Peran a-tokoferol terhadap Penanda Hemolisis dan Stres Oksidatif Sel Darah Merah Thalassemia-b Mayor = The Effect of a-Tocopherol in Hemolysis and Oxidative Stress Marker on the RBC of b-Thalassemia Major

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Abstrak

Akumulasi rantai globin-Î± berlebihan pada membran SDM thalassemia-Î² mayor menyebabkan hemolisis, eritropoiesis tidak efektif dan anemia kronik sehingga memerlukan transfusi sel darah merah (SDM) terus menerus. Transfusi rutin dan hemolisis mengakibatkan besi bebas sebagai radikal bebas dan membentuk radikal peroksil lipid di membran SDM sehingga memperberat hemolisis. Antioksidan Î±-tokoferol menghambat pembentukan radikal peroksil lipid tersebut.

Penelitian ini bertujuan untuk menilai peran Î±-tokoferol terhadap hemolisis dan stres oksidatif. Penelitian ini merupakan uji klinis acak tersamar ganda pada thalassemia-Î² mayor usia 5–18 tahun yang mendapat transfusi dan kelasi besi rutin di Pusat Thalassemia RSUP dr.Ciptomangunkusumo Kiara. Intervensi plasebo dan Î±-tokoferol diberikan selama empat minggu. Suplementasi Î±-tokoferol berdasarkan rekomendasi Institute of Medicine (IOM), 4–8 tahun 200 mg/hari; 9–13 tahun 400 mg/hari; 14–18 tahun 600 mg/hari. Penilaian penanda hemolisis menggunakan haptogobin (Hp), hemopeksin (Hx) dan fragilitas osmotik SDM. Penanda stres oksidatif yaitu MDA, GSH, GSSG, rasio GSH/GSSG dan Î±-tokoferol. Pemeriksaan laboratorium dilakukan sebelum dan setelah diberikan plasebo/Î±-tokoferol, sesaat sebelum transfusi SDM. Analisis uji t-tidak berpasangan untuk melihat perbedaan antara kelompok studi dan uji korelasi untuk melihat hubungan antara variabel.

Pada bulan Desember 2016 hingga Juli 2017, 40 subjek mampu menyelesaikan penelitian, 20 subjek kelompok plasebo dan 20 subjek kelompok Î±-tokoferol. Nilai rerata Hp lebih besar pada kelompok Î±-tokoferol (3,01 mg/dL) dibandingkan kelompok plasebo (1,08 mg/dL), secara statistik berbeda bermakna (p = 0,021). Nilai rerata kadar Hx dan persentase hemolisis SDM tidak berbeda bermakna pada kedua kelompok studi (p > 0,05). Tidak ada perbedaan bermakna pada kelompok Î±-tokoferol dan plasebo untuk kadar MDA (1,003 nmol/L dan 1,07 nmol/L), GSH (5,81 µM dan 6,15 µM), GSSG (1,77 µM dan 1,86 µM) dan rasio GSH/GSSG (1,29 dan 1,31), (P > 0,05).

Antioksidan Î±-tokoferol dapat mengurangi hemolisis dan secara tidak langsung memperbaiki kadar Hp pada thalassemia-Î² mayor, akan tetapi tidak mampu memengaruhi stres oksidatif.
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The accumulation of excess unmatchedÎ±-globin chains in the red blood cell membrane of Î²-thalassemia major leads to hemolysis, ineffective erythropoiesis and chronic anemia which needs multiple red blood cell transfusion. Routine transfusions may lead to iron overload as free radical in the red blood cell membrane, resulting clinically as severe hemolysis. Alpha-tocopherol as an antioxidant has been known as a potent scavenger of hydroxyl lipid radical.

The aim of this study was to evaluate the effects of Î±-tocopherol in hemolysis and oxidative stress on the red cell membrane in Î²-thalassemia major. This randomized double-blind, placebo-controlled study was done in Î²-thalassemia major patients range aged 5–18 years old who regularly had transfusion and receiving iron chelating agents at Thalassemia centre, Kiara Ciptomangunkusumo Hospital. All subjects were randomized to receive either Î±-tocopherol or placebo orally for 4 weeks. Subjects in the experimental group received Î±-tocopherol, the doses based on the recommendation from Institute of Medicine (IOM) as follows: 200 mg/day for 4–8 years old; 400 mg/day for 9–13 years old; 600 mg/day for 14–18 years old. Laboratory analysis for hemolysis variables were haptoglobin, hemopexin, osmotic fragility test. Oxidative stress and antioxidant variables were MDA, GSH, GSSG, GSH/GSSG ratio, and Î±-tocopherol. All variable were evaluated before 4 weeks and after consuming Î±-tocopherol or placebo, just before they received a blood transfusion. The statistical analysis results using independent t-test and correlation test.

During December 2016–July 2017, 40 subjects completed the study, they were 20 subjects in the placebo group and 20 subjects in the Î±-tocopherol group. There was significant enhancement of haptoglobin mean level in the Î±-tocopherol group (3.01 mg/dL) compared to placebo (1.08 mg/dL), ($p = 0.021$). The mean level of hemopexin and the percentage of RBC hemolysis did not significantly different in both groups, ($p > 0.05$). We also did not find any significantly different in mean level of MDA (1.003 nmol/L and 1.07 nmol/L), GSH (5.81 µM and 6.15 µM), GSSG (1.77 µM and 1.86 µM) and GSH/GSSG ratio (1.29 and 1.31), ($p > 0.05$) for the Î±-tocopherol and placebo groups.

The effects of Î±-tocopherol may improve hemolysis and haptoglobin level indirectly in Î²-thalassemia major, but there was no significant role in oxidative stress.