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Gamma Glutamyl Transferase Activity (Ggt) In Albino Rats Treated With Orphenadol Analgesics

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Abstract: *The use of orphenadol as a wide spectrum painkiller (analgesics) has been reported to elicit some toxic effects. This research examined the hepatobiliary effect of orphenadol solution on hepatobiliary system in albino rats. Twenty male albino rats, distributed into four groups (A, B, C and D), with five rats in each group, were used in this research. Groups A, B and C were given oral treatment of 21, 42 and 84mg/kg respectively of the drug solution for seven days consecutively, while the animals in group D were kept as control. Treatment of animals with the drug sample resulted to a decrease in physical activities, body weights, and feed and water intake during the period of treatment relative to the control. Measurement of the total protein concentration in the serum of the rats did not reveal any significant difference (P>0.05) between the test and the control groups. The activity of gamma glutamyl transferase recorded in the test groups were significantly higher than the control (P<0.05). These effects of orphenadol solution on this enzyme and total protein concentration were found to be dose-dependent. The findings of this research indicate that the toxic effects or the adverse effect of orphenadol may include the hepatobiliary system.*

Keywords: *Orphenadol, analgesics, gamma glutamyl transferase and hepatobiliary system.*

I. Introduction

The word analgesic is derived from Greek “an” meaning without and “algia” meaning "pain". An analgesic is also known as painkiller, and is any member of the group of drugs used to achieve analgesia- relief from pain [1, 2, 3 and 4].

Analgesic drugs act in various ways on the peripheral and central nervous systems. They are distinct from anesthetics, which reversibly eliminate sensation, and include paracetamol (known in the US as acetaminophen or simply APAP), the non-steroidal anti-inflammatory drugs (NSAIDs) such as the salicylates, and opioid drugs such as morphine and opium. In choosing analgesics, the severity and response to other medication determines the choice of agent; the World Health Organization (WHO) pain ladder specifies mild analgesics as its first step [5, 6, 7 and 8]. Analgesic choice is also determined by the type of pain: for neuropathic pain, traditional analgesics are less effective, and there is often benefit from classes of drugs that are not normally considered analgesics, such as tricyclic antidepressants and anticonvulsants [9, 10 and 11].

Pain can be defined in many ways. It is usually described as a distressing sensation in the body system or, an unpleasant or hurtful sensation resulting from the stimulation of nerve endings by noxious stimulus/stimuli resulting a gross tissue damage. However, pain can also be explained as a mental or emotional suffering or torment. Various daily activities and actions may cause pain and aches like, headache, muscle cramp or a pinch from someone or engaging in strenuous exercises that can lead to muscle aches. Occasionally, pain also occurs through serious injuries and illnesses such as sore throats [12, 13, 14 and 15].

Orphenadol citrate is a salt of orphenadrine which appears as a white crystalline powder having a bitter taste. It is practically odorless; sparingly soluble in water and slightly insoluble in organic solvents (an example is alcohol) [16, 17, 18, 19 and 20].

Orphenadrine citrate exerts its analgesia by acting at the central nervous system (brain stem). It appears to selectively block facilitatory functions of the reticular formation. It does not produce myoneuronal block and does not also affect the crossed extensor reflexes [21 and 22]. Orphenadrine prevents nicotine-induced convulsions but not those produced by strychnine. Euphoria is an effect reported by many patients using orphenadrine, and orphenadrine has been investigated for use against depression, as first reported in June 1958 in the American Journal of Psychiatry. Like many first-generation antihistamines and chemically-similar anticholinergics, orphenadrine can also cause excitement and insomnia, particularly in children and the elderly [23, 24 and 25].

Gamma-glutamyltransferase or gamma-glutamyl transpeptidase (also γ-glutamyltransferase, GGT, GGTP, gamma-GT) (EC 2.3.2.2) is an enzyme that transfers gamma-glutamyl functional groups. It is found in many tissues, the most notable one being the liver, and has significance in medicine as a diagnostic marker. GGT catalyzes the transfer of the gamma-glutamyl moiety of glutathione to an acceptor that may be an amino acid, a peptide or water (forming glutamate). GGT plays a key role in the gamma-glutamyl cycle, a pathway for

the synthesis and degradation of glutathione and drug and xenobiotic detoxification. Other lines of evidence indicate that GGT can also exert a prooxidant role, with regulatory effects at various levels in cellular signal transduction and cellular pathophysiology [21, 23 and 24].

GGT has several uses as a diagnostic marker in medicine. GGT is primarily used to diagnose hypertension. Blood test results for GGT suggest that the normal value for men is 15-85 IU/L, whereas for women it is 5-55 IU/L [9] and [16].

II. Aims/ Objectives

Orphenadol has been reported to have some side effects on some tissues and organs. This research was to investigate the possible adverse effects of orphenadol on hepatocyte and other tissue or organs. By measuring the level of gamma glutamyl transferase activity (mark enzyme), the hepatic effects of orphenadol as well as its analgesia on albino rats is determined.

III. Materials And Methods

Methods

Collection of Samples

Collection of Albino Rats

Twenty male albino rats were purchased from the Biochemistry Department of the University of Nigeria Nsukka and were transported down to Abakaliki to the Biochemistry Laboratory of Ebonyi State University.

Collection of Drug Sample

Orphenadol drug was bought from Chris Pharmacy, Onitsha, Anambra State.

Preparation Of Drug Sample

485mg of orphenadol drug drug was dissolved in 400ml of distilled water to obtain concentration of 12.1mg/ml.

Animals Handling And Treatment

Animal Grouping

The animals were grouped in four cages, five per group and were labeled accordingly.

Measurement Of The Weight Of The Animals

The weights of the animals were taken daily using chemical balance. The results obtained were used to monitor weight changes and determine the volume of the sample to be administered to each of the animal.

Administration Of Sample

The animals were fed with growers and water on daily basis for seven days for acclimation. The samples were administered to the animals using 2ml syringe. The animals in groups A, B, and C were given 21, 42, and 84mg/kg body weights respectively. While the animals in group D (the control) were given distilled growers and water for seven consecutive days.

Collection Of Samples From The Animals

After seven days of treatment with the drug sample, the animals were starved for 24 hrs and their blood samples were collected into a sterile bottle.

IV. Results

Physical Activities

During the period of treatment of animal, the albino rats in test groups (A, B, G and C) were observed to show relatively decreased movement for water intake, unlike the animals in the control group. But during the first 3 days, the reduction in movement for water intake was not observed that much. Other physical activities of the treated generally reduced.

Changes In Body Weight

The result on the average body weights (g) of animals during seven days of treatment is represented in table 1 below.

Table 1 average weight of rats during seven days of treatment

DAYS	BODY WEIGHT OF GROUP A(G)	BODY WEIGHT OF GROUP B(G)	BODY WEIGHT OF GROUP C(G)	BODY WEIGHT OF GROUP D(G)
1.	80±.7.21	88±7.88	74 ± 7.16	91±7.46
2.	89± 7.90	96±7.73	83±7.57	102±7.03
3.	92±7.18	102± 7.95	88±7.55	110±7.81
4.	85 ± 6.36	96 ± 6.93	82 ± 7. 43	110 ± 7.14
5.	82 ± 7.24	86 ± 5.94	78 ±7.03	107 ± 7.04
6.	82 ± 4.83	82 ±4.47	74 ± 7.94	105 ± 7.00
7.	80 ± 5.24	76 ± 5.42	69 ± 6.51	100 ± 7.07

All values are mean ± standard derivation n=5

Table 1 shows that the mean values of test groups increased during the first 3 days of treatment after which it reduced consecratory compared to that of the control group.

Gamma Glutamyl Tramsferse (Ggt) Activity And Total Protein Concentration

The result on the protein concentration, enzyme activity and specific enzyme activity is shown in table 2 below.

Table 2 average enzyme activity, protein concentration and specific enzyme activity after seven days of treatment.

Animal Group	Average enzyme activity (u/l)	Total protein conc. (mg/ml)	Specific enzyme activity (u/1mg/ml)
1.	24.86 ± 3.68^{b}	0.34 ± 080^{a}	156.30 ± 7.83^{c}
2.	37.95 ± 41.31^{c}	0.41 ± 0.17^{a}	109.8 ± 7.02^{p}
3.	66.96 ± 7.44^{u}	0.30 ± 0.13^{a}	305.22 ± 7.33^{u}
4.	17.42 ± 1.63^{a}	0.65 ± 0.30^{a}	39.32 ± 7.44^{a}

Table 2 shows the average enzyme activity, protein concentration and specific enzyme activity of the rat after seven days of treatment. The different observed between the enzyme activity and total enzyme activity having the differ superscripts is significant ($P<0.05$) the enzyme activity and specific enzyme activity of the test groups increased while that of the control decreased conversely. The protein concentration of the test groups having the same superscripts did not differ significantly ($P>0.05$).

V. Discussion

During the periods of treatment, the test animals were observed to experience decrease in their physical activities, rate of food and water intake, while the animals in the control grouped thrived. The mechanism or reason to support the reduction in agility is not well understood at the level of this research. However, this could be as a result of the metabolic responses/changes of the animals to the drug sample (chemical constituents of the drug sample). This is may be because of the side effects like, dizziness, itching, euphoria. The main reason that may back up the loss of weight observed in the test groups (table 1) is still obscure even at the level of this research. But this reason may be attributed to the reported decrease in food intake as well as water intake, during the periods of treatment of the animals as in the case of metabolic responses to the drug sample.

Between the animals in the test group (treated) and those in the control group, the protein concentration did show a significant difference in their protein level (table 2). Thus, the drug (orphenadol) with its chemical constituent may have played a significant role/function biologically in the rate of the biosynthesis and degradation of protein.

The gamma ghtamyl transferase activity in the serum of the albino rats in the treated animals increase, while that of the control decreased (tabled 2). The biochemical back up/reason for this increase in GGT is still not clear. Since GGT is a marker found in the hepatocyte (liver cell) the reason for the increase in the level of the enzyme (even though it is still obscure) may be as a result of the administration of the drug sample which may have exhibited toxic effect on the red blood cell (RBC), causing the enzyme to leak out from the liver into blood stream thereby decreasing the level of gamma glytamyl tramsferase.

The elevation or elevated level of GGT corresponds with respective doses of the administered drugs and may indicate that the dose used may have effect on the liver thereby allowing the presence of the enzyme in the blood sream, indicating a liver disease, which could be inter-or post-hepatic biliary obstruction.

VI. Conclusion

From the precedent/foregoing observation, it can conclusively be stated that the high dose adverse effects which may involve over activation of GGT resulting to its elevation in the serum indicating the either inter-or post-hepatic bilary obstruction. It is therefore suggested, that more researches should be carried out to determine the exact possible mechanism responsible for the elevated level of GGT as well as its increased rate of activity.

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