OA-D-29

EVALUATION OF CANDIDATE GENETIC VARIATIONS AS PHARMACOGENETIC MARKERS FOR METFORMIN AMONG FILIPINOS

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INTRODUCTION

This study aims to determine the genetic polymorphisms associated with drug response to metformin in type 2 diabetes mellitus (T2DM).

METHODOLOGY

Unmatched cases and controls were used to test the association of genetic polymorphisms in candidate genes to test drug response to metformin. Two hundred fifteen patients with type 2 diabetes who were diagnosed within the past 3 years, without recent T2DM treatment were enrolled simultaneously from three (3) hospitals from Luzon, Visayas and Mindanao and various communities around its area. The participants were started on metformin as monotherapy for 3 months. Glycosylated hemoglobin (HbA1c) was measured at baseline and after 3 months of treatment. Genotyping was done using customized Illumina Infinium microarray chips. Candidate variants were then correlated with response using logistic regression analysis.

PRELIMINARY RESULTS AND DISCUSSION

There are three (3) candidate genetic variants significantly associated to metformin response in this study. The two most significant single nucleotide polymorphisms (SNPs) are variants of the gene FK506-binding protein 5 gene (*FKBP5*) (AA > AC > CC: OR 3.44, 95% CI 1.67, 7.76; *p-value* 0.0004 and CC > CT > TT: OR 3.45, 95% CI 1.64, 8.06; *p-value* 0.0006, respectively).

CONCLUSION

The study revealed SNPs that were not previously associated with metformin response. Genetic variation exists among Filipinos and these influence treatment responses to oral hypoglycemic agents. This study on the genetics of Filipinos with diabetes will potentially benefit the population with use of appropriate medications.

KEY WORDS

pharmacogenetics, diabetes mellitus, type 2, metformin

OA-D-30

EVALUATION OF CANDIDATE GENETIC VARIATIONS AS PHARMACOGENETIC MARKERS FOR GLICLAZIDE AMONG FILIPINOS

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INTRODUCTION

To determine the genetic polymorphisms associated with drug response to gliclazide in type 2 diabetes mellitus (T2DM).

METHODOLOGY

This was an unmatched case-control study comparing response to gliclazide. Participants were enrolled from three (3) institutions (Philippine General Hospital, Corazon Locsin Montelibano Memorial Regional Hospital and Southern Philippines Medical Center) and its surrounding communities. One hundred thirty-nine adult Filipinos with newly diagnosed T2DM were enrolled to determine the association of genetic variants in response to gliclazide. Glycosylated hemoglobin (HbA1c) collected 3 months apart was used to determine response. DNA from blood samples were genotyped using Infinium iSelect beadchips. Candidate variants were then correlated with response to gliclazide using t-test, chi-square and univariate logistic regression analysis.

PRELIMINARY RESULTS AND DISCUSSION
Four (4) candidate genetic variants associated with response to gliclazide were revealed. The two most significant single nucleotide polymorphisms (SNP) are variants of the gene 5-hydroxytryptamine receptor 2C (*HTR2C)* (CC > > GC > GG: OR 28.20, 95% CI 2.59, 1,464.13; *p-value* 0.0015 and AA vs. GG + AG: OR 0.04, 95% CI 0.00069, 0.389; *p-value* 0.0015 respectively). The third SNP is a variant of the gene high mobility group 20A (*HMG20A*) (AA > AG > GG: OR 3.70, 95% CI 1.50, 10.03; p-value 0.0018).

CONCLUSION
The study revealed SNPs that were not previously associated with response to gliclazide. These may be further investigated and validated to identify markers for response to this medication. This will be the basis for matching of patients with the appropriate medications and hence provide improved outcomes.

KEY WORDS
pharmacogenetics, diabetes mellitus, type 2, gliclazide

OA-D-31

CORRELATION OF CANDIDATE GENETIC VARIATIONS FOR SUSCEPTIBILITY AND RISK ASSESSMENT OF TYPE 2 DIABETES MELLITUS AMONG FILIPINOS

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OBJECTIVES
The study aims to determine genetic variants associated with type 2 diabetes mellitus (T2DM) that can help in the development of personalized care for Filipinos.

METHODOLOGY
A total of 201 unrelated adult Filipinos were enrolled in this matched case-control study (67 cases with T2DM to 134 controls). DNA from blood was genotyped via customized Illumina (GoldenGate Genotyping and Infinium iSelect) microarray beadchips, investigating 357 candidate genetic variants associated with T2DM. Correlation with T2DM was done via permuted Pearson chi-square tests of allelic/genotypic association, Bonferroni correction for multiplicity, and Efron conditional logistic regression analysis.

RESULTS AND DISCUSSION
Three (3) candidate variants exhibited significant association with T2DM among Filipinos. A *CDKAL1* (cyclin-dependent kinase 5 regulatory subunit-associated protein 1 like 1 gene) variant showed the greatest risk in association (AA > AC > CC: OR 10.08, 95% CI 5.21, 19.53; *p* 0.0145). Other variants showed significance, namely a *SERPINF1* (serpin family member 1 gene) variant (CC > CT > TT: OR 5.43, 95% CI 2.84, 10.38; *p* 0.0164) and a *GPR45* (G protein-coupled receptor 45 gene) variant (CC > CT > TT: OR 2.56, 95% CI 1.43, 4.59; *p* 0.0206).

CONCLUSION
Preliminary results present variations in *CDKAL1*, *SERPINF1*, and *GPR45* significantly associated with T2DM which may be further investigated through clinical validation to develop diagnostic/prognostic markers for T2DM in Filipinos. Though Philippine genetic studies for T2DM are limited, the emergence of genetic research and genotyping technology presents the opportunity to better optimize T2DM management and treatment in the Filipino individual.

KEY WORDS
diabetes mellitus, type 2, genetic susceptibility, genotyping