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Investigation of the physiology effects of amikacin and the protective role of L-carnitine and vitamin C in adult male rats

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ABSTRACT- The aim of this study is to show the powerful role of amikacin without or with L-carnitine or vitamin C in some bodily criteria. This can give more insight on how to use amikacin with or without additives. The animals were divided into four groups (12 for each group). The first group as a control group, and the second group was injected with amikacin 30 mg/kg b. w for 28 days. The third group was dosed with vitamin C 500 mg/kg b. w and amikacin injection 30 mg/kg b. w for 28 days. The fourth group received L-carnitine 600 mg/kg b. w and amikacin 30 mg/kg b. w also for 28 days. The blood samples taken from the animals were slaughtered when the experiment was completed. As a result of exposure to amikacin, we notice an increase significantly in the level of cholesterol, T.G, LDL, VLDL, ALT, AST, CPK, MDA compared with control group and other groups, in contrast with HDL, while noted nearly no-significantly ($p \geq 0.05$) level of cholesterol, T.G, LDL, VLDL, HDL, ALT, AST, CPK, MDA in male rats of the third and fourth groups compared with control group. The study's conclusion indicates that amikacin has a wide range of physiological adverse effects. As a result, antioxidants such as (L-carnitine and Vitamin C) are recommended as a protective measure against amikacin.

Keywords- Amikacin, kidney function, L-carnitine, lipid profile, Liver enzymes, vitamin C.

1. INTRODUCTION

Amikacin is sizeable in medicine due to the fact it is a mighty antibiotic that could treat bacterial infections which can be extreme and probably fatal however resistant to different drugs. Particularly powerful towards Gram-bad microorganisms that motivate infections of the lungs, pores and skin, stomach, blood, mind, urinary gadget, bones, and joints encompass amikacin-producing Pseudomonas, Acinetobacter, Enterobacter, E. Coli, Proteus, and Serratia [1, 2, 3]. Amikacin eye drops also can be used to deal with bacterial eye infections [4]. Amikacin does, however, have many shortcomings and restrictions. Serious damaging effects from amikacin encompass allergies, renal problems, hearing loss, stability problems, and paralysis [5]. Amikacin should as a result be administered carefully and under

cautious statement of the affected person's blood degrees and renal characteristics. [6] Amikacin has to no longer be taken when pregnant or nursing when you consider that it could leave the unborn infant permanently deaf [7]. Moreover, amikacin may additionally interact with other pills, including cisplatin, diuretics, and other antibiotics, to reduce their efficacy or enhance their toxicity [8].

Bacterial resistance is another problem that amikacin should cope with as it lowers its effectiveness and increases the opportunity of treatment failure. Acetylation by way of the enzyme AAC (6′)-Ib, which alters the antibiotic and prevents it from attaching to the bacterial ribosome, is the number one resistance mechanism towards amikacin. Developing AAC (6′)-Ib inhibitors, mixing amikacin with other antibiotics, or converting the shape of amikacin to lessen its susceptibility to acetylation are some strategies to combat this resistance [9].

When taking amikacin as an antibiotic, there is an excessive danger of toxicity. Amikacin may additionally have harmful consequences, such as nephrotoxicity, which could result from renal damage and decreased kidney function [10]. Increased risk of contamination, fluid retention, and electrolyte imbalance can result from this. Ototoxicity is an additional dangerous effect. Amikacin might also set off vertigo, tinnitus, or hearing loss by means of affecting the inner ear [11]. Depending on the remedy's dosage and length, this may be irreversible or permanent. Amikacin also can impede nerve impulse transmission, resulting in neurotoxicity, which can induce seizures, tingling, numbness, or weakening within the muscle mass [12]. Patients with neuromuscular conditions like Parkinson's sickness or myasthenia gravis can be especially vulnerable to this.

A nutrition and dietary supplement known as L-carnitine is related in the synthesis of electricity and the metabolism of fat. Although there are probably a few blessings for fertility, mind feature, and weight loss, there could also be a few negative consequences and interactions. A substance called L-carnitine aids the frame's process of converting fats into power. It has been used to treat some of illnesses, together with renal and cardiac troubles in addition to muscular problems. According to certain research, L-carnitine can also provide a few safeties against amikacin poisoning, a dangerous facet impact of a commonplace antibiotic [13].

L-carnitine has the ability to reduce the degree of amikacin-induced nephrotoxicity or the drug's negative consequences on the kidneys. L-carnitine changed determined to decorate kidney function and shape by using the authors of this take a look at, who also assessed the renal biochemical parameters and histology of rats dealt with amikacin and L-carnitine. Additionally, they performed clinical research on hospitalized sufferers receiving amikacin and found that L-carnitine decreased the negative outcomes of medication,the second study investigated the effects of cholecalciferol (vitamin D3) and L-carnitine on amikacin-caused nephrotoxicity in rats and humans, and the effects have been mentioned in the Biomedical and Pharmacology Journal2. The findings validated that while cholecalciferol turned into more beneficial than L-carnitine in lowering the renal damage brought on by way of amikacin, both substances reduced renal damage. The authors came to the belief that cholecalciferol is an ideal desire to L-carnitine for decreasing the results of nephropathy due to amikacin [14].

While most individuals find L-carnitine to be safe, some humans may additionally experience negative side effects which include nausea, vomiting, diarrhea, and seizures [15].

Because vitamin C shields the cochlear hair cells from oxidative stress, it could lessen the ototoxicity, or hearing impairment, produced by means of amikacin and other aminoglycosides [16]. Since renal damage from amikacin and different aminoglycosides is broadly speaking linked to the drug's high blood concentration, diet C won't have an effect on this [17]. If eaten up in extra, diet C itself could have harmful results, including acidifying the urine, generating nausea and diarrhea, disrupting the antioxidant balance, and in certain instances, encouraging iron overload [18]. My research objectives are to decide the impact of L-carnitine and Vitamin C on Amikacin-brought toxicity in rats via lipid profile, liver enzyme, and kidney feature analysis.

2. MATERIAL AND METHODS

2.1. Experimental design

The existing research has been completed, and 48 adult male rats were between 11-13 weeks old; weight 180-225 grams. Animals, leave it for ten days to adapt to the environment under normal conditions, under 25 temperatures. The experiment will be completed between September and October 2023. In four groups, Rats were distributed, each group consisting of 12 adult rats in each group: -

- The control group: distilled water only was given to animal
- Group 2: injected with amikacin 30 mg/kg b. w daily for 28 days [19].
- Group 3: injected with amikacin 30 mg/kg b. w, and 600 mg/kg b. w daily (carnitine) for 28 days, Oral dose [20].
- Group 4: injection of amikacin 30 mg/kg b. w, and 500 mg/kg b. w daily (vitamin C) for 30 days, oral dose [21].

Blood 1was collected from the heart by using a 5ml disposable syringe, then put the blood sample in the gel tube until it thickened, and then centrifuged at 3000 rpm for 15 minutes to obtain the serum sample is separated into many Eppendorf tubes to avoid repeated thawing. All test tubes are stored under (-20c) until use

2.2. Biochemical assay

The biochemical analyses were done on liver enzymes (ALT, AST, ALP), Lipid profile (HDL, VLDL, LDL, T.G, Cholesterol), and kidney function (AST, ALT, CPK) and tests for at the technical institute/ kut using the Fujifilm device, where special kits were used for these tests and they're of Japans manufacturer. When the separated serum from the blood was placed in his tube the blocks were defined on the device and an instruction was given that it takes the device five minutes for the results to appear printed on the papers.

2.3. Statistical analysis

The mean± SEM was applied in the present work to represent the data, and analysis of variance (ANOVA) was applied by using the SPSS program. *P<0.05, **P<0.01, ***P<0.001, and ****P<0.0001.was considered a significant difference. The least significant difference (LSD) was measured to test the difference between means [22].

3. RESULTS AND DISCUSSION

3.1. Liver functions

The data obtained by conducting this study revealed the effect of different treatments on liver, kidney, and lipid profiles. Figure 1 shows the levels of AST, ALT, and CPK in control, G1, G2, and G3, respectively. For AST, ALT, and CPK, the amikacin group showed the highest level (P<0.05) in comparison with the control, vitamin C, and L. carnitine groups, respectively. L. carnitin group showed no significant (P>0.05) difference in comparison with the control group (Figure 1).

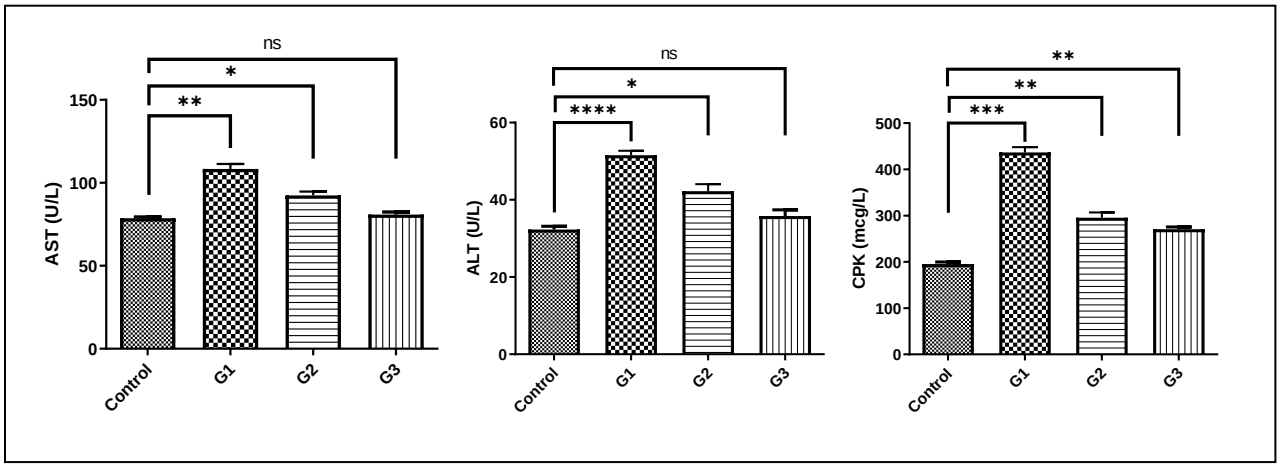

FIGURE 1. Shows AST, ALT, and CPK levels in Control, G1: Amikacin (35mg/kg) for 30 days, G2: Vitamin C (500 mg/kg) + Amikacin (35mg/kg) for 30 days, and G3: L. carnitin (600mg/kg)+ Amikacin (35mg/kg) for 30 days. Ordinary one-way ANOVA and Newman-Keuls post hoc. N=12. Ns:non-significant, *P<0.05, **P<0.01, ***P<0.001, and ****P<0.0001.

The G1, G2, and G3 AST, ALT, and CPK le-vels of the control group. The group tre-ated with amikacin showed the highest level of AST, ALT, and CPK when compared to the control, vitamin C, and L. carnitine groups (P<0.05). It seems that levels of liver enzymes can be increased due to Amikacin uptake. It can make levels rise to three to five times the typical ranges, but it usually does not damage the liver. Live-r enzymes are prote-ins that perform everyday tasks for the liver. When the live-r gets hurt, these e-nzymes get into our blood. We can find the-m through blood tests. ALT (Alanine transaminase) and AST (Aspartate- transaminase) are liver e-nzymes. If their leve-ls go up, it might mean the liver has been harmed by a medicine- [23].

In rare cases, amikacin can also cause hepatitis or hepatitis. Blood tests that monitor levels of liver enzymes and bilirubin the red stains that form when red blood cells are removed diagnose liver disease [24].

Amikacin sometimes poses a serious risk to the liver, leading to liver failure, though this is extremely rare. Signs of liver failure range from organ damage, blee-ding, swelling, and confusion, to a state of coma. Bloodwork can show ammonia, a harmful matter that is usually re-moved by the liver, and other tests that can potentially signal liver failure [25]. Despite this, [26]. confirmed that le-vels of AST, ALT, and CPK might increase if the liver is exposed to dange-rous chemicals. These spe-cifics show that liver cells are hurt and normal live-r function changes.

3.2.Kidney functions

To find out the effect of different treatments on kidney functions, BUN and creatinine were measured. Figure 2 revealed that control group had the lowest (P<0.05) BUN and creatinine levels in comparison with G1, G2, and G3 groups. However, treatment with Vitamin C and L. carnitin had a significant (P<0.05) lowering effect in comparison with G1: Amikacin group.

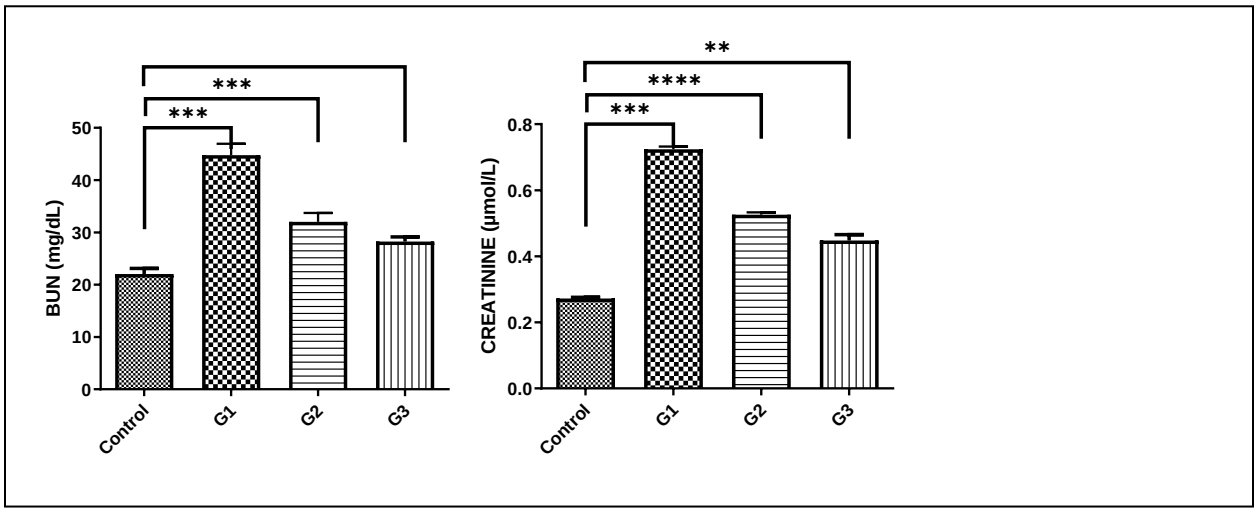

FIGURE 2. Shows BUN and Creatinine levels in Control, G1: Amikacin (35mg/kg) for 30 days, G2: Vitamin C (500 mg/kg) + Amikacin (35mg/kg) for 30 days, and G3: L. carnitin (600mg/kg)+ Amikacin (35mg/kg) for 30 days. Ordinary one-way ANOVA and Newman-Keuls post hoc. N=12. Ns:non-significant, *P<0.05, **P<0.01, ***P<0.001, and ****P<0.0001.

Measuring blood creatinine levels is one method of keeping an eye on kidney health. One waste product that the kidneys often eliminate from the blood is creatinine. A high creatinine level may indicate reduced renal function or kidney disease. On the other hand, certain drugs have the ability to raise blood creatinine levels without really

damaging the kidneys. This is known as a falsely elevated creatinine level. Among the drugs that may result in a falsely elevated creatinine level is amikacin [27].

Blood urea nitrogen, or BUN, is an additional waste product that the kidneys eliminate from the blood. renal disease or diminished renal function may also be indicated by a high BUN level. Amikacin does not obstruct the laboratory procedure used to quantify BUN, in contrast to creatinine. As a result, amikacin's impact on BUN levels accurately represents renal function. However, dehydration, feeding, liver function, and medical treatment could be important factors that can effect on BUN levels. As a result, BUN values have to be evaluated in combination with other clinical indices and creatinine levels [28]. mentioned that a rise in the level of these parameters is caused by any kidney-related issue [29].

3.3. Lipid profile

Since detecting of lipid profile is very beneficial in reflecting the status of lipid metabolism in the body, cholesterol, TG, HDL, LDL, and VLDL were detected in all study groups; control, G1, G2, and G3. Figure 3 showed that G1 group had the highest levels ($P<0.05$) regarding cholesterol, TG, and VLDL in comparison with control and other G2 and G3 groups. Nevertheless, HDL had the lowest level in G1 group in comparison with other groups. In general, G3 had the best effect since it had no significant ($P>0.05$) difference in comparison with control group and could ameliorate the effect of amikacin alone.

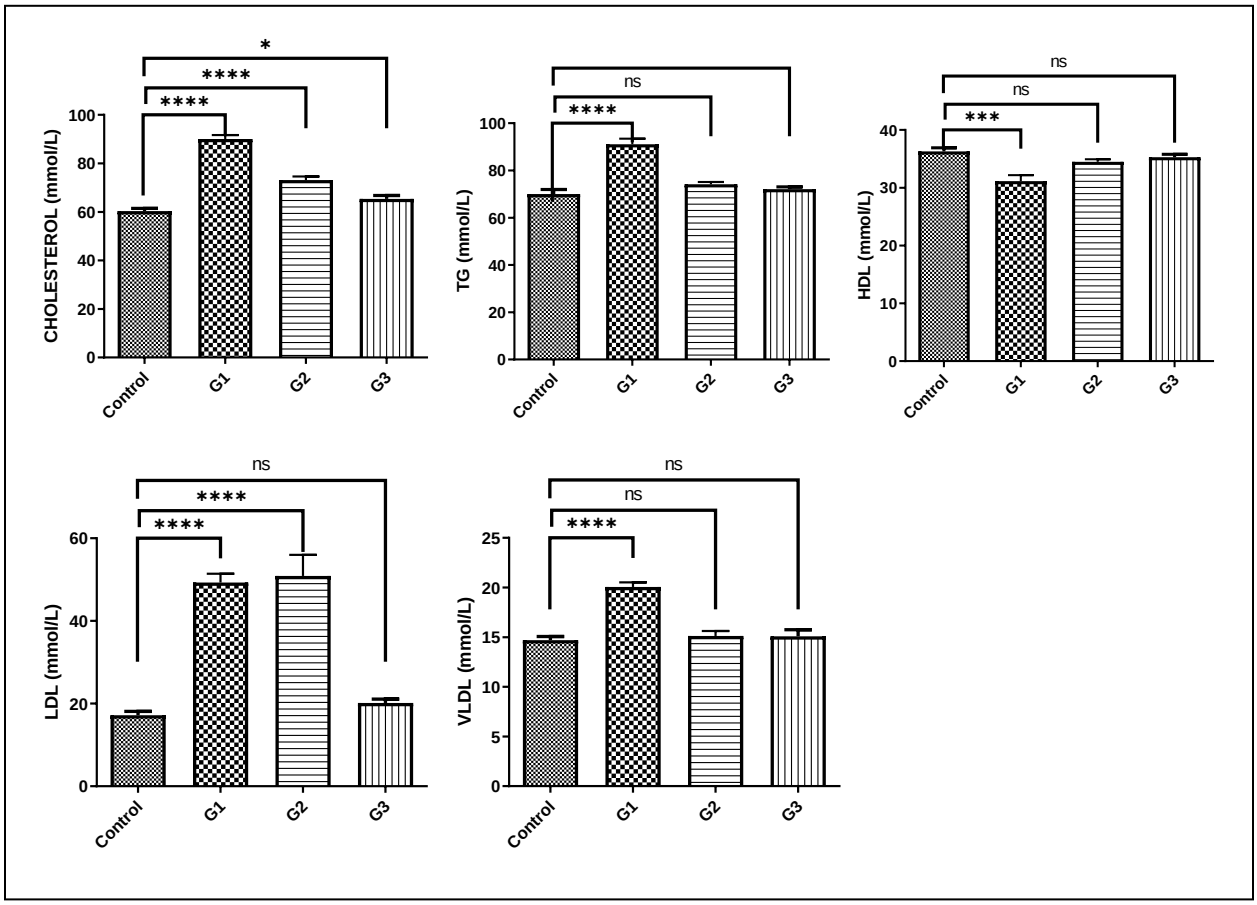

FIGURE 3. Shows lipid profile levels in Control, G1: Amikacin (35mg/kg) for 30 days, G2: Vitamin C (500 mg/kg) + Amikacin (35mg/kg) for 30 days, and G3: L. carnitin (600mg/kg)+ Amikacin (35mg/kg) for 30 days. Ordinary one-way ANOVA and Newman-Keuls post hoc. N=12. Ns:non-significant, *P<0.05, **P<0.01, ***P<0.001, and ****P<0.0001.

Amikacin may have the following effects on lipid profile and lipid peroxidation: it may raise levels of triglycerides (Tg), low-density lipoprotein cholesterol (LDL-Ch), and total cholesterol (TCh), which are cardiovascular disease risk factors; it may lower levels of phospholipids (PL), total lipids (TL), and high-density lipoprotein cholesterol (HDL-Ch), which are good for the integrity and function of cell membranes; and it may have adverse effects on the kidneys, liver, and other organs [30]. Certain antibiotics, such as gentamicin, can cause toxicity to certain organs, including the liver and kidney, when their lipid profiles are high, with the exception of HDL. For this reason, it's critical to keep an eye on the oxidative state and lipid markers of patients receiving amikacin treatment. Ascorbic acid, a vitamin C derivative, may enhance antioxidant defense and reduce oxidative stress, hence protecting against amikacin-induced lipid peroxidation and profile modification, according to certain studies [31].

4. CONCLUSION

The conclusion of the present study indicates that amikacin has a wide range of physiological adverse effects. As a result, antioxidants such as (L-carnitine and Vitamin C) are recommended as a protective measure against amikacin.

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