. A p-value of < 0.05 was considered to be statistically significant.

Results

The patients' demographic properties such as age range, fetus abortion occurrence, the couple number being relative, unwanted gestation occurrence, the number of mothers with taking medicine during pregnancy record have been analyzed. Based on table 1 showing the highest level of embryo abortion occurring was seen in pregnant women in age rang below 25 years

(46/51%) and also the lowest level was related to women in 25-35 age range (23/25%).

Table 1 The number of women with abortion in the study in certain age range

Age	< 25 years	25-35 years	>35 years
Percentage (n)	45/51% (20)	23/25% (10)	30/24% (13)

On the other hand, based on Table 2, out of 43 pregnant women who suffered abortion, 8 couples were relative and out of control group women, only 1 couple was relative.

Table 2 Comparing two groups related to demographic information

Group / Parameter	Suffering group percentage (cases/total)	Control group percentage (cases/total)
Relative background	18.6% (8/43)	2.32% (1/43)
Unwanted pregnancy	32.55% (14/43)	11.62% (5/43)
Family abortion background	25.58% (11/43)	11.62% (5/43)
Medical taking background during pregnancy	11.62% (5/43)	2.32% (1/43)

The analysis of, the results indicate that unwanted pregnancies and family abortion background and taking medicine during gestation in women suffering from embryo abortion have been meaningfully higher than those of the control group. In this experiment, serum samples of women with abortion and also control group women have been analyzed in terms of essential metals such as selenium (Se) and copper (Cu) and the relation between their serum concentration and unwanted abortion occurrence in pregnant women has been compared that the results were presented based on Table 3.

Table 3 Selenium and copper-serum concentrations in serum of women suffering from fetus abortion and control group

Group / Concentration	Suffering from abortion	Control	*P*-value
Selenium	0.779 ± 0.16	0.973 ± 0.112	P > 0.05
Copper	42.326 ± 0.176	51.326 ± 0.072	P < 0.05

The results showed that no significant correlation was seen between abortion occurrence and the selenium serum levels in any of the groups ($p > 0.05$). The serum copper concentrations in women suffering from abortion showed significant differences with the control group ($p < 0.05$).The average Cu and Se levels in non-pregnant subjects were 51.326 ± 0.072 µg/dl and 0.973 ± 0.112 µg/dl, whereas Cu and Se levels in aborted women were 42.326 ± 0.176 µg/dl with 17.64% and 0.779 ± 0.16 µg/dl with 20% less, respectively (Table 3).

Discussion

Modification in trace element levels during pregnancy depend on many factors (15). Essential trace elements are especially important for children and pregnant women (16). The demand for both energy and nutrients is increased during pregnancy (18). Se and Cu are involved in many biological processes that are vital for life (15, 18). The results indicated that the highest incidence of second-trimester induced abortion was occurred in pregnant women below 25 years old (45.51%). Also, the lowest abortion incidence was seen in 25-40 years age range (23.25%); but, following, the occurrence of abortion was increased in women above 35 years. On the other hand, genetic disorders in fetus followed may lead to some gestational disorders such as blighted ovum, defect in nestling, and missed abortion. Besides, family background of missed abortions can provide a robust genetic background for pregnant women facilitating abortion incidence due to unknown origin. For example, suffering from pre-eclampsia, pregnancy diabetes, still child born background, childbirth heavier than 4 kg. Another influential and highly significant factor increasing unwanted abortions incidence probability is taking medicine during pregnancy. Many pregnant women take medicine willfully due to lack of knowledge about their side effects, tratogenic and provoking effects of abortion; for instance, medicine such as methatrexate , colchicines and angetansin converting enzyme controlling drugs can lead to abortion. Even taking aspirin during pregnancy can create disorders in pregnancy. Because of medicine´s tratogenic effects during pregnancy, drugs have been divided into classes showing their complications levels. Thus taking drugs willfully especially when pregnant is absolutely forbidden and taking medicine should be done under doctor's supervision (12-15, 17,19). Analyzing serum selenium and copper concentrations in the serums of women with abortion and control group women indicate that both metals in the serum

of control group suffering from abortion. Some previous studies found a significant drop in serum Se levels in aborted women compare with normal pregnant ones (12-15, 19).

Glutathione peroxidase (GPx) is a Se-dependent enzyme that has an antioxidant activity. Since there is an increase in free radicals and reactive oxygen species in miscarrying, Se may have an important role in abortion (20). Also Cu acts as a cofactor in superoxide dismutase. This antioxidant enzyme has a role in placental function (18).

Conclusion

Our study described that the trace elements levels were decreased in abortion, but more studies are needed to find out the association of lower values with any abnormalities. Therefore, essential metals such as copper and selenium deficit in pregnant women can increase the probability of unwanted abortion occurrence. The deficiency of these metals can be due to malnutrition, not pursuing medical examination during pregnancy. As a result, consuming supplementary substances during pregnancy and paying attention to the genetic and family background of pregnant women, not taking drugs willfully, doing genetic tests before and during pregnancy can decrease unwanted abortions occurrence and save mother and child lives (15, 17). Thus, at the end, we recommend that in order to take nutrition importance in pregnant women's diet and the patients with abortion into account, sampling be done several times during several weeks and the values mean be calculated and analyzed in every woman regarding every patient's conditions.

Acknowledgment

This research project has been conducted under the financial support of Mazandaran University of Medical Sciences.

Conflict of interests

Nothing to declare.

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