



OxiDates

ZeptoMetrix Corporation

Oxidative Stress/Free Radical News

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TBARS and Women's Health

Increased oxidative stress is a factor throughout the lifespan of a woman and has been linked to a number of gender-related health issues (1). Current studies report elevated levels of lipid peroxides measured as TBARS, together with decreased antioxidant (AOX) protection involving enzymatic or non-enzymatic mechanisms. These include changes precipitated by lack of estrogen, which is a natural AOX (2). This age-induced imbalance can influence risk for developing disease in females. Biomarkers commonly used estimate lipid peroxidation, oxidized LDL (oxLDL), enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), paraoxonase (PON1) and total AOX capacity (TEAC). The relevance of each of these are reviewed in the following abbreviated summary:

Pregnancy. TBARS and SOD are present in plasma of normal, non-pregnant women. However, they increase steadily during pregnancy (3). In contrast, patients with Type 1 diabetes are significantly higher in TBARS, whereas SOD and GPx are reduced even when good glycemic control is achieved.

Prenatal Hypoxia. In term infants, urinary TBARS is increased following acute asphyxia or chronic hypoxia (4). Mechanical resuscitation or intrauterine meconium further increased the TBARS value.

Prematurity. TBARS are elevated in paired plasma and urine specimens obtained from pre-term infants (5). One day after delivery, both plasma and urine TBARS are elevated showing the utility of urine samples.

Pre-eclampsia. TBARS are also increased in the plasma of women who develop hypertension and other complications during pregnancy (6). High blood pressure correlated with a significant decrease in erythrocyte GPx as well as in cord blood and gestational diabetes. Supplementation with AOX significantly reduced the risk of developing pre-eclampsia (7) and the TBARS/AOX ratio is proposed to monitor complicated pregnancies (6).

Polycystic Ovary Disease. Oxidative stress is thought to produce a pro-inflammatory condition in this disorder (8).

Endometriosis. A positive, but weak association was found with TBARS in women aged 18-40 years (9). However, antioxidants were lower than controls in cultured endothelial stromal cells (10). This imbalance could contribute to the growth of endometrial cells. Approximately 50% of infertile women have endometriosis, a disease characterized by a sterile, inflammatory reaction (11). Lipid peroxides are elevated in the endometrium (2.61 +/- 0.66 pmol/ug protein vs. 1.50 +/- 0.25 in normals). TBARS is markedly elevated in peritoneal fluid (3.34) as well. AOX's are decreased and this redox imbalance pre-disposes obese women to endometriosis. (10).

Anorexia Nervosa, Bulimia Nervosa, and Amenorrhea. Eating disorders influence menstrual dysfunction and infertility (12) and these patients have low antioxidants (13).

Obesity. There is a rapidly growing prevalence of overweight, premenopausal women (14) and a recent study found that TBARS was increased, $p < 0.04$ (15). This was correlated with increased lipid peroxides measured by HPLC. Dietary restriction and weight loss resulted in a decrease of peroxidation indices during a 16 week trial.

Menopause. A recent PUBMED search indicates more than 90 papers linking oxidative stress with menopause. Women who have undergone a hysterectomy-ovariectomy show an increase in TBARS which is correlated with the homozygous Q carrier of PON 1, whose enzyme activity is also elevated under these conditions (16). As the interval after surgery is extended, PON 1 increases more while TBARS decreases. In women who achieve menopause naturally, TBARS is increased relative to younger females but decreases after 4 months of estradiol treatment (17). The AOX activity of estradiol is due to its phenolic structure and its catechol metabolites. However, in the presence of redox-active metals, it can become a pro-oxidant via Fenton-type reactions (18). Conversely, TEAC decreases prior to hormone replacement therapy and increases following the treatment period. Another study looked at cardiovascular risk in menopause and found that levels of TBARS and oxLDL were increased in early menopause and then decreased 6 months after treatment (19). PON 1 activity also responded to estrogen intervention (20). The TBARS in post-menopausal women with Type 2 diabetes is reduced by hormone replacement coupled with vitamin C plus E (21).

Osteoporosis. In elderly women, AOX is depleted and correlates with reduced bone density (22). Since this decrease is due to enzyme and non-enzyme mechanisms, the Zeptomatrix TEAC assay will be useful.

Carcinoma. TBARS, SOD, and GPx are each increased in cancer or breast tissue compared to uninvolved mammary tissue (23). Furthermore, the extent of lipid peroxidation is more pronounced in Stage 3 than in Stages 1 and 2. Upregulation of AOX protection is suggested as a growth advantage for tumor cells. TBARS is increased and TEAC decreased, including AOX enzymes, vitamin C and E in patients with ovarian cancer relative to controls (24). Another investigator reported elevated TBARS in ovarian cancer and proposed its diagnostic value (25). Similar findings were found in cervical cancer (26-27). Lowered protection is speculated to involve increased utilization during oxidative stress due to continuous ovulation and epithelial inflammation. These biomarkers were measured in plasma or erythrocytes and each showed the characteristic up or down shift.

In summary, the papers reviewed in this issue of

Oxidates emphasizes the importance of TBARS in women's health. These various authors cite the need for obtaining more data in disease situations to strengthen the role of TBARS in prognostic-diagnostic medicine. Furthermore, other Zeptomatrix kits such as GPx and Arylesterase/Paraoxonase and in-house assays like TEAC are available to enhance research relating to oxidative stress.

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