Evaluation of Plasma Na, K, Urea, and Creatinine in Rabbits Given Amoxicillin Overdose Supplemented with Cucumber (Cucumis sativus) Fruit Juice

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Abstract

Study Background: Raw cucumber (Cucumis sativus) fruit juice contains substances of health benefits. Na, K, urea, and creatinine are indices of nephrotoxicity. Overdose of amoxicillin, an antibiotic, could cause hemolysis and nephrotoxicity. Aim and Objective: This work was therefore designed to evaluate plasma Na, K, urea, and creatinine in rabbits given amoxicillin overdose supplemented with cucumber (C. sativus) fruit juice. Materials and Methods: Fifteen rabbits of the same sex weighing 0.9–1.4 kg divided into three groups of five rabbits each were used for the study. Group A – Five control rabbits; Group B – Five rabbits given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days which was followed by 30 mL raw cucumber fruit juice supplementation for 14 days; Group C – Five rabbits given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h and raw cucumber fruit juice supplementation for 14 days simultaneously. Plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL) were determined in the rabbits biochemically by spectrophotometry using COBAS 111. Results: There was a significant decrease in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than when they were given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days with P < 0.05. There was a significant increase in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days than when they were given 30 mL of raw cucumber fruit juice supplementation for 14 days; basal samples; and also than the results obtained from the control rabbits with P < 0.05. There was also a significant increase in the plasma values of K (mmol/L), following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than the results obtained from the control rabbits with P < 0.05. Conclusion: This work revealed possible nephrotoxicity following the administration of amoxicillin overdose as indicated by raised plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL), while the supplementation of raw cucumber fruit juice revealed nephroprotective and decrease in plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL). Raw cucumber fruit juice could be applied to reduce drug-induced nephrotoxicity.

Keywords: Amoxicillin overdose, creatinine, K, Na, rabbits, raw cucumber (Cucumis sativus) fruit juice, urea

INTRODUCTION

The flesh of cucumber fruits is mostly made of water and rich in phytonutrients (Vitamin A, Vitamin C, folic acid, magnesium, molybdenum, silica, and potassium), essential for the human body. It also contains ascorbic and caffeic acids that prevent water loss.[1,2] Amoxicillin is applied in the treatment of acute otitis media, streptococcal pharyngitis, pneumonia, skin infections, urinary tract infections, Salmonella infections, Lyme disease, and chlamydia infections.[3] It has the following side effects: jaundice, nausea, vomiting, rashes, bleeding, lethargy, mental changes, and insomnia.[4,5] The primary cations and anions of electrolytes include sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺), magnesium (Mg²⁺), chloride (Cl⁻), hydrogen phosphate (HPO4²⁻), and hydrogen carbonate (HCO₃⁻).[6] Potassium is the major intracellular cation, while sodium is the major extracellular cation. The cation such as potassium

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and sodium and the anions such as bicarbonate and chloride constitute common examples of blood electrolytes used to determine water–electrolyte imbalance and renal dysfunction. Plasma potassium can also be affected by blood hemolysis. Creatinine and urea are nonprotein nitrogen useful in the diagnosis of renal dysfunction. Creatinine is a product of creatine and creatine phosphate in the muscle tissue, while urea is the end product of protein metabolism involving deamination of amino acids in the liver. They are excreted in the urine through the kidney. Nonprotein nitrogen can be converted to protein by microbes.

Cucumber (Cucumis sativus) fruit contains phytochemicals and phytonutrients of health benefits. Amoxicillin is an antibiotic treated to bacterial infections. It is used by many people in Nigeria to treat common infections such as Salmonella infection. There is little information on the evaluation of Na, K, urea, and creatinine in rabbits given amoxicillin overdose supplemented with raw cucumber fruit juice, hence the need for this work.

**Materials and Methods**

**Materials**

**Study area**

This work was carried out at the animal house of Achievers University, Owo, Nigeria. Achievers University is in Owo, Ondo state, Nigeria. The university is a private-sector initiative, established in 2007 and accredited by the National Universities Commission. It is located on land in the Ido Community of Owo, consisting of Ulale 1, Ulale 11, Ulema, Ijegunma, Isijogun, and Amurin Elegba (formerly Amurin, Oga). The university sprang from the Achievers Group of Education and Training Organization, located in Ibadan, Oyo state of Nigeria, owned and run by Hon. Dr. Bode Ayorinde and other educationalists. The university commenced academic activities during the 2007/2008 academic session. In the Nigerian National University Commission Annual University rankings for 2013, it was rated 53rd. It has three colleges which include College of Natural and Applied Sciences; College of Engineering and Technology; and College of Social Science and Management including a postgraduate school.

**Study population**

Fifteen rabbits of the same sex divided into three groups of five rabbits each was used for the study. The rabbits was bought animal farm in Owo, Nigeria, and was presented to Federal School of Agriculture, Akure, for confirmation.

- **Group A** – Five control rabbits were fed with normal meal and water throughout the period of investigation.
- **Group B** – Five rabbits given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days which was followed by 30 mL raw cucumber fruit juice supplementation for 14 days.
- **Group C** – Five rabbits given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h and raw cucumber fruit juice supplementation for 14 days simultaneously.

**Administration of amoxicillin**

Amoxicillin was bought from a registered pharmaceutical shop in Owo, Nigeria. Overdose of 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days.

**Preparation of cucumber (Cucumis sativus) fruit juice**

Cucumber (C. sativus) was bought from fruit vendors in Owo, Nigeria. The fruit was presented to Federal School of Agriculture, Akure, for confirmation. The fruit was washed in sterile water and then sliced. The sliced fruit was blend together using an electronic blender. The raw fluid was extracted using a sterile sieve. The raw liquid extract was served to the rabbits as juice. 30 mL was given to the rabbits on daily basis. The juice will always be freshly prepared.

**Specimen (blood) collection**

Five milliliters of venous blood was collected from each of the rabbits into lithium-heparinized bottles for the biochemical analysis.

**Methods**

Biochemical analysis of Na, K, urea, and creatinine was carried out using auto-chemistry analyzer – COBAS C111 using Roche reagent.

**Potassium**

Sodium tetraphenylboron reacts with potassium ions in a protein-free alkaline medium to produce a turbid suspension of potassium tetraphenylboron. The amount of turbidity produced is proportional to the potassium concentration.

**Sodium**

Sodium is determined enzymatically via sodium-dependent β-galactosidase activity with ONPG as substrate. The absorbance at 405 nm of the product O-nitrophenyl is proportional to the sodium concentration.

**Creatinine**

Creatinine in alkaline solution reacts with picric acid to form a colored complex. The amount of the complex formed is directly proportional to the creatinine concentration.

**Urea**

Urea is hydrolyzed in the presence of water and urease to produce ammonia and carbon dioxide. The ammonia produced in the first reaction combines with α-oxoglutarate and NADH in the presence of glutamate-dehydrogenase to yield glutamate and NAD+.

**Method of data analysis**

The results obtained in this study was subjected to statistical analysis to determine mean, standard deviation, Student’s “t” and probability value at 0.05 level of significance using IBM SPSS 18.0 (New York).
Results

There was a significant decrease in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than when they were given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days with \( P < 0.05 \) [Tables 1 and 2 and Figure 1].

There was a significant increase in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days than when they were given 30 mL of raw cucumber fruit juice supplementation for 14 days; basal samples, and also than the results obtained from the control rabbits with \( P < 0.05 \) [Tables 1 and 2 and Figure 1].

There was also a significant increase in the plasma values of K (mmol/L), following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than the results obtained from the control rabbits with \( P < 0.05 \) [Tables 1 and 2 and Figure 1].

There was no significant difference in the plasma value of Na in the results obtained from the rabbits before and after they were given supplement of raw cucumber fruit juice and amoxicillin overdose, including the values obtained in the experimental rabbits compared with the control rabbits with \( P > 0.05 \) [Tables 1 and 2 and Figure 1]. There was no significant difference in the plasma value of creatinine (mg/dL) and urea (mg/dL) obtained in the basal samples and samples obtained from the rabbits after the administration of raw cucumber fruit juice supplement compared with the control rabbits with \( P > 0.05 \) [Tables 1 and 2 and Figure 1]. No significant difference was obtained in the plasma value of K (mmol/L) obtained from the rabbits after the administration of raw cucumber fruit juice supplement compared with their basal samples with \( P < 0.05 \) [Tables 1 and 2 and Figure 1].

Table 1: Mean and standard deviation of plasma values of Na (mmol/L), K (mmol/L), creatinine (mg/dL), and urea (mg/dL) obtained in the rabbits

|                  | Control rabbits A | Group B  | Group C  |
|------------------|-------------------|----------|----------|
|                  |                   | B1       | B2       | B3       | C1       | C2       |
| Na (mmol/L)      | 133±11            | 134±10   | 138±12.0 | 136±10.0 | 134±10.0 | 136±11.0 |
| K (mmol/L)       | 3.1±0.1           | 3.3±0.2  | 15.6±0.4 | 4.0±0.2  | 3.2±0.2  | 3.5±0.3  |
| Creatinine (mg/dL) | 1.0±0.2          | 1.2±0.1  | 5.1±0.3  | 2.0±0.2  | 1.3±0.3  | 1.2±0.2  |
| Urea (mg/dL)     | 13±2.0            | 12.0±1.0 | 29.0±3.0 | 14±2.0   | 13±1.0   | 12±2.0   |

Table 2: Comparative analysis of the mean and standard deviation of plasma values of Na (mmol/L), K (mmol/L), creatinine (mg/dL), and urea (mg/dL) obtained in the rabbits

|                  | A versus B1 | A versus B2 | A versus B3 | A versus C1 | A versus C2 | B1 versus B2 | B1 versus B3 | B2 versus B3 | C1 versus C2 |
|------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Na (mmol/L)      | t           | −0.14       | −0.38       | −0.283      | −0.14       | −0.27       | −0.26       | −0.14       | 0.128       | −0.133     |
|                  | P           | 0.45        | 0.37        | 0.402       | 0.45        | 0.41        | 0.411       | 0.45        | 0.455       | 0.453      |
| K (mmol/L)       | t           | −0.894      | −30.32      | −4.02       | −0.477      | −1.27       | −27.50      | −2.47       | 25.94       | −0.83      |
|                  | P           | 0.233       | 0.0005*     | 0.028*      | 0.349       | 0.167       | 0.001*      | 0.07        | 0.001*      | 0.247      |
| Creatinine (mg/dL) | t           | −0.89       | −6.008      | −0.687      | −0.832      | −0.707      | −12.33      | −0.42       | 4.73        | 0.149      |
|                  | P           | 0.233       | 0.013*      | 0.282       | 0.247       | 0.276       | 0.003*      | 0.356       | 0.021*      | 0.448      |
| Urea (mg/dL)     | t           | 0.447       | −5.657      | −0.354      | 0.354       | −7.60       | −0.89       | 5.30        | 0.45        |
|                  | P           | 0.349       | 0.015*      | 0.38        | 0.5         | 0.379       | 0.01*       | 0.233       | 0.017*      | 0.35       |

*Significant
**Discussion**

There was a significant decrease in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than when they were given 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days. This is attributable to the fact that the fruit juice of cucumber also contain antioxidant flavonoids, such as quercetin, apigenin, luteolin, Vitamin C, water, electrolyte content, and kaempferol 1, 6, which provide additional benefits. Cucumber has also been applied conventionally as antitoxin. These properties made it possible for the reversal the abnormal increase in plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL), indicating renal problem.\[1,2\]

There was a significant increase in the plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) following the administration 30 mg/kg BW subcutaneous injection of amoxicillin every 24 h for 7 days than when they were given 30 mL of raw cucumber fruit juice supplementation for 14 days; basal samples; and also than the results obtained from the control rabbits. Increase in plasma values of K (mmol/L), creatinine (mg/dL), and urea (mg/dL) could indicate nephrotoxicity as a large overdose of amoxicillin could affect the kidneys, possibly causing poor kidney function or even kidney failure.\[4,5\] as this may reduce the normal excretion of these parameters from the body through the kidney.\[6-8\] It is also important to expect that an overdose could cause any of the usual amoxicillin side effects which may be more severe. For instance, it is possible that nausea, vomiting, hemolysis, yellowing of the skin or eyes, unusual bleeding or bruising, and diarrhea would occur which could cause dehydration, leading to increased plasma level of these parameters.\[4,5\]

There was also a significant increase in the plasma values of K (mmol/L), following the administration of 30 mL raw cucumber fruit juice supplementation for 14 days than the results obtained from the control rabbits and basal samples. Hyperkalemia can also be a result of taking some drugs. Overdose of amoxicillin could cause jaundice and jaundice is a product of massive red blood cell destruction, and potassium is a major intracellular cation found on red blood cells which upon destruction leak to the plasma (extracellular fluid [ECF]), thereby causing raised plasma level of potassium.\[6-8\]

**Conclusion**

This work revealed possible nephrotoxicity following the administration of amoxicillin overdose as indicated by raised plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL) while the supplementation of raw cucumber fruit juice revealed nephroprotective and decrease in plasma K (mmol/L), creatinine (mg/dL), and urea (mg/dL).

**Recommendation**

Raw cucumber fruit juice could be applied to reduce drug-induced nephrotoxicity.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Schieberle P Ofner S, Grosch W. Evaluation of potent odors in cucumbers (Cucumis sativus) and muskmelons (Cucumis melo) by aroma extract dilution analysis. J Food Sci 1990;55:193.
2. Huang S, Li R, Zhang Z, Li L, Gu X, Fan W, et al. The genome of the cucumber, Cucumis sativus L. Nat Genet 2009;41:1275-81.
3. Fischer J, Ganellin CR. Analogue-based Drug Discovery. Publisher: John Wiley and Sons, USA; 2006. p. 490.
4. Roy J. An Introduction to Pharmaceutical Sciences Production, Chemistry, Techniques and Technology. Cambridge: Woodhead Pub; 2012. p. 239.
5. Gillies M, Ranakusuma A, Hoffmann T, Thorning S, McGuire T, Glasszio P, et al. Common harms from amoxicillin: A systematic review and meta-analysis of randomized placebo-controlled trials for any indication. CMAJ 2015;187:E21-31.
6. Chemeycky CC, Berger BJ. Electrolytes panel – Blood. In: Chemeycky CC, Berger BJ, editors. Laboratory Tests and Diagnostic Procedures. 6th ed. St. Louis, MO: Elsevier Saunders; 2013. p. 464-67.
7. DuBose TD. Disorders of acid-base balance. In: Skorecki K, Chertow GM, Marsden PA, Taal MW, Yu AS, editors. Brenner and Rector’s the Kidney. 10th ed., Ch. 17. Philadelphia, PA: Elsevier; 2016.
8. Coso JD, Estevez E, Baquero RA, Mora-Rodriguez R. Anaerobic performance when rehydrating with water or commercially available sports drinks during prolonged exercise in the heat. Appl Physiol Nutr Metab 2008;33:290-8.
9. Howard TE. Clinical Chemistry. New York: John Wiley and Sons; 1989. p. 4, 58-62.
10. Traynor J, Mactier R, Geddes CC, Fox JG. How to measure renal function in clinical practice. BMJ 2006;333:733-7.
11. Klein JD, Blount MA, Sands JM. Urea transport in the kidney. Compr Physiol 2011;1:699-729.
12. Hosten AO, Kenneth WH, Dallas HW, Willis HJ, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990.