J Pharmacogenomics Pharmacoproteomics 2016, 7:3 (Suppl)
http://dx.doi.org/10.4172/2153-0645.C1.010

Hyperthermia improves the chemopreventive effects of Tamoxifen in the treatment of triple-negative breast cancer

Zhaleh Behrouzkia[1], **Zahra Joveini**[1], **Nader Riahi-Alam**[2] and **Reza Zohdi Aghdam**[1]
[1]Urmia University of Medical Sciences, Iran
[2]Tehran University of Medical Sciences, Iran

The anti-estrogen agent, Tamoxifen, is the most widely endocrine therapy drug for the treatment or prevention of breast cancer. However, many triple negative patients are low reactive or resistant to it. Hyperthermia which exerts selective antitumor effects has been applied clinically either alone or in the combination of different approved therapies in the treatment of various malignancies like breast cancer. In this study, we aimed to explore whether hyperthermia has the additive effects of tamoxifen in the triple negative breast cancer therapy. The antiproliferative activity of tamoxifen alone and in combination with hyperthermia in 4T1 balb/c mammary breast carcinoma cell line was assessed by the standard colorimetric 3-(4,5-dimethyl-2-thiazolyl)-2,5 diphenyl-2H-tetrazolium bromide assay (MTT method). We also use Acridine Orange/Propidium Iodide fluorescent staining for approving the inhibitory effect. After determining the IC50 of tamoxifen, we expose the cells to 43 ºC for 30 minutes in a regular incubator and then assess the viability rates after 24 hours in single and combination groups. The findings indicate that tamoxifen alone weakly inhibited the proliferation of 4T1 cells by the IC50 of 8 μM and in combination with hyperthermia the viability rates of cells reduced but not very much. Fluorescent staining showed this low rate of apoptosis, too. It was concluded that hyperthermia cannot enhance the killing effect of tamoxifen. These findings support that two modal treatments is not so effective for triple negative patients.

zahrajoveini@gmail.com

Genetic variation in *CYP4F2* and *VKORC1*: Pharmacogenomics implications for response to Warfarin

Zinhle Cindi
University of Cape Town, South Africa

Background: Warfarin is the most commonly used drug in the management of thromboembolic disease. However, there is a huge variability in the time, number of doses or starting doses for patients to achieve the required international normalized ratio (INR) which is compounded by a narrow therapeutic index. Many genetic-association studies have reported on European and Asian populations which have led to the designing of specific algorithms, these are used to assist in warfarin dosing. However, very few or no studies have looked at the pharmacogenetics of warfarin in African populations.

Objective: We set out to investigate the distribution of 3 *SNPs CYP4F2 c.1347C>T, VKORC1 g.-1639G>A and VKORC1 c.1173C>T* among South African Mixed Ancestry (MA) and Black African patients.

Methods: DNA was extracted from 383 participants and genotyped using PCR/RFLP for the *CYP4F2 c.1347 (V433M) (rs2108622), VKORC1g.-1639 (rs9923231)* and *VKORC1 c.117 3(rs9934438)* SNPs.

Results: Comparing the Black and MA groups, significant differences were observed in the distribution of the following genotypes; *CYP4F2 c.1347C/T* (23% vs. 39% p=0.03), all *VKORC1 g.-1639*G>A genotypes (p<0.006) and all *VKORC1 c.1173C>T* genotypes (p<0.007).

Conclusion: *CYP4F2 c.1347T* (V433M) reduces *CYP4F2* protein levels and therefore expected to affect the amount of warfarin needed to block vitamin-K recycling. The VKORC1 g-1639A variant alters transcriptional regulation therefore affecting the function of vitamin-K epoxide reductase in vitamin-K production. The *VKORC1 c.1173T* variant reduces the enzyme activity of *VKORC1* consequently enhancing the effectiveness of warfarin. More genetic characterization is required to understand all the genetic determinants affecting how patients respond to warfarin.

zinhle.a.cindi@gmail.com