

Oxidative stress and antioxidant status in menstrual cycle



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Evaluation of oxidative stress and antioxidant status during normal menstrual cycle

Abstract:

Background & Objectives: Oxidative stress has been investigated to explain various physiological as well as pathological basis of many medical conditions. But very few data concerning the oxidative stress during normal menstrual cycle of eumenorrheic women are available. Thus, the purpose of study was to examine the physiological role of oxidative stress during normal menstrual cycle.

Methods: 120 young healthy female subjects of reproductive age group (17-27 yrs), having regular menstrual cycle, were examined. Serum malondialdehyde (MDA), an oxidative stress biomarker and serum ascorbic acid (vitamin-C), an antioxidant vitamin were assessed in the follicular phase (on 7th day) and in the luteal phase (on 21st day) of normal menstrual cycle.

Results: In the present study, significant higher ($p < 0.0001$) levels of MDA and lower but non-significant ($p > 0.05$) levels of ascorbic acid were observed in the luteal phase when compared to the follicular phase. Non-significant negative correlations were also observed between MDA and ascorbic acid in both the phases of normal menstrual cycle. Significant increase in serum MDA level coincided with the increased progesterone and estrogen levels during the luteal phase. High levels of estrogen may be the initiator of lipid peroxidation process which eventually ends up with cellular injury during the luteal phase.

Interpretation & Conclusion: Oxidative stress has an important role to play in physiological phenomenon of the menstruation.

Keywords: Antioxidants, ascorbic acid, malondialdehyde (MDA), menstrual cycle, oxidative stress.

Abbreviations: MDA, malondialdehyde.

Introduction

Menstrual cycle is the result of complex interacting processes involving interaction of the hypothalamus, pituitary, ovaries, uterus, prostaglandins and neuroendocrine factors ¹.

The normal menstrual cycle is a twenty eight day period which is divided into two phases i. e. follicular phase and luteal phase. The follicular phase is characterised by a low level of estrogen and progesterone which is followed by rise in estradiol, lutenizing hormone, and follicle stimulating hormone at the time of ovulation, while the luteal phase is associated with increased levels of progesterone and estrogen. These phases are associated with various changes in blood parameters along with variations in the sex hormones.

Several powerful reactive oxygen species or free radicals or oxidants are produced during the course of metabolism in blood cells and most other cells of the body. These oxidants are very reactive molecules that can react with proteins, nucleic acids, lipids and other molecules which changes physicochemical status of the cell to alter their structure and cause tissue damage. Lipid peroxidation is a well established mechanism of cellular injury

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in human and is used as an indicator of oxidative stress in cells and tissues. Malondialdehyde (MDA) is one of the important byproduct of lipid peroxidation process which is widely used as an indicator of lipid peroxidation ² .

These free radicals are the target for the enzymatic and non-enzymatic scavenging systems ³ , which includes the antioxidants such as superoxide dismutase, glutathione peroxidase, vitamin-A, vitamin-C, vitamin-E etc. that scavenge the free radicals and protect the tissues from oxidative stress.

Oxidative stress has been implicated in various physiological as well as pathological bases of many medical conditions including reproductive system. Evidences have shown the dual effects of oxygen radicals in the physiological reproductive processes such as oocyte maturation, ovulation, menstruation, luteolysis, luteal maintenance in pregnancy, implantation and blastocyst development ^{4, 5, 6}, as well as in the pathological conditions like spontaneous abortions and infertility in females ⁷ .

The imbalance between free radicals and antioxidants resulting from either an overproduction of free radicals or a deficit in antioxidant protection leads to oxidative stress ⁸ .

Although, reports regarding variations of oxidative stress across the normal menstrual cycle in eumenorrhic women have been published, specially in reference to MDA (a marker of oxidative stress and an important byproduct of lipid peroxidation), but these are sparse and have conflicting trend.

by the absorbance coefficient of malondialdehyde-thiobarbituric acid complex.

Serum ascorbic acid was estimated spectrophotometrically, by using 2, 4-dinitrophenyl hydrazine ¹⁰. The underlying principle was based on the oxidation of ascorbic acid to dehydroascorbic acid followed by coupling with 2, 4-dinitrophenyl hydrazine under controlled conditions, in the presence of Thiourea as a mild reducing agent which gives red coloured osazones.

The data thus obtained was subjected to statistical analysis using the PRIMER OF BIOSTATISTICS software. The comparison of variables was done using the Student paired 't' test and correlation between variables was estimated by using Karl Pearson's correlation coefficient. The significance level was considered at $p < 0.05$.

Results

The mean serum MDA and serum ascorbic acid levels during the follicular and luteal phases of menstrual cycle are presented as in Table 1. In the present study, the mean serum MDA (nmol/ml) level was greater during the luteal phase (4.294 ± 1.60 nmol/ml) as compared to follicular phase (2.119 ± 0.83 nmol/ml). The difference between MDA levels in the luteal phase was highly significant ($p < 0.0001$) when compared with the follicular phase.

Lower values of serum ascorbic acid were found in luteal phase when compared to follicular phase. The mean values observed were 0.9399 ± 0.40 mg/dl & 0.8963 ± 0.37 mg/dl in follicular phase and luteal phase, respectively. But, the changes were not significant statistically ($p > 0.05$).

In this study, a negative correlation was also observed between serum ascorbic acid (mg/dl) and serum MDA (nmol/ml) levels in both follicular and luteal phases but the correlation was found to be non-significant in both follicular phase (r value=-0.026, p> 0.05) as well as in luteal phase (r value=-0.010, p> 0.05).

Table 1: Mean+SD levels of serum Malondialdehyde (MDA) and serum Ascorbic acid during follicular and luteal phases of menstrual cycle.

Parameters	Follicular phase (Mean+SD)	Luteal phase (Mean+SD)	p value
Serum MDA (nmol/ml)	2.119±0.83	4.294±1.60	<0.001*
Serum Ascorbic acid (mg/dl)	0.9399±0.40	0.8963±0.37	> 0.05**

Data expressed as mean and SD, * Highly significant, ** Non-significant.

Discussion

Present study has revealed the role of oxidative stress in the physiology of menstruation. We observed a significant higher levels of MDA while a non-significant lower levels of ascorbic acid in the luteal phase when compared with the follicular phase of the menstrual cycle.

Previous studies also have correlated increased serum MDA levels during the luteal phase with the physiological phenomenon of menstruation in the healthy normal menstruating females which support our study results ^{6, 11} . While, no significant differences in MDA levels throughout the normal menstrual cycle also have been reported ^{12, 13, 14} .

Unlike our study results, a progressive significant rise in plasma ascorbic acid levels has been reported from menstrual to ovulation ¹⁵ . Similarly, “ a sharp increase in the fasting level of plasma Vitamin C” also has been showed in some women during the middle of the menstrual cycle ¹⁶ . Whereas, some other researchers found no evidences of unusual variability of plasma ascorbic acid values throughout the menstrual cycle, which supports our study ¹⁷ .

The significant rise of MDA and depletion of ascorbic acid levels during the luteal phase of menstrual cycle coincides with the increased levels of estrogen and progesterone, which is a characteristic feature of this phase ¹⁸ . Increased levels of estrogen and progesterone cause the proliferation of uterus while the initiation of sloughing of the endometrium is mainly due to the rise in the estrogen levels ^{18, 19, 20} .

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Thus, the high estrogen level from developing follicles may be the initiator of lipid peroxidation process ²¹, which eventually causes the cellular injury followed by release of cytokines especially tumour necrosis factor-alpha, which generates reactive oxygen species from the tissues which in turn causes lipid peroxidation ²². The generated free radicals may play an important role in spasm of the highly vascularised vessels leading to vascular necrosis and menstrual flow, when hormonal support for the endometrium is diminished.

High levels of oxidative stress have been coincided with high levels of female sex hormone such as estradiol in previous studies also ^{6, 21, 23}. While, in other studies a significant negative correlation between these parameters in regularly menstruating females also have been established ²⁴. Whereas, some evidences show no significant correlation between ovarian hormones and oxidative stress during the follicular and luteal phases of menstrual cycle ²⁵.

Present study perhaps therefore suggests that the high MDA level in the luteal phase may play an important role in the initiation of menstruation which is a well established cellular injury based phenomenon.

Conclusion

In conclusion, these results suggest that increase of serum MDA levels may play an important role in the physiological phenomenon of menstruation.

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