ABCB1 AND SLCO1B1 GENE POLYMORPHISMS PREDICT METHOTREXATE-RESISTANCE IN LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA

Manasawee Srisuttayasathien¹, Nutthada Areepium², Ruangsak Lertkhachonsuk¹

¹ Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn, University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand

² Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand

INTRODUCTION

Methotrexate, as a single agent, has long been used successfully and is preferred worldwide for the treatment of low-risk gestational trophoblastic neoplasia. However, up to 26% of patients develop resistance and require changes to second-line chemotherapy. In the search for personalised treatment approaches, a link has been found between the pharmacogenomics of methotrexate response in various diseases

OBJECTIVES

To explore the effects of ABCB1 and SLCO1B1 gene polymorphisms and the methotrexate treatment response in patients with low-risk gestational trophoblastic neoplasia. Secondary objectives were to investigate the association of single nucleotide polymorphism (SNP) genotypes with toxicity profiles, and to evaluate other factors associated with the response.

METHODS

Records of all patients with low-risk gestational trophoblastic neoplasia were reviewed and patients who received methotrexate as a first-line single agent were invited to participate in the study.

DNA was extracted from peripheral blood samples from 18 patients and assessed for ABCB1 (3435C>T) and SLCO1B1 (521T>C).

RESULTS

For the ABCB1 polymorphism, CT was the most common genotype (61.1 %), followed by CC (27.8 %) and TT (11.1 %). Patients with TT had a 1.6-fold higher risk of methotrexate-resistance when compared to the wild-type and heterozygous alleles. The risk of methotrexate-related toxicity was 2.67-fold higher in CT/CC patients who showed a better response to methotrexate. SLCO1B1 gene was not associated with treatment outcomes.

ABCB1	Methotrexate Response		Odds ratio	95%CI
	Resistant	Sensitive		
TT	2	0	1.6	1.095-2.339
CT/CC	10	6		

ABCB1	Adverse Effects		Odds ratio	95% CI
	Yes	No		
TT	0	2	2.67	1.417-5.020
CT/CC	10	6		

CONCLUSION

ABCB1 polymorphism might be useful as a biomarker for predicting the response to methotrexate in patients with low-risk gestational trophoblastic neoplasia.