The Activities of Vitamin D and Anti-Thyroperoxidase (Anti-TPO) Antibodies in Uncontrolled Type 2 Diabetes

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Abstract

The fat soluble vitamin D and anti Thyroperoxidase (anti TPO) enzyme, an enzyme involved in thyroid hormone synthesis have a role in uncontrolled type 2 diabetes mellitus (T2D). Vitamin D has diverse functions in human body and it carries out its function via vitamin D receptors (VDR). These VDRs are present in most types of immune cells. The immuno modulator property of vitamin D is due to its effects on T and B lymphocytes. Thus, vitamins D modifies cell mediated immune responses and regulate inflammatory T cell activity. In T2D, there is insulin resistance (high titers of insulin antibodies), decreased vitamin D activity and increased anti TPO activities. This study concludes a probable relation between immune related activity, signaling molecules in T2D which increases the progression of this condition to autoimmune thyroid disease.

Keywords: Vitamin D; Anti TPO antibodies; Type 2 diabetes; Insulin resistance

Introduction

Vitamin D plays a pivotal role in calcium metabolism and its deficiency may be associated with serious diseases including cancer, cardiovascular disease, and type 2 diabetes(T2D) (Holick MF, 2007). The T2D represents a global health problem and its onset is in adulthood (above 35 years) due to insufficient production of insulin (or) may be due to over production of insulin leading to insulin resistance (American Diabetes Association, 2013). The insulin resistance is mostly seen in overweight or obese individuals. Vitamin D plays an important role in the regulation of calcium and this calcium helps to control the release of insulin thus, vitamin D helps in proper insulin function via calcium (Mitri, 2011). Anti Thyroperoxidase (anti-TPO) antibodies are the antibodies secreted against the action of the enzyme thyroperoxidase, involved in oxidation of iodide in thyroid hormone synthesis. Anti TPO antibodies levels are raised in autoimmune disease, Hashimoto’s thyroiditis (HT). HT is an autoimmune disease caused by the destruction of thyroid gland in various degrees via numerous immune mechanisms (Fatma Dilek Dellal, 2013). The present study aims to determine the association of vitamin D and anti TPO antibodies in uncontrolled type 2 diabetes.

Materials and Methods

The study includes 30 samples of age group between 40-65 years collected from diabetic people type 2 category (not autoimmune) and 30 age matched healthy control samples attending the Out Patient (OP) department of Chalmeda Anand Rao Institute of Medical Sciences hospital. There history revealed that they are diabetics taking medication since 5- 15years.

Inclusion Criteria:
Type 2 Diabetics with Fasting Blood glucose (FBS) above 150mg/dl and Post lunch blood glucose (PLBS) above 220mg/dl.

Exclusion Criteria:
Pregnant women, diabetics under control (FBS Below 150mg/dl & PLBS below 220mg/dl).

The samples are collected in fasting (12 hours) and Postprandial (2 hours after lunch) conditions. These samples were allowed to clot for 30minutes and then
centrifuged at 3000rpm for 15 minutes then serum is separated for analysis.

The blood glucose estimation (fasting and postprandial conditions) was done by GOD POD (Glucose Oxidase and Peroxidase) method. The vitamin D levels are estimated by chemiluminiscence analyzer (Snibe Company, China) and anti TPO levels are analyzed by ELISA method (AESKULISA kit).

**Statistical Analysis**
The mean and SD values are calculated using paired student t test using graph pad prism.

**Result**
The fasting and postprandial blood glucose levels are more than the diabetic range (more than 200 mg/dl). The mean and SD values of anti TPO activities of sample (34.3± 30.16) and controls (17.57± 9.4) were statistically significant; similarly vitamin D levels of sample (19.08 ± 15.77) and control (62.6 ± 23.7). The p values are significant (< 0.01 for sample group and < 0.001 for control group) (Table 1).

<table>
<thead>
<tr>
<th>Anti TPO</th>
<th>Vitamin D</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (Sample group)</td>
<td>34.3 ± 30.2</td>
<td>19.1 ± 15.8</td>
</tr>
<tr>
<td>Mean ± SD (Control Group)</td>
<td>17.6 ± 9.4</td>
<td>62.6 ± 23.7</td>
</tr>
</tbody>
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**Discussion**
The prevalence of anti TPO antibodies in diabetic persons has been variously reported as ranging from 8–22% (Pettit, 1961; Landing, 1963; Whittingham, 1971; Goldstein and Maccuish, 1975). It has been suggested that diabetic people should be routinely screened for evidence of thyroid dysfunction (Feely and Isles, 1979). There are reports that treatment of diabetes with sulphonylurea led to an increased incidence of goiter and hypothyroidism (Hunton, 1965). This sulphonylurea has goitrogenic potential and has ability to decrease the serum thyroid binding proteins (Ganz and Kozak, 1974; Prince, 1980). In uncontrolled T2D the plasma insulin levels are high and sensitivity to insulin is decreased making the body insulin resistant. High titers of antibodies to insulin (exogenous insulin) are seen in T2D which may also contribute to insulin resistance. The anti TPO measurement is reliable in autoimmune thyroid disorders (AITD) (Sabitha kandi and Pragna Rao, 2012). In conditions like Insulin resistance and AITD there are decreased vitamin D levels. In T2D, the role of vitamin D is due to the presence of vitamin D Receptor (VDR) on pancreatic islet cells. The present study shows that there is an insulin resistance which caused a raised anti TPO levels (33%) and decreased vitamin D status (54%) of T2D individuals. Vitamin D plays a role in Immune modulation, improves insulin sensitivity and increases insulin secretion. Vitamin D exerts its function through vitamin D receptor (VDR) which is found in immature immune cells of thymus and CD8 and also β cells of pancreas (Kostoglou-Athanassiou, 2013). The immunomodulator properties of vitamin D are due to its effect on T and B lymphocytes mediated by VDR. This VDR activates IL-4 and IL-5 production, suppresses interferon, gamma and IL-2 production. Thus, vitamins D modulates cell mediated immune responses and regulates inflammatory T-cell activity (Boonstra, 2001; Van Halteren, 2002; Mahon, 2003; Van Halteren, 2004).

Vitamin D ↓

exerts its effect via

Vitamin D receptor (VDR)
↓
Inhibit dendritic cell dependent T cell activation
↓
Promote regulatory T cell properties
↓
Activates CD4 T cells
↓
Increases production of IL-4 & IL-5

Decreases Interferon, Gama, IL-2 production

Vitamin D supplementation decreased 19% chances of developing T2D because of its role in regulation of calcium and indirect role in controlling insulin secretion. Every 4ng/ml increase in vitamin D was associated with a 4% lower risk of getting T2D later in life (Mitri, 2011; Davidson, 2013; Belenchia, 2013).
Conclusion

In uncontrolled T2D, the management includes high dose of insulin which leads to insulin resistance because of high titers of antibodies to insulin. This insulin resistance decreases the expression of insulin receptors on cells, thus decreasing the VDR function on β cells of pancreas. As vitamin D exerts its function either to lower or decrease calcium levels, the decreased VDR expression on the cells in turn lowers the calcium levels and increases the activities of anti TPO antibodies; thus there is an inverse relationship between the activities of calcium and anti TPO antibodies. In uncontrolled T2D there are decreased vitamin D levels and increased chances of AITD.

Further studies are required to know the probable hormonal signaling pathways involved in the actions of insulin receptors, VDR and anti TPO antibodies in uncontrolled T2D as most of T2D on long run leads to complications of thyroid diseases.

References
