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DISERTASI

HUBUNGAN POLIMORFISME GEN HLA-DRB1 DENGAN ALLOANTIBODI ERITROSIT PADA PASIEN TRANSFUSI BERULANG DENGAN INKOMPATIBILITAS *CROSSMATCH*

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ABSTRAK

HUBUNGAN POLIMORFISME GEN HLA-DRB1 DENGAN ALLOANTIBODI ERITROSIT PADA PASIEN TRANSFUSI BERULANG DENGAN INKOMPATIBILITAS *CROSSMATCH*

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Transfusi darah merupakan terapi suportif sangat vital dalam penatalaksanaan pasien hemato-onkologi yang ditransfusi secara berulang. Tranfusi darah berulang berisiko terjadi alloimunisasi sehingga terbentuk alloantibodi yang dapat menyebabkan inkompatibilitas *crossmatch*. Pembentukan alloantibodi dipengaruhi oleh beberapa faktor termasuk faktor genetik. Tujuan penelitian ini mengetahui hubungan polimorfisme gen HLA-DRB1 dengan alloantibodi eritrosit pada pasien transfusi berulang dengan inkompatibilitas *crossmatch*.

Penelitian observasional analitik dengan rancangan potong lintang dilakukan pada 47 pasien hemato-onkologi yang mendapat transfusi berulang di Bagian Ilmu Penyakit Dalam RSUP Dr. M. Djamil Padang berusia ≥18 tahun dengan riwayat transfusi eritrosit minimal tiga unit *packed red cell* (PRC) dalam tiga bulan terakhir. Pasien dengan riwayat penyakit autoimun, sedang hamil, *direct coomb's test* positif dan *C-Reactive Protein* >100 mg/L dikeluarkan dari penelitian ini. Alloantibodi positif ditentukan dari hasil *indirect coomb's test* positif, inkompatibilitas *crossmatch* ditentukan dari hasil *crossmatch* mayor positif dan polimorfisme gen HLA-DRB1 ditentukan menggunakan *PCR-Sequence Specific Primer* dan sistem elektroforesis untuk alel HLA-DRB1*04, HLA-DRB1*09. HLA-DRB1*11 dan HLA-DRB1*15.

Hasil penelitian pada 47 pasien hemato-onkologi yang mendapat transfusi berulang didapatkan alloantibodi positif sebanyak enam pasien (12,8%). Semua pasien dengan alloantibodi positif mengalami inkompatibilitas *crossmatch*, yang terdapat pada pasien dengan diagnosis *Acute Myeloblastic Leukemia* dan Leukemia Granulositik Kronik masing-masing sebanyak 33,3% diikuti oleh *Myelodysplastic Syndrome* dan *Multiple Myeloma* masing-masing 16,7%. Persentase alloantibodi yang positif lebih tinggi pada alel HLA-DRB1*15 positif dibandingkan dengan HLA-DRB1*15 negatif yaitu 100% berbanding 2,4%. Persentase alloantibodi positif juga lebih tinggi pada alel HLA-DRB1*04 positif dibandingkan dengan HLA-DRB1*04 negatif yaitu 60% berbanding 7,1% dan secara statistik perbedaan tersebut bermakna (P<0,05), sedangkan persentase alloantibodi positif pada alel HLA-DRB1*11 positif juga lebih tinggi dibandingkan dengan alel HLA-DRB1*11 negatif yaitu 33,3% berbanding 11,4%, tetapi tidak bermakna secara statistik (P>0,05). Alloantibodi positif tidak ditemukan pada alel HLA-DRB1*09 positif.

Hasil penelitian ini disimpulkan bahwa terdapat hubungan polimorfisme gen HLA-DRB1 yaitu alel HLA-DRB1*15 dan HLA-DRB1*04 dengan alloantibodi eritrosit yang menyebabkan inkompatibilitas *crossmatch* pada pasien transfusi berulang.

Kata kunci: transfusi berulang, alloantibodi, inkompatibiltas *crossmatch*, polimorfisme gen HLA-DRB1

ABSTRACT

RELATIONSHIP BETWEEN HLA-DRB1 GENE POLYMORPHISMS AND ERYTHROCYTE ALLOANTIBODIES IN REPEATED TRANSFUSION PATIENTS WITH CROSSMATCH INCOMAPATIBILITY

Zelly Dia Rofinda

Blood transfusion is a vital supportive therapy in the management of hemato-oncology patients which is blood needs to be transfused repeatedly. Repeated blood transfusions increase the risk of alloimmunization in patients resulting in the formation of alloantibodies that can cause crossmatch incompatibility. The formation of alloantibodies is influenced by several factors including genetic factors. The purpose of this study was to determine the relationship between HLA-DRB1 gene polymorphisms and erythrocyte alloantibodies in repeated transfusion patients with crossmatch incompatibility.

An analytical observational study with a cross-sectional design was conducted on 47 hemato-oncology patients who received repeated transfusions at the Internal Medicine Department, Dr. M. Djamil Central Hospital, Padang aged 18 years with a history of erythrocyte transfusion of at least three PRC units in the last three months. Patients with a history of autoimmune disease, pregnant, positive DCT and CRP >100 mg/L were excluded from this study. Positive alloantibodies were determined from positive indirect Coomb's test results, crossmatch incompatibility was determined from positive major crossmatch results and HLA-DRB1 gene polymorphisms were determined using PCR-Sequence Specific Primer and electrophoresis system for the allele HLA-DRB1*04, HLA-DRB1*09. HLA-DRB1*11 and HLA-DRB1*15.

The results of a study conducted on 47 hemato-oncology patients who received repeated transfusions found that six people were positive alloantibodies (12.8%). All patients with positive alloantibodies had crossmatch incompatibility, which was found in patients with acute myelocytic leukemia and chronic myelocytic leukemia diagnoses of 33.3%, followed by myelodysplastic syndrome and myeloma multiple of 16.7%, respectively. The percentage of positive alloantibodies was higher in the positive HLA-DRB1*15 allele compared to the negative HLA-DRB1*15 which was 100% versus 2.4%. The percentage of positive alloantibodies was also higher in the positive HLA-DRB1*04 allele compared to the negative HLA-DRB1*04, namely 60% versus 7.1% and the difference was statistically significant ($P<0.05$), while the percentage of positive alloantibodies the positive HLA-DRB1*11 allele was also higher than the negative HLA-DRB1*11 allele, namely 33.3% versus 11.4%, but not statistically significant ($P>0.05$).

From the results of this study, it can be concluded that there is a significant relationship between the alleles of HLA-DRB1*15 and HLA-DRB1*04 with erythrocyte alloantibodies that cause crossmatch incompatibility in repeated transfusion patients.

Keywords: repeated transfusion, alloantibody, crossmatch incompatibility, HLA-DRB1 gene polymorphisms