Association of the T-786C, G894T and 4a/4b polymorphisms of the endothelial nitric oxide synthase gene with vasculogenic erectile dysfunction in Iranian subjects

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Abstract: We know that nitric oxide (NO) plays a significant role in penile tumescence. NO is produced during enzymatic conversion of L-arginine to L-citrulline by three distinct isoforms of NO synthase (NOS), namely, inducible (iNOS), endothelial (eNOS) and neural (nNOS). The endothelial isoform of NOS (eNOS), encoded by the NOS3 gene, is the main source of NO.

We determined all three eNOS gene polymorphisms in men with vasculogenic erectile dysfunction. There was a significant difference between the group of men with vasculogenic erectile dysfunction and normal healthy men when compared by genotype distribution.

OBJECTIVE

to investigate the association of the T-786C, G894T and variable number of tandem repeats (VNTRs) in intron 4 (a/b) polymorphisms of the eNOS gene in Iranian subjects with vasculogenic erectile dysfunction (ED).

PATIENTS AND METHODS

to a total of 322 consecutive patients with vasculogenic ED were recruited. Patients with concomitant risk factors for ED were excluded.

to Patients with ED were identified based on history-taking, detailed physical examination, serum biochemistry, sex hormone measurements, application of the International Index of Erectile Function (IIEF) questionnaire, and penile duplex Doppler ultrasonography after intracavernosal injection of 20 μg prostaglandin E(1). The control group comprised 318 age-matched healthy male volunteers.

to Genotyping was performed by polymerase chain reaction-restriction fragment length polymorphism and the T-786C, G894T and VNTR intron 4 polymorphisms of the eNOS gene were determined.

RESULTS

to After multivariate regression analysis, significant differences were seen in the frequencies of genotypes and alleles of the two T-786C and G894T polymorphisms when patients with ED and normal controls were compared.

to In a multiple logistic regression analysis, the odds ratio (OR) of increased ED was strongly associated with the T-786C allele [adjusted OR = 3.12, 95% confidence interval (CI) = 2.28-4.25; P = 0.001] and the 894T allele (adjusted OR = 3.87, 95% CI = 2.53-4.87; P = 0.001).
The data showed a higher prevalence of the T-786C CC genotype (adjusted OR = 2.72, 95% CI = 1.88-3.65; P = 0.006), and the G894T GT (adjusted OR = 1.72, 95% CI 1.24-2.83; P = 0.037) and G894T TT genotypes (adjusted OR = 3.42, 95% CI 2.42-4.26; P = 0.001) in patients with ED than in the controls.

CONCLUSIONS

center dot The findings of the present study suggest that the eNOS T-786C and G894T polymorphisms are strong predictors of the predisposition to ED in addition to traditional risk factors, signifying a genetic influence for this multifactorial disease.

center dot Further studies in different ethnic populations are needed to better elucidate the role of eNOS gene polymorphism in the pathogenesis of ED.

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