ORIGINAL ARTICLE

PROTECTIVE ROLE OF CURCUMIN AGAINST ASPIRIN INDUCED TOXICITY OF PROXIMAL CONVOLUTED TUBULE IN ALBINO RATS

SABA AMJAD, SABA SALEEM, KANWAL SHARIF, ZAHRA FATIMA,
MAHRUKH MALIK, MUHAMMAD SUHAIL.
Department of Anatomy, Shaikh Zayed Postgraduate Medical Institute,
SKZ Medical and Dental College, Lahore.

ABSTRACT

Background: Aspirin is a well-known anti-inflammatory, analgesic and anti-pyretic drug. Turmeric powder commonly known as "Haldi" has an active ingredient curcumin which is being widely used in ayurvedic medicine.

Objective: To determine the nephroprotective role of curcumin on dose related nephrotoxicity induced by aspirin in adult albino rats.

Methods: It was Experimental study. The duration of study was 30 days. We divided the rats into four groups, 15 rats in each. The rats were given 200 mg/kg body weight of aspirin through orogastric catheter to induce toxicity in kidneys of group B (positive control) and groups C and D (experimental). The rats of groups C & D also received 15 mg/kg & 30 mg/kg body weight of curcumin along with toxic dose of aspirin through orogastric catheter.

Results: Current study depicted that groups B, C & D showed smaller diameters of the PCT (proximal convoluted tubules) in comparison with group A. The effects in diameters were dose related. The difference among the groups showed highly significant p-value <0.001. (Table.1)

Conclusion: The results of current research have proved the nephroprotective ability of curcumin is by its antioxidant properties due to a counteraction of free radicals.

Key words: Aspirin, kidneys, curcumin, proximal convoluted tubules, adult albino rats

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Correspondence to: *Saba Amjad,*
Assistant Professor,
Department of Anatomy,
UCMD, University of Lahore, Pakistan.

Email: dr.sabawaqas14@gmail.com

INTRODUCTION

Aspirin is widely used effective analgesic, anti-inflammatory and anti-pyretic drug, that induces nephrotoxicity through inhibition of prostaglandins synthesis.[1] It causes suppression of the production of thromboxanes and prostaglandins as a result of irreversible inhibition of cyclooxygenase.[2] Aspirin is a commonly available, well known and cost effective medicine that causes constriction of blood vessels and smooth muscles atrophy in kidneys through inhibition of production of prostaglandins.[3]

Inhibition of prostaglandin synthesis has a tremendous effect on perfusion of kidneys as well as GFR (glomerular filtration rate).[4] Previous research data also showed that adult female rats are more prone to nephrotoxicity by aspirin than male rats and immature rats.[5] The underlying fact is that females have

comparatively low levels of serum aspirin esterase which metabolizes aspirin slowly, resulting in more nephrotoxic effects.[6] Therapeutic use of aspirin is very common in various illnesses that reduce the risk of Alzheimer's disease, various cardiovascular diseases and colorectal carcinoma.[7] Aspirin reduces the chances of development of atherosclerotic disease phenomenon through inhibition of cyclooxygenase resulting in loss of normal cytoprotective role of prostaglandins. It is contraindicated in intracranial hemorrhage, gastrointestinal bleeding, alcoholism and gastric ulcer disease.[8]

The active ingredient of turmeric is a polyphenol component extracted from the Curcuma Longa plant, generally known as turmeric[9] which belongs to a ginger family,[10] being used as a food flavouring and spice agent.[11] It is commonly harvested in sub-tropical and tropical areas.[12] The active ingredients of curcumin which are derived from turmeric are Diferuloylmethane, bisdemethoxycurcumin and demethoxycurcumin .[13,14] along with resins proteins, volatile oils and sugars in minor quantities. Curcuminoids are also known as "Indian Saffron"[15] that has anti-human immunodeficiency virus, anti-inflammatory, anti-atherosclerotic,[16] antispasmodic, antioxidant, anti-bacterial, nematocidal and anti-protozoal properties.[12] It also has well established role against sprain injuries and joint swellings.[17] In another study it was also observed that it has a significant role in improvement of arthritis, hepatotoxicity, inflammatory bowel disease, wound healing and gall stones formation.[19] The underlying mechanism is lipid peroxidation, inhibition of generation of free radical that results in protection of DNA against oxidative insult.[20] It also lowers glomerulosclerosis Index (GI), arteriolopathy and fibrosis,[21] hence preventing structural damage of blood vessels. Downregulation of the activity of cytochrome P450, a drug metabolizing enzyme, is also an important factor to prevent the toxicity of aspirin. [22] Curcumin exerts both indirect and direct antioxidant effects, indicating that it is a bifunctional antioxidant agent.[23]

Curcumin is one of the commonly used food additives hence, the present study was intended to prove the nephroprotective role of curcumin on the diameters of PCT against aspirin induced nephrotoxicity in adult albino rats.

METHODS

The study was carried out in SZPGMI in the Department of Anatomy Lahore.

The rats were retained in animal house of PGMI, Lahore. The rats of all 4 groups were kept in separate cages and were provided with sufficient food and water. They were kept at room temperature of 27°C with 12 hourly light and dark cycle after 15 days of acclimatization. All 4 cages were properly labelled as A, B, C and D with 15 rats in each cage. The initial body weight was measured before the experiment followed by at the end of the experiment. [24]

Extract of turmeric was prepared at PCSIR food laboratory, Lahore and quantification of extract through GC-MS (Gas Chromatography - Mass Spectrometry) from Forman Christian College, Chemistry Department, Lahore. The turmeric extract was administered through orogastric catheter according to following dose schedule to all the 3 groups for 30 days.

Healthy Control Group - Group A: 10ml / kg body weight / day of distilled water.

Positive Control Group - Group B: 100mg / kg body weight / day of aspirin

Experimental Group I - Group C: 15mg / kg body weight of curcumin & 100mg / kg body weight / day of aspirin simultaneously

Experimental Group II - Group D: 30mg/kg body weight of curcumin & 100mg/kg body weight/day of aspirin simultaneously

The diameters of proximal convoluted tubules were taken with ocular micrometer (µm) starting from basement membrane on one side to the basement membrane of the other side of tubule with 40X eye piece lens in all 4 groups. 2 diameters of proximal convoluted tubules were measured and their mean was calculated. The total number of PCT present per mm^2 field were observed and counted along with their measurements. Both the diameters were taken perpendicular to midpoint of each other. [25]

The rats were dissected and the kidneys were removed for histological observation and measurement of diameters of proximal convoluted tubules through micrometer.

SPSS 22.0 was used to enter and analyze the data. The quantitative data for diameter of proximal convoluted tubule was reported as mean ± S.D and comparison among groups was performed by using ANOVA (one way). Post hoc analysis was done through Tukey test and ≤ 0.05 P-value was taken as significant.

RESULTS

Control group A had diameter of proximal convoluted tubule 43.3 ± 2.2 µm. Smaller diameters were observed in groups B, C and D in comparison with control group A. Minimum mean value recorded was 31.3 ± 2.1 µm. (Fig.1, Table.1)

The difference in the diameters of PCT among four groups were highly significant having <0.001 p-value as mentioned in Table 2.

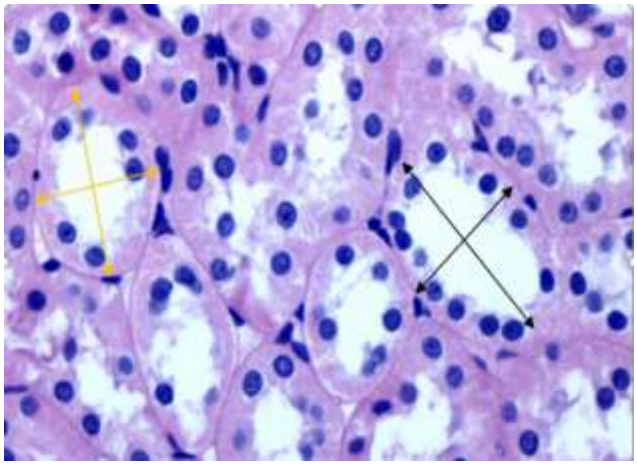

Fig No.1 Photomicrograph indicating measurement of diameter of proximal convoluted tubule (yellow arrow). (H&E, 40x)

Table No. 1: Diameters of PCT in control group A, positive control group B and experimental groups C & D.

Groups	PCT Diameter µm			
	Mean	SD	Minimum	Maximum
A	43.3	2.2	40	48
B	37.9	1.5	33	40
C	32.1	2.0	28	35
D	31.3	2.1	28	35

The results of group wise comparison showed that there were significantly smaller diameters of PCT in groups C & D in comparison with control group B. P-value was found highly significant <0.001. All the 3 groups B, C & D were observed having significantly smaller diameters in comparison with group A with p-value <0.001. The difference among the experimental groups was not significant with p-value 0.632. (Fig.2)

Table No. 2: Comparison of diameters of PCT in control group A and groups B, C & D

	Sum of Squares	Df	Mean Square	F	P-value
Among Groups	1407.12	3	469.04	119.10	0.000**
Within each Groups	220.53	56	3.94		
Total	1627.65	59			

Based on ANOVA

DISCUSSION

The most cost effective and conveniently available non-steroidal anti-inflammatory drug is Aspirin. It has been employed in variety of ailments and possesses analgesic, anti-platelet, anti-inflammatory and anti-pyretic characteristics. It has joint healing properties[3,8] In Asia turmeric is used as a food pigment & flavoring agent.[26]

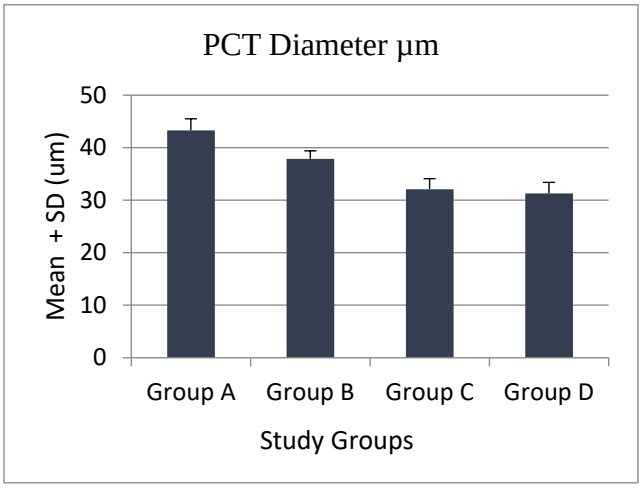

Fig No.2 Bar diagram showing diameters of PCT in control group A and groups B, C and D

The current study depicted that the group B and C & D had smaller diameters of the PCT in comparison with group A and significant difference was found having <0.001 p-value. (Table.1) Significantly smaller diameters have been observed in groups C & D in comparison with group B having <0.001 p-value, but the difference among groups C and D was not significant having p-value 0.632 (Table No.2 & Fig No.2).

The findings are analogous to one study which depicts that atrophy of tubules decreases epithelial cell size and the outer and luminal diameters of the tubules [27] The DNA damage will result because of the disparity between antioxidants defense system and generation of oxygen free radicals. Impaired results in increase in oxidative insult results due to insufficient generation of antioxidants resulting in failure of protective mechanisms. Hence, curcumin with abundant antioxidant characteristics contribute towards improvement of tubular atrophy. In another study improvement in tubular atrophy was observed after giving antioxidant agent. [28]

CONCLUSION

The current study showed that prophylactic treatment of curcumin with aspirin ameliorated tubular atrophy in PCT in rats.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board of Federal Postgraduate Medical Institute /Shaikh Zayd / National Health Research Complex, Lahore via Ref No. F-39/NHRC/Admin/IRB/228 Dated: June 11, 2014.

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AUTHOR'S CONTRIBUTIONS

SA: Manuscript writing
SS: Statistical analysis, Proof reading
KS, MM, MS: Proof reading
ZF: Research compilation, Proof reading