Pathological Studies on the Effect of Melatonin Administration in Experimental Diabetes in Goats

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Abstract
In the present study, induction of oxidative stress was carried out through alloxan (at 80 mg/kg body weight Intra Venus) and its amelioration was attempted by melatonin (at 40 mg/goat sub-cutaneous for five days). The animals were divided into two groups of four goats each i.e. groups A and AM. Group A was treated with alloxan monohydrate and group AM was treated with alloxan + melatonin. Pathological changes were studied in pancreas, liver, kidneys and spleen in both the groups. Pathological changes in pancreas revealed presence of extravasated blood, damage to the cells of islets and creation of empty space around islets of Langerhan of pancreas. Liver showed congestion of large blood vessels, sinusoidal congestion, mild vacuolar degeneration, presence of pseudo bile duct and moderate Kupffer cell proliferation. Kidneys showed severe interstitial hemorrhages, congestion of glomerular capillaries and hyperplasia and fragmentation of the cells in glomeruli. Kidney tubular epithelial (KTE) cells showed vacuolar degeneration and coagulative necrosis. Spleen showed severe depletion of lymphoid cells from the white pulp. It was concluded from the present study that melatonin is unable to attenuate the tissue changes associated with hyperglycemia in diabetic goats.

Key words: Experimental diabetes, Goats, Melatonin, Pathology.

1. Introduction
Goats are disseminated all over the world because their great adaptability to varying environmental conditions and the different nutritional regimen under which they were evolved and subsequently maintained. They proved useful to man throughout the ages due to their productivity, small size, and non-competitiveness with food for humans. In the developing countries, goats make a very valuable contribution, especially to the poor in the rural areas and so termed as “Poor man’s cow”. But the importance of this valuable genetic resource is underestimated and its extent of contribution to the livelihood of the poor is inadequately understood. India holds the second largest population of goat in the world as 125.7 million which is 14.6 per cent of world’s goat population and 24.4 per cent of Asia’s goat population and number of goats in the world has been increasing since 1990 by about 1 per cent to 4 per cent each year (FAOSTAT, 2008). This increment amounts to the biggest among the livestock species during the last 20 years (Dubeuf and Boyazoglu, 2009). The population of goat in Uttarakhand state is 11.58 lakhs and is increasing at the growth rate of 3.10 per cent per annum (Anonymous, 2007). Diabetes mellitus is characterized by hyperglycemia, defects in reactive oxygen species scavenging enzymes and high oxidative stress induced damage to pancreatic beta cells. In diabetic animals, free radicals are rapidly accumulated and cause oxidative stress, which may impair the structure and function of liver and kidney characterized by suppressed antioxidative activities and enhanced lipid peroxidation. Melatonin (MT, N-acetyl 5-methoxy serotonin), a hormone secreted by the pineal gland in the brain, has been shown to function as a direct free radical scavenger (Tan et al., 1993) and an indirect antioxidant via its stimulatory actions on antioxidative enzymes (Reiter et al., 2000; Rodriguez et al., 2004). It has been used in both experimental and clinical studies for its antioxidative effects. Perception of the mechanisms and reactions associated with oxidative stress can be of immense help in designing specific antioxidant therapies in general and diabetes in particular. The present investigation was therefore,
undertaken to evaluate the role of melatonin in reducing the tissue changes in alloxan induced experimental diabetes in goats.

2. Materials and Methods

Provision of study and experiment was approved by the Institutional Animal Ethics Committee. Eight apparently healthy female goats (Capra hircus) weighing 23.66 ± 2.22 kg, aged 2-4 years were maintained in the experimental shed of Department of Veterinary Physiology and Biochemistry, College of Veterinary and Animal Sciences, GB Pant University of Agriculture and Technology, Pantnagar. Goats were grazed on local pasture in the morning and evening. They were also fed concentrate mixture (gram, wheat bran, jiggery fortified with mineral mixture, vitamins and salt) at the rate 250 g/goat/day and had free access to fresh drinking water. All goats were off fed 12-18 hours before exposure of alloxan and melatonin.

The animals were allocated randomly into two groups (viz. A i.e. alloxan and AM i.e. alloxan + melatonin) comprising of four animals in each group. In both the groups, diabetes was induced by intravenous injection of a freshly prepared aqueous solution of alloxan monohydrate (10% alloxan solution in normal saline solution at 80 mg/kg body weight Intra Venus). Establishment of diabetes was insured by estimating fasting blood sugar (FBS), performed by Accu check in overnight fasted animals. These levels of FBS in diabetic animals (two days after alloxan treatment) were in the range of 266-323 mg/dl compared to 58-69 mg/dl in pre experimental animals. These animals showed clear signs of polyuria, polyphagia, polydipsia and were considered diabetic. After two days of alloxan treatment, group A goats received normal saline solution at 4 ml per goat as placebo whereas group AM were treated with melatonin at 40 mg/goat subcutaneously for five days (Rohilla and Ali, 2012).

Pathological studies were conducted on the dead animals and all the dead animals were subjected to detailed post mortem examination and gross lesions were duly recorded. The representative samples from pancreas, liver, kidney and spleen were collected in 10% neutral buffered formalin and processed as per standard protocol for histopathological examination (Luna, 1968).

3. Results and Discussion

Three goats from group A died at 17th, 20th and 24th day and one goat from group AM died at 21st days after alloxan treatment. This might be due to the treatment of diabetic goats with melatonin in the present study (Kumar, 2014). This indicated that melatonin can effectively ameliorate the stress accompanying the diabetes in goats. This is in agreement with the earlier reports in rabbits (Winiarska et al., 2006). The melatonin might have helped in restoring the beta cells of IL to some extent but not completely as reported in an experimental study in rats (El-Desouki et al., 2007) thereby reducing the number of animals died in group AM.

3.1 Gross Pathology

There was no significant difference in the gross lesions in the organs of animals died from group A and AM. In animals of both the groups, pancreas revealed slight reduction in the size in all the 4 animals that died during the course of experiment. Liver was reddish, appeared congested and slightly enlarged also. Kidneys were severe red in color at places, showed subcapsular hemorrhages and slightly enlarged. Spleen was reduced in size in all the 4 dead animals.

3.2 Histopathological Examination

3.2.1 Pancreas

Pancreas revealed presence of extravasated blood in between the acini at many places. There was severe reduction in size of islets of Langerhans (ILH). There was creation of empty space around the ILH. In many of the ILH, only few cells were left (Fig 1). The lesions found in pancreas, in this study, are in accordance to the lesions reported earlier by other workers due to alloxan induced oxidative stress (Nermeen et al., 2010). There was creation of empty space around the ILH which might be due to damage to the cells of the islets. In many of the ILH, only few cells were left which might be due to necrosis of cells of ILH.

3.2.2 Liver

Liver depicted mild to moderate congestion of large blood vessels at many places along with sinusoidal congestion (Fig 2). There was mild to
moderate vacuolar degeneration and swelling of hepatocytes throughout the parenchyma. There were presence of pseudo bile ducts around large blood vessels at many places (Fig 2) and moderate kupffer cells proliferation. There were foci of coagulative necrosis at few places. Similar pathological lesions in liver due to alloxan induced oxidative stress had been reported by earlier workers (Mir et al., 2013).

3.2.3 Kidney

The renal cortex showed severe interstitial hemorrhages in between the tubules along with congestion of the glomerular capillaries throughout the parenchyma. Glomeruli revealed hyperplasia of the cells. Many of the kidney tubular epithelial (KTE) cells were exhibiting vacuolar degeneration and coagulative necrosis while many others were showing pyknotic nuclei only. In many of the tubules, KTE cells were sloughed off from the basement membrane which coalesced with each other to form a mass in the center of kidney tubule (Fig 3). Kidneys in the present experiment manifested similar pathological lesions as reported by earlier workers due to alloxan induced oxidative stress (Mir et al., 2013).

3.2.4 Spleen

Spleen showed moderate to severe depletion of lymphoid cells from the white pulp (Fig 4). The lesions observed in the present study were similar to those reported earlier in spleen due to alloxan induced oxidative stress (Mir et al., 2013).

4. Conclusion

It was concluded from the present study that melatonin may not reverse the tissue changes produced as a result of alloxan induced hyperglycemia in diabetic goats.

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