Journal of Education for Pure Science- University of Thi-Qar
Vol.13, No.3 (Sept.2023)
Website: jceps.utq.edu.iq Email jceps@eps.utq.edu.iq

DOI: http://doi.org/10.32792/utq.jceps.10.01.01

Potential modulation pancreas gland activity in hyperprolactimic male Rats (*Rattus norvegicus*) by vitamin D3 treatment

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Received 13/7/2023, Accepted 14/8/2023, Published 21/9/2023

Abstract:

Hyperprolactinemia status is commonly known as abnormal levels of prolactin hormone in the blood due to endocrine disorder. So far, there is no evidence explaining whether hyperprolactinemia affected Pancreas gland and vitamin D level in male. Therefore, this study aimed to eliminate hyperprolactinemia affecting the Pancreas gland by treating it with vitamin D supplements. Eighteen male rats were equally divide into three groups: The first group (6 rats): received normal saline for 42 days. The second group (6 rats): rats were given 5 mg/kg metoclopramide by intraperitoneal injection for hyperprolactinemia induction for 14 days. The third group (6 rats): hyperprolactinemic rats received 2.5 mg/kg vitamin D3 for 28 days.

After the end of experimental) 42days(,hormonal parameters (prolactin, insulin, and vitamin D3) were measure, and the Pancreas gland was remove for routine paraffin-embedded section staining with hematoxylin and eosin staining. The result of the study revealed a significant decrease ($P \leq 0.01$) in prolactin hormone concentration and a significant increase ($P \leq 0.01$) in D3 concentration and insulin hormone Group 3compared with Group2. Histological examination of parts of the pancreas gland treated with vitamin D showed a remarkable recovery in the size and number of cells, and the cells became abundant in the cytoplasm. It was also noted that the nuclei returned to a size close to normal and took on a regular, spherical shape and central location compared to the hyperprolactinemia group. The study concluded that vitamin D had a protective effect on Pancreas gland by stabilizing insulin hormone level and restoration histological architectures throughout pancreas gland.

Key words: Hyperprolactinemia, prolactin, vitamin D3, Pancreas gland

Introduction: -

Hyperprolactinemia is an increase in the concentration of prolactin in the blood as a result of disorders in the pituitary gland [1-2].The most common cause of hyperprolactinemia is the presence of tumors in the pituitary gland or useing of certain drugs[3]. Among the drugs that lead to an increase in the level of prolactin in the blood is metoclopramide[4-5], which is a common drug used to increase the movement of the digestive system and empty the stomach. Metoclopramide was first described by Jastin-Besaucon and Lavillen in 1964[6]. Its long-term useing leads to hyperprolactinemia[7] . The pancreas contains receptors for the hormone prolactin, which indicates the effect of prolactin in regulating metabolism[8]. Vitamin D is an element of the nutrients that the body needs. It is synthesize by subcutaneous cells from an inactive chemical compound related to the vitamin through exposure of the skin to ultraviolet radiation and has a function in the physiological commitment of the element calcium. Vitamin D can be obtained from some foodstuffs in fatty fish [9]. Vitamin D has a major role in treating pancreatic disorders, lowering blood sugar levels, and improving insulin secretion by pancreatic cells[10-11]. The current study was aimed to evaluate the use of vitamin D3 to restoration of damaged histological architectures components of pancreas tissue.

Materials and Methods: -

Animal's husbandry: eighteen male rat (weight 210-239 g) were use in our study. The rats were put in the animal house in the college of Education Pure Sciences in Thi-Qar university under standard conditions of temperature (22 ± 3) ºC and lighting (12:12hr light: dark cycle) for two weeks before and through the experimental work, the rats being maintained on a food rat and tap water is available *ad-libitum*.

Experimental design:- The animals were randomly divided into 3 groups (6 rats in each group) as follows:**Group1:** (negative control): received normal saline (N.S) intraperitoneal (IP) injection for 42 days.

Group2: (Hyperprolactinemia group): The animals received a single dose of metoclopramide (MC) 2.2 mg/Kg b.wt to induce hyperprolactinemia ,rats daily given by injection for 14 days according to[12]

Group3: (Hyperprolactinemia group treated with vitamin D**)** Received 0.5 mL of Vitamin D (5 µg/kg b.wt) for 28 days by intraperitoneal injection [13.]

At the end of the experiment, animals of each group were anesthetized by ether and sacrificed, Pancreas gland of all groups were removed and kept in 10% formalin for histopathological study.

Biochemical analysis:

Determination of serum Prolactin, Insulin hormone, Vitamin D3, levels

Prolactin(PRL) , Insulin hormone, Vitamin D3were determined using commercial kits (Elisa, Monobind ,U.S.A.).

Histopathological study

Pancreas samples were fixed in a 10% formalin solution for 48 hours. They were then processed (washed with water, passed through escalating grades of ethyl alcohol, cleaning in xylene, and

imbedded in paraffin wax at 70 ^{0}C.5m of tissue thickness was put on clean glass slides and stained with hematoxylin and eosin [14].

Statistical Analysis

The results of the present study were analyzed by using one-way covariance (ANOVA) Tukey's test in all study. All statistical calculations were carried out by the aid of the statistical package SPSS V. 17 (SPSS Inc.). The data were express as means ±standard error (Mean ± SE) [15]

Results: -

Hormonal change :

The results of the current study showed that there is a significant decrease in the level of the prolactin hormone as in (Figure 1) and a significant increase in the level of vitamin D3 and insulin hormone, as in (Figures3-2), in the vitamin D - treated group compared with the hyperprolactinemia group, where the levels of hormones in the vitamin D treated group became close to the levels of hormones in the negative control group.

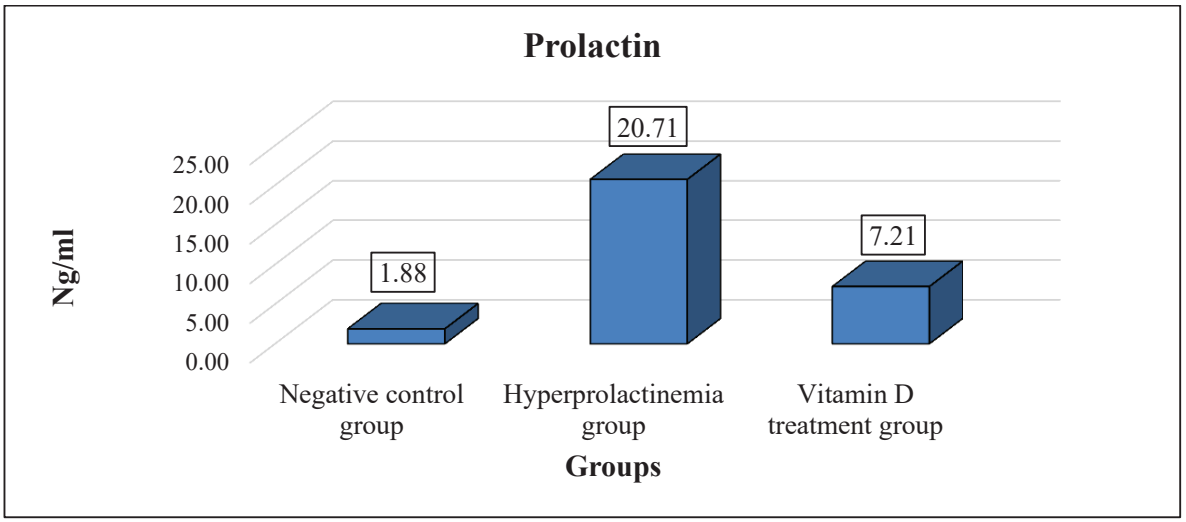

Figure1: PRL hormone level in all groups

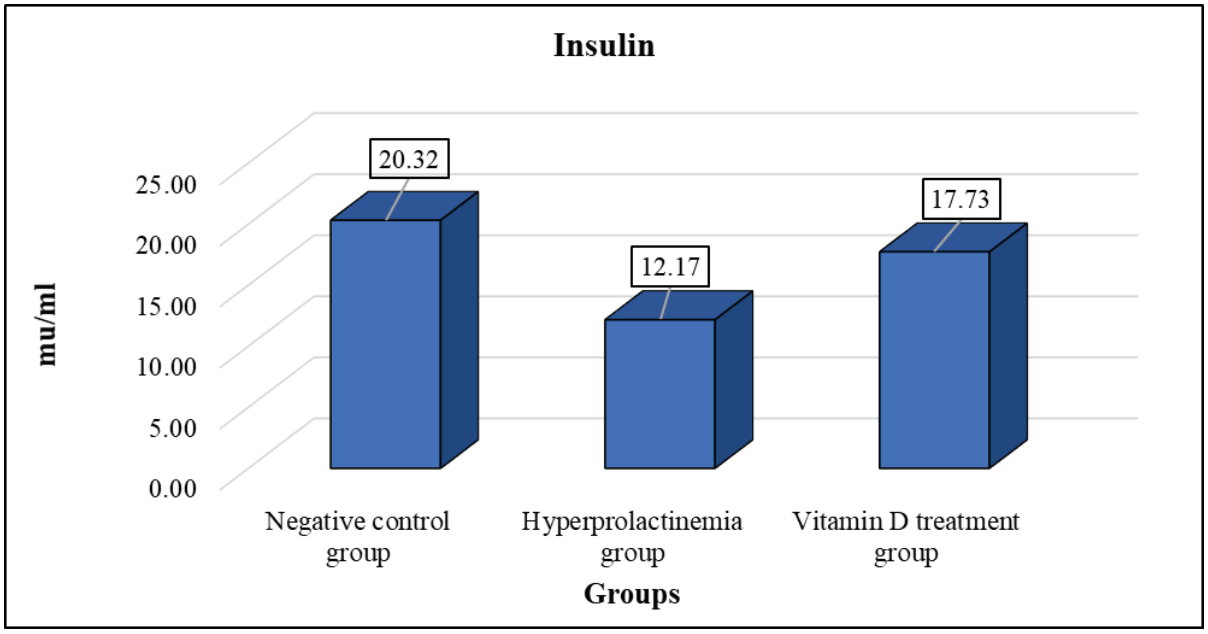

Figure 2: Insulin hormone level in all groups

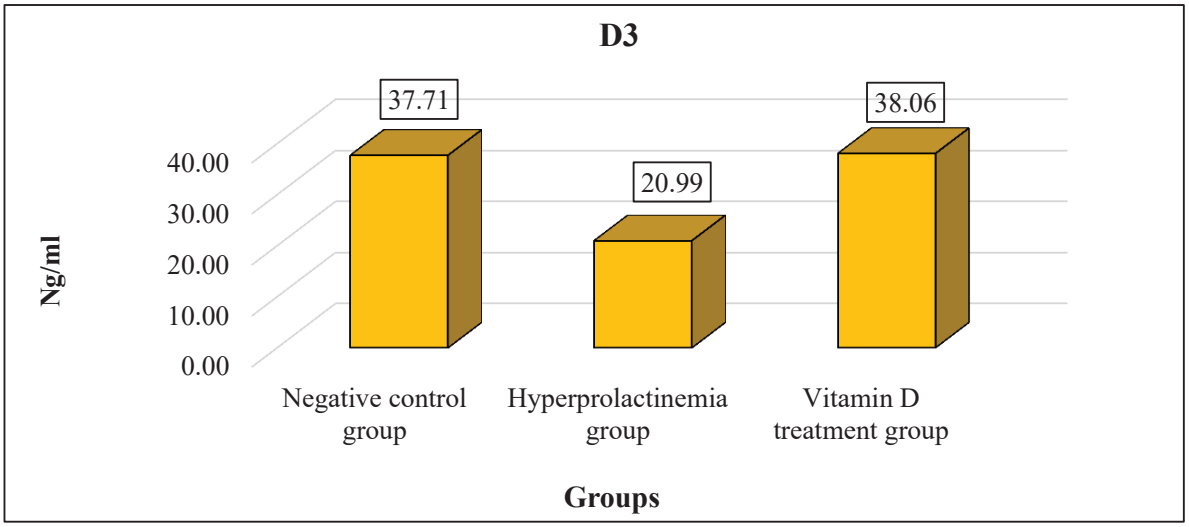

Figure 3: Vitamin D hormone level in all groups

Histological study

The results of the current study showed the occurrence of histological changes in the pancreas gland in the hyperprolactinemia group ,Where atrophy occurred in the islets of Langerhans and a decrease in the number of its cells, as it was observed degeneration in some cells, and the cells were empty of the cytoplasm and thickening in some nuclei, as was observed in the connective tissue surrounding the cells (Figure5).

The tissues showed a repair response in the group of rats treated with vitamin D, as there was an activation of the pancreas gland. The size of the Langerhans islets was larger, and the number of their

cells was more. It was also observed that the cells recovered their cytoplasm and nuclei of normal size (Figures 6), where the tissue was near the negative group, as in (Figures

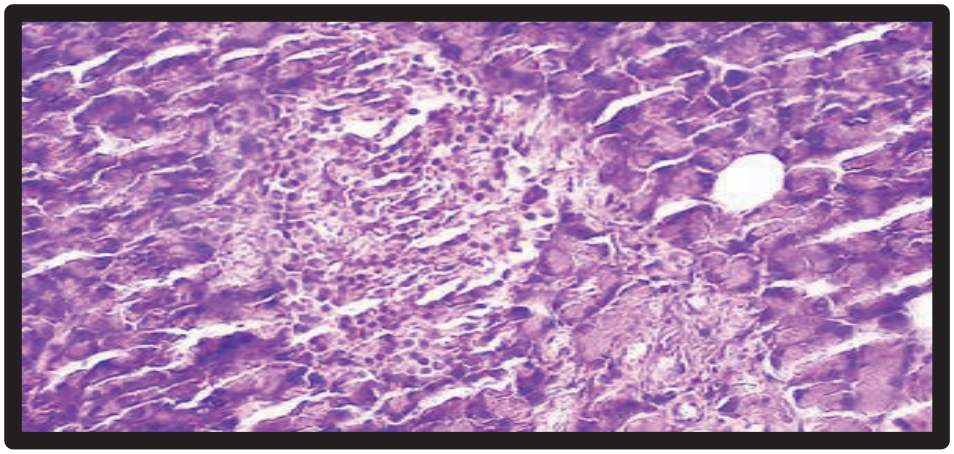

Figure 4: normal histostructures of pancreas gland tissues in the control group showing normal structure of and Langerhans islets normal appearance of cells.
Photomicrograph (400 X).

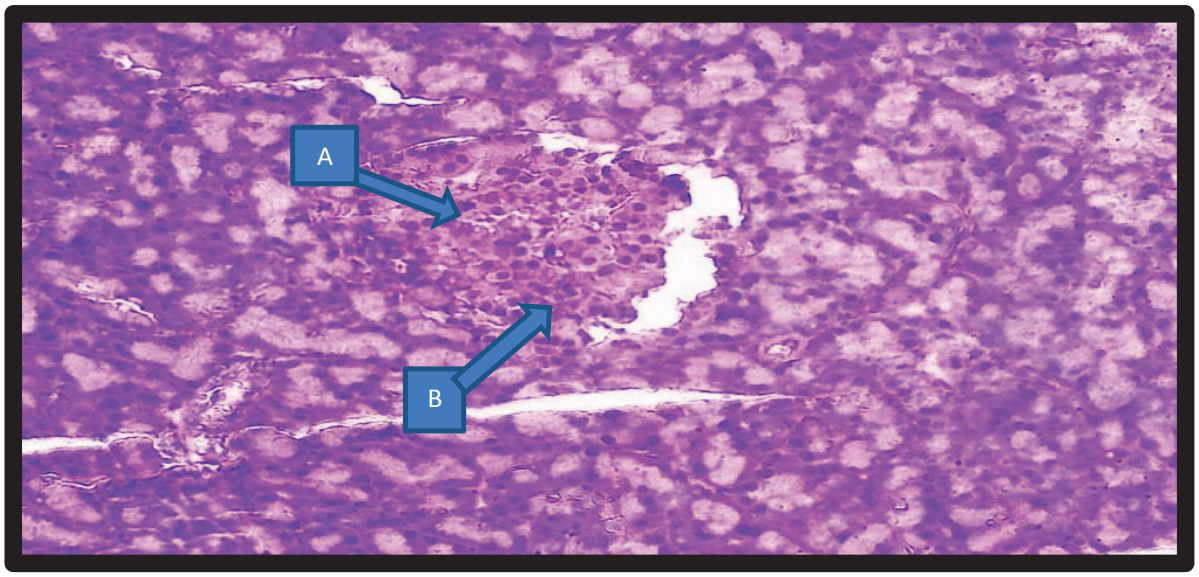

Figure 5: histostructures of pancreas gland tissues in the hyperprolactinemia group showing vacuolated cytoplasm (A), thickened nuclei (B) .Photomicrograph (400 X).

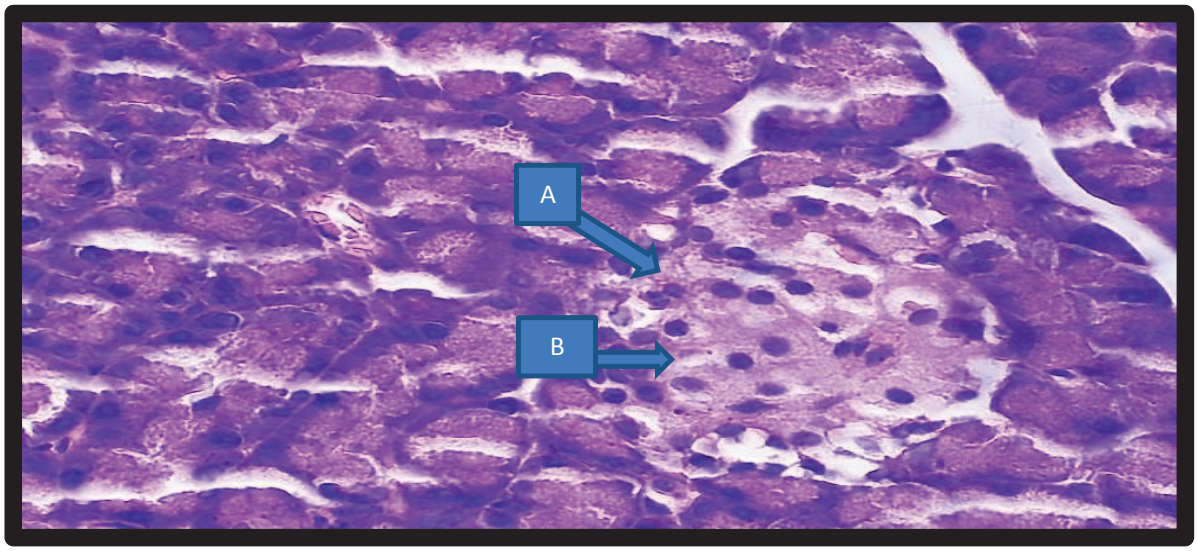

Figure 6: histostructures of Pancreas gland tissues in the in vitamin D -treated group showing normal sizes of Langerhans cells(A) full of cytoplasm and nuclei of normal structure (B). Photomicrograph (400 X).

Discussion: -

The current study aims to know the role of vitamin D in reducing levels of prolactin hormone and improving the function of the pancreas gland and repairing its tissues. Vitamin D affects many biological functions due to the presence of receptors for vitamin D in various organs in the body. The pancreas gland contains vitamin D receptors, which indicates the role of vitamin D. The important thing is in the function of the pancreatic gland, as vitamin D deficiency leads to a malfunction in the function of the pancreatic gland and its secretions[16] .The results of the current study showed an increase in prolactin levels, which led to a defect in the secretion of the pancreas gland that led to in a drop the secretion of insulin hormone. In addition, the vitamin D level decreased in the hyperprolactinemia group, and this deficiency may be attributed to pancreas dysfunction agree with (Ramos-Martínez et al., 2022 and Mohd Ghozali et al., 2022)[17-18].

However, the results of vitamin D treatment showed a decrease in the prolactin level in the vitamin D group. Vitamin D has an effective role in increasing blood absorption of calcium. and when the level of calcium rises, this leads to a decrease in the level of the hormone prolactin, which inhibits the production of prolactin by the pituitary gland[19-20]. This study demonstrated the role of vitamin D in improving the pathological return to their normal levels, compared to the hyperprolactinemia group. The results of the current study showed the presence of histological changes in the hyperprolactinemia group, where it was noted that the size of the islets of Langerhans decreased and the number of cells decreased, especially in the center of the islet of Langerhans , which contains beta cells that secrete the hormone insulin significantly, where it was observed that there was a thickening of the nuclei and the cells were devoid of cytoplasm compared with the control group. negative control .The current study showed that in the group treated with vitamin D, the islets of Langerhans were larger in size, the number of cells was closer to the normal state, the cells had restored their cytoplasm, and their nuclei appeared in normal sizes, with the presence of many newly

formed cells., indicating the role of vitamin D in tissue repair.

Conclusion:-

The study concluded that vitamin D3 has an encouraging effect on the pancreas by stabilizing the hormone insulin and remodeling tissue structures.

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