INTISARI

PERBEDAAN VARIASI GENETIKA NKX2-5 DEFEK SEPTUM ATRIUM FAMILIAL DENGAN NON-FAMILIAL DI RSUP DR. SARDJITO

Rozqie, R., Dinarti, L. K., Mumpuni, H.

Latar Belakang: Faktor transkripsi NKX2-5 sangat penting untuk perkembangan jantung selama tahap embrio. Variasi genetika gen NKX2-5 ditemukan pada banyak penyakit jantung bawaan, terutama defek septum atrium (DSA). Variasi gen NKX2-5 di Asia berdasarkan populasi Tionghoa ditemukan dalam kasus familial dan sporadis. Apakah varian yang sama dari NKX2-5 juga terlibat dalam populasi Asia Tenggara masih belum diketahui. Oleh karena itu, kami menyelidiki keberadaan variasi gen NKX2-5 pada populasi defek septum atrium di Indonesia dan membandingkan antara familial dan non-familial.
Tujuan: Penelitian ini bertujuan untuk mengetahui peran variasi gen NKX2-5 pada kejadian DSA familial dan non-familial di RSUP Dr Sardjito Yogyakarta.
Metode: Kami mengumpulkan 97 pasien dengan DSA (termasuk 25 pasien familial *vs* 72 pasien non-familial) untuk dilakukan pemeriksaan variasi genetik pada gen NKX2-5. Sampel DNA diekstraksi dari sampel darah vena. Seluruh ekson pengkode dari gen NKX2-5 dari sampel DNA diamplifikasi dengan metode PCR dan dilakukan *sequencing*. Variasi dideteksi dengan membandingkan genom referensi standar. Distribusi frekuensi genotipe pada penyakit defek septum atrium familial dan non-familial dianalisis dengan statistik.
Hasil: Kami mengidentifikasi 3 varian genetik NKX2-5 yaitu c.63 A> G (rs2277923) pada ekson 1, c.413 G> A (rs1366528649) dan c.561G> A (rs767559311) pada ekson 2. Variasi pertama ditemukan pada 83 pasien (85,6%) dan memiliki 3 genotipe AA, GA, dan GG. Uji *Mann-Whitney* menunjukkan kesamaan genotipe antara kelompok familial dan non-familial (p = 0,813). Variasi kedua dan ketiga adalah heterozigot dan ditemukan pada lokus yang sama, sehingga dinamakan sebagai variasi heterozigot ganda. Variasi ini diidentifikasi hanya pada DSA familial (3 pasien, 3,1%). Uji eksak *Fisher* menunjukkan perbedaan yang signifikan antara familial dan non-familial (p = 0,016).
Simpulan: Ditemukan tiga variasi genetik NKX2-5, yaitu rs2277923 memiliki distribusi yang sama antara familial dan non-familial, sedangkan rs1366528649 dan rs767559311 teridentifikasi secara signifikan hanya pada DSA familial.
Kata Kunci: NKX2-5, DSA familial, variasi genetika.

ABSTRACT

DIFFERENCES OF GENETIC VARIATION OF NKX2-5 IN ATRIAL SEPTAL DEFECT BETWEEN FAMILIAL AND NON-FAMILIAL AT DR. SARDJITO HOSPITAL

Rozqie, R., Dinarti, L. K., Mumpuni, H.

Background: The transcription factor NKX2-5 is essential for heart development during embryonic stages. Genetic variations of NKX2-5 gene are detected in many congenital heart diseases, especially atrial septal defect (ASD). NKX2-5 variants in Asia based on Chinese population are founded in familial and sporadic cases. Whether the same variant of NKX2-5 is also involved in Southeast Asia population is still unknown. Therefore, we investigate the presence of NKX2-5 gene variant in atrial septal defect population in Indonesia and compare between familial and non-familial.

Objectives : This study investigates the role of genetic variation of NKX2-5 in familial and non-familial ASD patients at RSUP Dr Sardjito Yogyakarta.

Methods: We screened 97 patients with ASD (including 25 familial patients vs 72 non-familial patients) for genetic variations in NKX2-5 gene. DNA samples were extracted from venous blood samples. The whole two coding exons of the NKX2-5 gene from DNA samples were amplified by multiplex PCR and directly sequenced. Variations were detected by comparison with the standard reference genome. The distribution of genotype frequency in atrial septal disease familial and non-familial were analyzed.

Results: We identified 3 genetic variants of NKX2-5 which are c.63 A>G (rs2277923) at exon 1, c.413 G>A (rs1366528649) and c.561G>A (rs767559311) at exon 2. The first variation was founded in 83 patients (85,6%) and has 3 genotypes AA, GA, and GG. Mann-Whitney test showed similar genotypes between familial and non-familial groups (p = 0,813). The second and third variations were heterozygote and founded in the same locus, so we named as double heterozygote variation. These variations were identified only in familial ASD (3 patients, 3,1%). Fisher's exact test was showing a significant difference between familial and non-familial (p = 0,016).

Conclusion: We discovered three genetic variations of NKX2-5, which are rs2277923 has similar distribution between familial and non-familial, while rs1366528649 and rs767559311 are significantly identified only in familial ASD.

Keywords: NKX2-5, familial ASD, genetic variation.