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Evaluation of the Morphological Condition of the Pancreas in Alloxan-Induced Diabetic Rats Under Chronic Pesticide Exposure

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Abstract: *This study explores the effects of chronic pesticide exposure (chlorpyrifos) on the pancreas morphology in rats with experimental diabetes induced by alloxan. The study showed significant histological and morphometric alterations between the control, diabetic, and diabetic + pesticide groups, providing evidence for a synergistic toxic effect of diabetes and pesticide exposure. The results highlight the detrimental impact of environmental toxins, particularly chlorpyrifos, on pancreatic morphology in diabetic conditions.*

Keywords: *Diabetes, Alloxan, Pesticides, Chlorpyrifos, Pancreas, Morphology, Rats.*

INTRODUCTION

Diabetes mellitus (DM) is a leading chronic metabolic disorder characterized by hyperglycemia, which occurs due to either insufficient insulin secretion or a lack of insulin action. Among the organs affected by diabetes, the pancreas, particularly the islets of Langerhans, is significantly involved. The beta-cells of the pancreas, which are responsible for insulin production, undergo degeneration in diabetic conditions, leading to impaired glucose metabolism.

Environmental factors, especially pesticides, are increasingly recognized as contributing to the exacerbation of diabetes, either by interfering with insulin signaling or by promoting inflammation and oxidative stress. Chlorpyrifos, an organophosphorus pesticide, is commonly used in agriculture and has been shown to affect various organ systems, including the pancreas. Studies have demonstrated that exposure to chlorpyrifos can disrupt pancreatic function, leading to insulin resistance and promoting oxidative stress. However, the combined effect of diabetes and pesticide exposure on the pancreas has not been well-studied. This research aims to investigate the morphological and histological changes in the pancreas of rats subjected to chronic chlorpyrifos exposure after alloxan-induced diabetes.

MATERIALS AND METHODS

Animal Model:

A total of 30 male Wistar rats weighing between 180 and 200 grams were selected for the study. The animals were housed under standard laboratory conditions with a 12-hour light/dark cycle and allowed free access to food and water. The rats were divided into three groups:

1. Control group (n=10): No treatment, these rats were used as baseline controls.

2. Diabetic group (n=10): Diabetes was induced by a single intraperitoneal injection of alloxan monohydrate at a dose of 150 mg/kg.

3. Diabetic + pesticide group (n=10): Diabetes was induced as in the diabetic group, and starting from the 3rd day, chlorpyrifos (5 mg/kg) was administered daily by oral gavage for 60 days.

Histological Examination:

After 60 days of treatment, the rats were euthanized, and their pancreases were immediately excised and fixed in 10% formalin solution for 24 hours. Tissue samples were then processed and embedded in paraffin. Sections (5 µm thick) were prepared and stained with hematoxylin and eosin (H&E) for histological analysis. The slides were examined under a light microscope, and histopathological changes were noted.

Morphometric Analysis:

The following parameters were evaluated:

1. Islet number and area: The number of islets per section and the total islet area were measured using a digital microscope and software.

2. Cellular changes: The presence of vacuolization, nuclear pyknosis, and cell degeneration was recorded.

3. Capillary status: The number of capillaries within the islets and their morphological changes were assessed.

4. Necrosis and inflammation: The extent of necrosis and the presence of inflammatory cells were evaluated.

Statistical Analysis:

Data were analyzed using one-way ANOVA followed by Tukey's post hoc test for multiple comparisons. Results were expressed as mean ± standard deviation (SD), and $p < 0.05$ was considered statistically significant.

RESULTS

Control Group:

In the control group, the islets of Langerhans appeared normal, with well-defined borders andno evidence of damage. The beta-cells were densely packed, and the nuclear-to-cytoplasm ratio was normal. The capillaries within the islets were well-formed, and no inflammatory cells were present. There were no signs of vacuolization, necrosis, or fibrosis.

Diabetic Group:

In the diabetic group, significant changes were observed in the pancreas. The number of islets was significantly reduced, and some islets showed signs of atrophy. The beta-cells exhibited vacuolization, a hallmark of cellular degeneration, and the nuclear density decreased. The capillaries in the islets were

dilated, and areas of necrosis were observed. Some islets were infiltrated by lymphocytes, indicating an inflammatory response.

Diabetic + Pesticide Group:

In the diabetic + pesticide group, the morphological alterations were more severe compared to the diabetic group. The number of islets was drastically reduced, and many islets exhibited complete degeneration, replaced by fibrous tissue. The beta-cells showed advanced degenerative changes, including nuclear pyknosis and cytoplasmic vacuolization. In several areas, necrosis was extensive, with hemorrhage and tissue infiltration observed. Inflammatory cell infiltration was more prominent in this group, and the pancreatic tissue exhibited signs of fibrosis. The capillaries within the islets were disrupted, and some areas showed complete loss of islet architecture.

DISCUSSION.

The results of this study clearly demonstrate that alloxan-induced diabetes alone leads to significant histological changes in the pancreas, including reduced islet number, beta-cell degeneration, and the presence of necrosis. However, the addition of chronic chlorpyrifos exposure exacerbated these changes, showing a synergistic toxic effect between diabetes and pesticide exposure. Chlorpyrifos is known to cause oxidative stress and mitochondrial dysfunction, both of which can contribute to the degeneration of pancreatic cells. The pesticide's ability to disrupt cellular membranes and impair the function of various cellular organelles likely contributes to the enhanced pathological effects observed in the diabetic + pesticide group. Furthermore, the chronic exposure to chlorpyrifos in diabetic rats may result in a heightened inflammatory response, as evidenced by the increased presence of inflammatory cells in the pancreatic tissue. Our findings are consistent with previous studies that have demonstrated the toxic effects of pesticides on the pancreas, including alterations in insulin secretion and cellular damage. The interaction between pesticides and diabetes is an important area of research, as it highlights the need to consider environmental exposures as a potential exacerbating factor for individuals with diabetes.

CONCLUSION.

1. Alloxan-induced diabetes causes significant degenerative changes in the pancreas, including a reduction in islet number and beta-cell damage.

2. Chronic exposure to chlorpyrifos worsens these changes, resulting in more severe morphological alterations, including necrosis, fibrosis, and cellular atrophy.

3. The combined effects of diabetes and pesticide exposure lead to a synergistic deterioration of pancreatic function, suggesting that environmental toxins may contribute to the progression of diabetic complications.

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