ORIGINAL ARTICLE

Protective Effect of Commercial Green Tea on Ibuprofen Induced Changes in Renal Function Tests of Adult Rats

Afnan Gul[1], Muhammad Bahadur Baloch [2]

Postgraduate Trainee, Department of Anatomy, National University of Medical Sciences[1]
Postgraduate Trainee, Department of Anatomy, University of Health Sciences[2]

ABSTRACT

Background: Nephrotoxicity of ibuprofen is a growing international public health problem in the wake of excessive use of the drug for the treatment of a broad spectrum of diseases in both adults and pediatric patients.

Objectives: To present an overview of the protective effect of the green tea on ibuprofen-induced changes in the biochemical markers of the adult rat kidneys.

Materials & Methods: It is an experimental study conducted in the department of Anatomy, Army Medical College Rawalpindi. The investigation was led on 30 male and non-pregnant female Sprague Dawley rodents of 9-11 weeks old enough and going in weight from 200-330 gm. The animals were divided into three groups consisting of 10 animals each; group A served as control, each animal in group B was given ibuprofen at a dose of 120 mg/kg/day and each animal in group C was given both green tea at a dose of 1ml/100g/day and Ibuprofen 120mg/kg body weight for a period of 9 weeks. Ibuprofen manufactured by Abbot Laboratories (Pvt.) Limited was utilized. Green tea was obtained from local market. Data was collected at the end of experimental period and was analyzed using SPSS version 22. One Way ANOVA was exerted, afterwards by post-hoc Tukey test to find out intergroup differences for quantitative variables. The results were depicted as mean ± standard deviation (mean ± SD). A p value < 0.05 was believed significant.

Results: Green tea administration had a significantly favorable effect on serum urea (mg/dl) (Group A=21.9 ± 2.8, Group B=93.2 ± 3.9, Group C=36.4± 3.0; p<0.001) and serum creatinine (mg/dl) (Group A=0.9 ± 0.22, Group B=2.4± 0.52, Group C=0.97 ± 0.3; p<0.001).

Conclusion: Green tea had ameliorative effects on the ibuprofen-induced changes in the biochemical markers

Key Words: ibuprofen, green tea, nephrotoxicity

Corresponding Author:
Dr. Muhammad Bahadur Baloch
Postgraduate Trainee
Department of Anatomy
University of Health Sciences
Email address: dr.sakhani@gmail.com

INTRODUCTION

Ibuprofen, classified as non-steroidal anti-inflammatory drugs (NSAIDs), was discovered by Dr. Stewart Adams in 1961 in Nottingham UK at the Boots Company laboratories. It is a one of the frequently administered medicines and is extensively available over the counter as well[1, 2]. It is generally used against fever, to relieve pain and an agent to eliminate inflammation. The greatest advantage of this medication is discovered to be

particularly helpful in the remedy of joint inflammation and other musculoskeletal conditions. Ibuprofen is likewise much of the time the medication of choice for alleviation of dental agony, headache, dysmenorrhea, flu and cold[2].

Various results influencing different viscera are related with long term utilization of ibuprofen. The drug, therefore, has been related to cause a number of nephrotoxic effects resulting in damage to renal architecture, thus increasing the risk of renal failure. In other organ systems, ibuprofen has been found to cause gastric and duodenal ulcers, hepatitis and cardiac failure[3]. The neph-rotoxic effects of ibuprofen mainly result from the oxidative damage to renal tissue caused by reactive oxygen species which are generated during the metabolism of the drug[4].

The kidney is actively involved in the bio-transformation of different medications and is thus widely exposed to their unfavorable side-effects. The degenerative effects of NSAIDs, especially ibuprofen on kidneys have been reported and well-accepted[5].

Green tea (Camellia sinensis) is quite possibly the most well-known, profoundly devoured drinks all throughout the planet. It has been found to be a powerful nephron protective specialist against the unhealthy effects of various medications. Green tea contains polyphenols; mostly flavonoids amo-ng which 80-90% are catechins. The green tea catechins have strong antioxidant properties[6] and defends the renal tissue against oxidative stress, hence forestalling the harm brought about by reactive oxygen species generated from ibuprofen biotransformation[7].

In addition to its nephron-protective properties, green tea has long been believed to have beneficial effects on cardiovascular and gastro-intestinal systems. To date, antibacterial, antiviral, anti-inflammatory, anticancer and anti-hypertensive benefits of the constituents of the green tea have been observed[8]. Knowledge of the beneficial effect may highlight its significance for clinical utilization as a part of treatment regime which could be best assessed by renal function tests.

MATERIALS AND METHODS

This laboratory based experimental study was conducted at the Anatomy Department, Army Medical College Rawalpindi, for duration of one year. The study was performed following the approval of ethical committee on animal experiments, of Army Medical College, Rawalpindi.

Thirty (30) adult male healthy rats along with non-pregnant female Sprague Dawley rats of 9- 11 weeks of age and weights ranging from 200-330 gm were used in the experiment and were acclimatized in the animal house of National Institute of Health (NIH), Islamabad. Rats were segregated into three groups (n=10 in each group) where male rats were kept in isolated confines from the females. Rats were fed NIH standardized lab diet for sixty days and water was supplied ad libitum. Ibuprofen manufactured by Abbot Laboratories (Pvt.) Limited was utilized. Green tea was obtained from local market. At the end of 9 weeks but 24h after administration of last dose, five milliliters of blood were taken through intracardiac route and collected in labeled vials. The samples were sent to Pathology Laboratories, Army Medical College for biochemical analysis of serum urea and creatinine (Table 1).

Statistical Analysis

The data was analyzed using statistical package for social sciences (SPSS version 22). The biochemical parameters were narrated as mean ± standard deviation and the critical contrast was resolved utilizing analysis of variance (ANOVA), after which Post-hoc Tukey test. Results were believed significant at p value of <0.05.

Table 1: Experimental Grouping of Animals, Mode of Intervention and Dosage of Drugs

Groups	Intervention& Dosages	Number of Administrations (per day)	Route of Administration	Duration of Administration (weeks)
A	Distilled water & NIH lab diet	Once	Orally by gavage tube	9
B	Ibuprofen (120mg/kg body weight)	Once	Orally by gavage tube	9
C	• Green tea extract ml/100g bodyweight • Ibuprofen 120mg/kg body weight	Once	Orally by gavage tube	9

Table 2: Mean Values of Biochemical Analysis of Control Group A, Interventional Groups (B and C) and Intergroup Comparison of p-values (n = 10)

| Parameters	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	Group A vs. B	Group A vs. C	Group B vs. C
Serum urea (mg/dl)	21.9 ± 2.8	93.2 ± 3.9	36.4± 3.0	0.000	0.000	0.000
Serum creatinine (mg/dl)	0.9 ± 0.22	2.4± 0.52	0.97 ± 0.3	0.000	0.819	0.000

RESULTS

The serum levels of urea and creatinine after ibuprofen administration were generally higher in the experimental group B when compared to control group A. The biochemical markers clearance levels in tea given group C were found to be lower when compared to the other experimental group.

For serum urea, significant disparity in statistical terms was seen among all the groups (Figure 1). For serum creatinine, statistically substantial distinction was noticed between control group A and experimental group B but not between control group A and experimental group C. The comparison between experimental groups B and C, nevertheless, revealed a statistically significant difference (Table 2, Figure 1 and 2).

DISCUSSION

Kidney is an exceedingly active organ involved in metabolism and is accountable for the metabolism of a vast range of chemicals and drugs. In metabolic terms, the reactive intermediates consequence of the metabolic conversion of most of the drugs cause the nephrotoxic effects[9]. Ibuprofen is utilized for the therapy of pyrexia, dental & post-operative pain, dysmenorrhea, migraine, rheumatoid and osteoarthritis, disorders of the soft tissue and various inflammatory dis-orders on a vast scale[10].

The detrimental effect of Ibuprofen on renal tissue is well-documented and is mostly consequence of its potential to generate the quantity of reactive oxygen species which subsequently lead to the per oxidative reaction damaging the renal tissue. These
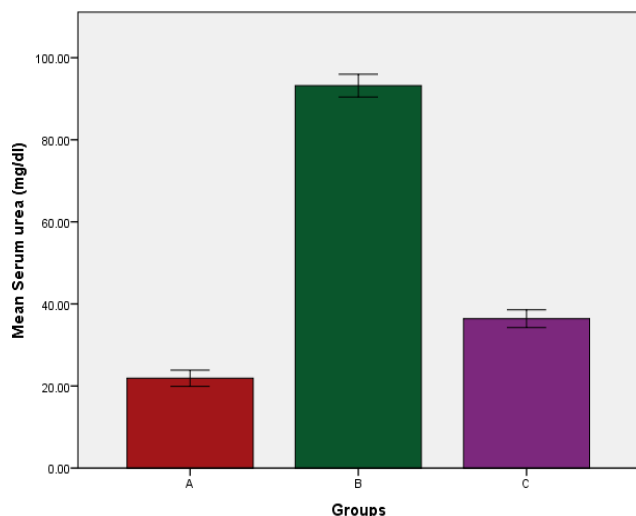
Figure 1: Bar charts illustrating the correlation of mean values of serum urea in control group A and interventional groups B and C

incorporate renal failure and interstitial nephritis on acute basis, tubular necrosis, acute necrosis, and quickened chronic renal failure[11].

Green tea, primarily by quality of its preventive activity against oxidative stress, has strong protective effects on renal tissue. It protects against glomerulosclerosis and reduces serum creatinine and urea[11]. The tea was also ascribed to have a shielding impact not in favor of injury to the renal ischemia and renal tubules triggered by cyclosporine A[12]. Biochemical parameters including serum urea and creatinine, were evaluated for all rodents in all groups. The levels of urea and creatinine in the serum came out elevated significantly in experimental group B when compared to control A. Abbas and Abed proven that ibuprofen elevated urea and creatinine in the serum on significant terms[13]. These two parameters are key markers of intense kidney injury, particularly in youngsters. Subsequently, ibuprofen instigated intense kidney infection in youngsters will in general be more extreme and set aside more effort to recuperate than in grown-ups[14]. An investigation directed on Holstein calves showed expanded serum urea and creatinine following 10-day ibuprofen administration[15]. An investigation
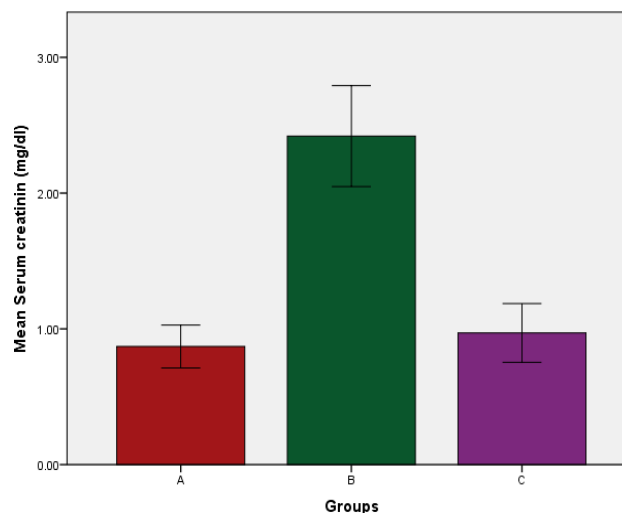
Figure 2: Bar charts illustrating the comparison of mean values of serum creatinine in control group A and experimental groups B and C

comparing acetaminophen vs ibuprofen performed on rabbits by revealed that ibuprofen raised up levels of urea and creatinine more compared with the latter, employed as an alternative[16]. Elevated values of blood-urea and creatinine depict substantial renal damage and are credited to oxidative stress caused by reactive oxygen species generated from the metabolism of the ibuprofen. Green tea administration in experimental group C brought about huge betterment of serum urea and creatinine levels when contrasted with group B. Consequently, action of green tea polyphenols against oxidation is liable for keeping up these markers of renal operation inside typical cutoff points.

CONCLUSION

Green tea had ameliorative effects on the ibuprofen-induced changes in the biochemical markers of the adult rat kidneys.

Acknowledgements

Conflicts of interest

The authors declare that they have no conflict of interests.

Contributors

Dr. Afnan Gul contributed to concept, design of the study& data collection. Drafting & data analysis was done by Dr. Muhammad Bahadur Baloch. Dr. Afnan Gul critically revised the article and approved the final version.

REFERENCES

1. Davies M. Stewart Adams: pharmacologist who discovered ibuprofen. Brit Med J. 2019; 364: l898.
2. Obituary. Dr. Stewart Sanders Adams (16 April 1923 to 30 January 2019)-Pioneer in the discovery of ibuprofen, that from meagre beginnings to become world's best-selling pain-killing drug. Inflammopharmacology. 2019; 27(1): 1-4. doi: 10.1007/s10787-019-00576-7.
3. Abireh IE, Ozioko OM, Ozor II, Finbarrs-Bello E, Ozioko US, Egbo F. Azadirachta indica (neem) leaf extract effect as an option of treatment of ibuprofen-induced nephrotoxicity. J Adv Med Med Res. 2020; 25: 56-62.
4. Nadimohamed N, Mahmoud B, Abdel-Reheim ES, Abdel-Moneim A. Olive and basil leave extracts protect against Ibuprofen induced nephrotoxicity in albino rats. Res J Pharm Technol. 2020; 13(9): 4190-4.
5. Aziz ND, Ouda MH, Ubaid MM. Comparing the toxic effects of non-steroidal anti-inflammatory drugs (Celecoxib and Ibuprofen) on heart, liver and kidney in rats. Asian J Pharm Clin Res. 2018; 11(6): 482-5.
6. Reygaert WC. An update on the health benefits of green tea. Beverages. 2017; 3(1): 6.
7. Semen KO, Weseler AR, Janssen MJ, Drittij-Reijnders MJ, Noble JL, Bast A. Effects of monomeric and oligomeric flavanols on kidney function, inflammation and oxidative stress in runners: A randomized double-blind pilot study. Nutrients. 2020; 12(6): 1634.
8. Hara Y, Yang CS, Isemura M, Tomita I. Health Benefits of Green Tea: An Evidence-Based Approach. Tokyo: CABI; 2017. Available from: https://www.cabi.org/nutrition/ebook/20173328607 (accessed 17.03.2021)
9. Ogidi OI, Ogoun TR, Njoku CO, Charles EE, Amgbare EB, Omotehinse ET. Toxicity Studies on the Effects of Non-Steroidal Anti-Inflammatory Drugs in Wistar Albino Rats. Elixir Pharmacy. 2020; 149: 55010-14.
10. Krasniqi D, Thaqi E, Berisha D, Bibaj G, Kryeziu F. The use of Ibuprofen and our knowledge about it. Med Nurs Pharm Nat Sci. 2019: 31.
11. Gul A, Asad A, Soha il S,Qamar K. Meliorative effect of commercial green tea on ibuprofen induced histomorphological alteration in luminal diameter of proximal renal tubule. Pak Armed Forces Med J. 2020; 7: 6-9.
12. Sarhan O, Abdel-Ghany M, Abdel-Hamid M. Development, evaluation and application of transfersomal green tea extract (Camellia sinensis) formulations. Development. 2020; 2(02): 21-39.
13. Abbas MT, Abed RM. The effect of olive oil on ibuprofen induced renal toxicity in female rats. Karbala J Pharma Sci. 2017; 13: 167-77.
14. Su L, Li Y, Xu R, Luo F, Gao Q, Chen R, et al. Association of ibuprofen prescription with acute kidney injury among hospitalized children in China. JAMA Netw Open. 2021; 4(3): e210775.
15. Walsh P, Carvallo Chaigneau FR, Anderson M, Behrens N, McEligot H, Gunnarson B, et al. Adverse effects of a 10-day course of ibuprofen in holstein calves. J Vet Pharmacol Ther. 2016; 39(5): 518-21.
16. Ojiako OA, Nwanjo HU. Effects of co-administration of chloroquine with paracetamol or ibuprofen on renal function of rabbits. Afr J Biotechnol. 2006; 5(8): 668-70.