HISTOMORPHOLOGICAL CHANGES OF LIVER IN DRUG INDUCED DIABETIC RATS

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Abstract

The study of the changes in the histomorphology of the liver induced by the administration of diabetogenic dose of alloxan was undertaken using one hundred and twenty male Albino (Wistar) rats. The animals were randomly separated into four groups. A, B, C and D, of thirty rats each. The first group (A) was used as the primary Control group, the second group (B), the third group (C) and the fourth group (D) were used as test groups. The test groups were administered with 200mg per kg body weight of alloxan which is the diabetogenic dose. The second group (B) was used to study the direct effect of alloxan on the histology of the liver. The third group (C) was used to study effect of diabetes mellitus on the morphology of the liver. The fourth group (D) was used to study the effect of the therapeutic agents on the liver. Histological examination of the liver of the test groups showed various accumulation of degenerative fatty vacuoles and areas of necrosis while the control showed normal histology of the liver.

Key words: Histomorphology, Liver, Diabetic Rats, Alloxan, Degeneration, Fatty Vacuoles

Introduction

Diabetes mellitus can be defined as a chronic disorder characterized by a raised level of glucose in the blood (Guyton and Hill, 1996; Gale, 2001). Diabetes can be the outcome of many different causes, some hereditary, some environmental and some hormonal (Greenspan and Baxter, 1994; Granner, 1995; Biesenbach, et al; 2000). The aetiology of the commontest forms of diabetes is unknown and these are referred to as primary diabetes. These include, type I or juvenile-onset diabetes; type II or maturity-onset diabetes and the much rarer types of diabetes which are usually associated with other hereditary disorders (Bloom and Ireland, 1980; Edwards, et .al., 1995; Agarwal, et.al., 2001).

The cause of some forms of diabetes is known and are classified as secondary diabetes. These include diabetes due to destruction of the pancreas by drugs, disease, autoimmunity or surgery and diabetes due to hormonal imbalance (Tierney, et. Al., 1996; Greenspan and Baxter, 1994; Balsells, et.al; 2000; Berger, et.al. 2001).

Diabetes has been known to mankind since time immemorial and was described as a disease with "honeyed urine" (Turner, 1966). The first clear account of diabetes was given by Aretaeus in about 170 AD. He described it as "This mysterious affection, being a melting down of flesh and limbs in urine, thirst unquenchable, and death inevitable" (Blood and Ireland, 1980).

It has been shown that intravenous or intraperitoneal injection of alloxan or streptozotocin into experimental animals, causes degenerative lesions in various organs but with proper dosage, it produces prompt and selective coagulative necrosis of the beta cells of the islets of Langerhans resulting in a syndrome resembling clinical diabetes mellitus (Barnes and Eltherington, 1964; Steiner and Freinkel, 1972; Govan, 1992; Yala, et.al; 2003)

Since the liver is the site of metabolism and detoxification in the body, any derangement of the liver tissue may lead to impaired body function. The present study examines the significant histological changes in the liver in drug – induced diabetes rats.

Materials and Methods

The experimental drug was alloxan crystals contained in a 250gms bottle. The alloxan crystals weighing 1.2gms were dissolved in 10mls of injection water amounting to 1.2gm/10ml. 0.3ml of the 1.2gm/10ml solution which is equivalent to 40mg of alloxan was administered as the diabetogenic dose according to Barnes and Eltherington, (1964); Barbato and Landau, (1977); Bowman and Rand, (1985); Greespan and Baxter, (1994).

The test animals were 120 male Albino (Wistar) rats which were separated into four groups A, B, C, and D of thirty rats each. The first group (A) was the primary control group. The second, third and fourth groups (B, C and D) were used as the test groups and were administered with 0.3ml of 1.2gm/10ml solution of alloxan equivalent to 200mg per kg body weight which contained 40mg of alloxan. This single diabetogenic dose of alloxan was administered to the test animals through the intraperitoneal route (IP) while the Control group received normal saline through the same route.

The group B animals were the first test group and were used to study the effect of alloxan on the liver during diabetic induction. The second test group C. was used to study

the effect of diabetes mellitus on the histology of the liver, while the third test group (D) was used to study the influence of therapeutic agent, insulin in the resuscitation of the liver.

Animals from each of the groups were anaesthetized and their abdomen opened by a midline incision and part of the liver was excised. These tissues were placed in cold normal saline until excision of the tissues were completed. The tissues were fixed using 10% neutral formalin and Bouins fluid. The technique of tissue processing used were both manual and automatic tissue processing techniques using Histokinette bench model tissue processor obtainable from the Department of Human Anatomy, ABU., Zaria.

The tissues were embedded in paraffin wax and sections between 5-8 microns were made using the Rotary microtome. The tissues were stained using Haematoxylin and Eosin (H and E) method and Periodic Acid Schiff (PAS) methods. These methods were used as outlined by Drury and Wallington, (1973); Gurr, (1992); Culling (1993).

Results

The results of the microscopic examination of the liver, show the normal liver architecture with cord arrangement of cells from group A animals as shown in plates 1 and 2. Animals in group B, C, and D, show fatty vacuoles in some hepatocytes as in plate 3 while some in addition to fatty vacuoles, contain inflammatory cells as in 4 and small area of necrosis as in plate 5. The liver from group D animals treated with insulin, show plant-like enlarged hydropic cells as shown in plate 6.

Plate 1: A section of liver from the Control group (A), Showing normal liver architecture with cord radiating from the Central Vein (V). H and E x100.

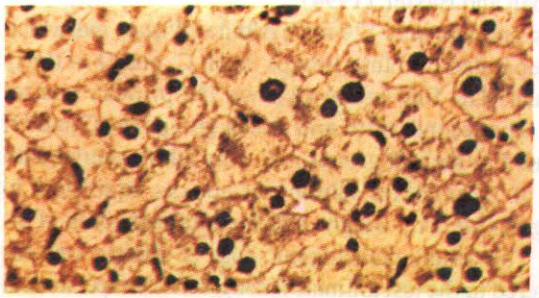

Plate 2: A section of liver with higher mag. from group A, showing normal hepatocytes The cellular components are highly PAS positive indicating high glycogen content.PAS x400

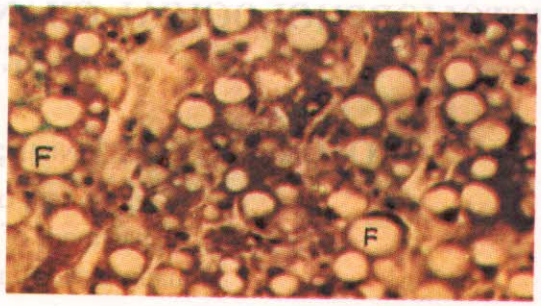

Plate 3: A section of liver from the test group (B), showing fatty infiltration resulting in vacuolation of some hepatocytes (F). H and E x 400.

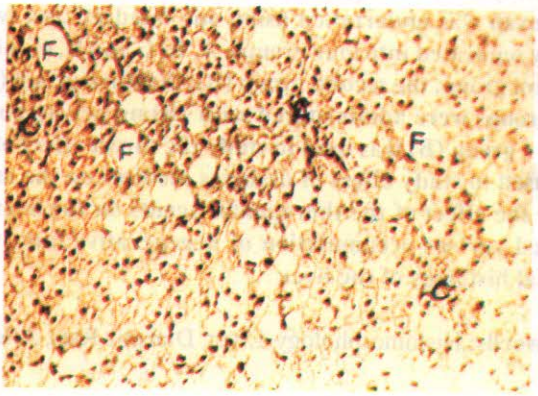

Plate 4: A section of Liver from the test group (C), showing fatty infiltrated hepatocytes causing vacuolation of some hepatocytes (F) and presence of inflammatory cells (C) in the liver. H and E x 400.

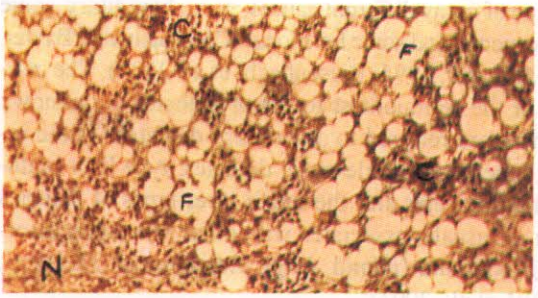

Plate 5: section of liver from the test group (D), showing fatty infiltrated and vacuolated hepatocytes (F), small area of necrosis (N) and inflammatory cells (C) in the liver. H and E x400.

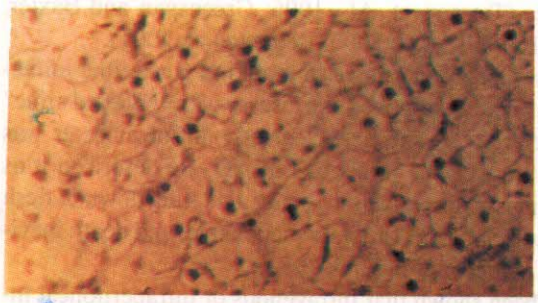

Plate 6: section of liver from the test group (D), treated with insulin, showing plant-like cell pattern with hepatocytes overladen with glycogen. H and E x400.