ASSESSMENT OF THYROID PARAMETERS IN ALCOHOLIC LIVER DISEASE

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ABSTRACT

Normal level of thyroid hormone is important for normal hepatic function as it maintains the metabolism of bilirubin by playing a role in the enzymatic activity of glucuronyl transferase and by regulating the level of ligandin. The liver in turn glucuronidates and sulphates the thyroid hormone, excretes into bile and regulates their systemic endocrine effects. Therefore, hepatic dysfunction is commonly observed in patients with thyroid disease. Mean levels of Gamma-glutamyl transferase are increased in alcoholic cirrhosis with alcohol abuse of <10 years duration. In this study thyroid function tests and liver function tests were performed on the 200 subjects, of which 100 subjects were patients with Alcoholic Liver Disease, 100 were healthy controls and it was found that the serum tri-iodothyronine and free tri-iodothyronine levels were decreased and levels of Thyroid stimulating hormone were increased in patients with Alcoholic Liver Disease as compared to controls.

KEYWORDS: ALD, Thyroid hormones, Deiodinase, Gamma-glutamyl transferase.

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INTRODUCTION

Alcoholic liver disease is a term that encompasses the liver manifestations of alcohol overconsumption, including fatty liver, alcoholic hepatitis, and chronic hepatitis with liver fibrosis or cirrhosis. Of all chronic heavy drinkers, only 15–20% develop hepatitis or cirrhosis, which can occur concomitantly or in succession. 80% of alcohol passes through the liver to be detoxified. Additionally, the liver has tremendous capacity to regenerate and even when 75% of hepatocytes are dead, it continues to function as normal. Alcoholism causes development of large fatty globules the liver and can begin to occur after a few days of heavy drinking. Alcohol is metabolized by alcohol dehydrogenase (ADH) into acetaldehyde, then further metabolized by aldehyde dehydrogenase (ALDH) into acetic acid, which is finally oxidized into carbon dioxide (CO$_2$) and water (H$_2$O). Gamma-glutamyl transferase (GGT) is an enzyme that transfers gamma-glutamyl functional groups. It is found in many tissues, the most notable one being the liver. GGT plays a key role in the gamma-glutamyl cycle, a pathway for the synthesis and degradation of glutathione. Isolated elevation or disproportionate elevation compared to other liver enzymes (such as ALP or ALT) can indicate alcohol abuse or alcoholic liver disease. Alcohol might increase GGT production by inducing hepatic microsomal production, or it might cause the leakage of GGT from hepatocytes. GGT is a sensitive and highly specific test of liver cell injury in suspected alcoholics and is superior to transaminase determination. GGT remains the best of simple lab screening test and is superior to transaminase determination. GGT from hepatocytes. GGT is a sensitive and highly specific test of liver cell injury in suspected alcoholics and is superior to transaminase determination. GGT remains the best of simple lab screening test and is superior to transaminase determination. GGT might increase GGT production by inducing hepatic microsomal production, or it might cause the leakage of GGT from hepatocytes. GGT is a sensitive and highly specific test of liver cell injury in suspected alcoholics and is superior to transaminase determination. GGT remains the best of simple lab screening test and is superior to transaminase determination. GGT plays a key role in the gamma-glutamyl cycle, a pathway for the synthesis and degradation of glutathione. Isolated elevation or disproportionate elevation compared to other liver enzymes (such as ALP or ALT) can indicate alcohol abuse or alcoholic liver disease.

MATERIALS AND METHODS

The present study consists of 200 subjects, 100 subjects were patients with alcoholic liver disease 100 were healthy controls. The study was conducted at Goa Medical College and Hospital, Bambolim-Goa during the period of 2013-2014. Ethical clearance was obtained from the institution's ethical committee. 7-8ml of fasting samples were collected in plain bulbs by venepuncture, under aseptic conditions of the 200 subjects. Serum was seperated by centrifuging blood samples at 3000 rpm in clinical centrifuge for 10 minutes. Serum was used to perform thyroid function tests and liver function tests on the above mentioned 200 subjects. All tests were performed on Ci2000 autoanlyser. ARCHITECT Total T$_3$(tri-iodothyronine) assay is a two step immunoassay to determine the presence of Total T$_3$ in human serum and plasma using CMIA (Chemiluminescent Microparticle ImmunoAssay) technology with flexible assay protocols, referred to as chemiflex. The sample and anti T$_3$ coated paramagnetic microparticles are combined. T$_3$ present in the sample binds to the anti-T$_3$ coated microparticles. After washing, T$_3$ acridinium-labeled conjugate is added. Pre-trigger and trigger solutions are then added to the reaction mixture, the resulting chemiluminescent reaction is measured as relative light units (RLUs). Reagent contains microparticles 1 or 4 bottles (6.6ml/27.0ml) anti-T$_3$ coated particles in MES buffer with sheep IgG Stabilizers and 1 or 4 bottles (5.9ml/26.3ml) T$_3$ acridinium-labeled conjugate in citrate buffer with NaCl and triton X-100 stabilizers. Antimicrobial agent is used as preservative. Calibrator range is 0.0-8.0ng/mg. Expected value of TT$_3$ is 0.58-1.59ng/mL. The sample and anti T$_4$ coated paramagnetic microparticles are combined. T$_4$ present in the sample binds to the anti-T$_4$ coated microparticles. After washing, T$_4$ acridinium-labeled conjugate is added. Pre-trigger and trigger solutions are then added to the reaction mixture, the resulting chemiluminescent reaction is measured as RLUs. Reagent contains microparticles 1 or 4 bottles of anti-T$_4$ coated particles in TRIS buffer. Calibrator range is 0.0-24.0 µg/dL. Expected value of TT$_4$ is 4.87-11.72 µg/dL. The ARCHITECT TSH assay is a two step immunoassay to determine the presence of thyroid stimulating hormone (TSH) in human serum and plasma using CMIA technology with flexible assay protocols. The sample and anti-β TSH antibody coated paramagnetic microparticles and TSH Assay Diluent are combined. TSH present in the sample binds to the anti-TSH coated microparticles. After washing, anti-α TSH acridinium labeled conjugate is added. Pre-trigger and trigger solutions are then added to the reaction mixture, the resulting chemiluminescent reaction is measured as RLUs. Reagent contains microparticles 1 or 4 bottles (6.6ml/27.0ml) anti-β TSH coated particles in TRIS buffer with protein (bovine) Stabilizers. Minimum concentration is 60 ng/mL. Calibrator range is 0.0000-100.0000 µIU/mL and expected value is 0.35-4.94 µIU/mL. The ARCHITECT Free T$_3$ assay is a two step immunoassay to determine the presence of free (unbound) T$_3$ in human serum and plasma using CMIA technology. The sample and anti T$_3$ coated paramagnetic microparticles are combined. Free T$_3$
present in the sample binds to the anti-T3 coated microparticles. After washing, T3 acidinium-labeled conjugate is added. Pre-trigger and trigger solutions are then added to the reaction mixture, the resulting chemiluminescent reaction is measured as RLUs. Reagent contains microparticles 1 or 4 bottles (6.6ml/27.0ml) anti-T3 coated particles in MES buffer with sheep IgG Stabilizers. Calibrator Range is 0.0-30.0 pg/ml. Expected value is 1.0, 6.0 pg/ml. Quality control procedures for TT3, TT4, TSH, FT3, FT4 requires a single sample of all control levels tested once every 24 hours each day of use. The ARCHITECT TT3, TT4, TSH, FT3, FT4 utilizes a 4 parameter logistic curve fit data reduction method to generate a calibration curve. Total Bilirubin-Total (conjugated and unconjugated) Bilirubin couples with diazoreagent in the presence of surfactant to form azobilirubin. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total Bilirubin concentration. Expected values are 0.2 to 1.2 mg/dL in adult serum. Direct (conjugated fractions) bilirubin couples with a diazonium salt in the presence of sulfamic acid to form the coloured compound azobilirubin. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total Bilirubin concentration. Expected values are 0.0 to 0.5 mg/dL in adult serum. Aspartate Aminotransferase (AST) present in the sample catalyzes the transfer of the amino group from L-aspartate to α-ketoglutarate, forming pyruvate and L-glutamate. Oxaloacetate in the presence of NADH and lactate dehydrogenase (MDH) is reduced to L-malate. In this reaction, NADH is oxidized to NAD. The reaction is monitored by measuring the rate of decrease in absorbance between L-2-amino-2-nitrobenzoate is measured as an increase in absorbance which is proportional to the GGT activity in the sample. Expected values are 0.2 to 1.2 mg/dL in adult serum. 

Table 1

<table>
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<th>Parameters</th>
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B - 773
The present study consists of 200 subjects, 100 subjects were patients with alcoholic liver disease and 100 were healthy controls. In this study, patients with alcoholic liver disease were evaluated for thyroid function tests and it was found that the serum T₃ and FT₃ levels were decreased and levels of TSH were increased as compared to controls. The mean serum T₃ level in patients with ALD was 0.41±0.082 and in control group was 0.96±0.27. This difference was statistically significant (p value <0.001). The mean serum FT₃ level in patients with ALD was 1.35±0.41 and in control group was 2.29±0.62. The mean serum TSH level in patients with ALD was 4.28±2.21 and in control group was 2.29±1.33. This difference was statistically significant (p value <0.001).

**DISCUSSION**

Thyroid hormones are essential for normal organ growth, development, function and regulation of the basal metabolic rate of all cells and therefore, its alteration can affect the entire metabolism. Most affected organs include liver and heart. So, it alters the liver enzymes like ALP, AST, ALT, GGT and cardiac enzymes like CPK, LDH and AST. These biochemical changes, usually mild, are also reversible with adequate thyroid replacement therapy. The findings of our study is in corroboration with findings of the study by Yadav A. et al. and Pandey R. et al. Malik and Hodgson et al who mentioned that thyroid hormones T₃ and T₄ regulate BMR of hepatocytes and modulate all the organ functions. The liver, muscle and kidney in turn metabolizes thyroid hormones and...
regulates their systemic endocrine effects. Therefore, thyroid dysfunction may disturb liver, muscle and other organ functions and vice versa. Thyroid hormones regulate the basal metabolic rate of all cells including hepatocytes. The liver in turn metabolizes the thyroid hormones and regulates their systemic endocrine effects.

Israel et al. may have thyroiditis, hyperthyroidism or hypothyroidism functions. (ii) Some patients with chronic liver diseases have alterations of thyroid hormone metabolism or tests secondary to liver disease. And (iv) Liver or thyroid disorders related to the therapy of thyroid or liver disease.

Elevated serum T3 and T4, elevated rT3, and normal TSH values have been observed. In patients with alcoholic liver disease Israel et al. reported an inverse correlation between serum T3 concentrations and the severity of liver dysfunction as well as a progressive T3 increase suggesting that T3 concentrations in patients with alcoholic liver disease may be considered as helpful prognostic indicator. The low total and free T3 levels may be regarded as an adaptive hypothyroid state that serves to reduce the basal metabolic rate within hepatocytes and preserve liver function and total body protein stores. Indeed, a recent study in cirrhotic patients showed that the onset of hypothyroidism from intrinsic thyroid disease of various aetiologies during intrinsic thyroid disease of various aetiologies during liver cirrhosis resulted in biochemical improvement in liver function. 

CONCLUSION

Hepatic dysfunction is commonly observed in patients with thyroid disease. The mean T3 and FT3 levels were decreased in patients with alcoholic liver disease has compared to controls probably because type I deiodinase which is the major enzyme in liver carries out 5’ deiodination of T4 to form T3. Type II 5’ deiodinase is important for providing the T3 required to stimulate the pituitary to synthesize and secrete TSH.

CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES