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The protective effect of taurine against liver disorder induced by gentamicin in male rats

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Abstract:-

The present study was carried out to investigate the effects of an amino acid taurine on gentamicin-induced liver disorder in male rats. Twenty four male rats were used in this study, the animals divided into four groups, each group contained six rats including: G1 normal group, G2 injection IP with 100mg/kg of gentamicin only for 10 days, G3 injection IP with 100mg/kg of taurine only for 10 days, G4 injection IP with 100mg/kg of gentamicin and injection IP with 100mg/kg of taurine for 10 days, The result shows significant increase ($p<0.05$) in liver enzymes ALT, AST, ALP and significant increase in TC, TG, LDL with marked decrease in HDL levels in gentamicin group compared with normal group. This animal study suggests that the treatment with gentamicin plus taurine protects against gentamicin-induced acute liver injury by a significant ($p<0.05$) and improvement in the biochemical markers of liver and normalized lipid profiles.

Key words: Gentamicin, Taurine, Liver, Rats. ALT, AST, ALP, TC, TG, LDL, HDL.

Introduction:-

Gentamicin is an antibiotics, it is one of the aminoglycosides group, it more effective against G negative bacteria (Ho and Barza, 1987), such as Pseudomonas, Proteus bacteria (Tangden *et al*., 2011; Shrestha and Haylor, 2014). But its uses are declined because of its serious adverse effects as nephrotoxicity. It produced by micrmonospora pupurea. It can be used in different type of infections, including gram positive and gram negative bacteria. In addition, it has significant effect against pseudomonas. Gentamicin works by inhibiting protein synthesis. It binds very strongly to ribosome's (30 S) sub unit and interferes with protein synthesis. Gentamicin enters the cell by binding to negatively charged phospholipids and enters the cytosol via electron transport linked system and thus need oxygen and ATP to enter cytosol and be effective. Therefore, gentamicin antibiotics are effective only in aerobic bacteria (Kumana and Yuen, 1994). It reported that up to 30% of patients who taken of gentamicin would develop some symptoms of nephrotoxicity (Martinez-Salgado *et al*., 2007 and Ali *et al*., 2011).

Taurine is an intracellurar amino acid, it consider as one of the most plentiful amino acids in the body of the human (Lourenço and Camilo, 2002), it isolated firstly from bile of bull in 1827, but in rodent it is non-essential, it present is essentially in cat and may be conditionally in humans (Jacobsen and Smith, 1968). Recent experimental studies on the animals and also human did confirms its importance, its present in the nutrient is essential as nutritional supplement (Stapleton *et al*., 1997). The main physiological functions are limited and prevented the oxidation in many tissues (Chesney, 1985; Huxtable, 1992). According to the experimental on the animals, taurine may cause hypolipidemia (Niittynen *et al*., 1999). It an antioxidant, a scavenger of carbonyl compounds, a modulator of cytosolic calcium, an analgesic, and to have neurotrophic properties (Pop-Busui *et al*., 2001; Schaffer *et al*., 2009). The effect of taurine as an antioxidant is due to its ability in stabilized biomembrane (Wright *et al*., 1986). It scavenges reactive oxygen species (Wright *et al*., 1985) and reduced the level of malondehyde (Huxtable, 1992).

The present study was designed to assessment the defensive effects of taurine against liver disorders induced by gentamicin in male rats.

Experimental animals:-

Twenty four healthy adult male rats (*Rattus norvegicus*) weighing (190-200 g) of 9-10 weeks old were used in the present study. Animals were

housed in the animal house of Department of Biology, College of Science, University of Thi-Qar, Iraq. Experimental animals were divided into four groups (6 rats in each group), upon the following designed.

Experimental design:-

Group-1: Control group; treated orally with distill water daily for 10 days.
Group-2: Gentamicin group; were injected (IP) with (100mg/kg) of gentamicin only daily for 10 days.
Group-3: Taurine group; were injected (IP) with (100mg/kg) of taurine only daily for 10 days.
Group-4: Gentamicin and taurine group; were injected (IP) with (100mg/kg) of gentamicin, and after one hour the rats injected (IP) with (100mg/kg) of taurine daily for 10 days.

Rats were sacrificed at the end of experimental period (10 days). Blood samples was collected from the heart by 10 ml disposable syringe of 22G needles (Parasuraman, *et al.*, 2010), the blood putting into plain tube without EDTA and centrifuged at 3000 rpm for 15 minutes to obtain the serum which then transferred into Eppendorf tubes and stored at -20ºC till used for measurement of biochemical parameters like liver enzymes and lipid profiles (Gray *et al.*, 2003).

Statistical Analysis:-

Statistical analysis was done using the software SPSS version 15.0; the results were expressed as mean ± standard deviations (mean ± SD) and LSD. Two-way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

Results:-

Table (1) explain that the administration of gentamicin was associated with a significant increase ($P<0.05$) in serum ALT, AST and ALP activities when compared with the control group. While when taurine is administered separately to the animals, it has no effect was observed on serum ALT, AST and ALP enzymes compared with the control group enzyme values. The high in serum level of the ALT, AST and ALP enzymes that result from gentamicin injection were reduced significantly ($P<0.05$) in group 4 after administration of taurine in dose of 100 mg/kg with gentamicin compared with those in the control group.

Lipid profile parameters in serum of the different groups were shown in table (2). Intraperitoneal injection of gentamicin (100 mg/kg/WB) for 10 days had significantly increased ($p<0.05$)the serum cholesterol, triglycerides, LDL levels and a significant deceased in HDL level when compared with the control group. While injection of taurine alone caused non-significant differences of cholesterol, TG, HDL and LDL compared with the control group, Co-administration of gentamicin with taurine showed a significant prevented ($p<0.05$) the changes recorded in serum cholesterol, triglycerides, non HDL, LDL concentrations as compared with the control group.

Table (1): The protective effects of taurine on ALT, AST and ALP of male rats treated with gentamicin (mean ± SE)

Groups	ALT U/L	AST U/L	ALP U/L
G-1	17.81±0.51c	37.93±0.92d	184.02±2.04b
G-2	45.15±0.65a	93.30±1.94a	241.55±2.35a
G-3	17.38±0.66c	43.79±1.47c	188. 9±2.13b
G-4	25.16±0.75b	53.40±2.03b	201.86±0.85b
LSD	2.54	5.85	22.51

Table (2): The protective effects of taurine on lipid profile of male rats treated with gentamicin (mean ± SE)

Groups	Chol mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl
G-1	45.87± 1.49b	25.69±0.72b	27.56±0.62a	13.17±1.6b
G-2	87.33 ±1.28a	40.66±1.01a	12.34±0.76b	66.52±1.84a
G-3	45.06 ± 0.55b	26.11±0.7b	26.65±1.20a	13.24 ±1.3b
G-4	47.62 ± 1.01b	28.17±0.71b	26.57±1.14a	15.37±1.39b
LSD	7.82	3.84	5.62	14.7

Discussion:-

The result indicating impaired liver function. These results is in agreement with results of Mohamed *et al.*, (1992) and Galaly *et al.*, (2014) who found that treatment of experimental with 100 mg/kg/ BW gentamicin for 21 days produced a significant elevation of liver enzymes, increasing levels of AST and ALT in plasma is mainly due to the leakage of these enzymes from the liver cytosol into the blood stream (Concepcion *et al.*, 1993). Releasing of AST and ALT from the cell cytosol can occur as secondary changes to cellular necrosis (Gaskill *et al.*, 2005). Gentamicin induces an increase in the oxidative stress and production of free radicals and suppresses the antioxidant defense system in liver (Ademiluyi *et al.*, 2013; Galaly *et al.*, 2014). The exacerbated increase of lipid peroxidation by gentamicin impairs membrane lipids and causes hepatocytes necrosis and damage. The suppressive effect of gentamicin on the nonenzymatic and enzymatic antioxidants results in an excess

production of reactive oxygen species which not only deleteriously affects membrane lipids but also deteriorates proteins and nucleic acids. This in turn leads to liver toxicity, dysfunction and damage (Galaly *et al*., 2014). The elevation in serum enzymes activities observed in the present study may reflect hepatotoxic potency of gentamicin on liver.

The capacity of taurine in liver protection against gentamicin was due to free radicals scavenging. The result is agreed with the results of Taghizadiyeh and Kermanizadeh, (2011) who's confirmed the benefit effect of taurine against hepatotoxin caused by methotrexate. Gordon *et al*., (1986) used supplemental taurine as a protective agent against lipid peroxidation. The study demonstrated the protection effect of taurine in bronchioles of hamaster from alteration or disturbance caused by NO2. Administration of taurine showed improved in the liver function after mercury intoxicated in animal by decline in increased of liver enzymes (AST, ALT and ALP) in serum. Also the decreased level of antioxidant system (GSH, GPx, CAT and SOD) has been promoted levels (Jagadeesan and Pillai, 2007). On the other hand Lee *et al*. (1992); Ebrahim *et al*. (2001) and Tasci *et al*. (2007&2008) showed that the taurine has protective effect against acute pancreatitis, it cause a significant correction in all studied parameters dependent on time of treatment. These results may be attributed to the magic physical and chemical characteristic powerful of taurine which immediately stop cancer from spreading and start killing existing cancer cells, acts as a free radical scavenger, decreases lipid peroxidation production via increases β-oxidation in the mitochondria matrix, rebuild the immune system and damaged tissue. So, the body can naturally transform or expel any tumorous masses and eliminate the causal factors that destroyed immune system in the first place. Hagar (2004) demonstrated that the administration of taurine administration (1% in the drinking water) for 3 days before and concurrently during CsA injections improved liver functions, as indicated by decline of serum transaminases and GGT levels and elevation of serum total protein. Moreover, taurine significantly reduced hepatic TBARS and increased GSH content and catalase and GSH-Px activities in the hepatic tissue.

Also the results in table 2 indicated a significant increase in cholesterol, triglyceride and LDL levels, with significant decreased in HDL in animals of group -3 who treated with gentamicin. This is in agreement with Rashid and Khan, (2017) who reported that treatment of rats with gentamicin (80 mg/kg) increased the levels of total cholesterol, triglycerides and LDL in serum as compared with control animals. Ahmadvand *et al*., (2016) reported that gentamicin significantly increased TG, TC, LDL in rats treated with 100 mg/kg/day for 12 days as compared with control group. Also, Ademiluyi *et al*., 2013, reported that the plasma atherogenic lipids (triglycerides and total cholesterol) were increased in gentamicin treated rats. The high levels of triglycerides may be due to inhibition of 7ahydroxylase activity (Hussein *et al*., 2014). Also the high levels of LDL-C may be attributed to a down regulation in LDL receptors (Hussein *et al*., 2014) moreover, this increase in LDL-c level might be explained via involvement of two enzymes namely cholesterol ester hydrolase and cholesterol ester synthetase. These enzymes balance the cholesterol levels in the blood. Hence, it is logical to assume that the elevation in plasma cholesterol is mediated through increased cholesterol turnover and influenced by the relative balance between cholesterol ester hydrolase and cholesterol ester synthetase activity. With increased esterifying activity (when cholesterol ester hydrolase: cholesterol ester synthetase is lowered) cholesterol will be predominantly in its ester form (as in LDLc) and can lead to the development and progression of atherosclerosis (Hussein *et al*., 2014). HDL plays an essential role in the transport of cholesterol to the liver for excretion into bile duct (Ademiluyi *et al*., 2013). Azab, *et al*. (2016) reported that treatment of guinea pigs with 100mg/kg body weight/ day gentamicin for 10 days induced hepatotoxicity. Furthermore, impaired hepatic function may also have affected cholesterol metabolism leading to hypercholesterolemia and hypertriglyceridemia (Ademiluyi *et al*., 2013). Administration of taurine cause a significant decrease in cholesterol, triglyceride and LDL levels in a group-4 whose treated with gentamicin and taurine, this was probably achieved by means of its antioxidant nature (Rodriguez-Martinez *et al*., 2004) against lipid peroxidation induced by gentamicin. These result agreed with Auda *et al*., (2018**)** these actions suggest that high levels of taurine may be protective against coronary heart disease (CHD) (Wójcik *et al*., 2010).

Conclusions:-

Based on the previous findings, it can be concluded that, gentamicin had adverse effects the liver and lipids

profile. Taurine administration showed a remarkable amelioration of these abnormalities in gentamicin treated male rats, which may be due to its antioxidant property.

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