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The role of vitamin E In reducing the side effects of Gabapentin on some histological parameters related to the heart in male albino rats

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Abstract

The study was designed to evaluate the role of vitamin E in reducing the side effects of gabapentin on the heart in male albino rats,(30) males were used, who were divided into three equal groups : The control group was given physiological saline solution in concentration(0.9%), the treatment group T1 was given gabapentin at a concentration of (100mg / Kg) of body weight, treatment group (T2) was given gabapentin at a concentration of (100mg / Kg) of body weight and vitamin E at a concentration of 80 mg/kg of body weight,The results showed that the drug algapapentin caused tissue changes in the heart muscle, represented by atrophy of the cardiac muscle fibers, the appearance of spaces between them, and congestion in the blood vessels ,Vitamin E helped reduce them.

Keywords: Gabapentin, vitamin E,heart

Introduction

Gabapentin (GBP) is marketed commercially under the name Neurontin, often used as an adjunct to other antiepileptic drugs. It is a highly bioavailable drug, undergoes minimal metabolism, and is excreted via the kidneys (15,21).GBP is a new, second-generation drug that was approved by the US Food and Drug Administration in 1993 and has been available generically in the United States since 2004 (9).

Its original use was as a muscle relaxant and anticonvulsant but its potential as an anticonvulsant and adjunct to more potent anticonvulsants has been demonstrated. It is prescribed off-label for a range of disorders including bipolar disorder, trigeminal neuralgia, pruritus, and migraine (12,17).

The pharmacokinetics of the drug make GBP ideal due to its rapid absorption, limited metabolism, and low risk of drug interactions. The drug does not inhibit or stimulate hepatic enzymes, which reduces the possibility of interaction with other drugs. The drug also does not inhibit or stimulate metabolism like other drugs (6,14).

Vitamin E is one of the most important fat-soluble vitamins and biological antioxidants that break free radical chains to protect tissues from lipid peroxidation damage (3). It is considered essential for the safety and function of the reproductive, muscular, circulatory, nervous, immune, and circulatory systems (10,11). It is one of the essential vitamins for humans and animals, as the body needs it because it is unable to manufacture it (2,4).

Vitamin E has multiple physiological effects. Although the mechanism of physiological action is not fully known, most of the biological activities of this vitamin are due to its activity as an antioxidant. It plays an important role in preventing the oxidation of lipids in biological membranes by reducing free radicals and other oxidizing agents and preventing the formation of peroxides (8,13).

Materials and methods

In this study, 30 adult male white rats aged (3-4) months and weighing between 16-170 kg were used. The animals were divided into three groups as follows:

1-Control group C: included (10) animals given the physiological solution for 60 days.

2-The first treatment T1: included (10) animals given Gabapentin only at a concentration of (100 mg/kg) of body weight for 60 days (20).

3-The third treatment T2: It included (10) animals that were given Gabapentin at a concentration of (100 mg/kg) of body weight and then Vitamin E at a concentration of (80 mg/kg) of body weight for 60 days.

After the specified period of the experiment, the animals were anesthetized by placing the rats inside a container with a tight lid containing cotton soaked in chloroform for a few seconds. After that, the animals were dissected and the heart was removed. The tissues attached to it were removed and preserved in formalin at a concentration of 10% for 48 hours for the purpose of conducting tissue sections. The formalin solution was prepared according to the method of Bancroft (2013) by mixing 10 ml of formaldehyde fixative at a concentration of 40-37% with tap water in a volume of 90 ml.

Results

Histological Changes In Heart

Histological sections of the heart of male white rats in the control group C showed normal cardiac tissue, where the normal histological arrangement of cardiac muscle fibers was observed with the presence of peripheral nuclei within these muscle fibers .as in Figure (1-4) and (2-4)

As for the treatment group T1 and the treatment with GBP at a concentration of 100 mg/kg, the histological examination showed clear atrophy in the cardiac muscle fibers, where the loss of the histological arrangement of the cardiac muscle fibers was observed, as the cardiac fibers appeared small and round with small spherical nuclei in addition to the presence of wide spaces between them, and congestion of the blood .vessels within the cardiac muscle was observed as in Figure (3-4) and (4-4)

As for group T2 treated with 100 mg/kg GBP and 80 mg/kg vitamin E, It showed slight histological changes when compared with group T1, where very little congestion of the blood vessels Inside the cardiac muscle was observed, and the cardiac muscle fibers were normal with elongated peripheral nuclei and simple spaces .between them as shown in Figure (7-4) and (8-4)

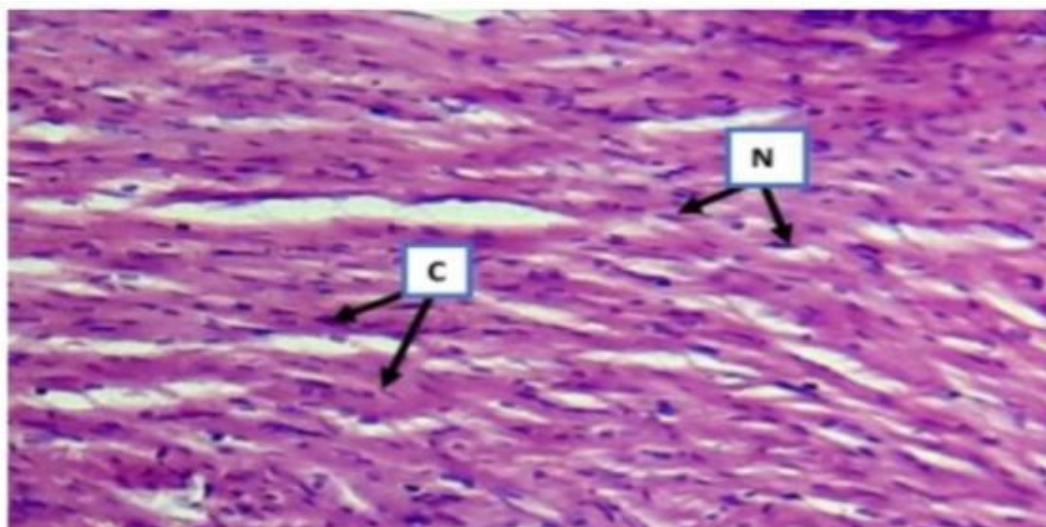


Figure (1): A rat heart from the control group C – normal heart tissue is observed, where the normal tissue arrangement of cardiac muscle fibers is observed ©, with peripheral nuclei within these muscle fibers (N) (10X H&E).

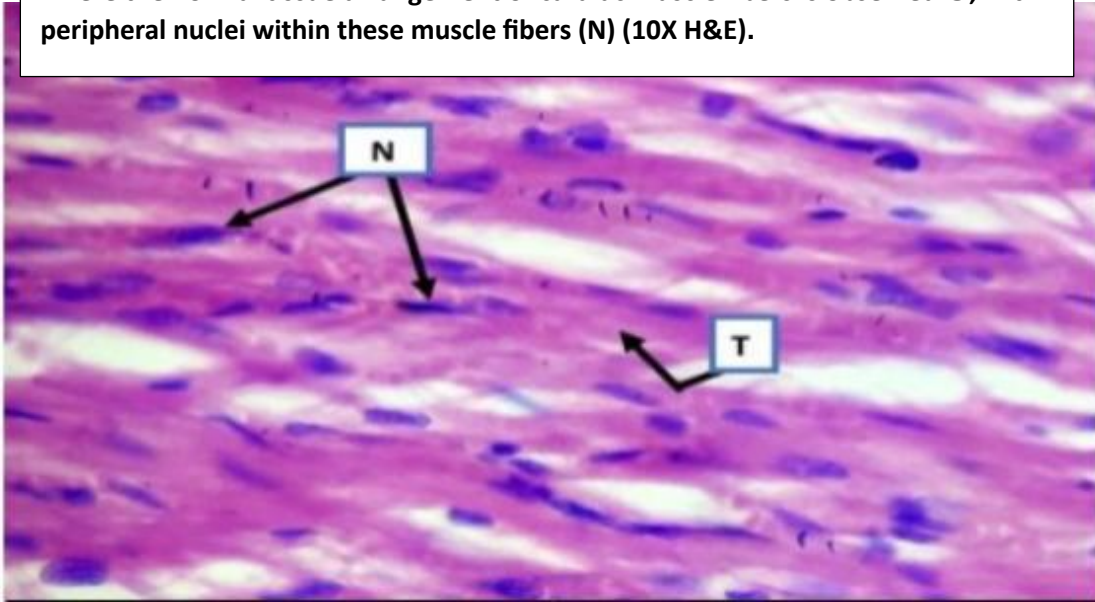


Figure (2): Heart of a rat from the control group C: - Magnified section. Cardiac muscle fibers are observed with transverse striation (T) and peripheral elongated nuclei within these fibers (N). (40X H&E).

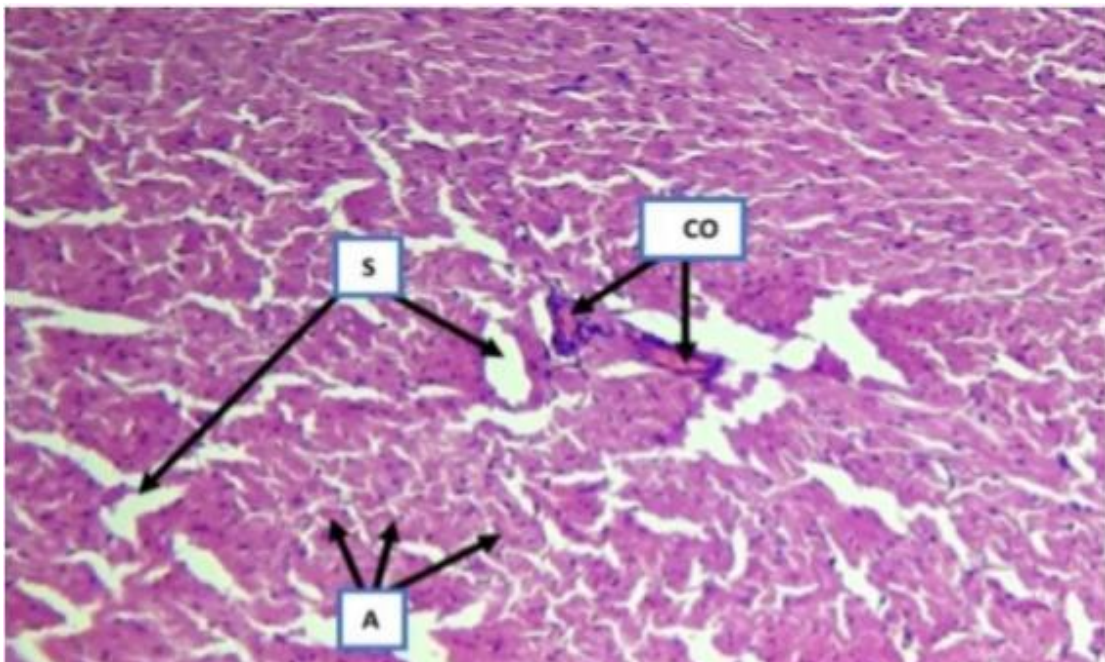


Figure (3): Rat heart from the T1 drug group: - Clear atrophy in the cardiac muscle fibers (A), where loss of the tissue arrangement of the cardiac muscle fibers is observed, and there are wide spaces between them (S), with congestion of the blood vessels (CO). (10X H&E).

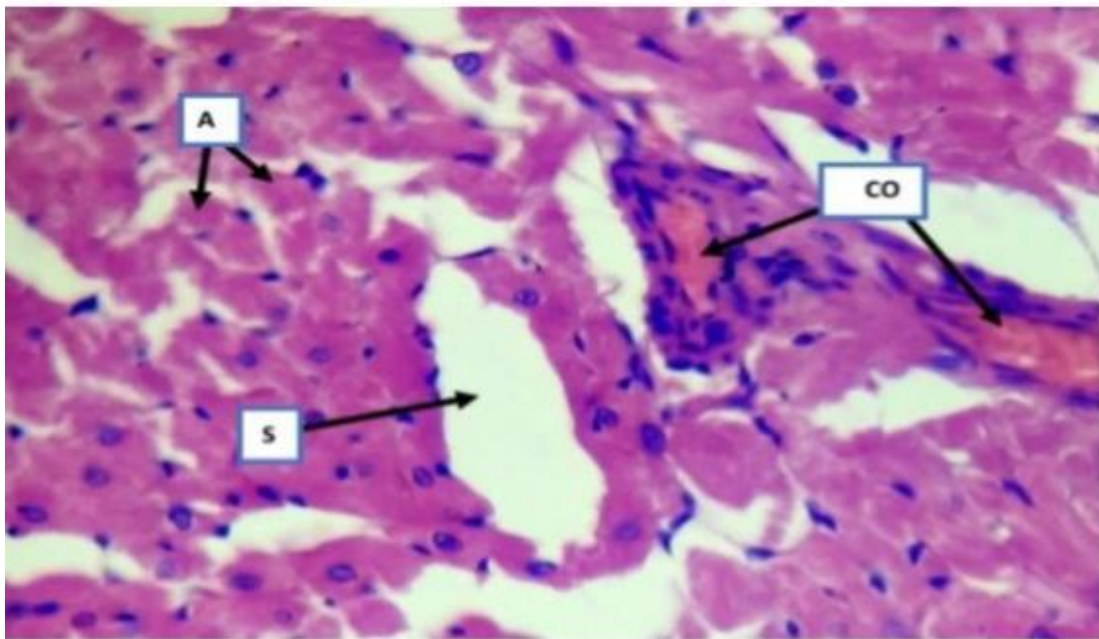


Figure (4-4): Rat heart from the T1 group. Magnified section. We notice clear congestion of the blood vessels inside the myocardium (CO) and clear atrophy of the cardiac muscle fibers (A), as the cardiac fibers appear small and round with small spherical nuclei. Also, wide spaces are observed between the cardiac muscle fibers (S).

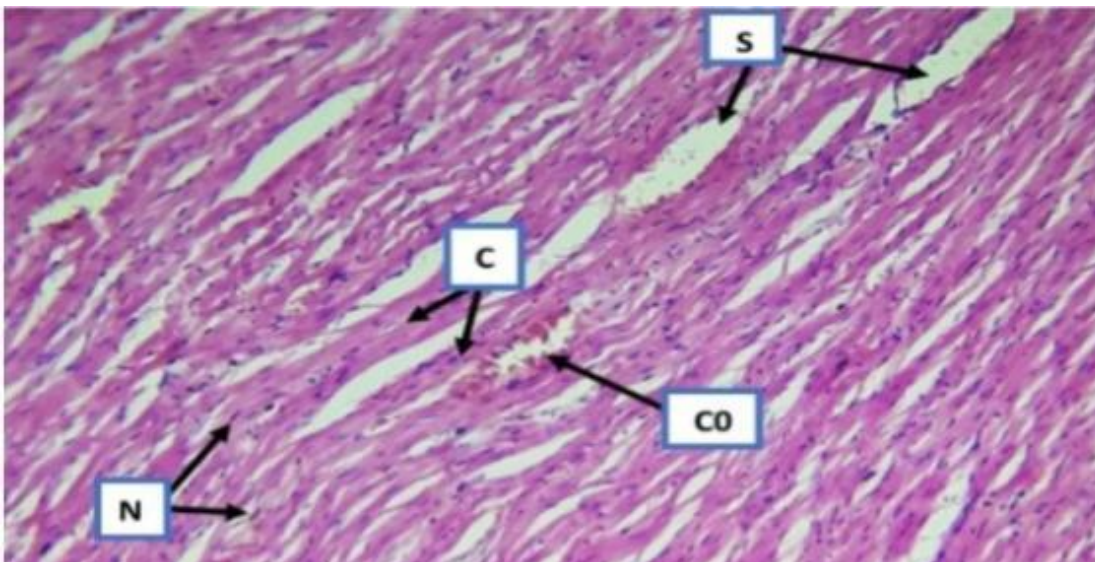


Figure (5): A rat heart from the T3 drug group + vitamin E. The histological arrangement of the cardiac muscle fibers (C) is noted with the peripheral elongated nuclei located (N) where slight degeneration of the muscle fibers is noted with the presence of simple spaces between them (S). Also, very little congestion of the blood vessels inside the cardiac muscle is noted (CO) (10X H&E)

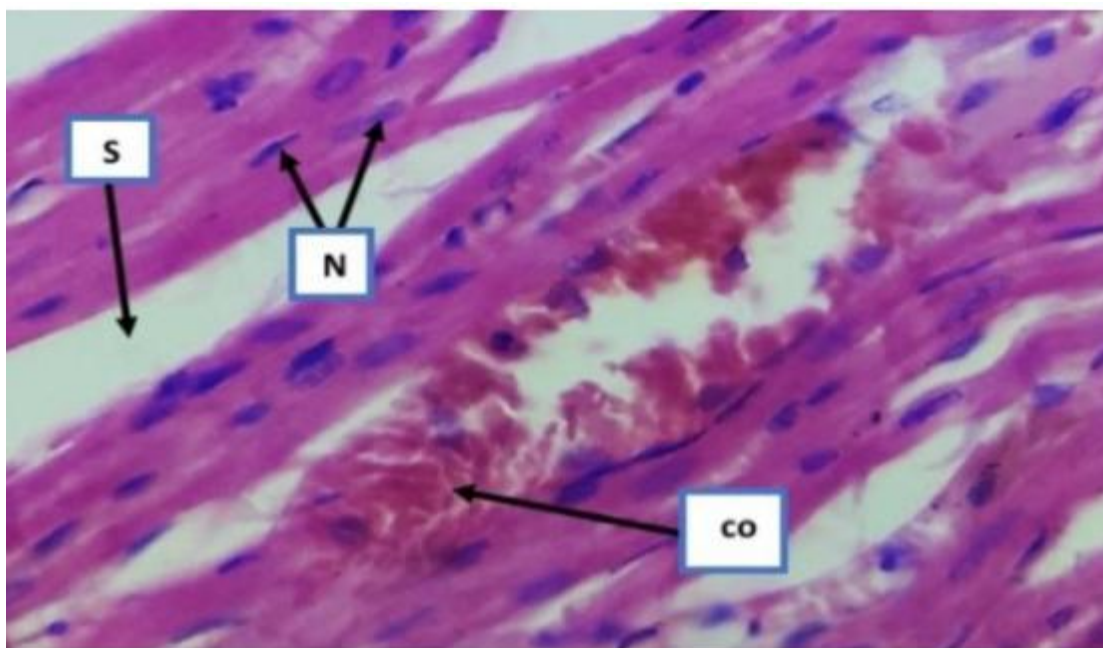


Figure (6): Rat heart from the T3 drug + vitamin E group. Magnified section. Very little congestion of blood vessels is observed within the myocardium (CO) and the cardiac fibers are normal with elongated peripheral nuclei (N) and small spaces between them (S). (40X H&E).

Discussion

The tissue sections of the T1 group treated with GBP at a dose of 100 mg/kg of body weight showed a clear atrophy in the cardiac muscle fibers, where the loss of the tissue arrangement of the cardiac muscle fibers was observed, as the cardiac fibers appeared small and round with small spherical nuclei and the presence of wide spaces

between them, and congestion in the blood vessels was observed compared to the control group C. The atrophy of the cardiac muscle fibers occurs due to the insufficiency of blood supply to the heart muscle ischemia, which is a pathological structural change, and the main reason for these changes is inflammation of the cardiac muscle cells Myocarditis, and it is also observed that there are spaces in the cytoplasm of the cells and congestion in the blood vessels and the occurrence of programmed death apoptosis of the cardiac cells with the development of the condition of cardiac muscle atrophy (19), and the GBP drug can cause damage to both sides of the heart, but the left ventricle is more susceptible to the effect than the right ventricle due to the strength of the contraction and the role it plays in cardiac contraction due to its muscle mass , and on this basis, examining the function and structure of the left ventricle is the real standard for diagnosing and evaluating the heart condition (5) .

These negative structural and functional tissue changes that may occur due to GBP can be attributed to several reasons, but the most likely reason, which was addressed by most of the research and studies that we reviewed during the preparation of this thesis, is oxidative stress and the generation of active oxygen species, as free radicals can induce nucleolysis and then the process of programmed death (1).

While the histological sections of the heart in the T2 groups showed a close to normal shape with very little congestion of blood vessels within the myocardium and small spaces between the myocardial fibers when compared with the T1 group that was dosed with GBP only, these results were consistent with the results of ,who found that treating rats with vitamin E showed an almost normal heart structure. This study was also consistent with the results of (16), who found that treating male rats with vitamin E prevented an increase in the myocardial fiber atrophy index, congestion in the blood vessels, and the presence of wide spaces between the myocardial fibers. The reason for this is that vitamin E can protect heart failure by maintaining a normal oxidative stress state by reducing the production of MDA, as it is known that vitamin E reduces the production of free radicals, Therefore, we conclude from the above that vitamin E is able to heal the heart muscle and prevent pathological structural changes in the heart (18), because this antioxidant activates the defense mechanism in heart cells because it is effective in scavenging free radicals and reducing oxidative stress, in

addition to its role in preventing the biosynthesis of enzyme proteins that contribute to oxidation and reduction reactions, and in return, it activates the gene expression for the synthesis of Actine proteins in cardiac muscle fibers in an attempt to compensate for damaged proteins , It is an antioxidant capable of preventing the formation of free radicals and removing previously formed free radicals at the same time (7).

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