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Repercussions of Thyroid Profile Hormones Triggered by Oxidative Stress in Infertile Females among the Allahabad-India

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Abstract:

This study has been designed to investigate the impact of oxidative stress on the thyroid hormones profile in the fertile and infertile females of the child bearing age. To achieve this aim 500 married female were included for this study and were divided in two groups: group I: 250 fertile married females and group II : 250 infertile married females falling between the reproductive age 25-35 yrs and having no history of any metabolic disorder. Melondialdehyde (MDA) is considered as oxidative stress marker in the present study. Thyroid profile tests (total $T_{3,}$ total T_4 and TSH) were measured in both the groups. Results indicates from this study that level of MDA showed a significant ($p > 0.0001$) increase in the infertile group in comparison to the fertile group. On the other hand significant ($p>0.0001$) increase in the total $T_{3,}$ total T_4 and TSH in the infertile group when compared to the fertile group. In the correlation study MDA had a significant positive correlation with the T3 ($r= 0.2421, p= 0.00011$) as well as with T4 ($r=0.1463, p=0.020663$).Similarly a significant positive correlation was also found in between the MDA and the TSH ($r=0.020663, p=<0.00001$).

It was concluded that high value of melondialdehyde could be used as a marker for alteration in thyroid profile which is responsible for many complications including fertility rate in females.

Key Words: Infertility, Oxidative stress, Melondialdehyde, Thyroid.

Introduction

Oxidative stress is a condition in which there is an imbalance between the productions of ROS and the ability of the biological system to detoxify the reactive intermediates or easily repair the resulting damage (1). Increase in the level of Reactive oxygen species and decrease in the antioxidant scavenging enzyme leads to the condition of oxidative stress (2). All forms of life maintain a reducing environment within their cells. Normal cellular aerobic metabolism also results in the generation of ROS. Minimal levels of ROS act through signaling pathways, which is necessary for the normal physiological functions in the female reproductive tract (3). The normal cellular metabolism also produce free radicals and are also important to some extent for contribute to normal physiological functions such as cellular differentiation, cell signaling, second messenger pathways, bactericidal activities, and apoptosis as well as adverse effects such as lipid peroxidation, protein oxidation, and DNA damage. Oxidative stress can cause tissue injury or even cell death which can occur essentially by two mechanism, necrosis and apoptosis (4). Oxidative stress also effects the human fertilization and can induce apoptosis which can further result in failure in implantation, fragmentation of the embryo or can cause abortions. Many of the unsuccessful reproductive performance such as infertility, miscarriage and preeclampsia are found to be related to adverse health effects of oxidative stress (5). Successful pregnancy is a combination of a long list of

complex biological steps like, ovulation, production of competent sperm and oocyte in the reproductive tract, proper fertilization, successful transportation of the conceptus to the uterus and implantation of the embryo etc. Disruption in one or more of these complex biological steps can lead to infertility (6). It is proposed that oxidative stress (OS) precipitates the range of pathologies that currently are thought to afflict the reproductive function of female body (7). Study conducted on rats by introducing experimentatal hyperthyroidism was accompanied with increased oxidative stress and with the consumption of antioxidant enzyme in induced oxidative aggression (8). Melondialdehyde (MDA) is the one of the final products of polyunsaturated fatty acids peroxidation in cells. An increase in free radical is causing overproduction of MDA and is commonly treat as a marker for oxidative stress (9).

Material and Methods

The present study were carried out in faculty of Health Sciences, SHIATS and the experimental protocol was approved by the Institutional Ethical Committee in the meeting held on 3rd October 2011, Reg No-2011/A/010. The blood sample of infertile and fertile married females having child bearing age (25-35 yrs) without any metabolic disorder (known from the history of the patient) were collected from different gynecologist clinical hospitals and infertility centers of Allahabad city. The screening of the sample were done on the basis of history given by the females with their written concern as well as performing blood analysis for MDA, and thyroid profile.5ml of venous blood sample were collected from each selected fertile and non fertile married females in Allahabad and were divided in two groups Group I consist of 250 fertile married females having children and Group II includes 250 infertile married females who doesn't have children.

The level of Melondialdehyde was determined by procedure described by Satoh (10**)**) total $T_{3,}$ total T_4 and TSH was measured by Chemiluminescent microparticle immuno assay method (11). Data were analyzed for significance level by Graph Pad online software for T test analysis. This was done by online using www.graphpad.com/quickcals/.

Results

During this study it was found that there was a significant difference in the plasma MDA mean values levels of the two groups, with increase in the group II (3.00±0.295 nmol/ml) as compared to group I (0.85±0.0603 nmol/ml). The results showed significant increment in the MDA value of infertile group which strongly indicates the lipid peroxidation and denotes presence of oxidative stress in the infertile females. Lipid peroxidation measured as MDA content is considered to be indicator of oxidative damage from stress (12)

Results in table 3.2 was reveals that there is a significant difference in the thyroid hormone mean values of the two groups with increase in the group II. The results showed significant increment in the total $T_{3,}$ total T_4 and TSH value of group II when compare to group I. Significantly increased free T_4 values were also observed in the study done (13**)** on rats by inducing experimental hyperthyroidism. Their results suggested that experimental hyperthyroidism (caused by inducing L thyroxin 10µg/animal/day) is accompanied with increased oxidative stress and with the consumption of antioxidant enzyme in induced oxidative aggression.

Correlation between MDA and Thyroid hormones in infertile females: Table 3.3 representing correlative study among MDA and the Thyroid hormones i.e. T3, T4, TSH. The results indicates a significant positive relation with the thyroid hormones.MDA had a significant positive correlation with the T3 (r= 0.2421,p= 0.00011) as well as with T4 (r=0.1463, p=0.020663).Similarly a significant positive correlation was also found in between the MDA and the TSH (r=0.020663,p=<0.00001).

Discussion

The results show significant increment in the MDA value of infertile group which strongly indicates the lipid peroxidation and denotes

presence of oxidative stress in infertile women. As Melondialdehyde is known to be an oxidative stress marker and is only formed in the lipid peroxidation. The finding of present study was in agreement with the earlier reports or studies (14, 15). The results shows a significant positive correlation of MDA with thyroid hormones.Thus it is indicated that increase in the MDA level causes increase in the level of thyroid hormones which means the condition of hyperthyroidism. In this state of over activity of thyroid gland the female ovulation become irregular or even complete lack of menstrual cycle and thus effect the fertility. The major source of energy production in the body is oxidation which predominantly in mitochondria (16) as well as thyroid hormone also targets mitochondria. There is constant production of hydrogen peroxide during the thyroid hormone synthesis, which is absolutely indispensable for iodine oxidation in presence of thyroid peroxidase. The synthesis of thyroid hormone depends on the hydrogen peroxide, which works as a donor of oxidative equivalents for thyroperoxidase (17). The toxic effect of hydrogen peroxide its synthesis must always remain in equilibrium with the hormonal synthesis. Thyrocytes contains various enzymatic systems ,such as catalase ,superoxide dismutase, glutathionine peroxidase that contribute to limit their limit cellular injuries when hydrogen peroxide or other are produced in excess (18,19,20). The most important factor involved in the regulation of basal metabolic state and the oxidative metabolism is thyroid hormone (21) .Thyroid hormones play a very essential role in the metabolic activities of the body as they can cause many changes in the number and activity of mitochondrial respiratory chain enzyme, which may result in the increased generation of ROS (22,23).

Many experimental studies suggest that hyperthyroidism is associated with a general increase in tissue oxidative stress. Some studies suggest the thyroid hormone, especially thyroid stimulating hormone (TSH), plays a role in infertility (24). Pregnancy as well as various aspects reproduction is disrupted by thyroid dysfunction.

Many studies highlight role of thyroid hormones as disturbance in their levels in the clinical conditions such as hyperthyroidism or hypothyroidism causes disturbance in menstrual cycle causing anovulatory cycles and increases morbidity in pregnancy (25, 26, and 27). It is known that thyroid hormones have major effects on the female reproductive system (28). They are critical for growth, development and differentiation. *In vitro* and *in vivo* data indicate that anovulations of estrogen and thyroid hormone levels can alter each other's functions. One possible mechanism for interaction may be that thyroid and estrogen receptors, having structural similarities, bind to an identical half-site, AGGTCA, of their cognate hormone response elements and thereby can compete with each other at this level (29).

.**Conclusion:** With the results observed in this study it may be concluded that oxidative stress, adversely affect the female reproduction and may also lead to infertility. As ROS are naturally made up by the human body and is a part of normal healthy metabolic activity but increased amount of ROS burdens immensely the fertility rate of the females. Thus to counter the ROS, the protective attempt i.e. antioxidants supplementation in the diet may be very beneficial for the body. The a positive correlation indicates that a change in the value of one variable will predict a change in the same direction in the second variable i.e increase in one variable may also cause increase in the second variable whereas the negative correlation result indicates that the change in the value of one variable predicts a change in the opposite direction in the second variable i.e increase in one variable may cause decrease in the other variable and vice versa. Thus the result indicates that high value of MDA level may act as trigger for thyroid hormones which mean the condition of hyperthyroidism or over active thyroid gland. In this state of over activity of thyroid gland it causes

Table 3.1. Serum MDA level in Fertile female and Infertile female.

S.No	Parameters	Group I	Group II	t-test
1	MDA	.85±.0603	3.00±0.295	126.111*

Normal Range: MDA (nmol/ml):0.5-2.0

Table 3.2. Thyroid hormone profile in fertile and infertile females.

S.No	Parameters	Group I	Group II	P.Value Significance	t-Test
1.	Total T_3 (Triiodothyronine) (ng/mL)	91±1.107 .	2.02±1.293 significant (>0.0001)	Statistically	10.31
2.	Total T_4 (Thyroxine) (µg/dl)	6.48±1.587	11.66±1.742	Statistically significant (>0.0001)	34.75
3.	TSH (Thyroid stimulating **hormone)** (µIU/ml)	1.48±.603	4.47±1.069	Statistically significant (>0.0001)	**38.51**

T_3 (Triiodothyronine) (ng/mL): 0.58 - 1.59 Total T_4 (Thyroxine) (µg/dl): 4.50-12.60
TSH (Thyroid stimulating hormone) (µIU/ml):0.35-5.5

Table 3.3. Correlation factors of serum Melondialdehyde with the thyroid function test i.e. T_3, T_4, TSH (thyroid stimulating hormone) in infertile women

MDA Verses	Parameters	r value	p. value	Significance level
Thyroid	**T_3**	**0.2421**	0.00011	Significant at p<0.05
hormones.	**T_4**	**0.1463**	0.020663	Significant at p<0.05
	TSH	**0.020663**	<0.00001	Significant at p<0.05

the overt activity of metabolism. It also effects the female ovulation as it causes irregular or even complete lack of menstrual cycle and thus affecting the fertility.

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