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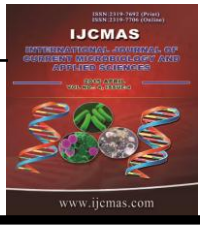

Original Research Article

Study of Effect of Thyroidectomy on Serum Oxidant-Antioxidants Status

Alaa A. Faisal[1], Raid M. H. Al-Salih[1]* and Ali N. Assi[2]

[1]Chemistry Department, College of Science, Thi-Qar University, Iraq
[2]Consultant Surgeon, Dept. of Surgery, Medical College, Thi-Qar University, Iraq
**Corresponding author*

Keywords

Thyroidectomy, Preoperative, Postoperative, Oxidant-antioxidants Status

A B S T R A C T

The aim of this study was to investigate the effect of thyroidectomy on serum oxidant-antioxidants status. Using the lipid peroxidation marker, malondialdehyde (MDA) and preventative antioxidants ceruloplasmin (Cp), transferrin (Tf) and albumin (Alb), in serum of patients with euthyroid goiter. Blood samples were obtained from (100) patients with euthyroid goiter, as well as (50) healthy subjects as a control group. They divided into three groups as the following: Group A (control):- Included fifty healthy subjects aged (15-60 years). Group B (preoperative):- Included fifty preoperative patients aged(15-60 years). Group C (postoperative):- Included fifty postoperative patients aged (15-60 years). The results show a presence of a significant increasein MDA and Cp in all groups of patients in preoperative and postoperative in comparison with control group. But, Albumin and transferrin levels showed a significant decreasein all groups of patients preoperative and postoperative in comparison with control group. Also, MDA, and ceruloplasmin showed a significant increase in all patients groups in postoperative in comparison with control group. While, transferrin showed in significant decreasein all groups of patients in postoperative as compared to the control group. MDA and Cp was decrease in the postoperative group when compared with preoperative group. But, albumin and Tf showed insignificant increase in patients groups in the postoperative group when compared with preoperative group.

Introduction

The thyroid is one of the largest endocrine glands in the body. **(1).** The thyroid gland is an endocrine structure that synthesizes and releases triiodothyronine (T_3) and thyroxin (T_4) **(2)**.These hormones are the only iodine-containing amine hormones in the human **(2)** and are needful, for optimal growth, development, and function of tissues**(3).** They have vital effect on oxygen consumption and metabolic rates of all cells including hepatocytes thus alter hepatic function**(4).** The liver in turn metabolizes thyroid hormones through conjugation, excretion, peripheral deiodination, and in the synthesis of thyroid-binding globulin, and thus controls their endocrine impact **(5).**

The earliest account of thyroidectomy is probably that given by Roger Frugardi of Salerno in 1170 [6]**.** Thyroidectomy remained a rarely performed procedure, William Halsted [7]. Finding accounts of only eight operations in which the scalpel had been used on the thyroid between 1596 and1800, and of only 69 more cases between 1800 and 1848.

The morbidity and mortality, usually from uncontrolled bleeding and sepsis, were prohibitive but advances in general anesthesia, antisepsis and homeostasis paved the way for surgeons at the turn of the century to make thyroidectomy a safe and acceptable operation. At the forefront of these developments was Theodor Kocher of Berne [8] who performed thousands of thyroidectomiesbringing the mortality down to under 1%. Today, thyroidectomy should be an extremely safe and uneventful procedure when performed by a trained endocrine surgeon.

Nodular Abnormalities – Goiter

Multinodular Goiter

Goiter is a common problem, with women affected more often than men [9]. The spread of MNG is particularly high in regions with iodine deficiency, where it occurs at a younger age [10 ,11]**.** The reason is thought to be multi factorial, involving hereditary factors, dyshormonogenesis, iodine deficiency or goitrogens contributing to intermittent stimulation of thyroid follicle cells by thyroid-stimulating hormone(TSH) from the pituitary gland. Exposure to radiation may also cause nodular thyroid disease [12]. Most patients with MNG have normal thyroid function [13]. Surgical treatment can consist of total thyroidectomy (TT), neartotal thyroidectomy (NTT) and subtotal thyroidectomy (STT) [10 ,11] .

Subtotal Thyroidectomy

Subtotal thyroidectomy(STT), which leaves a small unilateral or bilateral remnant in site .The main reason for conducting a subtotal thyroidectomy is a presumably lower incidence of post operative complications, including recurrent laryngeal nerve (RLN) paralysis and hypo para thyroidism, and an anticipated post operative euthyroid state by leaving a small residue of thyroid tissue in situ to maintain adequate hormone production. There is, however, a risk that the disease will persist or recur in the remnant [14, 15] .Nevertheless, the recurrence rate is high after STT, which causes reoperation morbidities. Most of the patients also need thyroxin replacement therapy while undergoing STT [16].

Lipid Peroxidation (LPO)

Lipid peroxidation (LPO) can be defined as the oxidative deterioration of lipid containing a number of double bonds between carbon [17].

LPO, being a free radical reaction, happens when the hydroxyl radicals, perhaps oxygen, react with the unsaturated lipids of the bio-membranes, resulting in the generation of lipid peroxide radicals (ROO•), lipid hydroperoxide (ROOH) and fragmentation products such as Malondialdehyde (MDA) [18].

Antioxidant Defense System

The term "antioxidant" refers to any molecule capable of stabilizing or deactivating free radicals before they attack cells.

Humans have evolved highly complex antioxidant systems (enzymic and nonenzymic), which act synergistically, and

in combination with each other to protect the cells and organ systems of the body against free radical damage.

According to their function, the antioxidant are classified into three types:

(a) Enzymatic Antioxidant catalyzing the breakdown of FRs such as superoxide dismutase (SOD), catalase and glutathione peroxidase(GPX) [19].

(b) Preventative Antioxidants (sequestration of metal ions)- these which prevent the participation of transition metal ions in FRs generation such as transferrin (Tf), ferritin, albumin (Alb) (Diplock et al, 1998). and ceruloplasmin–Cu containing has ferroxidase activity "prevents Fe^{2+} from reacting with H_2O_2 [20].

(c) Chain Breaking Antioxidants (Scavengers), those which are FRs scavengers such as ascorbic acid, uric acid, bilirubin and vitamin E [21].

Ceruloplasmin (Cp) is major antioxidant proteins that are synthesized in many tissues, including brain. Cp inhibits the peroxidation of membrane lipids catalyzed by metal ions, such as iron and copper. It also acts as ferroxidase and superoxide dismutase, and it protects polyunsaturated fatty acids in red blood cell membranes from active oxygen radicals [22].

Albumin (Alb) is a single polypeptide consisting of 585 amino acids with M.W. of approximately 66,248 Dalton, synthesized by the liver. It is most abundant in human plasma. Usually, it constitutes about 55–60% of all plasma proteins and has a serum half-life of about 20 days [23].Albumin synthesis happen only in the liver.

The aim of this study is to investigate the oxidative stress by measuring the lipid peroxidation marker (MDA) in patients with simple goiter, to evaluate serum antioxidant status in the mentioned disease by measurement (ceruloplasmin (Cp), transferrin (Tf) and albumin (Alb)) preoperative and postoperative the thyroidectomy and compared with control group.

Patients and Method

Design of Study

This study conducted at AL-Hussein Teaching Hospital in Thi-Qar, The Endocrine Gland Center in Thi-Qar Governorate, Biochemistry Laboratory, at the period between 10/9/2013 to 1/6/2014. It included (150) subjects, control (50) and patients(100).

There were (150) women subjects, control and patients with euthyroid goiter aged (15-60) years were included in this study. they divided into three groups as the following :-

Group A (control):- Included fifty (50) healthy subjects aged (15-60).

Group B (preoperative):- Included fifty (50) preoperative patients aged(15-60).

Group C (postoperative):- Included fifty (50) postoperative patients aged (15-60).

Collection of Blood Samples:

About (6mL) of blood samples from patients with simple euthyroid goiter (before and after conducting subtotal thyroidectomy) and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm) for 10 min. The serum samples were separated and stored at (-20ºC) for later measurement of biochemical parameters, unless used immediately.

Biochemical Parameters

Lipid peroxidation Marker (Serum MDA)

Determination of serum MDA level that consider as a lipid peroxidation marker were performed according to the method of **Fong** [24]. MDA concentrations were calculated, using the molar extinction coefficient of MDA (ε_{MDA}) equal to 1.56 x10^5 mol^{-1}. Cm^{-1} [25]. MDA formed from breakdown of polyunsaturated fatty acid, serves as a convenient index of peroxidation reaction.

Serum Antioxidants

Serum Cp concentration was measured by the method of Menden et al.,(1977) which using the extinction coefficient of Cp (ε Cp) equal to (0.68) to calculate it concentration.

The bromocresol green (BCG) method, colorimetric method, is the simplest technique which have been developed to determine Alb concentration [26].

The iron-binding protein transfesrring in serum is saturated upon treatment with an axcess of Fe (iii) ions. Unbound(excess) iron is absorbed onto aluminium oxide and precipitated . The trasferrin-bound iron (TIBC) in the supernatant is then determined [27 , 28].

Statistical Analysis

Statistical analysis was done using the software SPSS version 17.0; the results were expressed as mean ± standard error (mean ± SE). One way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

Result and Discussion

General Comparison for Some Studied Parameters

Lipid Peroxidation Status (Malondialdehyde)

Table (2) showed a significant increase in concentrations of serum MDA in preoperative group in comparison with control group ($P \leq 0.05$). However, there was a significant reduction in the serum concentration of MDA in postoperative group as compared to preoperative group ($P \leq 0.05$), but was still significantly higher than the control group ($P \leq 0.05$). This result is similar to the result of Akinci [29] who reported that serum MDA levels as the stable end product of lipid peroxidation before thyroidectomy and post-thyroidectomy, were significantly higher, compared to control group. However, in post thyroidectomy, the serum MDA level significantly decreased compared to pre thyroidectomy levels but was still significantly higher than the control group's level. This rising in MDA level is directly associated with the degree of lipid peroxidation which is one of the most important measurement of oxidative stress [30]. The higher level is correlated with the functional status of thyroid cells, in multinodular goiters [31].

Increased markers of oxidative stress were found in plasma of Graves' disease patients, even when they are rendered euthyroid [32].Significantly higher values have also been observed in patients with subclinical hyperthyroidism due to multinodular goiter [33].The decrease of MDA levels as reported in this study was compatible with the findings of Komosinska [34] and Adalı [35] who reported that the increased MDA levels decreased after the therapy. It is well known

that thyroid hormones exert a wide range of effects on lipid synthesis and degradation and also influence antioxidant activity [36] Thyroid dysfunctions increase LPO reactions and ROS as documented by considerable studies[37,38].

Serum Antioxidants

Serum Ceruloplasmin Concentration

Table (3) showed a significant increase in concentrations of serum Cp in preoperative group in comparison with control group (P≤0.05). However, there was a significant reduction in the serum concentration of Cp in postoperative group as compared to preoperative group (P≤0.05), but was still significantly higher than the control group (P≤0.05). The increase in concentration of serum ceruloplasmin in preoperative group was probably due to catalysis of the liver cells synthesis of Cp against iron overload status [39] and elevation in serum copper level [40] as a defiance function. Also the reduction in Cp concentration could be to counter balance of the ROS radicals generated in the lipid peroxidation processes and presence of iron or copper ions [41]. Thyroid hormones regulate the synthesis and degradation non-enzymatic antioxidants, such as transferrin, and ceruloplasmin. Undoubtedly, the changes in enzymatic and non-enzymatic substances affect the redox balance in the body and, in turn, enzymatic feedback regulates thyroid function [42]. In general antioxidative defense pathways of the organism play a crucial role in reducing the increased levels of free radicals generated by thyroid gland dysfunction [43].

Serum Transferrin Concentration

Table (4) showed a significant decrease in concentrations of serum Tf in preoperative group in comparison with control group (P≤0.05). Yet, there was a significant increase in the serum concentration of Tf in postoperative group as compared with preoperative group (P≤0.05), but was still significantly lower than the control group (P≤0.05). The low plasma transferrin concentration found in humans with increased iron stores may be due to a negative feedback of storage iron levels on transferrin synthesis [44]. Lower Tf concentration in patients with thyroid diseases perhaps due to that Tf is one of protective antioxidants that prevent the formation of free radicals. The associated metals prevent it from interacting with the H_2O_2 to form free radicals, as well as Tf works to remove O^{2-} the root of superoxide anion. The major carrier protein of iron is transferrin. Iron ions are delivered in the blood by the protein transferrin, each transferrin molecule can carry two iron ions [45]. The antioxidant property of transferrin is its ability to bind with iron ions and storage it as a ferritin and prevent the oxidative role of iron which allows to generate free radicals by Fenton and Haber-Weiss reactions [46].

Serum Albumin *(*Alb*)* Concentration

Table (5) showed a significant decrease in concentrations of serum Alb in preoperative group in comparison with control group and postoperative group (P≤0.05). On the other hand, no significant differences can be observed between postoperative group and control group. Our results are matched with the results of study Ömer [47]. who reported that albumin levels increased after thyroidectomy. Vlassara [48] has been reported that this decrease is due to the increase in synthesis of lipid peroxide and elevation in formation of free radicals which result in the increase of membranes permeability and leaking the proteins outside the vascular system. In the present

work, we focused on the antioxidant activity of albumin because oxidative stress is thought to play a significant role in the pathogenesis of many diseases .These highly reactive species are able to induce oxidative degradation of protein [49]. The albumin is a negative acute phase protein. It accounts for about 60% of the total serum protein and plays important physiological roles [50].

Table.1 Data of patients and controls groups

Groups	NO.
Patients	100
Controls	50

Table.2 Serum MDA concentrations for studied groups

Groups	NO.	MDA concentration (nmol/ml) Mean ± S.E
Control	50	18.65 ± 0.77 [c]
Pre	50	29.53 ± 0.89 [a]
Post	50	24.63 ± 0.75 [b]
LSD	3.01	

Table.3 Serum Cp concentrations for studied groups

Groups	NO.	CP concentration (g/L) Mean ± S.E
Control	50	2.11 ± 0.07 [c]
Pre	50	3.55 ± 0.16 [a]
Post	50	2.87 ± 0.09 [b]
LSD	0.43	

Table.4 Serum Tf concentrations for studied groups

Groups	NO.	Tf concentration (g/L)Mean ±S.E
Control	50	2.77 ± 0.04 [a]
Pre	50	2.12 ± 0.09 [b]
Post	50	2.54 ± 0.09 [c]
LSD	0.22	

Table.5 Serum Alb concentrations for studied groups

Groups	NO.	Alb concentration (g/L) Mean ± S.E
Control	50	43.09 ± 0.40 [a]
Pre	50	40.66 ± 0.60 [b]
Post	50	43.48 ± 0.62 [a]
LSD	2.05	

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