Original Article

Thyroid Disorders and the Level of Malondialdehyde

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Summary:

Background: Free radicals have been implicated in many pathological processes, including ischemia, inflammation, and malignancy. The free radicals may affect tissues damage by lipid peroxidation which generate malondialdehyde (MDA) as a by byproduct of the reaction. The objective of this study is to examine the dynamics of lipid peroxidation in patients with thyroid disorders using the measurement of malondialdehyde level as a marker for the degree of thyroid disorder.

Methods: Two hundred and forty five subjects were enrolled in this study. Hundred and ninety five were patients with different thyroid disorders (88 yperthyroidism, 63 hypothyroidism and 44 thyroid carcinoma) the remaining 50 subjects were healthy ones without any apparent functional disorders served as a control. Malondialdehyde (MDA) level was estimated in the sera of all subjects.

Results: A significant increase in the level of serum MDA concentration was observed in patients with all types of thyroid disorders as compared with the control groups.

Conclusion: The findings obtained showed a high rate of lipid peroxidation.

Keywords: Thyroid Disorders, malondialdehyde**.**

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Introduction:

Oxidative stress is defined as the imbalance between production of oxygen-derived free radicals and their removal by antioxidants (1). If mild oxidative stress occurs, tissues often respond by making extra antioxidant defenses. However, severe oxidative stress can cause cell injury and death. Free radical-induced cell death can proceed as necrosis or apoptosis (2). Furthermore, increased oxidative stress at the cellular level can come about as a consequence of many factors, including exposure to alcohols medications, trauma, cold, infections, poor diet, toxins, radiation, or strenuous physical activity (3). The oxidants that are typically generated in biological systems such as hypochlorite, hydroxiradical, peroxyl radical, peroxynitrite are very reactive, and short-lived with half-lives of only few seconds (4). By contrast, some of the modifications in biological macromolecules have relatively long half-lives, ranging from hours to weeks. Thus, modified lipids, proteins, and nucleic acids in tissues can serve as reporter groups for the presence of oxidative stress. Among these modified molecules are: malondialdehyde, isoprostance, nitrotyrosine , breath alkanes(5) and several others that have been established or proposed. Malondialdehyde (MDA) is the most commonly marker that is used to investigate the presence of oxidative stress in biological systems.

Approximately 20% of end-products derived from oxidative damage of lipids in vitro are MDA. Others are short- and long- chain aldehydes, ketones, alka (e) nes, and diens. The cytotoxicity effects of aldehydic carbonyl compounds arise from their ability to react with cellular biomolecules and forming a duct, which in turn cause the cell to loss its biological function(6).

In biological systems, MDA is present in both, free and bound forms. Some MDA arises from lipid peroxidation in vivo, and circulates either in body fluid bound to protein or in the free form. Another portion of MDA is generated in vitro, from decomposition of lipid hydro peroxides. Malonaldehyde is a significant byproduct during enzymatic synthesis of prostaglandins and it can be removed by renal clearance.

Thyroid hormones T3 and T4 act in many tissues to increase basal metabolic rate, partly by regulating mitochondrial ATP synthesis (7). Hence, because the actions of thyroid hormone are in the broad sense stimulatory, the manifestations of hyperthyroidism usually reflect the increased functioning of various organ systems to meet the demands imposed by hyperthyroidism [8,9,10]. Therefore, this study was carried out to explain the effect of the pathological changes of thyroid hormones (hyperthyroidism, hypothyroidism, and thyroid carcinoma) on the lipid peroxidation process by measuring the MDA level in the three disorders to look if it can mark the degree and type of the disorder.

Patients and Methods:

Two hundred and forty-five subjects were involved in this study all of them were selected from individuals attending the outpatient clinic at Al-Kadhumia Teaching Hospital. Hundred and ninety five subjects were diagnosed patients with different types of thyroid disorders: Eighty-eight (88) patients with an age

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range between (18-71) years, 48 females and 40 males were diagnosed as overt hyperthyroidism. Sixty-three (63) patients with an age range between (19-66) years, 33 females and 30 males had overt hypothyroidism. Forty-four (44) patients with an age range between (31-83) years, 22 males and 22 females were confirmed to have papillary thyroid carcinoma.

The following criteria were used for the diagnosis of the cases: clinical examinations, serum hormones (T3, T4 and TSH), computed tomography (CT scan), Pathological examination, and fine needle aspiration (If needed).

The remaining 50 subjects were normal healthy persons with an age range (18-55) years, 29 females and 21 males were used as a control. Five milliliters of venous blood from fasting subjects were withdrawn by utilizing disposable plastic syringes in the morning and transferred into a sterile test tube. The blood was allowed to clot and centrifuged at 1000rpm for 10 minutes. Sera were then separated and stored at -20°C until analysis.The thiobarbituric acid method of was use to measure the malondialdehyde (MDA), which reacts with thiobarbituric acid (TBA) to give a pink color that is read at (535nm). The malondialdehyde concentration was calculated using the molar extinction coefficient of 1.5x105. The results were expressed as µmol MDA/L serum.

Results:

The mean level of MDA in the healthy subjects was (0.67±0.23µmol/L). However the level showed a definite significant stepwise increase in the different forms of thyroid disorders. In patients with hypothyroidism the mean level was (1.12±0.69µmol/L). in patients with hyperthyroidism the level was (1.28±0.59 µmol/L). While the highest level of MDA was recorded in patient with thyroid carcinoma as it was (1.59±0.73µmol/L), as shown in figure (1).

The results shown in the figure indicate a highly significant difference between each type of the thyroid disorders compared to that of the control ($P<0.05$).

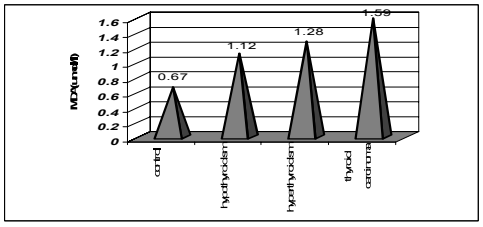

Figure (1): The mean serum concentration of MDA in patients with hyperthyroidism, hyperthyroidism, and thyroid cancer in comparing with normal subjects

Discussion:

The generation of reactive oxygen species (ROS) is considered as a primary event of a variety of stress conditions. The consequences of ROS formation depends on the intensity of stress and on physicochemical conditions in the cell. It has been generally accepted that active oxygen species produced under stress is a determinant factor, which causes lipid peroxidation, enzyme inactivation, and oxidative damage to DNA[11]. However, during the recent years evidence has accumulated on the participation of ROS and their oxygenated products in a signal transduction cascade. Antioxidant status and redox state of the cell are the main components in the fine regulatory mechanism of ROS signal specificity. ROS seem to affect the cell through a combination of the following factors: the amount of ROS produced (correlates with the severity of the stress) and biochemical status of the cell (i.e. activity of antioxidative and other enzymes, antioxidant content, pH, energy resources, integrity of membranes, redox characteristics etc.) The particular mechanisms and place of ROS in the signal transduction cascade are not yet known[12].

Besides stimulating cell growth, ROS also have toxic effects. ROS were first implicated in cytotoxicity based on the similarity observed between oxygen poisoning and radiation toxicity. Because of their high reactivity, ROS affect various molecular components of the cell such as fatty acids, proteins, and DNA (13, 14). Excess of ROS inevitably leads to cell degeneration and death (13, 15). In mammalian cells, high levels of ROS are encountered either in experimental or in certain pathological situations like the inflammatory response [16]. The mechanisms by which ROS include lethal effects are dependent on many factors including the nature of the free radicals involved and the characteristics of the target.

As mentioned previously, thyroid hormone synthesis involves the oxidation of iodide followed by the iodination of the tyrosyls of thyroglobulin and the coupling of the resulting iodotyrosyls in iodothyronines by an H_2O_2 generation system coupled to a peroxidase [17]. H_2O_2 is produced in large amounts under stimulation by thyroid-stimulating hormone (TSH) and can exert its toxic action through oxidative damage to the DNA, proteins and lipids of the cells. To prevent massive cellular destruction, the thyroid cells use various anti-oxidative systems, including enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase. Activated mononuclear cells and macrophages are able to produce interleukin-1 (IL-1), interleukin-6 (IL-6) and the tumor necrosis factor (TNF) (18), which have a prooxidant and proinflammatory properties [19,20]. Additionally, high concentrations of thyroid hormones may change the metabolism of oxygen in the cell and stimulate the production of free radicals (21).

In the current study there was a significant increase in MDA level in all groups of patients with thyroid disorders compared to the level of the control group.

Rom-Boguslavskaia (20) et al. studied lipid oxidation in euthyroid and thyrotoxic tissue samples of the human thyroid gland. The authors observed that

the content of TBA-active lipid peroxidation products was increasing in hyperthyroid tissue and the activity of antioxidant enzymes (catalase, GSH-Px) was decreasing. Similar studies by Sewerynek et al (21) have shown the ratio of CD/MDA decreased in the hyperthyroid patients, as compared to the controls. They believe that their results indicated a high rate of lipid peroxidation during hyperthyroidism (22).

The cut-off values of the result obtain (mean + 2SD) can give a distinct differentiation between thyroid carcinoma and the control. However the cut-off value can not differentiate between hyper and hypothyroidism although the two shown a significant difference between them.

On the other hand, many researchers [23, 24] studied lipid peroxidation in hypothyroidism patients. They observed that the MDA concentrations were significantly increased in hypothyroidism patients that suggest an oxidative damage. Free radicals are known to reduced the activity of membrane Na^+-K^+-activated ATPase in beef erythrocytes and rat brain .The similar influence to the activity of iodothyronines 5-monodeiodinase activity (MA) of T4 (and rT3) are two very common phenomena. Free radicals may influence hepatic iodothyronines MA by inducing lipid peroxidation or another form of oxidative damage to tissue components, e.g. reduction of thiol cofactors necessary for the MA or damage to protein or carbohydrate components of the enzyme (24).

Table (1): The Cut-off values of MDA in studied groups

	control	hypothyroidism	hyperthyroidism	Thyroid carcinoma
Cut off value (mean + 2SD) (µ MOL/I)	1.13	2.5	2.46	3.05

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