ABCC4 polymorphisms and tenofovir pharmacodynamics; a molecular calculation analysis

Rujittika Mungmumpuntipantip1*(https://orcid.org/0000-0003-0078-7897)

Viroj Wiwanitkit2 (https://orcid.org/0000-0003-1039-3728)

126 Medical Center, Bangkok, Thailand

2 Honorary professor, dr DY Patil University, Pune, India

*Corresponding author: Rujittika Mungmumpuntipantip, Email: rujittika@gmail.com

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Abstract
Human immunodeficiency virus (HIV) infection is an important infectious disease that cannot be cured at present. The standard treatment is the use of antiretroviral drug therapy. In the present day, there are many new effective antiretroviral drugs such as tenofovir. The pharmacodynamics of the new antiviral drug is an interesting clinical pharmacology issue. The background genetic effect on pharmacodynamics of new tenofovir is widely mentioned. The effect of ABCC4, polymorphisms on pharmacodynamics of tenofovir is an interesting in HIV medicine research. Here, the authors use a standard molecular calculation analysis to assess the molecular change due to important ABCC4, polymorphisms, ABCC4 4131T → G and ABCC4 3463 A → G. Further implications on the oral clearance and blood concentration of tenofovir can be well explained based on the finding from present molecular calculation analysis.

Keywords: Polymorphism, Cytochrome, Polymorphism tenofovir, Concentration
Introduction

Human immunodeficiency virus (HIV) infection is an important infectious disease that is the big problem in medicine in the present day (1). This infection can be mainly transmitted by sexual contact or blood contact. The infection can be detectable worldwide and it is still not curable at present. The available standard treatment is the use of antiretroviral drug therapy for controlling of the HIV viral load in HIV infected patients.

In the present day, there are many new effective antiretroviral drugs for HIV infection management. Tenofovir is an example of new antiretroviral drug widely used at present. In clinical pharmacology, the pharmacodynamics of the new antiviral drug is an interesting issue. The effect of genetic variation on pharmacodynamics of new tenofovir is mentioned in the literature. Of many genetic polymorphisms, ABCC4, polymorphisms are widely mentioned for the interrelationship with pharmacodynamics of tenofovir (2, 3). Here, the authors use a standard molecular calculation analysis aiming at determining the molecular change due to important ABCC4, polymorphisms, ABCC4 4131T → G and ABCC4 3463 A → G.

Materials and Methods

In the present report, standard clinical bioinformatics analysis is performed in order to access the effect of ABCC4 polymorphisms and tenofovir pharmacodynamics. The focused studied genetic variants are ABCC4 4131T → G and ABCC4 3463 A→G. The molecular calculation analysis is done is based on standard molecular quantum calculation technique as described in the previous studies (4, 5).

Results

According to the molecular calculation analysis, The magnitude of molecular weight change in ABCC4 4131T → G and ABCC4 3463 A → G are equal to +25.02 g/mol (126.11 to 151.13 g/mol) and +16 g/mol (135.13 to 151.13 g/mol), respectively. This mean there will be a less final phenotypic expression per mol in G variant comparing to naive type for both 4131T → G and ABCC4 3463 A → G variants. Also, a higher change is observed in ABCC4 4131T → G indicating a more effect on final phenotypic expression than ABCC4 3463 A → G.

Discussion

Tenofovir is a new antiretroviral drug that is mentioned as a good antiretroviral drug (6). Pharmacologically, tenofovir can be excreted via kidney and the MRP4, encoded by ABCC4, plays important role in tenofovir excretion. Hence, the effect of genetic variant on the pharmacodynamics system of tenofovir in HIV infected patient is an interesting issue (7). A poor pharmacodynamics process of tenofovir in HIV infected patient might result in failure of HIV therapy and might further induce tenofovir related nephrotoxicity (8). Some specific variants such as ABCC4 polymorphisms are mentioned for relationship with oral clearance and blood concentration of tenofovir (2, 3).
In the present report, the authors focus interest on the effect of ABCC4 4131T→G and ABCC4 3463 A → G polymorphisms on pharmacodynamics of tenofovir. It can show that there is a significant change of molecular weight of ABCC4 due to each studied genetic variant. For sure, true observed molecular change could result in altered phenotypic expression, pharmacodynamics process. Effects on the oral clearance and blood concentration of tenofovir can be expected. A less expression of ABCC4 activity can imply alteration of pharmacodynamics process of tenofovir. This pharmacodynamics change is a possible explanation for alteration of oral clearance and renal elimination of tenofovir in HIV infected with the studied genetic variants.

**Conclusion**

Based on the present study, the interrelationship between studied genetic variants and the oral clearance and blood concentration of tenofovir can be shown based on the result from molecular calculation analysis.

**Authors’ contribution**

RM and VW wrote the manuscript equally.

**Conflicts of interests**

The authors declare that they do not have any conflicts of interest.

**Ethical considerations**

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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**References**