THYROXINE PRESERVES THE ARCHITECTURE OF PANCREATIC ISLETS OF LANGERHANS IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

BACKGROUND: In experimental animal models, Streptozotocin (STZ) induced diabetes, causes disruption of the normal architecture of the islets of Langerhans and exogenous administration of thyroxine in diabetic rats preserves the anatomy of endocrine pancreas.

OBJECTIVE: This study was performed to observe the effect of thyroxine on the pancreas of albino rats during STZ induced diabetes.

MATERIAL AND METHODS: This is a Prospective experimental study was conducted in Anatomy department at BMSI, JPMC, Karachi from 01 November to 15 December 2013. In this study sixty healthy adult albino rats were included in the study and divided equally into 3 groups for 6 weeks. Group-A was taken as control. Group-B received STZ (I/P) in a dose of 37 mg/kg body weight. Group-C received STZ in the same dose and additionally received thyroxine (1 mg/kg (s.c.) thrice a week for 6 weeks.

RESULTS: STZ significantly increased serum glucose level and decreased weight in group B animals, whereas in group C, thyroxine significantly restored serum glucose level but could not restore the body weights reduced by streptozotocin. Moreover, thyroxine significantly preserved the morphology of pancreatic islets in group C animals.

CONCLUSION: Thyroxine restores the structure of pancreatic islets distorted by STZ and reduces hyperglycemia, but cannot restore the body weight.

KEYWORDS: Streptozotocin, Thyroxine, Diabetes Mellitus, Hyperglycaemia, islets of Langerhans, Albino rats.

INTRODUCTION

Diabetes and thyroid disease are common in our population. There is a continuous association of thyroid hormones and insulin in glucose metabolism^{1,2}. Normal thyroid status is a prerequisite for the normal growth and development of many tissues³. The thyroid hormones increase the metabolic activities of almost all the tissues of the body. About 93 per cent of the metabolically active hormones secreted by the thyroid gland is thyroxine, and 7 per cent triiodothyronine. Thyroxine is eventually converted to triiodothyronine in the tissues¹. Insulin resistance is the main metabolic feature of diabetes and several studies indicate

the effect of thyroxine in reducing insulin resistance⁴.

Thyroid hormones exert profound effects in the regulation of glucose homeostasis. Glucose homeostasis is achieved by an extremely complex mechanism involving, along with food intake, the regulation of insulin secretion and its action at a target tissue level⁵. Thyroid disorders have a major impact on glucose control. When thyroid dysfunction ensues the glucose homeostatic balance is broken⁶.

Streptozotocin (STZ) is a naturally occurring compound that has a wide range of antibacterial properties⁷. It is the most commonly used agent to induce experimental diabetes in rodents as it

causes destruction of the pancreatic beta cells⁸. Pancreatic β -cells are the easy target of damage due to release of free radicals as they have a very low potential to overcome oxidative stress⁹. Several studies have proved the association between insulin resistance and hypothyroidism, indicating the effect of thyroxine in reducing insulin resistance³. Abnormal thyroid function can have a major impact on diabetes control and increase a person's risk of developing diabetic complications³. Because of the complications that can result from untreated thyroid disorder, regular screening is recommended to allow early detection and treatment.

In consideration of these statements, this study was planned to observe the effect of thyroxine on the pancreatic islets in diabetic rats. Its effects on body weight and serum glucose were also observed.

MATERIAL AND METHODS

This study was conducted in the department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Centre (JPMC), Karachi. The duration of study was 06 weeks. Sixty healthy adult albino rats, both male and female, weighing around 260–290 grams were selected for the experiment from the animal house. The experimental protocol was reviewed and approved by the Ethics committee of BMSI. The albino rats were weighed, identified and housed in well labeled plastic cages in the experimental room of animal house and given a routine balanced diet. A glucometer was used to monitor serum glucose of all the animals from the tail vein. Animals were divided into 3 groups, and each group contained 20 animals. Group-A animals served as control. Group-B animals received STZ (Intraperitoneally) at a dose of 37 mg/kg¹⁰ body weight (dissolved in 1 ml of citrate buffer at pH of 4). Group-C additionally received thyroxine 1mg/kg (subcutaneously) thrice a week for 6 weeks. STZ, during administration, was freshly prepared by dissolving it in a citrate buffer at a pH of 4. Rats were fasted overnight a day before the administration of STZ.

Serum glucose levels were monitored by glucometer twice weekly. After 6weeks of treatment, weights of the animals were recorded. Differences in weights and serum glucose levels were evaluated in all the three groups and measured by performing t-tests, using SPSS-17. The pancreas was isolated, placed in 10% formalin and processed further for chrome alum hematoxylin stain¹¹ to be viewed under a research light microscope.

RESULTS

There was a normal physiological increase in the weights of the animals belonging to group- A, whereas a highly significant decrease in the weights were recorded in group- B animals. Similarly, in group- C, the results regarding weights were almost similar to those of group- B (Table-2).

The data showed a highly significant increase ($p<0.001$) in serum glucose level in group- B as compared to group A (Table-1), highlighting the deterioration of beta cells of the pancreas in group-B (Fig-2). Serum glucose of group- C rats was significantly decreased as compared to group B. Administration of thyroxine to group- C animals significantly preserved the morphology of pancreatic beta cells (Fig-3) as no vacuoles were seen and the arrangement of islets was also preserved.

Table-1: Mean $\pm$ Standard error of mean bodyweight in different groups

*Statistically Significant at $p < 0.01$,

**Statistically highly significant at $p < 0.001$ as compared to control group.

The table above shows the highly significant ($p < 0.001$) effect of STZ in raising serum glucose

Laboratory data	Group A (control)	Group B (STZ treated)	Group C(STZ + Thyroxine)
Initial S. Glucose (mg/dl)	85.18 $\pm$ 0.810	89.82 $\pm$ 0.900	85.94 $\pm$ 0.920
Final S. Glucose (mg/dl)	89.98 $\pm$ 1.750	354.70 $\pm$ 0.880**	109.61 $\pm$ 0.960*

levels and also the significant ($p < 0.01$) effect of thyroxine in decreasing serum glucose levels.

Table-2: Mean $\pm$ Standard error of mean bodyweight in different groups

Groups	Initial weight of body(grams)	Final weight of body(grams)
A	276.0 $\pm$ 1.249	280.2 $\pm$ 1.246
B	275.3 $\pm$ 1.179	253.2 $\pm$ 1.193**
C	281.3 $\pm$ 1.238	260.0 $\pm$ 1.248**

*Statistically Significant $p < 0.01$, **Statistically highly significant $p < 0.001$ as compared to control group.

The table above shows the highly significant ($p < 0.001$) effect of STZ in reducing body weight. However, thyroxine could not restore the body weight in STZ treated group.

Figure 1(Group A): photomicrograph of a 5 μ m thick chrome alum hematoxylin stained section from a normal rat pancreas showing a normal architecture of islets of Langerhans with alpha cells, beta cells and delta cells x 1000

Figure 2(Group B): photomicrograph of a 5 μ m thick chrome alum hematoxylin stained section from STZ treated rat pancreas showing a distorted architecture and formation of vacuoles in islets of Langerhans x1000.

Figure 3 (Group C): photomicrograph of a 5 μ m thick chrome alum hematoxylin stained section from STZ and Thyroxine treated rat pancreas showing preserved architecture of islets of Langerhans x 1000.

DISCUSSION

Several studies have been conducted to investigate the effect of thyroxine on different organs of the body during diabetes. The results obtained from these studies yield different results. In one of the study conducted by Jorns et al. (2002)¹², it was demonstrated that thyroxine induces apoptosis of rat pancreas, leading to a reduction of insulin secretion, which is unlike

our results. Another study was conducted by Fernández-Alvarez et al.(2004)¹³, showing the proliferative effect of tungstate on pancreatic beta cells damaged by STZ. In a study conducted by Takiguchi et al. (1989)¹⁴, it was demonstrated that thyroid hormone deficiency was responsible for the altered reactivity of the rat mesenteric vasculature at the early period of diabetes.

A study revealed that T3 and insulin both stimulate the expression of hexokinases and glycogen synthase which are respectively responsible for uptake and disposal of glucose via formation of glucose-6- phosphate and glucose-1 phosphate¹⁵. It was reported by Ledda et al. (2005)¹⁶ that T3 is a powerful inducer of pancreatic acinar cell proliferation in rodents¹⁶. Ortega et al. (2008)¹⁷ demonstrated that T3 concentrations were positively associated with insulin secretions and stated that T3 may play a role in the insulin secretions.

No significant change in the weight of the animals was observed in group-C, and the reason is that, the thyroid gland causes a hypermetabolic state, leading to increased energy expenditure¹⁸, weight loss, reduced cholesterol levels, increased lipolysis, and gluconeogenesis¹⁹.

It has been observed that hyperglycemia produced by administration of STZ, reduces the response of serum glucose to insulin, although the numbers of insulin receptors in a cell are increased⁹. Hyperglycemia increases the level of free radicals in the blood which in turn leads to insulin resistance and metabolic syndrome¹⁰. It was demonstrated in our study that thyroxine has the potential to protect pancreatic β -cells against damage exerted by STZ, leading to the proliferation and conservation of pancreatic islet cells.

CONCLUSION

Based on the present study, we come to the conclusion that thyroxine significantly restores the morphology of pancreatic islets, distorted by STZ-induced hyperglycemia in albino rats. Therefore, it can play a promising role in

protecting pancreatic beta cells from damage in diabetic patients. We can also consider administering thyroxine to diabetic patients who undergo surgery for implantation of beta cells, as it would help in proliferation of beta cells, once implanted.

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