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Pharmacogenetic association of anti-vascular endothelial growth factor treatment in neovascular age-related macular degeneration

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Abstract

We conducted a prospective study on pharmacogenetic association of anti-vascular endothelial growth factor (anti-VEGF) treatment in neovascular age-related macular degeneration (AMD). 201 consecutive patients treated with an as-required regimen of ranibizumab or bevacizumab were genotyped for seven tagged single nucleotide polymorphisms (SNPs) in VEGFA gene. 224 patients were also genotyped for seventeen AMD risk-associated SNPs in the CFH, CFHR1-5, LOC387715/ARMS2, C3, C2, CFB and F13B genes. Multivariate data analysis was used to determine the role of genotype variants on treatment outcome. Of the seven examined SNPs in the VEGFA gene, SNP rs3025000 was the only SNP significantly associated (p value < 1x10-4) with visual outcome at 6 months. The presence of the T allele at this SNP predicted a better outcome of +7 letters at 6 months. Analysis of the seventeen AMD risk-associated SNPs revealed that the AA genotype at rs11200638 - HTRA1 promoter SNP (p =0.001) and GG genotype at rs10490924 (A69S) in LOC387715/ARMS2 (p=0.002) were significantly associated with poorer VA outcome at 12 months. The Mean change in VA from baseline in patients with AA genotype at rs11200638 was -2.9±15.2 letters after 12 months, compared with +5.1±14.1 letters in patients with AG or GG genotypes at this SNP. SNPs rs11200638 and rs10490924 were in high linkage disequilibrium (LD, r2 = 0.92). None of the other examined SNPs was associated with outcome. These findings may suggest a pharmacogenetic association and lead to a personalised treatment regimen, based on genotype to achieve optimal outcome in certain groups of patients.

Biography:

Dr Farshad Abedi obtained his MD from Iran University of Medical Sciences, Tehran, Iran. He completed a Doctor of Medical Science (DMedSc) in ophthalmic research at the University of Melbourne, Australia. His research was focused on predictors of outcome of anti-VEGF treatment in neovascular AMD. He currently works at St Vincent's Hospital in Sydney Australia.