

## ORIGINAL ARTICLE

# Impact of Celecoxib on Serum Creatinine along with Beneficial Effects of Lycopene on Albino Rats; an Observational Study

SADIA SUNDUS<sup>1</sup>, MARIA KHAN<sup>2</sup>, SARWAT FATMEE<sup>3</sup>, MUHAMMAD IMRAN<sup>4</sup>, SAFIA NAZ<sup>5</sup>, MADIHA AJAZ<sup>5</sup><sup>1</sup>Associate Professor Department of Anatomy Iqra Medical & Dental College, Karachi<sup>2</sup>Assistant Professor Department of Anatomy Dr Ishrat-Ul-Ebad Khan Institute Of Oral Health Sciences, DUHS<sup>3</sup>Associate Professor Department of Anatomy Fatima Jinnah Dental College, Karachi<sup>4,5</sup>Assistant Professor Department of Pharmacy Iqra University<sup>6</sup>Department of Human Nutrition & Dietetics Iqra UniversityCorresponding author: Sadia Sundus, Email: [usadsun\\_dr@yahoo.com](mailto:usadsun_dr@yahoo.com), Cell: 0092-300-2850489

## ABSTRACT

**Objective:** To assess the impact of celebrex on serum creatinine with augmentation by lycopene.**Study design:** observational study.**Place of study:** Animal House, JPMC, Karachi,**Period of study:** 4<sup>th</sup> May 2015 to 3<sup>rd</sup> June 2015.**Materials and Methods:** Forty fully-grown male Albino rats of 200-220gm weight and 3-4 months old were reserved for this study and separated into 4 groups, control was selected as A1, In A2 50 mg/kg Celebrex was given by oral route, In A3 50 mg/kg Celebrex was given by oral route along with lycopene and In A4 50mg/kg lycopene was given by oral route. At completion of experimental study, all animals were dissected and preserved.**Results:** In A2 animals serum creatinine level was significantly elevated, however level was improved in A3 animal group.**Conclusion:** Experiment discloses that lycopene improve the raised serum levels of A2.**Keywords:** Celebrex, GI adversity, cyclooxygenase, PG.

## INTRODUCTION

They are frequently used medications in senior citizens with various comorbidities. Unnecessary usage of NSAIDs can adversely effected CVS & kidney function and make complications in it because it disturbs the steadiness of vasodilators and vasoconstrictors mechanisms of renin-angiotensin system. It effects on kidney and causes interstitial nephritis, lipid peroxidation and focal necrotic changes in renal tubules, DNA damage followed by un-controlled cell proliferation.<sup>1,2,3</sup>

Discriminatory NSAIDs which are called COX-2 inhibitors have same painkiller properties like NSAIDs however they have least side effects. They ensure pharmacological prevention of PG synthesis by deterring inflammatory COX-2 enzymes only so as to reduce COX-1- intervened side effect e.g platelet dysfunction and GI bleeding.<sup>4,5,6</sup> It abstemiously revert the reproductive defects, neurobehavioral insufficiencies and had anticancerous activities thru pharmacological prevention of enzyme COX-2 but it causes renal dysfunction.<sup>5,6,7</sup> Celebrex suppresses COX-2 because COX-2 is overexpressed in malignancies and stimulates angiogenesis, immunosuppression and cell division, so it diminishes proliferation of malignant cells and act as an anticancerous agent.<sup>8,9,10</sup>

Lycopene is a noncyclic rosy carotenoid pigment and phytochemical compound which is insoluble in water. It is present in asparagus, parsley, Momordica cochinchinensis, Spreng fruit, papayas, tomatoes, watermelons, apricots and vegetables.<sup>11</sup> It is preventive against lipid, protein, and DNA oxidation. It can go through oxidative, thermal and photo deprivation, so it is 100 times more chemopreventive against various types of cancers and renal impairment.<sup>12,13</sup> It keeps strong antioxidant, antiautophagic, and antiapoptotic properties and defends cells beside injury due to reactive oxygen species. It is more effective as compared to  $\beta$ -carotene and vit E because it contain numerous conjugated double bonds.<sup>14,15,16</sup> It has the utmost singlet oxygen-quenching capability in all types of carotenoids and ability to decrease the risk of prostate cancer, uterine and liver cancers, Alzheimer's disease, and cardio-vascular diseases.<sup>17,18,19</sup> It prevents process of ageing, cell membrane lipid peroxidation and DNA impairment.<sup>20,21</sup>

In the prevailing time period, any study regarding the impact of celebrex on serum creatinine with augmentation by lycopene didn't came in notice, thus this study is planned and we also relate the outcomes with preceding researches.

## MATERIAL AND METHODS

Experimental procedure was permitted by the Animal Care unit of BMSI and 40 Adult masculine rats were retained in coops underneath proper temperature and aeration for a week on standard rat food. Subsequently after a week they were arbitrarily separated into four groups.

Ia: healthy set

IIa: Celebrex 50 mg/kg by oral route. (Unhealthy set)

IIIa: Celebrex with lycopene 50 mg/kg by oral route.

IVa: Lycopene 50 mg/kg by oral route.

Rats were sedated and blood were taken by cardiac puncture for serum creatinine assesment. Creatinine assessment was accomplished by Cat No 3L81-22, 3L81-32 and 3L81-41reagent kits

## RESULTS

Ia: These healthy animals were stayed in their best of fitness. Their eating behaviors and reaction to Impetuses were suitable till the termination of study. The mean assessment of serum creatinine level in set Ia was  $0.54 \pm 0.01$ .

IIa: These animals were appearing diseased, languid and slothful. Their eating habits became minimize and reaction was sluggish. The mean assessment of serum creatinine level in set IIa was  $1.14 \pm 0.09$ . There was a highly noteworthy upsurge ( $P < 0.001$ ) was perceived in the serum creatinine level in set IIa, when linked with set Ia. (Table-A, Figure- A)

IIIa: Animals of this set was relatively prospering and energetic in comparison with IIa. Their eating habits were usual. The mean assessment of serum creatinine level in IIIa was  $0.59 \pm 0.02$ . A noteworthy upsurge ( $P < 0.05$ ) was perceived in the mean value of serum creatinine level in IIIa, when linked with set Ia. An extremely noteworthy reduction ( $P < 0.001$ ) was perceived in the mean assessment of serum creatinine level in IIIa, as compare to IIa. (Table-A, Figure- A)

IVa: The consequences of set IVa were analogous to set Ia.

Table-A: Mean Assessment Of Serum Levels Of Creatinine (Mg/Dl) In Numerous Groups Of Albino Rats

Groups	Management given	Serum level of creatinine
Ia (n:10)	ND	$0.54 \pm 0.01$
IIa (n:10)	Celecoxib	$1.14 \pm 0.09$
IIIa (n:10)	Celecoxib + Lycopene	$0.59 \pm 0.02$

\*Mean $\pm$ SEM

Arithmetical assessment of the dissimilarities in the serum levels of creatinine in Albino rat groups.

Arithmetical assessment	P-value
Ila vs. Ia	P<0.001****
IIla vs. Ia	P<0.05**
IIla vs. Ila	P<0.001****

Key:  
Non-significant\*  
Significant\*\*  
Moderately significant\*\*\*  
Highly significant\*\*\*\*

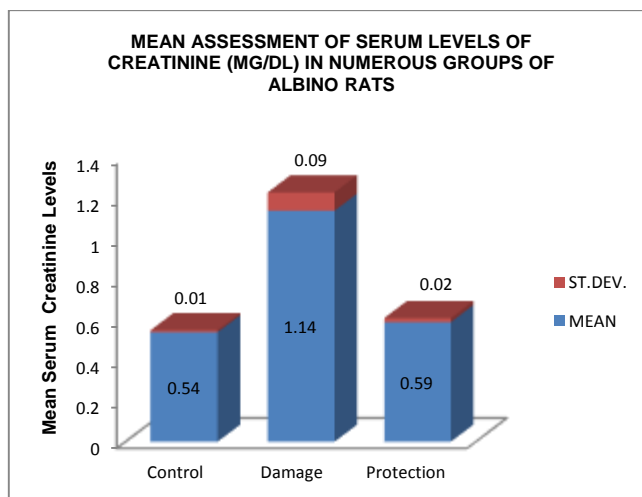


Figure A:

## DISCUSSION

NSAIDs are the internationally taken drugs burden mainly for old age patients, having several comorbidities. It signifies an auspicious circumstances for the inception of harmful effects caused by NSAIDs such as acute or chronic kidney damage.<sup>1,2</sup> COX-2 inhibitors, like Celebrex, have same pain-relieving effects, which are comparable with NSAIDs, however they have least harmful effects like platelet dysfunction and GI bleeding.<sup>3</sup>

Lycopene is chemically a red noncyclic carotenoid phyto- chemical medicine, which is commonly used as anti-oxidant and insoluble in water. It is present in asparagus, parsley, tomato puree, watermelons, apricots and vegetables. It plays a key role in the inhibition of lipid, protein, and DNA oxidation by undergoing oxidative, thermal and photo-degradation. It is 100 times more effective as compare to vit E, so it improves chemotherapeutic persuaded nephrotoxicity, neurotoxicity, hepatic injury. It is also an antioxidant and antiapoptotic agent.<sup>11,12,13</sup>

Ila animals were looking diseased, languid and slothful and there was a highly noteworthy upsurge was perceived in the serum creatinine level. Similar outcomes were observed by 7,8

IIla animals were looking active and an extremely noteworthy reduction was perceived in the mean assessment of serum creatinine level. Similar outcomes were observed by 13,15,21

## CONCLUSION

Investigation resolute that set II animals had noteworthy upsurge in serum creatinine level while III animals showed an extremely noteworthy reduction in serum creatinine level. So our construal from this research is that please avoid using unnecessary painkillers and if mandatory use it with lycopene, in order to decrease harmful effects.

**Conflict of Interest:** no conflict.

## REFERENCES

- Aderville Cabassi<sup>1</sup>, Stefano Tedeschi<sup>1,2</sup>, Stefano Perlini<sup>3</sup>, Ignazio Verzicco<sup>1</sup>, Riccardo Volpi<sup>1</sup>, Gianluca Gonzi<sup>4</sup> and Stefano Del Canale. Non-steroidal anti-inflammatory drug effects on renal and cardiovascular function: from physiology to clinical practice. *European Journal of Preventive Cardiology*, 2020, Vol. 27(8) 850–867.
- Ali Aghazadeh-Habashi, Waheed Asghar, Fakhreddin Jamali. Drug-Disease Interaction: Effect of Inflammation and Nonsteroidal Anti-Inflammatory Drugs on Cytochrome P450 Metabolites of Arachidonic Acid. *Journal of Pharmaceutical Sciences*, 2018; 756-763.
- T-T Ng, D Diamantaras, J Priestley, J Redman, N De Silva, V Mahanta. Is celecoxib a useful adjunct in the treatment of post-tonsillectomy pain in the adult population? A randomised, double-blind, placebo-controlled study. *The Journal of Laryngology & Otology*, 2017, 131, S18–S28.
- Zaher A. Radi and K. Nasir Khan. Cardio-renal safety of non-steroidal anti-inflammatory drugs. *The Journal of Toxicological Sciences (J. Toxicol. Sci.)*, 2019; Vol.44, No.6, 373-391.
- MingBai<sup>1,2</sup>, LiZhang<sup>1,3</sup>, BoFu<sup>1,3</sup>, JiuxuBai<sup>1</sup>, YingjieZhang<sup>1</sup>, GuangyanCai<sup>1</sup>, XueyuanBai<sup>1</sup>, Zh eFeng<sup>1</sup>, ShirenSun<sup>2</sup>, XiangmeiChen<sup>1</sup>. IL-17A improves the efficacy of mesenchymal stem cells in ischemic-reperfusion renal injury by increasing Treg percentages by the COX-2/PGE2 pathway. *Kidney International*, 2018; Vol 93, Issue 4, Pages 814-825.
- O.E.Kale<sup>1</sup>, T.O.Oyesola<sup>2</sup>, F.S.Raji<sup>1</sup>. Celecoxib a cyclooxygenase-2 inhibitor, offers chemoprevention against reproductive and neurobehavioural abnormalities induced by atrazine in male Wistar rats. *Environmental Toxicology and Pharmacology*, 2018, Vol58, pages 84-97.
- Asad Ullah, Muhammad Ashraf, Aqeel Javeed, Aftab Ahmad Anjum, Ali, Attiq, Sarwat Ali. Enhancement of anti-proliferative activities of Metformin, when combined with Celecoxib, without increasing DNA damage. *Environmental Toxicology and Pharmacology*, 2016; 227–234.
- Aderville Cabassi, Stefano Tedeschi, Stefano Perlini, Ignazio Verzicco, Riccardo Volpi, Gianluca Gonzi and Stefano Del Canale. Non-steroidal anti-inflammatory drug effects on renal and cardiovascular function: from physiology to clinical practice. *European Journal of Preventive Cardiology*, 2020, Vol. 27(8) 850–867.
- Estudio sobre el Efecto Tóxico de Diferentes Dosis de Diclofenaco Sódico en el Desarrollo del Riñón en el Período Postnatal A Study on the Toxic Effect of Different Doses of Diclofenac Sodium on the Development of the Kidney in the Postnatal Period. *Int. J. Morphol.*, 2019, 37(3):877-884.
- Derek E. Murrell<sup>1</sup>, James W. Denham<sup>2</sup>, and Sam Hariforooosh<sup>1</sup>. Histopathology and oxidative stress analysis of concomitant misoprostol and celecoxib administration. *J Toxicol Pathol* 2015; 28: 165–170.
- Narges Hedayati, Mehri Bemani Naeini, Alireza Nezami, Hossein Hosseinzadeh, A. Wallace Hayes, Sarasadat Hosseini, Mohsen Imenshahidi, Gholamreza Karimi. Protective effect of lycopene against chemical and natural toxins. *International union of biochemistry and molecular biology*, 2019, vol45; 5-23.
- Amayn Mohamed, Shalaby Dina, Fouad El Shaer. Lycopene protects against renal cortical damage induced by nandrolone decanoate in adult male rats. *Annals of Anatomy - Anatomischer Anzeiger*, July 2019, Volume 224, 142-152.
- Nenad Stojiljkovic, Sonja Ilic, Vladimir Jakovljevic, Nikola Stojanovic, Slavica Stojne, Iristina Kocic, Marko Stojanovic, and Gordana Kocic. The Encapsulation of Lycopene in Nanoliposomes Enhances Its Protective Potential in Methotrexate-Induced Kidney Injury Model. *Oxidative Medicine and Cellular Longevity*, 2018, 1-11.
- M Buyuklu, FM Kandemir, M Ozkaraca. Beneficial effects of lycopene against contrast medium-induced oxidative stress, inflammation, autophagy, and apoptosis in rat kidney. *Pubmed*, 2014; 22-29.
- Jia Lin, Jun Xia, Hua-Shan Zhao, Rui Hou, Milton Talukder, Lei Yu, Jian-Ying Guo, and Jin-Long Li. Lycopene Triggers Nrf2-AMPK Cross Talk to Alleviate Atrazine-Induced Nephrotoxicity in Mice. *J. Agric. Food Chem.* 2018, 66, 46, 12385–12394.
- Hasan Ikbali Atilgan, Arif Aydin, Murat Sadic, Meliha Korkmaz, Tolga Karakan, Elmas Ogus, Pelin, Borcek, Gokhan Koca. The Protective Effect Of Lycopene On Kidney Against Experimentally Induced Unilateral Ureteral Obstruction. *Acta Medica Mediterranea*, 2016, 32: 1631.
- Nenad Stojiljkovic, Sonja Ilic, Nikola Stojanovic, Sanja Stojanovic, and Milan Stojiljkovic. Lycopene improves methotrexate-induced functional alterations of the Madin-Darby kidney cells in a concentration-dependent manner. *J. Physiol. Pharmacol.* 2020, 98: 111–116.
- Somayeh Haghighipour, Rasool Soltani, Ali Anjomshoa. The protective effect of lycopene supplement against vancomycin-induced nephrotoxicity: a randomized double-blind placebo-controlled clinical trial. *J Renal Inj Prev.* 2020; 9(4), 32.
- Yi Zhao, Mu-Zi Li, Yue Shen, Jia Lin, Hao-Ran Wan, Milton Talukder and Jin-Long Li. Lycopene Prevents DEHP-Induced Leydig Cell Damage with the Nrf2 Antioxidant Signaling Pathway in Mice. *J. Agric. Food Chem.* 2020, 68, 7, 2031–2040.
- Cem Kaya, Ramazan Karabulut, Zafer Turkylmaz, Kaan Sonmez, Gamze Kulduk, Ozlem Gulbahar, Faik Kose & Abdullah Can Basaklar. Lycopene has reduced renal damage histopathologically and biochemically in experimental renal ischemia-reperfusion injury. *Ren Fail*, 2015; 37(8): 1390–139.
- Anup A. Patil<sup>1</sup>, Rajendra Doijad, Akshada Koparde. Renoprotective effect of Lycopene on Renal Functional and Histopathological changes in Gentamycin Induced Nephrotoxicity in Rats. *Research J. Pharm. and Tech.* 2020; 13(7): 3237-3240.