ORIGINAL RESEARCH

Changes in liver function, fluctuations in blood glucose, insulinsecretion and gender differences in patients with hyperthyroidism aftertreatment with propranolol hydrochloride tablets coalition withmethimazole tablets

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ABSTRACT

Introduction: Hyperthyroidism, an endocrine disorder characterized by an overactive thyroid gland, leads to increased levels of circulating thyroid hormones (T3 and T4), affecting numerous metabolic and physiological processes throughout the body. **Objective:** To find the changes in liver function, fluctuations in blood glucose, insulinsecretion and gender differences in patients with hyperthyroidism aftertreatment with propranolol hydrochloride tablets coalition withmethimazole tablets.**Methodology:** This comparative observational study was conducted and total of 165 patients diagnosed with hyperthyroidism were selected for this study. Patients with confirmed diagnosis of hyperthyroidism and had not previously received beta-blocker or antithyroid medication were included in the study. Patients with existing liver disease, diabetes, or other endocrine disorders that could impact metabolic outcomes were excluded. **Results:** Data were collected from 165 patients. Liver enzymes, specifically AST, ALT, and ALP, showed notable reductions of 25%, 30%, and 15%, respectively, with male patients experiencing greater enzyme decreases compared to females. Blood glucose levels also improved, with a 10% reduction in fasting blood glucose and a 15% decrease in OGTT levels, where females demonstrated a more pronounced improvement in glucose tolerance. The pre-treatment insulin sensitivity parameters reveal higher insulin resistance and fasting insulin levels in male hyperthyroid patients compared to females. Specifically, the mean HOMA-IR for males was 5.0 ± 1.2, while females had a slightly lower mean of 4.4 ± 1.0, indicating comparatively greater insulin sensitivity in females. **Conclusion:** It is concluded that combined propranolol and methimazole therapy is effective in managing hyperthyroidism by significantly improving liver function, blood glucose regulation, and insulin sensitivity.

INTRODUCTION

Hyperthyroidism, an endocrine disorder characterized by an overactive thyroid gland, leads to increased levels of circulating thyroid hormones (T3 and T4), affecting numerous metabolic and physiological processes throughout the body. Some of the signals include, rapid heartbeat, weight loss, increased food consumption and an overactive nervous system [1]. The effects of high doses of thyroid hormones on liver metabolism, on glucose homeostasis and on insulin release have recently become a subject of intense investigation in metabolic research because thyroid hormones are known to exert direct control on basal metabolic rate and energy expenditure [2]. Propranolol hydrochloride is a beta-adrenergic antagonist and methimazole is an antithyroid agent which are typically employed in practice for the treatment of the manifestation of the clinical syndome as well as control of hormone over production by the gland respectively [3]. Propranolol mainly concerns signs and symptoms of adrenergic form of hyperthyroid state that includes pass more, increased pulse rate, and anxiety. Understanding that beta-blockers do not affect thyroid hormone production,

this drug has been discovered to partially alleviate some sympathetic nervous system excitation due to hyperthyroidism, and to ease some of the more intolerable cardiac symptoms, to some degree [4]. Methimazole, on the other hand, inhibit the synthesis of thyroid hormones within the thyroid gland and therefore directly decreases concentration of these hormones in the body [5]. From the above details about hyperthyroidism, propranolol and methimazole used in combination, are employed on different aspects of hyperthyroidism and are effective in reducing the outlook of thyroid hormone levels and the related metabolism complications [6]. Hyperthyroidism is generally associated with the liver because the liver plays active part in the metabolism of hormones and glucose levels [7]. Hyperthyroidism raises the BMR and alters the activity of enzymes in the liver. These effects can change the function of the liver, the ability to synthesize bile acids and lipids metabolism and may cause liver damage in the severe condition. Hypothyroidism researches demonstrated that both propranolol and methimazole acting as thyroid hormones inhibitors also serve as regulators of liver enzymes and thus aid in stabilizing liver function. However, the kind of interaction between this improvement and the liver enzymes and the thyroid hormones are slightly different from one patient to another which gives hints to a probable genetic or lifestyle relation [8]. Patients with hyperthyroidism also have variation in blood glucose and insulin secretion. This remains true as thyroid hormones affect both glycogenolysis and gluconeogenesis and increased blood glucose levels. These changes result to glucose intolerance or even hyperglycemia in some patients who have underlying insulin resistance or even prediabetes [9]. Insulin secretion is affected in the same way as the level of glucose increases in the body, because of the efforts of the pancreas to secrete more insulin. All these have been seen to be compensated by the use of propranolol in combination with methimazole so as to supplement the normal formation of thyroid hormones thus curtailing the formation of glucose in the liver and boosting the manifestation of insulin [10]. However, even with these improvements, treatment outcome is stillPatient demographics strongly influence diabetes manifestation, and possibly sex also modulates blood glucose and insulin sensitivity. For example, some research that exists at the moment claims that the changes in blood glucose level can be greater among women because of hormonal changes and differences in body composition that affects insulin resistance [11]. Sexuality distinction makes hyperthyroidism a complex process because the symptoms and the reactions to the treatment depend on gender. For instance, the ability of the arteries to dilated, constricted or the rate at which drugs such as propranolol and methimazole are absorbed, distributed, metabolized and excreted from the body depends on the body weight, hormones and other differences [12].

OBJECTIVE

To find the changes in liver function, fluctuations in blood glucose, insulinsecretion and gender differences in patients with hyperthyroidism aftertreatment with propranolol hydrochloride tablets coalition withmethimazole tablets.

METHODOLOGY

This comparative observational study was conducted and total of 165 patients diagnosed with hyperthyroidism were selected for this study. Patients with confirmed diagnosis of hyperthyroidism and had not previously received beta-blocker or antithyroid medication were included in the study. Patients with existing liver disease, diabetes, or other endocrine disorders that could impact metabolic outcomes were excluded.

Data collection

Data were collected at baseline (before treatment) and after the 12-week treatment period. All patients received a standardized treatment protocol combining propranolol hydrochloride tablets (at a dose of 20–40 mg twice daily) and methimazole tablets (starting at 10–30 mg per day based on thyroid hormone levels). Thyroid function was adequately controlled and dosages of the agents were modified after four weeks with respect to TSH, Free T4, and T3. The duration of treatment was 12 weeks and the patients received strict follow up on their prescription refill and any side effects. Blood samples were also collected for aspartate aminotransferase [AST and alanine aminotransferase [ALT] activity and alkaline phosphatase [ALP] to check liver function. All the variations from the normal range of enzymes were documented. Blood glucose test was done after treatment and an oral glucose tolerance test (OGTT) was done to determine the body's response to glucose. Self monitoring of blood glucose levels before and after each meal compared to a standard level was done in the ability comparison. Select biochemical parameters included fasting serum insulin levels, and HOMA-IR was used to determine the level of insulin resistance and secretion. Insulin sensitivity was also compared with thyroid hormones levels. Levels of Free T3, Free T4 and TSH were measured in Baseline in order to examine the effectiveness of methimazole in reducing the synthesis of thyroid hormones.

Statistical Analysis

Data were analyzed using SPSS v11. Paired t-tests were used to compare pre- and post-treatment values within each group, while independent t-tests were conducted to analyze differences between male and female patients.

RESULTS

Data were collected from 165 patients. Liver enzymes, specifically AST, ALT, and ALP, showed notable reductions of 25%, 30%, and 15%, respectively, with male patients experiencing greater enzyme decreases compared to females. Blood glucose levels also improved, with a 10% reduction in fasting blood glucose and a 15% decrease in OGTT levels, where females demonstrated a more pronounced improvement in glucose tolerance. Additionally, insulin sensitivity metrics reflected a positive trend, as fasting insulin dropped by 20% and HOMA-IR values reduced by 22%, with males exhibiting higher improvements in insulin-related parameters.

Table 1: Clinical values of patients

Parameter	Baseline (Mean)	Post-Treatment (Mean)	% Change	Male % Change	Female % Change
Liver Function Tests					
AST (U/L)	75	56	-25%	-30%	-20%
ALT (U/L)	80	56	-30%	-35%	-25%
ALP (U/L)	150	128	-15%	-20%	-10%
Blood Glucose Levels					
Fasting Blood Glucose (mg/dL)	105	95	-10%	-8%	-12%
OGTT (2-hour Glucose, mg/dL)	160	136	-15%	-13%	-17%
Insulin and Insulin Sensitivity					
Fasting Insulin (μU/mL)	18	14.4	-20%	-25%	-15%
HOMA-IR	4.7	3.7	-22%	-27%	-18%

Free T3 and Free T4 levels both decreased by 60%, bringing hormone levels closer to the normal range, which indicates effective suppression of excess thyroid activity. Additionally, TSH levels increased from suppressed levels (<0.1 mIU/L) to 1.5 mIU/L, reflecting a restored regulatory feedback mechanism.

Table 2: Thyroid Function Test Results

Parameter	Baseline (Mean)	Post-Treatment (Mean)	% Change
Free T3 (pmol/L)	8.0	3.2	-60%
Free T4 (pmol/L)	30	12	-60%
TSH (mIU/L)	<0.1	1.5	-

The pre-treatment insulin sensitivity parameters reveal higher insulin resistance and fasting insulin levels in male hyperthyroid patients compared to females. Specifically, the mean HOMA-IR for males was 5.0 ± 1.2, while females had a slightly lower mean of 4.4 ± 1.0, indicating comparatively greater insulin sensitivity in females. Similarly, fasting insulin levels were higher in males at 19 ± 4 μU/mL versus 17 ± 3 μU/mL in females.

Table 3:Pre-Treatment HOMA-IR and Fasting Insulin Levels in Male and Female Hyperthyroid Patients

Insulin Sensitivity Parameter	Male (Mean ± SD)	Female (Mean ± SD)
HOMA-IR	5.0 ± 1.2	4.4 ± 1.0
Fasting Insulin (μU/mL)	19 ± 4	17 ± 3

For males, total cholesterol decreased by 8%, from 180 ± 15 mg/dL to 165 ± 12 mg/dL, while females saw a 7% decrease, from 170 ± 12 mg/dL to 158 ± 10 mg/dL. LDL cholesterol dropped by 9% in males and 8% in females, indicating reduced cardiovascular risk. HDL cholesterol, beneficial for heart health, increased by 12% in males (from 40 ± 6 to 45 ± 5 mg/dL) and by 7% in females (from 45 ± 5 to 48 ± 4 mg/dL). Triglycerides showed a 10% reduction in males and 9% in females.

Table 4: Pre-and post Treatment Lipid Profile in Male and Female Hyperthyroid Patients

Lipid Parameter	Gender	Pre-Treatment (Mean ± SD)	Post-Treatment (Mean ± SD)	% Change
Total Cholesterol (mg/dL)	Male	180 ± 15	165 ± 12	-8%
	Female	170 ± 12	158 ± 10	-7%
LDL Cholesterol (mg/dL)	Male	110 ± 10	100 ± 9	-9%
	Female	100 ± 8	92 ± 7	-8%
HDL Cholesterol (mg/dL)	Male	40 ± 6	45 ± 5	+12%
	Female	45 ± 5	48 ± 4	+7%
Triglycerides (mg/dL)	Male	150 ± 18	135 ± 15	-10%
	Female	140 ± 15	128 ± 13	-9%

DISCUSSION

These findings highlight not only the efficacy of this treatment in managing hyperthyroidism but also underscore notable gender differences in metabolic responses, suggesting the potential value of tailoring therapy based on gender-specific metabolic needs.Decreased levels of AST, ALT, and ALP post-treatment in hyperthyroid patients support the notion that, regarding hepatic function, increased metabolic rates and altered enzymatic activity resulting from excessive thyroid hormone are quite well known [13]. Male patients had significantly more profound decrease in enzyme levels that could be explained by difference in muscle mass and metabolic rate affecting the pharmacokinetics of propranolol and methimazole. This observation could suggest that the male patients gain more in healing of the hepatic organ under this combination therapy [14]. Nevertheless, it is necessary to control the hepatic function continuously, especially in females, who responded with significantly lower but still positive results. In regard to the treatment, the enhancements in the status of blood glucose levels and OGTT suggested that the treatment effectively attenuated the hyperthyroidism's effects on the increase in glucose production and enhancement in insulin action [15]. The treated hyperthyroidism is also shown to aggravate glucose intolerance because of its implication to increase the level of hepatic glucose output and effect on insulin resistance. Fasting blood glucose reduced by 10 percent and OGTT values increased by 15% after treatment implying that, it is possible to reverse these glomerular disturbances with normal thyroid hormone levels. Interestingly, female patients had numerically lower reductions in fasting glucose levels (-12%) than male patients (-9%) and a larger reduction in mean OGTT results (-17%) than male patients (-11%), seemingly related to hormonal influences on glucose and insulin metabolism [16]. For example, estrogen is involved in regulation of insulin sensitivity and glucose metabolism that can be one of the reasons for glucose tolerance improvement of female patients. This finding indicates that due to the differences in glucose metabolism therapy, it may be effective to consider sex-specific differences for therapy planning and the choice of the therapy protocol for female patients [17]. The authors observed a decrease in fasting insulin and HOMA-IR, therefore, they can state that normalising thyroid hormone parameters in hyperthyroidism promotes better insulin profiles. Male patients demonstrated even greater improvement of insulin sensitivity, with the decrease of fasting insulin to 25% and HOMA-IR to 27% [18]. This might be due to variation in the BMI where male individuals have more lean body mass, which improves glucose and insulin utilization. Furthermore, the impact of propranolol on insulin sensitivity appears to be more marked in men because of pharmacokinetic differences. Decreased free T3, and free T4 concentrations by 60% and normalized TSH level indicate the efficacy of methimazole in inhibiting thyroid hormone production [19]. It can be seen from the results that using propranolol to control adrenergic manifestations and methimazole to reduce thyroid hormone synthesis influenced patient treatment positively by reducing both symptomatic and metabolic consequences of hyperthyroidism. There were no sex-based differences in normalization of thyroid hormone levels which also explains the fact that the drug, methimazole works on both male and female bodies in regards to hormonal imbalance [20]. These variations call for individualized treatment approaches was evidenced by the gender differences detected in liver functioning, glucose control and insulin sensitivity. In male patients, if the liver function and insulin level were generally highly increased after treatment, the treatment plan may focus on the evaluation of liver function or intervention on insulin treatments. In contrast, for female patients, glucose metabolic control seems more responsive to thyroid hormone restoration, which may entail potential advantages for using additional treatment therapies aimed at glucose reduction in conjunction with thyroid treatment.

CONCLUSION

It is concluded that combined propranolol and methimazole therapy is effective in managing hyperthyroidism by significantly improving liver function, blood glucose regulation, and insulin sensitivity. This treatment approach not only lowers thyroid hormone levels but also alleviates hyperthyroidism-induced metabolic disturbances. The reduction in liver enzymes (AST, ALT, and ALP) suggests enhanced liver function post-treatment, particularly in male patients who experienced greater improvements in enzyme levels.

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