Molecular Analysis of Polymorphic Variants of MTHFR & CBS Gene of Homocysteine Metabolism in North Indian Cohort with Hyperhomocysteinemia

Avinash Lomash, Somesh Kumar, Sanjeev Pandey, Ankur Singh, Sunil Polipalli, Seema Kapoor

Division of Genetics, Department of Pediatrics, MAMC, New Delhi

ABSTRACT

Objective: Hyperhomocysteinemia may either be a primary presentation or be suspected as an association in certain disease scenarios and genetic defects in MTHFR & CBS gene result in elevated homocysteine level. The study is designed to evaluate whether genetic polymorphisms in these genes are associated with plasma Hcy conc. in a North Indian Cohort.

Materials and Methods: Fasting plasma total homocysteine conc.were measured using RP-HPLC & genotype frequencies at positions C677T & A1298C of the MTHFR & T833C of CBS gene were ascertained using PCR-RFLP method. The age groups at presentation were divided into 0-12years(pediatric),12-18years(adolescent)& >18years(adult).Statistical calculation was carried out with Kruskal Wallis test & p value less than <0.05 were considered significant.

Results: 40 patients screened for elevated homocysteine level from a total of 176 clinically heterogenous group of patients referred for plasma homocysteine estimation.20subjects demonstrated hyperhomocysteinemia in the pediatric age. Mean age at presentation was 6.22yrs(6.22±SD2.83).Commonest presentation was stroke(60%) & neuroimaging finding was an infarct(30%). 6 cases presented in the adolescent age group with mean age of 13.6yrs(13.6±SD 1.57).The commonest reason was stroke75% & seizures were seen in 33%cases.In the adult age group,14 cases with mean age at presentation was 25.43yrs(25.43±SD.5.97) presented with DVT(29%),Stroke(14%)& Recurrent abortions(14%).The frequencies of the AA,AC,CC genotype in cases&controls were 15%,72.5%& 10% and 87.5% & 12.5%.The frequencies of the CC,CT,TT genotype in cases&controls were 50%,50% and 75% & 25% respectively where only TT genotype from T833C found in case & controls.

Conclusions The odds ratios of the A1298C genotypes were significantly different(17.0RR) between Patients and normal controls.The frequencies of C677T haplotype were significantly higher(3RR)in the patients than in the control group. Hyperhomocysteinemia is a significant contributor to pediatric and adolescent stroke.Genotypes A1298C &C677T appear to confer significant susceptibility to the development of Hyperhomocysteinemia where genotype T833C of CBS gene do not affect hyper Hcy concentration.