A STUDY ON EVALUATION OF ISCHAEMIA MODIFIED ALBUMIN AND ITS RELATIONSHIP IN HYPERTHYROIDISM

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ABSTRACT

BACKGROUND

Hyperthyroidism is characterised by increased levels of thyroid hormones leading to hypermetabolic state. More common in females than males with sex ratio of up to 5:1. Thyroid hormone functions as a stimulus to metabolism and is critical for normal functioning of the cell. Under oxidative stress, Ischaemia Modified Albumin (IMA) is considered as one of the marker of ischaemia-reperfusion injury. Albumin has the tendency to attach to metals like copper and cobalt at N- terminus. Ischaemic conditions make albumin to lose its capacity to bind to metal ions due to change in its structural confirmation at the binding site.
Aim- This study was done to evaluate IMA and its relationship in hyperthyroidism.

MATERIALS AND METHODS

A descriptive, comparative study was done with 30 newly diagnosed hyperthyroid patients with elevated T3, T4 values and decreased TSH values were considered as cases, and 30 age and sex matched individuals with normal thyroid function tests were considered as controls. Thyroid profile was done by Enzyme linked immunofluorescent assay and IMA was estimated by colorimetric methodology.
Statistical Analysis**-** Independent sample t test was used. Statistical analysis was done by using SPSS version 13.0 (Statistical Package for the Social Sciences). Values are expressed as Mean ± SD, p value <0.05 was considered significant.

RESULTS

Ischaemia Modified Albumin levels were found to be significantly increased in hyperthyroid patients (0.73 ± 0.10 OD units) when compared to healthy controls (0.28 ± 0.01 OD units) (p=0.00).

CONCLUSION

Our study shows that there is significant elevation in IMA levels which may be due to the consequence of oxidative stress and ischaemia prevailing in hyperthyroid state.

KEYWORDS

Oxidative Stress, Hyperthyroidism, Ischaemia Modified Albumin.

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BACKGROUND

Under oxidative stress, Ischaemia Modified Albumin (IMA) is considered as one of the marker of ischaemia/reperfusion injury. Albumin has the tendency to attach to metals like copper and cobalt at N- terminus. Ischaemic conditions make albumin to lose its capacity to bind to metal ions due to change in its structural confirmation at the binding site. It also acts as a mortality predictor in renal disorder,[1] predictor of longterm outcome in myocardial infarction.[2] Alterations in the functional capacity of albumin in patients with decompensated cirrhosis is associated with increased mortality.[3] There is potentiation of ischaemia-reperfusion liver injury in hyperthyroidism.[4] Sheu et al found that the complications of ischaemic stroke were 1.44 times greater in hyperthyroidism patients.[5]

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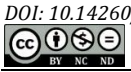

Free thyroid hormones are elevated in ischaemic stroke patients. Studies have shown that hyperthyroidism can aggravate neurological damage due to cerebral ischaemia leading to oxidative stress and modulates the outcome of ischaemic reperfusion injury.[6] Hyperthyroidism is characterised by increased levels of thyroid hormones leading to hypermetabolic state.[7] More common in females than males with sex ratio of up to 5:1.[8] Thyroid hormone functions as a stimulus to metabolism and is critical for normal functioning of the cell. Signs and symptoms include palpitation, heat intolerance, nervousness, insomnia, breathlessness, increased bowel movements, absent menstrual periods, fatigue, tachycardia, weight loss, muscle weakness, hair loss, dysphagia, staring look, etc.[9] Since IMA is considered as a marker of ischaemia and oxidative stress we took up this study of evaluating the IMA levels in hyperthyroidism.

MATERIALS AND METHODS

A descriptive, comparative study was done with 30 newly diagnosed hyperthyroid patients with elevated T3, T4 values, and decreased TSH values were considered as cases, and 30 age and sex matched individuals with normal thyroid function tests were considered as controls. Thyroid profile

was done by Enzyme linked immunofluorescent assay and IMA was estimated by colorimetric methodology.

RESULTS

Individuals with normal thyroid function tests i.e. T_3 (0.9-2.3 nmol/L), T_4 (60-120 nmol/L), TSH (0.25-5 µIU/mL) were considered as controls. The cases were selected from the medicine outpatient department after being investigated for hyperthyroidism for the first time. 23 females and 7 males were selected in our study as cases between the age group 35 to 55 years. 30 age and sex matched individuals as Controls were selected based on the thyroid function tests which were under the normal limits. Patients with history of chronic smoking; alcoholism; diabetes mellitus; liver, kidney, cardiac, endocrinal and immunological diseases were excluded in both the groups. Sample size was considered as per the convenience. Informed consent was taken from all subjects involved in the study which was approved by institutional ethics committee.

Under aseptic measures, blood sample was drawn and was used for analysis of thyroid profile and serum IMA levels. Bar-Or et al method was used for estimation of IMA levels. 200 µL of serum is incubated with 50 µL of 0.1% cobalt chloride in water for 10 min. at room temperature for adequate cobalt-albumin binding. 50 µL of dithiothreitol (DTT) was used for colourising the reaction for 2 min. before quenching with 1 mL of 0.9% NaCl. The absorbance (Optical density) was measured at 470 nm. Colour development with DTT was compared with serum-cobalt blank without DTT and expressed as OD units. Thyroid profile analysis was done by ELFA (Enzyme linked immunofluorescent assay) methodology. Reference range of different parameters are IMA (0.25-0.32 OD units), FT_3 (4-8.3 pmol/L), FT_4 (9-20 pmol/L).

Parameter	Cases (30)	Control (30)	p-value
Age (years)	47.23 ± 4.36	46.06 ± 3.375	
IMA (OD units)	0.73 ± 0.10	0.28 ± 0.01	0.001
T3 (nmol/L)	4.41 ± 0.93	1.63 ± 0.38	0.001
T4 (nmol/L)	255.70 ± 71.58	90.40 ± 15.77	0.001
TSH (µIU/mL)	0.03 ± 0.01	3.25 ± 0.71	0.001
FT3 (pmol/L)	8.71 ± 3.29	4.57 ± 0.36	0.001
FT4 (pmol/L)	24.34 ± 15.41	17.35 ± 1.38	0.016

Table 1

*p value <0.05 – significant, † Values – Mean ± SD.

Ischaemia Modified Albumin levels were found to be significantly increased in hyperthyroid patients (0.73 ± 0.10 OD units) when compared to healthy controls (0.28 ± 0.01 OD units) (p=0.00).

DISCUSSION

From the study, we can see that IMA levels are significantly elevated in hyperthyroid patients as compared to healthy controls (0.73 ± 0.10) (p value- 0.001). Ischaemia Modified Albumin (IMA) is considered as one of the marker of ischaemia/reperfusion injury in clinical conditions which include ischaemic events in their pathophysiology. The human serum albumin has the ability to bind to certain metal ions particularly cobalt and copper at the N-terminus. On exposure to ischaemic environment, structure of albumin N-terminus is changed such that it can no longer bind to metal ions. Hyperthyroidism is a clinical condition characterised by excess secretion of thyroid hormones (T3, T4) by thyroid gland with decreased TSH values. It is more common in females than males with sex ratio of up to 5:1. It is a hypermetabolic state known for high level of oxidation and ischaemic events leading to alteration in the albumin interaction site with metal ions.[10, 11] Studies have shown that hyperthyroidism can aggravate neurological damage due to cerebral ischaemia and modulates the outcome of ischaemic reperfusion injury. Free thyroid hormone levels are found to be elevated in ischaemic stroke patients. Sheu et al found that the complications of ischaemic stroke were 1.44 times greater in hyperthyroidism patients. IMA has been considered as biochemical marker for the myocardial ischaemia and coronary vasospasm.[12, 13] It has been proved in literature that IMA is a marker of oxidative stress, hence the increased IMA levels in hyperthyroidism points towards oxidative stress which could be due to production of reactive oxygen species as a result of ischaemia/reperfusion injury.[14,15]

CONCLUSION

Our study concludes that an elevated level of IMA is seen in hyperthyroidism, which may be due to oxidative stress and ischaemia which is prevailing in hyperthyroidism status. Major limitation of this study is the small sample size. Studies with larger sample size are needed for further evaluation.

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