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# Comparative Investigation of Amoxicillin and Cephalexin Administration on Some Biochemical Parameters in Male Rabbits

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**Abstract:** ***The effects of two antibiotics (amoxicillin and cephalexin) on biochemical parameters in male rabbits were investigated. Fifteen male rabbits were grouped at random into three, by five rabbits in each one. The control group was the first one and administrated distilled water with 1 ml once a day. The second and the third groups were dosed orally with 10 mg/kg of amoxicillin and 10 mg/kg of cephalexin, respectively for 14 days. The findings showed a significant elevation at P<0.05 in cholesterol concentrations in amoxicillin and cephalexin groups as compared with the control. A significant increase at P<0.05 in the means of triglycerides, VLDL-C, and atherosclerosis index in amoxicillin group was illustrated, while no significant difference in the values triglycerides, VLDL-C and atherosclerosis index in cephalexin group in comparison with control one. These findings revealed no significant difference at P<0.05 in the mean of HDL-C concentration in groups dosed amoxicillin and cephalexin compared with the control group. While, there was a significant elevation at P<0.05in the means of LDL-C in amoxicillin and cephalexin groups as compared with the animals of control group. Furthermore, the findings demonstrated a significant increase at P<0.05 in urea and creatinine means in the groups administrated amoxicillin and cephalexin compared with the control group. It is concluded from the present investigation that kidney failure and heart disease are the main side effect of repeated and continued administration of these antibiotics in laboratory animals. Therefore, it is important to monitor the levels of lipid profile and renal parameters periodically in the people who administrated these antibiotics.***

**Keywords:** amoxicillin, cephalexin, cholesterol, triglycerides, lipoproteins, creatinine, urea

## 1. Introduction

Antibiotic is a chemical material that put to death, or prevents the development of microbial organism (Olayinka and Olukowade; 2010, Habbeb, 2011). As the expansion in the use of antibiotics, different studies were carried out to determine their pharmacokinetics and adverse impacts. Though antibiotics are largely considered be safe and well sustained, they linked with a broad extension of side impacts. Side impacts are numerous, diverse and dangerous reliance on the kind of antibiotics, period of administration and microorganisms intended (Elmajdoub *et al.*, 2003; Habbeb, 2011; El-Magdoub et al., 2012).

Antibiotics are classified according to their chemical structures, action mode and broad spectrum. Antibiotics types depending on the chemical structures include Beta-lactams, Macrolides, Tetracyclines, Quinolones, Aminoglycosides, Sulphonamides, Glycopeptides and Oxazolidinones (Habbeb, 2011, Etebu and Arikekpar, 2016). Some antibiotics are lethal to bacteria; while others are frustrate bacterial growth. Antibiotics kill bacteria are called bactericidal while those that frustrate bacterial growth are called bacteriostatic (Etebu and Arikekpar, 2016).

Amoxicillin is as ampicillin is derived from the structural unit of penicillin nucleus, 6-aminopenicillanic acid (Olayinka and Olukowade, 2010). Amoxicillin is excreted by kidney tubules and glomeruli. It is a wide range antibiotic in the treatment of medical cases that have dangerous and important illnesses. Because of its pharmacodynamics and antibacterial activity, amoxicillin is largely administrated before surgical operation and as well as in veterinary medicine (Elmajdoub et al., 2003).

Cephalexin is a semisynthetic antibiotic derived from cephalosporin C but, it is well absorbed when administrated orally. Cephalexin is bactericidal to a wide range of bacteria. It classified into generations based upon the spectrum of anti- microorganism activity. Cephalexin is a first generation cephalosporin available for oral administration. Hypersensitivity is widespread impact of cephalosporins. Cephalexin, the more adverse impacts comprise nausea, vomiting and gastrointestinal (GI) disturbances (Agrawal *et al.*, 2014). Cephalexin is used to heal infections caused by bacteria including upper respiratory, eye and ear, skin, and urinary duct infections (Shafaa *et al.*, 2008).

The biochemical components of blood are enzymes, mineral elements, hormones, salts (such as urea, creatinine), lipids and lipoproteins. Total cholesterol is transported normally by the three types of lipoproteins: very low, low and high density lipoproteins (Al-Jowari, 2009). While in liver, triglycerides are incorporated with cholesterol, phospholipid and protein to form lipoprotein molecules termed very low density lipoproteins (Champe and Harvey, 1994; Denniston et al., 2001). VLDL are carried triglycerides from hepatic tissue to other tissues, such as adipose tissue and skeletal muscle (Al-Jowari, 2009). While LDL transported cholesterol to peripheral tissues and acts in regulating cholesterol concentrations in these tissues (Champe and Harvey, 1994). Finally, HDL are bound to cholesterol and carried it from peripheral tissues to the hepatic tissue (Denniston et al., 2001).

On the other hand, urea nitrogen test function is in the diagnosis of kidney and metabolic disorders. This measurement is an essential for the evaluation of kidney function. While serum creatinine test is important in the determination of normal glomerular filtration (Khargharia *et al.*, 2012).

In spite of the various side and adverse effects of these antibiotics, there is a few studies on the effect of antibiotics

on the biochemical parameters in laboratory animals, this work aims to evaluate the side effects of the same doses of two antibiotics; amoxicillin and cephalexin on lipids profile and kidney function parameters in male rabbits. The investigated parameters in the present work are total cholesterol, triglycerides, lipoproteins (which include; high, low and very low density lipoprotein), atherosclerosis index; renal parameters (blood urea nitrogen and serum creatinine).

## 2. Materials and Methods

**Laboratory Animals**

In this experiment, it was chosen fifteen male rabbits weighted between 1200- 1650 g and aged of about 3- 3.5 months. These animals were placed in metallic crates in Animal House of Department of Biology / College of Science. During the period of breeding and experiment, the constituents of food were vegetables, cereals and water tap. Respecting, the condition in Animal House, temperature was kept on between 22 - 25° C. and lighting time was lasted12 hours light and 12 hours dark (Al-Jowari, 2009).

**Administration of Antibiotics**

Fifteen male rabbits were grouped at random into three, by five rabbits in each one. The control group was the first one and administrated distilled water with 1 ml once a day. The second and the third groups were dosed orally with 10 mg/kg of amoxicillin and 10 mg/kg of cephalexin, respectively for 14 days (Al-Jowari, 2009).

**Collection of Blood Sample**

When the experimental time was finished, blood as about 2 ml, were collected by heart puncture. Blood was centrifuged at 250 rpm for 20 min at 35°C. and were kept on at -8°C until biochemical assays were done(Al-Jowari, 2009).

**Lipids Profile Tests**

Kitsfor lipid profile tests (Biomerixus, France) which depended on enzymatic hydrolysis (Cholesterol and triglycerides) and precipitation and supernatant reaction (HDL-C) were used. Then, the triglyceride value was divided on 5 to obtain VLDL-C.Concerning the value of LDL-C, it was calculated using Friedewald formula:

[LDL- C]= [Total-C] - [HDL-C] - [VLDL- C]

After that, LDL-C was divided on HDL-C to obtain atherosclerosis index (Dayspring and Helmbold, 2008).

**Renal Function Test**

Enzymatic kits for quantitative determination of urea and creatinine were used. Urease enzyme acts to cleavage urea into ammonia and carbon dioxide while colorimetric method was used in creatinine assay (Biomerieux, France).

**Statistical Test**

The results of the present study were arranged as mean ± standard deviation. The analysis of variance (ANOVA) test and Duncan multiple range test were used to analyze these results and to obtain the significance among means using SPPS program (version 19). The probability was calculated at P<0.05 (Basher, 2003).

## 3. Results

Results of the present study demonstrated a significant (P<0.05) elevation in the concentrations of total cholesterol in groups administrated amoxicillin and cephalexin compared with control animals. In amoxicillin and cephalexin groups, the cholesterol concentration means were 128.6 and 115.4mg/dl, respectively, while it was 104.8mg/dl in the control animals. These results also illustrated a significant increase at P<0.05in the means of triglycerides concentration in groups administrated amoxicillin dose, while no significant difference at P<0.05 in the means of triglycerides concentration in group administrated cephalexin in comparison with the control. Triglycerides mean in the control, amoxicillin and cephalexin groups' were65.2, 87.6and 69.4 mg/dl, respectively. Amoxicillin and cephalexin effects on the means of total cholesterol and triglycerides concentrations in male rabbits are illustrated in Table (1).

These results also revealed no significant difference at P<0.05 in the means of HDL-C in groups administrated amoxicillin and cephalexin in comparison with control group. The means of HDL-C concentration were 70.4, 72.8 and 72.6mg/dl in control, amoxicillin and cephalexin groups, respectively. While, there was a significant elevation at P<0.05 in the means of LDL-C in amoxicillin and cephalexin groups as compared with control. The means of LDL-C concentration were 21.36, 38.28 and 28.92 mg/dl in control, amoxicillin and cephalexin groups, respectively. Furthermore, these results also demonstrated a significant increase at P<0.05 in VLDL-C concentration in animals administrated amoxicillin dose, while it found no significant difference at P<0.05 in VLDL-C concentration groups administrated cephalexin as compared with control animals. The means of VLDL-C in control, amoxicillin and cephalexin groups were13.04, 17.52 and 13.88 mg/dl, respectively.

Regarding the impact of amoxicillin and cephalexin administration on atherosclerosis index, a significant elevation at P<0.05 in atherosclerosis index amoxicillin group, while no significant difference at P<0.05 in group administrated cephalexin in comparison with the control. Atherosclerosis indices were 0.305, 0.526 and 0.392 in control; amoxicillin an cephalexin groups (Table 2).

The results in Table (3) demonstrated that there was a significant elevation at P< 0.05 in the concentrations of urea as well as creatininein group's administrated amoxicillin and cephalexin in comparison with control group. Urea concentration means were19.33, 30.24 and 28.06 mg/dl in control, amoxicillin and cephalexin groups, respectively. While, the creatinine concentration means in these mentioned groups were 1.32, 3.14 and 2.64 mg/dl, respectively.

## 4. Discussion

The pharmacokinetic impacts of different antibiotics on the composition of blood, enzymes, chemicals as well as minerals were widely examined in the experimental animals (Elmajdoub et al., 2003).

In the present work, the measurement the levels of blood lipids (total cholesterol and triglycerides), lipoproteins (LDL and VLDL) as well as atherosclerosis index showed a significant increase (except HDL-C which decrease significantly) in amoxicillin group compared with cephalexin group at a dose of 10 mg/kg in male rabbits.

The observed elevation in cholesterol concentration in present study might be related to these antibiotics which inhibit CYPA, an enzyme necessary in the conversion of cholesterol molecules to bile acids. This might cause an actual increase in the level of cholesterol concentrations when these molecules are not converted into bile acids and stay in blood (Peters, 2013). Recent studies on the lipids of plasma membrane denoted that the ratio of total cholesterol/phosphoglycerides lipids ratio incorporated with other constituents are essential factors of cell membrane fluidity. This finding may propose a decline in plasma membrane fluidity; this would cause alteration in cell membrane functions (Olayinka and Olukowade, 2010, Olayinka et al., 2012).

Practically, a strong relationship between the level of cholesterol in the blood serum and cardiovascular disorder, especially atherosclerosis (thickness of the arteries). Cholesterol with other fat components in the blood, acts to a hardening of the arteries which lead to narrowing them. As narrowing elevated, more pressure is done to permit adequate blood flow, hypertension arises. Hypertension is also associated to coronary heart problems (Denniston *et al.*, 2001).

On the other hand, the elevation in the level of triglyceride level may be explained to the activation of the regulatory enzymes in the biosynthesis of triglycerides. As fat metabolism occurs in hepatic cells, the adverse impact of antibiotics uptake can lead to changes in serum lipid concentration (Peters, 2013).

In the present study, it was showed that amoxicillin and cephalexin induce renal failure in experimental animals. It was obvious from the values of kidney function assays. These assays showed a significant elevation in the means of serum creatinine and blood urea in experimental animals (Olayinka and Olukowade, 2010), which indicating that these substances cause a decline in glomular filtration rate (El-Magdoub et al., 2012, Elmajdoub *et al.*, 2014).

Blood urea has recorded to elevate to levels above its normal range in renal disorder (Olayinka and Olukowade, 2010). This increase in BUN may be related to nephrotoxicity which is defined by renallesions, especially to the proximal convoluted tubules (El-Magdoub et al., 2012, Elmajdoub *et al.*, 2014).

In addition, the significant elevation in serumcreatinine might be related to intrinsic factors such as renal damage, declined in the renal permeability, or drug impact on lower urinary canal (Olayinka and Olukowade, 2010, Olayinka *et al.*, 2012).

In general, any increase in serum creatinine concentration may lead to decrease in glomerular filtration rate of kidney. Furthermore, it has been found that there is a relationship between increased creatinine and heart problems. So it must check up the patients who had an elevation in creatinine level in order to avoid cardiovascular diseases (Samra and Abcar, 2012).

The accumulation of these drugs in the body especially in the liver and kidney might expose the organism to severe toxic and immune impacts. Further, repeated and low administration of these drugs may cause various diseases due to immunity destruction. Therefore, it is necessary to observe the immunological, hematological and biochemical effects of these antibiotics (Khargharia et al., 2012).

## 5. Conclusion

It is concluded from the present investigator that kidney failure and heart disease are the main side effect of repeated and continued administration of these antibiotics in laboratory animals. Furthermore, hepatotoxicity may be occurred in these animals due to circulating triglycerides which are an early and reliable indicator of hepatotoxicity.

It is recommended to monitor the levels of lipid profile and kidney parameters periodically in the people who administrated these antibiotics since the positive relationship between these biochemical parameters and amoxicillin and cephalexin levels in the blood serum.

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**Table1:** Effect of amoxicillin and cephalexin on cholesterol and triglycerides concentration

| Parameters / Groups | Cholesterol concentration (mg/dl) | Triglyceride concentration (mg/dl) | p-value |
|---|---|---|---|
| Control | 104.80 ± 3.70 [a] | 65.20 ± 3.96 [a] | p< |
| Amoxicillin | 128.60 ± 4.72 [b] | 87.60 ± 4.61 [b] | p< |
| Cephalexin | 115.4 ± 4.16 [c] | 69.40 ± 4.61 [a] | |

*Values are means ± SD
*Similar letters in the same column demonstrate no significant differences while different letters demonstrate significant differences at p< 0.05.

**Table 2:** Effect of amoxicillin and cephalexin on lipoproteins concentration and atherosclerosis index

| Parameters / Groups | HDL-C concentration (mg/dl) | LDL-Concentration (mg/dl) | VLDL-C concentration (mg/dl) | Atherosclerosis index |
|---|---|---|---|---|
| Control | 70.40 ± 4.77 [a] | 21.36 ± 4.08 [a] | 13. 04 ± 0.79 [a] | 0.305 ± 0.07 [a] |
| Amoxicillin | 72.80 ± 3.34 [a] | 38.28 ± 6.82 [b] | 17.52 ± 0.92 [b] | 0.526 ± 0.11 [b] |
| Cephalexin | 72.60 ± 4.62 [a] | 28.92 ± 6.54 [c] | 13.88 ± 0.92 [a] | 0.392 ± 0.10 [a] |

*Values are mean ± SD
*Similar letters in the same columndemonstrate no significant differences while different letters demonstrate significant differences at p< 0.05.

**Table 3:** Effect of amoxicillin and cephalexin on kidney functions parameters.

| Parameters / Groups | Urea concentration (mg/dl) | Creatinine concentration (mg/dl) |
|---|---|---|
| Control | 19.33 ± 2.96 [a] | 1.32 ± 0.38 [a] |
| Amoxicillin | 30.24 ± 3.51 [b] | 3.14 ± 0.50 [c] |
| Cephalexin | 28.06 ± 3.55 [b] | 2.64 ± 0.48 [b] |

*Values are means ± SD
*Similar letters in the same column demonstrate no significant differences while different letters demonstrate significant differences at p< 0.05.