Association of Additive Risk of Pioglitazone Use with the Presence of CYP1A1 Polymorphisms in the Occurrence of Bladder Cancer

Zainab Nizar Jawad1, Kamal A.R.2, W eam awad2
1Department of Biology, College of Education for Pure Sciences, University of Kerbala, Kerbala, Iraq.
2College of Medicine, University of Kerbala, Kerbala, Iraq.
E-mail: sarahnizar50@gmail.com

Article History: Submitted: 25.02.2020 Revised: 16.04.2020 Accepted: 07.05.2020

ABSTRACT
Tumor of urinary bladder nowadays is regarded as one of the most prevalent human cancers all over our planet. Many predisposing factors play a crucial role in the pathogenesis of this tumor including endogenous and exogenous blamed causes. Certain polymorphism of CYP1A1 gene recently has been linked to the occurrence of bladder cancer. Pioglitazone that used for treatment of diabetes mellitus type II for long time carry a risk impact on induction of this tumor.

Aim of this study: To evaluate the risk of using of pioglitazone in patients who carry CYP1A1 polymorphism to induce bladder carcinoma.

Materials and method: This study was conducted from 2017 to 2019, 80 patients with bladder cancer after being medically diagnosed and were assessed if using of pioglitazone with presence of CYP1A1 polymorphisms associated with high risk of CA bladder. DNA was extracted and molecular detection was performed to detect single nucleotide polymorphisms (SNPs) at genetic sites using PCR and PCR-RFLP techniques.

RESULTS AND DISCUSSION
The PCR program used to amplify CYP1A1: c.*1189T>C a gene is 94°C for 5 min for the initial denaturation, 35 cycles with 94°C for 45 sec, 59°C for 45 sec, and 72°C for 45 sec, and 72°C for 5 min for the final extension. The PCR product was digested by MspI (HpaII) in CYP1A1: c.*1189T>C a gene to two fragments of 209 and 133 bp for T allele, and the C allele 342 bp fragment. The data was expressed as (1) for sample with CYP1A1 polymorphism and (0) for negative samples, then these data were processed by using Chi-square test using sigma-plot software V.13.

This research demonstrate that there is significant association between using of pioglitazone and the presence of CYP1A1 polymorphism 1189T>C at p <0.05 (P=0.011769). This finding was due to many mechanisms, the most notable one is that presence of this polymorphism causing genomic instability (AM EIN, HAM DY et al. 2016). Over-expression of CYP1A1 polymorphism was shown to prohibit the protective apoptotic defense mechanism specifically against CA bladder (Verma, Sharma et al. 2018)

On the other hand, using of pioglitazone was shown to increase the risk for CA bladder due to abnormal activation of PPAR-gamma that may induce abnormal proliferation of urothelial cell (Ripamonti, Azoulay et al. 2020). This effect was not noticed for rosiglitazone suggesting that the risk of CA bladder is drug specific rather that drug class specific (Tuccori, Filion et al. 2016).

CONCLUSION
It can be concluded that assess the risk of pioglitazone use in patients bearing CYP1A1 polymorphism for induction of bladder carcinoma.
REFERENCES


