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## Combined effect of Levothyroxine and Oral Hypoglycemic agents on blood glucose level in hypothyroidism patients- A Prospective Observational Study

Anandkumar S\*, Shanmugapandiyan P

Department of Pharmacy, Ponnaiyah Ramajayam Institute of Science and Technology, (PRIST University), Thanjavur-613403, Tamilnadu, India



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### ABSTRACT

This study was aimed to evaluate the effect of levothyroxine combination therapy on blood glucose level in hypothyroidism patients. The Study was carried out in a private hospital at Tiruchengode as prospective observationally. Patients who were under the management of thyroid disorder and diabetes mellitus for 1 year period was screened and selected for the study. Effect of levothyroxine on blood glucose level and using a Mini mental state examination questionnaire their cognitive skills were also assessed. Independent sample t' test was used to compare the blood glucose level and complication of the management. There were 42 patients were included in the study and the patients who were on Levothyroxine and Glimepride with Metformin labeled as Group 1 and Glimepride with Metformin alone was labeled as Group 2. Glimepride with metformin therapy shows greater percentage of blood glucose level reduction and significant  $p < 0.05$  cognitive impairment was found in the combination therapy. Diabetes mellitus management with levothyroxine and glimepride with metformin has an association on the managing blood glucose level. Efficient management of blood glucose level was obtained with glimepride with metformin alone. Cognitive impairment was high in the combination therapy of levothyroxine and glimepride with metformin.

### \*Corresponding Author

Name: Anandkumar S  
 Phone: +91 9942541867  
 Email: sakumar0307@gmail.com

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### INTRODUCTION

Hypothyroidism is the metabolic disorder of the thyroid gland. During hypothyroidism clinical condition thyroid gland not produce sufficient amount of thyroid hormone for the metabolic need of the body. Human body has the largest endocrine gland

is known as thyroid gland it present in the neck that produce thyroid hormone. This weighs about 15-20 gm in human. Thyroid gland consists of two glands both the glands secrete thyroid hormone. The gland is composed of spherical follicles that secretes and stores thick, colloid, sticky protein material. Para follicular cells are present between the follicles, which secretes hormone calcitonin. This gland receives the blood from the inferior thyroid artery for the normal thyroid functions. Hypothyroidism requires proper management and improperly treated hypothyroidism resulting in metabolic management difficulty like diabetes mellitus ([Kostoglou-Athanassiou and Ntalles, 2010](#)).

Hypothyroidism and its management is the risk factor for diabetes mellitus. On other hand thyroid replacement therapy leads to disruptions of carbohydrate. Thyroid replacement therapy does not alter glucose levels but some time it raise the

blood glucose level faster than the normal. Excessive thyroid hormones lead to increase the glucose absorption in gastro intestinal tract and also resulting in insulin resistance and insulin degradation and resulting in diabetic complications (Porterfield, 2000).

Thyroid hormone leads to increase glucose absorption from peripherals and increase the glycogen productions resulting in difficulty in blood glucose management in diabetes mellitus patients. However hypothyroidism also managed with thyroid hormone that resulting in additional diabetic complication like diabetic ketoacidosis and insulin resistance (Hansen *et al.*, 2015). Patients with hypothyroidism and diabetes mellitus have risk of developing obesity and high dose was required for the diabetic management (McConnell, 1999; Samuels *et al.*, 2003; Adhimoolam and Arulmozhi, 2016).

So our study planned to compare and check the therapy of Glimepride 2mg and Metformin 500mg versus Levothyroxine 50mcg and Glimepride 2mg with Metformin 500mg combination therapy in blood glucose level and cognitive skills.

## MATERIALS AND METHODS

### Study design and sample

A prospective observational study was conducted in a Vivekananda Medical Care Hospital at Tiruchengode. The patients with hypothyroidism and diabetes mellitus with age group of 30 to 60 were included in the study.

### Sampling technique

Simple random sampling technique was employed in this study (Lemeshow *et al.*, 1990). According to this technique a sample group of 90 patients selected have an equal opportunity. According to the inclusive criteria of this study totally 42 patients were final participants until completion of the work. Chronically ill patients, Patients with multiple Drug therapy, improper availability of patients are not included in our study. Institutional Ethical committee approval was obtained from the Vivekananda Medical Care Hospital. Patients consent was obtained from the participants.

Totally 90 patients were included for our study from that proper follow up was from 42 patients so the study was performed with the same study populations. And the collected patients were separated into two groups. Patients were on the Levothyroxine 50 mcg with Glimepride 2mg with Metformin 500mg therapy was labeled as (Group 1), Patients were on the Glimepride 2mg with Metformin 500mg therapy was labeled as (Group 2) as mention in

Table 1. Blood glucose level and cognition was measured with suitable technique. Blood glucose level was measured by UV-Vis (Ultraviolet-Visible) method and Cognitive functions screening was measured with the help of Mini Mental State Examinations (MMSE) scale (Tombaugh and McIntyre, 1992). Score were calculated for the both the groups and data were compared and risk of cognition was also assessed in this study.

Group 1 was checked with Fasting Blood Glucose, Postprandial Blood Glucose initial phase and after 1 year of therapy for the both the groups. Group 2 was checked with Fasting Blood Glucose, Postprandial Blood Glucose and after 1 year of therapy for the both the groups. And cognition was analyzed for both the groups after 1 year of drug therapy and the mean was compared.

### Data collection tool

Data were collected through specially designed data entry format in order to collect the details of the Patient details including name, age, sex, known allergy, educational status, I.P No/O.P.No. Fasting Blood Glucose, Post Prandial Blood Glucose, Mini mental state examinations (MMSE) score and drugs treatment details were collected.

## RESULTS AND DISCUSSION

### Comparison on blood glucose level of both groups

In the group 1 before and after 1 year of management with Levothyroxine 50 mcg and Glimepride 2mg with Metformin 500mg therapy and the group 2 before and after 1 year of management of Glimepride 2mg with Metformin 500mg therapy shows significant reduction of Blood Glucose level. On comparison of both the groups does not show significant Blood Glucose Level reduction as mention in Table 2. Our study coincidence with similar study conducted on oral hypoglycemic agents and reported that metformin with glymepride have a significant glycemic control and between blood glucose level (Zhu *et al.*, 2013).

On the percentage of reduction in Blood Glucose Level between both the groups identified that Glimepride 2mg with Metformin 500mg shows greater percentage of reduction of Blood Glucose Level when compared to combination therapy of Levothyroxine 50mcg Glimepride 2mg with Metformin 500mg therapy. Our results shows that effective management of Blood Glucose Level was attain with the Glimepride 2mg with Metformin 500mg and also it proves that diabetes mellitus risk was increased significantly on combination therapy of

**Table 1: Demographic Characteristics of Patients**

Variables	Levothyroxine 50 mcg and Glimepride 2 mg with Metformin 500 mg (n=21)	Glimepride 2 mg with Metformin 500 mg (n=21)	Study Populations
Distribution of age			
30-40	04	02	06
41-50	11	09	20
51-60	06	10	16
Gender			
Male	08	09	17
Female	13	12	25

**Table 2: Mean Blood glucose level of Group 1 & Group 2**

Parameter (mg/dL)	Levothyroxine 50 mcg and Glimepride 2 mg with Metformin 500 mg	Glimepride 2 mg and Metformin 500 mg	Significance
Fasting Glucose Level	137.43±18.44	129.27±6.37	P>0.05
Post Prandial Glucose level	154.86±18.59	169.73±4.651	

Numbers indicate mean ± SD

P value of Student 't' test (Group 1 Vs Group2)

Significant P value (<0.05) in bold face

**Table 3: Percentage of reductions in blood glucose between group 1 & group 2**

Parameter (mg/dL)	Levothyroxine 50 mcg and Glimepride 2 mg with Metformin 500 mg	Glimepride 2 mg with Metformin 500 mg
Fasting Blood Glucose	19	62
Post Prandial Blood Glucose	28	33

**Table 4: Mini mental state Examination score between group 1 & 2**

Drugs	MMSE Score (mean±SD)	P Value
Levothyroxine 50 mcg and Glimepride 2 mg with Metformin 500 mg	13.43±2.3	P < 0.05
Glimepride 2 mg with Metformin 500mg	24.1±2.99	

P value of Student 't' test (Group 1 Vs Group 2)

Significant P value (<0.05) in boldface

Levothyroxine 50mcg Glimepride with Metformin 20mg as given in Table 3. Our study similar to the study concluded that the better glycemic control was attained in the diabetic mellitus patients alone (Kim *et al.*, 2014).

#### Comparison on cognition for both groups

MMSE was also calculated using the tools initial phase and after 1 year of therapy and its mean and standard deviation and its significance was identified that the patients with hypothyroidism and dia-

betes mellitus combined management patients have sever cognitive impairment (Biessels and Despa, 2018). And our study state that increased in age groups resulting in obviously decline in cognitive functions (Galea and Woodward, 2005).

Central nervous system functions was declined with the management of hypothyroidism patients with levothyroxine on other hand the patients with diabetic management alone not have any central nervous system dysfunctions. Diabetes management

alone not have cognitive impairment (Herath *et al.*, 2016).

When compared to Glimepride 2mg with Metformin 500mg therapy ( $24.1 \pm 2.99$ ) Levothyroxine 50mcg and Glimepride 2mg with Metformin 500mg ( $13.43 \pm 2.31$ ) combination therapy leads to significant cognition impairment ( $p < 0.05$ ) as mention in the Table 4. On study upon diabetic patient's population not have any cognitive decline throughout the study. On metformin drug therapy showed significant effects on cognitive functions. Diabetes mellitus patients have lesser cognitive impairment on compared to thyroid replacement therapy (Knouse and Safren, 2010).

## CONCLUSION

Hypothyroidism management along with diabetes mellitus management has an association on the managing Blood Glucose Level. Efficient management of blood glucose level was attaining with Glimepride with Metformin therapy. And the same time cognition impairment was high in the combination therapy of Levothyroxine and Glimepride with Metformin compared to the therapy of Glimepride with Metformin.

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