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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

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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.