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Research Article

HISTOLOGICAL CHANGES OF ENDOCRINE SECTION OF PANCREAS AND LIVER IN STREPTOZOTOCIN-INDUCED EXPERIMENTAL DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus has been considered as one of the major health concerns all around the world today. The present study was aimed to demonstrate the histological changes in the pancreas and liver of streptozotocin (STZ) induced diabetes in albino rat. Twenty four rats were separated into two groups. Group I served as normal control and group II served as diabetic. The diabetic condition was induced in group II by streptozotocin. Light microscopic assessment of islets showed highly disrupted cells with necrosis in diabetic rats. The present study revealed that induction of diabetes using STZ results in the alteration of the morphology of endocrine part of pancreas as well as liver in rats.

INTRODUCTION

Diabetes mellitus (DM) is a major health problem worldwide. The economic impacts of diabetes with its complications are large (Sarah *et al*., 2004). According to some estimates, the prevalence of diabetes mellitus is 4 percent worldwide and that indicates 143 million persons are affected which will increase to 300 million by the year 2025 (Analava *et al*., 2007). Streptozotocin (STZ) has been extensively used to induce diabetes for various diabetes studies in laboratory animals. STZ has been found to be a better chemical inducer for diabetes than alloxan (Szkudelski, 2001). The present study was designed to demonstrate the histological changes of endocrine section of pancreas and liver in STZ induced diabetes in rat.The common mechanism of action of alloxan, streptozotocin includesdegradation of pancreatic islet beta-cells by means of: 1) generation of oxygen free radicals (reactive oxygen species) thatdestroy the cells, 2) alkylation of DNA and subsequent activation of poly-ADPribose-synthetase - reduction of NAD to beta-cell, and 3) inhibition of active transport ofcalcium and calmodulin-activated protein kinase (Rees and Alcolado, 2005). In this typeof experimental models of diabetes mellitus streptozotocin (an N-nitrosourea derivative ofglucosamine) is most commonly used (McIntosh CHS, Pederson R.A, McNeill, 1999). The toxic effect of alloxan and streptozotocin oncells in pancreatic islets manifests itself not only by necrosis but also by apoptosis ofpancreatic islet beta-cells (Daisy *et al*., 2004).

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MATERIALS AND METHODS

Animals and housing

Adult male albino rats weighing 200±40g were maintained under standard laboratory conditions. Theanimals were fed standard rodent diet and water was provided *ad libitum*.

Generally different dosagesof STZ are used in the experiment (45-70 mg/kg) and route of administration (i.p., i.v.), to induce diabetes mellitus in rats (Srinivasan *et al*., 2007; Ziegler, 1990; Rakieten *et al*., 1963; Ar Rajab and Ahren, 1993). The highest STZ dose (70 mg/kg) is lethal to the animals, the doses of 50 and 60 mg/kg induce persistent hyperglycaemia (Gajdošík*et al*., 1999).

24 rats were separated into two groups. Group I served as normal control and group II served as diabetic. Diabetic group was separated as group A, B and C. Each group consisted of 6 rats.

In our experiment STZ was administered by i.p. injection in doses of 45 (group A), 50 (group B), and 60 mg/kg body weight (group C) dissolved in 0.1 M ice-cold citrate buffer (pH 4.5) to overnight-fasted rats (after Gajdošík *et al*., 1999; Babu and Prince, 2004).

Glucose tolerance test (GTT)

For glucose tolerance test (GTT) blood was collected first from the tail veins of control and STZ treated rats after 18 hr of fasting followed by challenge with glucose (25 mg glucose/100 g body weight) and at the following time point after glucose infusion: 1.5 hr, 2.5 hr and 24 hr. blood glucose was measured using a blood glucose monitoring system

(glucometer).

Histological analysis

Before autopsy, rats were anesthetized with chloroform. Pancreatic tissues and liver were dissected out and fixed in Bouin's fixative (Parakkal *et al.*, 1961). Tissues were embedded in paraffin, sectioned (5µm), mounted on glass slide and stained with hematoxylin-eosin for histological analysis.

RESULT

Blood glucose level

In the control rats the blood glucose level returned to the normal level after 24 hr of glucose feeding. Like control rats, in diabetic rats glucose level increased after 1.5 hr of glucose challenge but the elevated glucose didn't return to control level even after 24 hr of glucose challenge (Fig1).

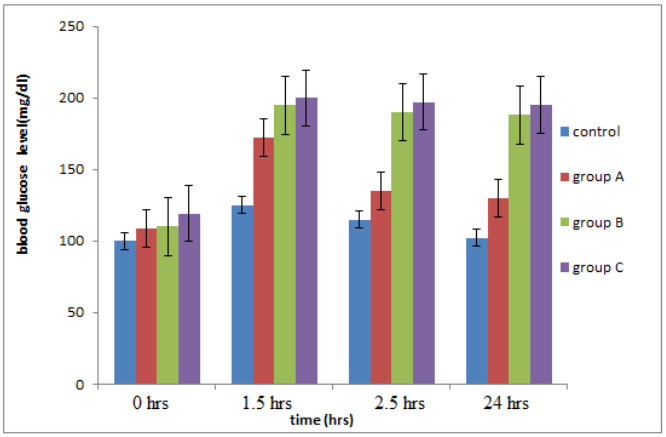

Figure 1 Blood glucose level in response to glucose tolerance test in control andSTZ treated diabetic rats. Values are expressed as mean ± SE. P-value < 0.05 is considered to be statistically significant.

Histology of pancreas

Control group showed a normal lobular architecture of the pancreas (Fig2A). Each islet consisted of lightly stained polygonal cells arranged in cords separated by a network of blood capillaries (Fig2A). The pancreatic sections of the diabetic group showed marked morphological changes (Fig 2B, C and D). Some islets cells showed pyknosis.A significant number of islets cells were found to be reduced in number.Treated tissues revealed marked necrotic changes in endocrine cells both in the central part and at the periphery of the islets. There was mild reduction in the number of islets cells in group A, but the periphery of islets was disrupted (group A) (Fig2B). Group B animals showed marked edema of the interlobular connective tissue with cellular infiltration (Fig 2C1 and 2C2). There was severe reduction in the number of islets cells in group C (Fig 2D1 and 2D2). The islets of group C appeared irregular in shape, reduced in the size, with some assuming 'star fish' appearance (Fig 2D2). Besides, there was an increase of mild degrees of fibrosis with infiltration of a few inflammatory cells were also observed in group C.

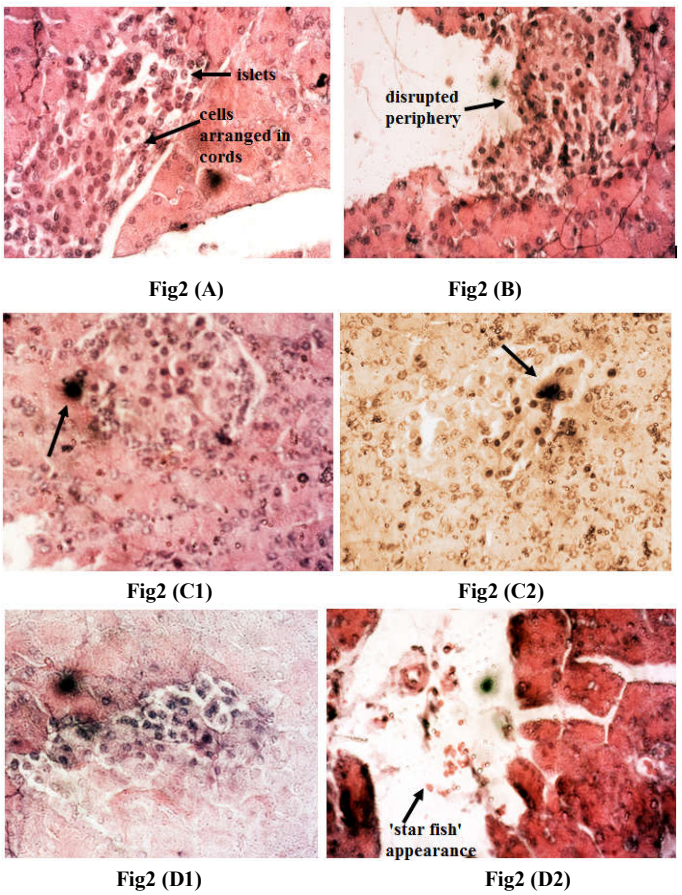

Fig2 (A) Fig2 (B)

Fig2 (C1) Fig2 (C2)

Fig2 (D1) Fig2 (D2)

Figure2 (A) Normal rat pancreatic islets (x 400), (B) Group A diabetic rat pancreatic islets (x 400),
(C1 and C2) Group B diabetic rat pancreatic islets (x 400), (D1 and D2) Group C diabetic rat pancreatic islets (x 400)

Histology of liver

The histological examination of the H-E stained control liver tissues showed normal cytoarchitecture with visible central veins with radiating cords of hepatocytes (Fig3A). Treatment with STZ caused central veincongestion (CVC) with significant dilatation of sinusoidal spaces. Liver section of diabetic group showed significant amount of empty spaces (ES) (Fig3B). The infiltration of inflammatory cells in treated liver was also noticed (black arrow)(Fig4).

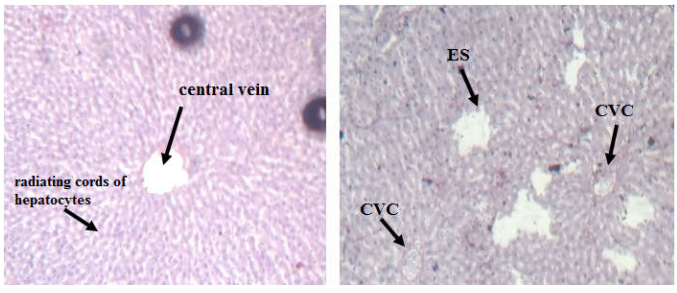

Fig3 (A) Fig3 (B)

Figure 3 (A) Normal rat liver (x 400), (B) diabetic rat liver (x 400)

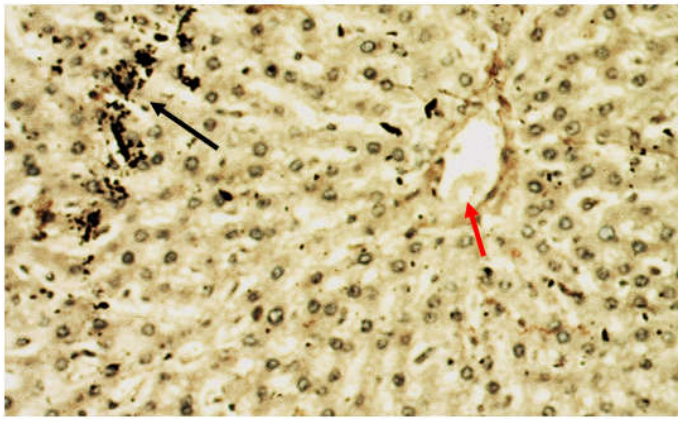

Figure 4 Liver section of treated rat revealedinfiltration of inflammatory cells (black arrow) with congestion of central veins (red arrow).x 400 H&E

DISCUSSION

It is known that type I diabetes develops when pancreatic beta cells are damaged due to certain inflammatory, autoimmune and other pathological processes (Kim *et al*., 2001). Selective organ-specific tissuedestruction of the insulin-producing pancreatic beta cells is associated with insulin deficiency resulting in impairment of glucose homeostasis (Guria *et al*., 2016; Guria *et al*., 2014). There are many experimental evidences emphasize the key role of apoptosis in the pathogenesis of diabetes mellitus (Kim *etal*., 2001; Severgina, 2002). Toxic effects ofcertain chemicals (e.g. alloxan, streptozotocin, etc.) are used to induce diabetes specifically in pancreatic beta-cells, manifest themselves by alkylation of DNA and formation of toxic compounds, such as superoxide anion, peroxynitrite, and nitric oxide (Rees and Alcolado, 2005). Our results exhibited that STZ rat developed atrophy of pancreatic islets and pyknosis of islets cells. Our result showed the 'star fish' like appearance of treated islets and increase of mild degrees of fibrosis with infiltration of a few inflammatory cells in treated pancreatic section, which is very much similar to the result of previous studies (Dhanush Krishna and Rao, 2012).

In STZ treated diabetic rat increments of blood glucose levels were observed after GTT and the hyperglycemia persisted even 24 h after glucose load. It is possible that STZ causes deleterious effects on beta cell function thereby impairing insulin secretion. This condition may provide an explanation for the decrease of glucose tolerance. STZ damages liverby destroying parenchymatous tissues and may hamper the process of glycogenesis.

The result of the present study corroborates the results of our previous studies (Guria, 2018; Guria *et al*.,2016; Guria *et al*.,2014; Guria *et al*., 2012).In conclusion, the results showed that STZ diabetes influence pancreatic islets morphology concomitant with cytomorphology of liver.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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