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Oxidative Stress in Thyroid Disorders

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Research Article
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Abstract:

Oxidative stress has been implicated in the etiopathogensis of several autoimmune disorders. There are evidences supporting the role of reactive oxygen species in the pathogenesis of thyroid disorders. The aim of the study was to investigate the role of free radicals and antioxidant status in hypothyroidism, hyperthyroidism and subclinical hypothyroid disorders.

Method: A total of 15 healthy subjects were included as the control group (Group I) 15 patients diagnosed with Hypothyroidism as (Group II), 15 patients with hyperthyroidism as (Group III), 15 patients with subclinical hypothyroidism as (Group IV) were enrolled in the study. Blood samples were analyzed for TT3, TT4 ,TSH Malondialdehyde, Vitamin E and Vitamin C.

Results: A highly significant increase in Malondialdehyde (MDA) and a decrease in Vitamin E and Vitamin C was observed in all thyroid disorders. A significant negative correlation was observed between MDA and Vitamin E (r2=0.075) and MDA and Vitamin C (r2=0.075). MDA is significant increased in all the three groups Group I ($p<0.0001$), Group II ($p<0.0001$) and Group III ($p<0.00001$) ,Vitamin E is significantly decreased in all the three groups with p value in Group I (<0.0001),Group II ($p<0.00001$) and Group III ($p<0.00001$).Vitamin C is significantly decreased in all the three groups with p value in Group I ($p<0.001$),Group II ($p<0.001$) and Group III ($p<0.01$) . A significant negative correlation was observed between MDA and Vitamin E (r2=0.075) and MDA and Vitamin C (r2=0.075).

Conclusion: Consequent antioxidant therapy should be included with thyroid replacement therapy.

Key words: Oxidative stress, Thyroid disorders, Vitamin E, Vitamin C.

Introduction:

Previous studies have suggested oxidative stress is induced by thyroid hormones. Thyroid disorders are associated with enhanced oxidative stress involving enzymatic and non-enzymatic antioxidants. Venditti and Di Meo [1], have reviewed mechanisms that could be the underlying cause enhanced nitric oxide synthase gene expression leading to increased nitric oxide over production, Activation of Hepatic NF −κB and consequent increase in the cytokines stimulating ROS generation, increased turnover of mitochondrial proteins, mitoptosis, influence on lipid composition is altered and therefore leading to increased susceptibility to oxidative stress leading to raise MDA [2]. The free radicals in turn enhance the activity of superoxide dismutase, glutathione peroxidase these enzymes in turn reduce the effect of free radicals. Vitamin E and Vitamin C efficiently scavenge singlet molecular oxygen and peroxyradicals. The aim of the study was to investigate the dynamics of oxidative stress and antioxidant status marker in all the thyroid understand the correlation of Vitamin E and Vitamin C with MDA [3,4].

Materials and Methods:

study population consisted of 60 subjects age and sex matched and were divided into four groups Group I (n=15) as Controls with mean TT3 as 1.04 ± 0.11 ,TT4 8.3 ± 1.0 and TSH as 2.58 ± 0.99 ,Group II (n=15) as Hypothyroidism with mean TT3 value <0.59 ± 0.43, TT4 as <4.09 ± 3.0 , TSH 87 ± 66 , Group III (n=15) as Hyperthyroidism with mean TT3 value > 1.9 ± 1.8 ,TT4 as > 11.4 ± 4.9 and TSH <0.04 ± 0.10 , Group IV (n=15) as subclinical hypothyroidism with mean TT3 as 0.9 ± 0.26 , TT4 9.0 ± 3.1 and TSH as 7.5 ± 1.5. All the patients and controls were recruited from NRI General Hospital and Medical College, Chinnakakani, Mangalagiri,

Andhra Pradesh, India. Exclusion criteria was smokers, alcoholics or suffering with acute or chronic disease such as Diabetes mellitus, Hypertension diseases of the liver and kidney or endocrine disorders.

After taking informed consent, the samples were collected in red colour vacutainer tube ,allowed to clot and was centrifuged at 3000 rpm for 5 – 10 minutes. The serum was separated and was analysed for TT3,TT4 ,TSH ,MDA ,Vitamin E and Vitamin C. The thyroid hormones were analyzed on Centaur CP, Seimens based on Chemiluminesence method. Appropriate calibration and quality control protocols were followed before analyzing the samples.

Measuring of MDA: The lipid peroxidation product MDA was measured using Thiobarbituricacid method, MDA reacts with Thiobarbituric acid at 100ºC in acid medium to give a pink colour complex. The colour intensity of MDA-TBA complex is measured at 535 nm in spectrophotometer.MDA concentration is calculated using the molar extinction co-efficient of MDA-TBA complex (1.5×10^{-5}) [5].

Measuring of Vitamin E: The principle of Vitamin E determination is the extraction of tocopherols into hexane after precipitation of proteins with ethanol. Tocopherol is oxidized to tocopherol quinone by the addition of ferric chloride reagent, and the Fe2+ in the resultant FeCl2 is complex with α, α - dipyridyl to produce a red color which measured as A510 [6].

Measuring of Vitamin C: Vitamin C is measured by 2,4D initrophenyl Hydrazine (DNPH) method, ascorbic acisd is oxidized by cupric ions to form dehydroascorbic acid which reacts with acidic [2,4] ,Dinitrophenyl Hydrazine to form red bishyrazone measured at 520nm [7].

Results:

Table 1: Thyroid function in patients with Hypothyroidism, Hyperthyroidism and Subclinical Hypothyroidism.

	Controls	Hypothyroidism	P value	Hyperthyroidism	P value	Subclinical hypothyroidism	P value
Age	45.2±11.8	38.5± 12.4		43.3±15.6		43.7±11.5	
T3units	1.04±0.11	0.59±0.43	0.0001	1.91±1.89	0.01	0.93±0.26	0.01
T4	8.32±1.01	4.09±3.01	0.0001	11.42±4.90	0.0001	9.0±3.16	NS
TSH	2.58±0.99	87.61±66.59	0.0001	0.04±0.10	0.0001	7.51±1.55	<0.00001

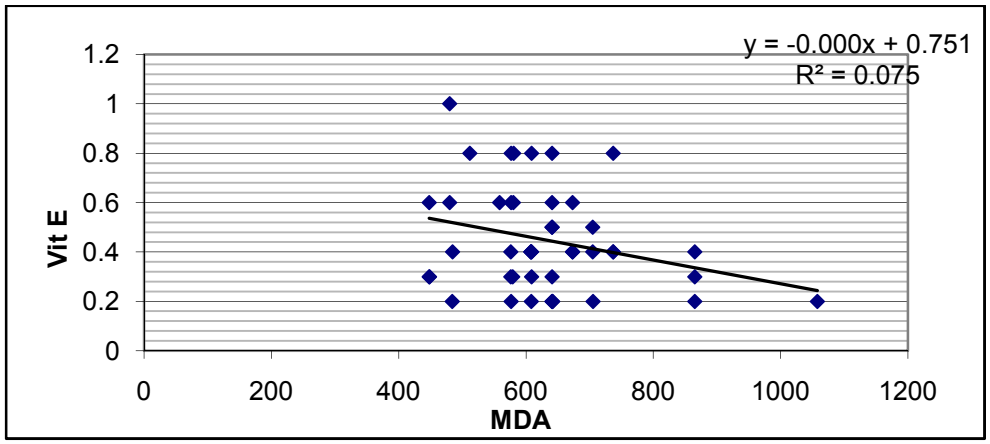
The results obtained from the control and the three groups are shown in Table 1. Group I as Controls with mean TT3 as 1.04 ± 0.11 ,TT4 8.3 ± 1.0 and TSH as 2.58 ± 0.99.Group II (n=15) as Hypothyroidism with mean TT3 value <0.59 ± 0.43 (p<0.0001), TT4 as <4.09 ± 3.0(p<0.0001) , TSH 87 ± 66 (p<0.0001) when compared with controls , Group III (n=15) as Hyperthyroidism with mean TT3 value > 1.9 ± 1.8 (p<0.01),TT4 as > 11.4 ± 4.9(p<0.0001) and TSH <0.04 ± 0.10(p<0.0001), Group IV (n=15) as subclinical hypothyroidism with mean TT3 as 0.9 ± 0.26 (p<0.01) , TT4 9.0 ± 3.1(p:Not significant) and TSH as 7.5 ± 1.5 (p<0.0001).

Table 2: Serum levels of MDA, Vitamin E and Vitamin C :

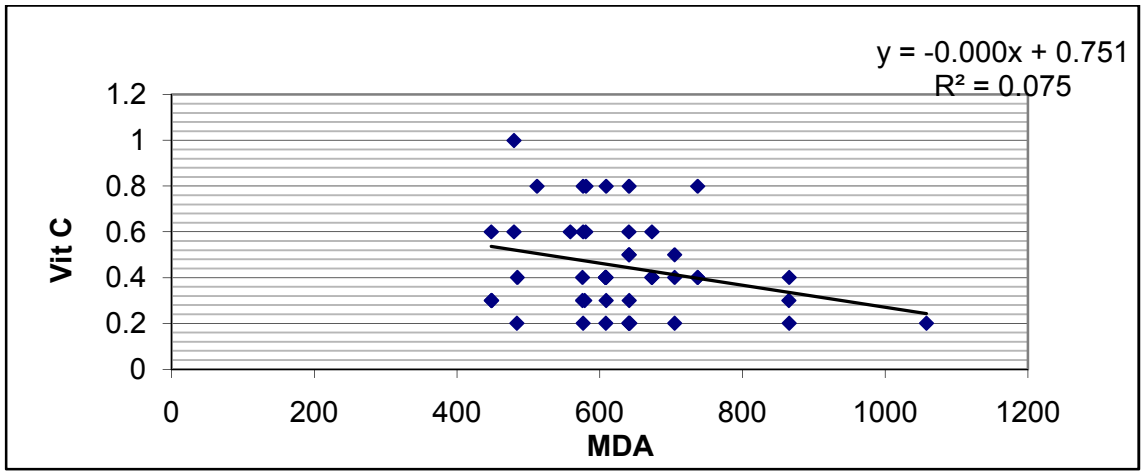
	Controls	Hypothyroidism	P value	Hyperthyroidism	P value	Subclinical hypothyroidism	P value
MDA	201.2±0.99	626.8±118.7	<0.0001	596.85±93.1	<0.00001	666.58±141.95	<0.00001
Vit E	6.8± 1.2	1.82±0.85	<0.0001	2.51±1.45	<0.00001	2.83±1.15	<0.00001
Vit C	0.91±0.19	0.48±0.24	0.001	0.53±0.24	0.001	0.61±0.45	0.01

The results of MDA levels were significantly elevated in all the three groups in Group II with highly significant p value (<0.00001) , in Group III with highly significant p value (<0.00001) and Group IV with highly significant p value (<0.00001) when compared with controls. Vitamin E was decreased in all the three groups when compared with controls with highly significant p value (p<0.00001 in all the three groups) .Vitamin C is also significantly reduced in all the three groups with p value (0.0001, 0.001 and 0.01) respectively. A significant negative correlation was observed between MDA and Vitamin E (r2=0.075) and MDA and Vitamin C (r2=0.075) as represented in Graph 1 and Graph 2.

Graph 1: Correlation between MDA and Vitamin E



Graph 2: Correaltion between MDA and Vitamin C



Discussion:

The study reveals correlation between thyroid hormones and oxidative stress.Thyroid hormones accelerate the cellular reaction and increase oxidative metabolism, they have the ability to target, influence and alter the metabolism of virtually every cell in the body. Oxidative stress arises when there is overwhelming production of free radicals and the available antioxidant defense mechanism falls short and unscavanged free radicals remain free which eventually oxidizes essentially components of cell i.e DNA , Proteins and membrane bound lipids. MDA is formed as a result of lipid peroxidation [1] and each cell has a counter mechanism to nullify the effects of free radical production by DNA repair enzymes and / or antioxidants [25,26].

If oxidative stress and antioxidants are not regulated properly they lead to a variety of chronic and degenerative diseases ageing and some acute pathologies [3]. In hypothyroidism Hyperthyroidism and subclinical hypothyroid there is an imbalance in thyroid hormones which lead to production of reactive oxygen species and concomitant use of antioxidants.

Resch et al [4,8,24] ,found that hypothyroidism was associated with enhanced oxidative stress and lipid peroxidation and proposed that this might lead to the development and progression of atherosclerosis.In our study MDA was significantly elevated in all the three

groups when compared with controls. In hyperthyroidism patients also due to excess hormones there was an increased production of MDA [9,27].

Vitamin E and Vitamin C are the antioxidant vitamins and are major defenses against harmful effects of Reactive Oxygen Species in cells. Vitamin E has an important role in quenching the free radicals produced and also increasing the capability of the immune system [14,16]. In our study Vitamin E levels are lowered indicating production of higher rate of free radical metabolism. The decreased level of Vitamin E is due to its use in preventing free radical damage that seems more extensive in thyroid dysfunctions and are on par with studies Gracin et al 1983 and Mano et al 1998 [10,17].

Studies have demonstrated that Vitamin E acts as a scavenger in thyroid follicular dysfunction and also they have demonstrated that active oxygen radicals inhibit the activity of an enzyme responsible for the conversion of T4 to the active hormone T3and that sufficient Vitamin E levels may mitigate that effect

Vitamin E as an antioxidant might have indirectly caused the destruction of H2O2 , the required oxidizing agent for iodide oxidation, thus leading to a decrease in thyroid hormone biosynthesis [12,13].Vitamin E is significantly reduced in our study explaining the role of Vitamin E as defensive antioxidant.

Vitamin C is also a very potent antioxidant because it is reduces the tocopherol back to alpha tocopherol. Vitamin E is a universal antioxidant and it reduces the peroxyl radical to much less reactive hydroperoxides and decreases the step in lipid peroxidation [12, 19, 20].

Conclusion:

In the present study a high significant inverse correlation was found between MDA and Vitamin E , also between MDA and Vitamin C in all the three groups of thyroid disorders.

There is an increase in reactive oxygen species induced by imbalance of thyroid hormones that can lead to oxidative stress condition with a consequent lipid peroxidation response. Antioxidant therapy and antioxidant diet should be advised along with thyroid hormone replacement therapy to diminish further complications.

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