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Arrhythmias and Clinical EP

IN SEARCH FOR GENETIC MARKERS OF NON-FAMILIA SICK SINUS SYNDROME

Poster Contributions
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Background: Sick sinus syndrome (SSS) can result from genetic and environmental factors. More than a dozen genetic loci are under investigations.

Objective: To investigate whether 5 connective tissue and 5 ion channel ***gens*** involved in the pathogenesis of non-familial SSS.

Methods: In the case-control study, DNA was isolated from peripheral blood of 284 unrelated SSS patients (65.65±11.0 years) and 243 healthy donors (62.56±14.05). 10 single nucleotide polymorphisms (SNPs) were genotyped by the real-time polymerase chain reaction. Logistic regression was used to detect the association of SNPs with SSS in different models.

Results: In the control group Hardy-Weinberg equilibrium was $P_{H\text{-}W}$=0.022 for ***CHRM2*** (***rs2350782***), $P_{H\text{-}W}$=0.081 for ***SYT10*** (***rs7980799***), $P_{H\text{-}W}$=0.18 for ***MYH6*** (***rs365990***), $P_{H\text{-}W}$=0.37 for ***FNDC3B*** (***rs9647379***), $P_{H\text{-}W}$=0.23 for ***MIR146A*** (***rs2910164***), $P_{H\text{-}W}$=0.0001 for ***MIR196A2*** (***rs11614913***). No statistically significant differences were observed in the CHRM2 rs2350782 frequency distribution ($\chi 2$=2.46, P=0.118 for alleles and $\chi 2$=3.41, P=0.18 for genotypes). Genotypes of the dominant model (T/T+T/C) were more common in the control group (36.2%) compared with SSS patients (28.9%) P_{adj}=0.052. Analysis, depending on the type of SSS, showed ***FNDC3B rs9647379*** C/C genotype was associated with bradycardia (P=0.05, OR=1.55). The protective effect was shown for the additive model ***FNDC3B rs9647379*** in (P=0.014, OR=0.71). In ion channel in the control group $P_{H\text{-}W}$=0.0001 was for HCN4 (rs7164883), $P_{H\text{-}W}$=0.49 for SCN10A (rs6795970), $P_{H\text{-}W}$=0.069 for KCNE1 (rs1805127), $P_{H\text{-}W}$=1.0 for CLCNKA (rs10927887), $P_{H\text{-}W}$=0.0001 for KCNN3 (rs13376333). KCNE1 rs1805127 was of statistical significance ($\chi 2$ = 8.40, P = 0.02), so the T/T genotype was more frequent in the control group, 15.64% vs. 8.45% in the SSS, OR = 0.50, 95% CI (0.29-0.86).

Conclusion: FNDC3B rs9647379, CHRM2 rs2350782 of connective tissue; T/T genotype of the KCNE1 rs1805127 and ***CLCNKA*** g.16351275A>G of ion channel genes may be risk factors for the non-familia SSS.