Efek Centella Asiatica terhadap Kulit Kering pada Penyandang Diabetes Melitus Tipe 2: Kajian terhadap Kadar N (6)-Carboxymethyl-lysine, Interleukin 1-, dan Aktivitas Superoksida Dismutase pada Stratum Korneum = The Effect of Centella asiatica in Type 2 Diabetics Dry Skin : A Study of N (6)-Carboxymethyl-Lysine Concentration, Interleukin 1-, and Activity of Superoxide Dismutase in Stratum Corneum

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Abstrak

Kelainan kulit kering banyak ditemukan pada penyandang DMT2. Patogenesis kulit kering pada DMT2 dipicu oleh kondisi hiperglikemia kronik yang meningkatkan Advanced glycation end products (AGE) N(6)-carboxymethyl-lysine (CML), sitokin proinflamasi dan stres oksidatif. Kombinasi Centella asiatica oral (CAo) dan topikal (CAt) diduga dapat meningkatkan efektivitas tatalaksana kulit kering DMT2. Penelitian bertujuan menganalisis efektivitas dan keamanan kombinasi CAo + CAt dalam memperbaiki kulit kering DMT2. Penelitian merupakan uji klinis acak tersamar ganda di Poliklinik Metabolik Endokrin Departemen Penyakit Dalam RSCM dan 5 puskesmas di Jakarta pada bulan Juli 2018–Maret 2019. Subjek dibagi menjadi 3 kelompok, yaitu kelompok CAo + CAt, plasebo oral (Plo) + CAt, dan Plo + Plasebo topikal (Plt) masing-masing berjumlah 53 orang. Perbaikan kulit kering secara klinis diukur dengan Specified Symptom Sum Score (SRRC) dan Skin Capacitance (SCap). Perbaikan secara molekular diukur CML, IL-1a, dan aktivitas superoksida dismutase (SOD). Keamanan kombinasi CAo + CAt dilakukan melalui penilaian efek simpang oral dan topikal. Pada ketiga kelompok, median HbA1c > 7%. Glukosa darah sewaktu (GDS) kelompok CAo + CAt hari ke-15 dan 29 semakin menurun. Efektivitas kombinasi CAo + CAt dinilai melalui analisis subgrup berdasarkan nilai HbA1c dan GDS. Pada glukosa darah terkontrol baik, persentase penurunan SRRC lebih besar pada kelompok CAo + CAt vs Plo + Plt (p = 0,04). Peningkatan SCap kelompok CAo + CAt lebih besar dibandingkan Plo + Plt (p = 0,01). Pada glukosa darah terkontrol kurang baik peningkatan SOD kelompok CAo + CAt lebih besar dibandingkan Plo + Plt (p = 0,01). Tidak terdapat korelasi antara CML, IL-1Î± dan SOD dengan SRRC atau SCap. Terdapat korelasi sedang sampai kuat dan arah korelasi sesuai antara CML dengan SOD (r = 0,58, p < 0,05) dan IL-1Î± dengan SOD (r = 0,70, p < 0,05) pada glukosa darah terkontrol baik. Tidak terdapat efek simpang oral dan topikal yang bermakna pada penggunaan CAo + CAt dibandingkan 2 kelompok. Simpulan: Pada glukosa darah terkontrol baik, perbaikan SRRC dan SCap kelompok CAo + CAt lebih besar dibandingkan Plo + Plt. Pada glukosa darah terkontrol kurang baik peningkatan SOD kelompok CAo + CAt lebih besar daripada Plo + Plt. Terdapat korelasi sedang sampai kuat antara CML atau IL-1Î± dengan SOD pada glukosa darah terkontrol baik. Tidak terdapat efek simpang oral dan topikal yang bermakna pada kelompok CAo + CAt dibandingkan 2 kelompok. Kata kunci: CML, DMT2, IL-1a, kulit kering, SCap, SOD, SRRC <hr /> Dry skin is a common findings in type 2 diabetes mellitus (T2DM). The pathogenesis of dry skin in T2DM rises from chronic hyperglycemic condition which

causes an increase in levels of Advanced glycation end products (AGEs) N(6)-carboxymethyl-lysine (CML), pro-inflammation cytokines and oxidative stress. Combination of oral and topical Centella asiatica (CA) is expected to ameliorate dry skin in T2DM patients more effectively. This study was a double blinded randomized clinical trial in T2DM patients with dry skin in outpatients clinic of Metabolic Endocrine, Internal Medicine Department, dr. Cipto Mangunkusumo Hospital, and 5 primary health cares in Jakarta from July 2018 to March 2019. The subjects were divided into three groups, CA oral (CAo) + CA topical (CAt) group, oral placebo (Plo) + CAt group, and Plo + topical placebo (Plt) which included 53 subjects respectively. Dry skin improvement was evaluated clinically using Specified Symptom Sum Score (SRRC) and Skin Capacitance (SCap). The molecular improvement was evaluated using levels of CML, inflammation interleukin 1-Î± (IL-1Î±) concentration, and oxidative stress superoxide dismutase (SOD). In the three groups, median of HbA1c > 7%. Random blood glucose (RBG) in CAo + CAt group in day-15 and 29 were further decreased. Effectivity of CAo + CAt combination were assessed via subgroup analysis based on HbA1c and RBG. In well controlled blood glucose, on day-29, percentage of SRRC decrement was greater in CAo + CAt compared to control group without CA (p = 0,04). SCap value in CAo + CAt group was greater than control group (p = 0,01). In the partially controlled blood glucose, increment of SOD activity of CAo + CAt group was greater than control group (p = 0,01). There was no correlation found between CML, IL-1Î± and SOD with SRRC nor SCap. There were medium to strong correlation between CML with SOD (r = 0,58, p < 0,05) and IL-1Î± with SOD (r = 0,70, p < 0,05) in well controlled blood glucose. Systemic and topical adverse events were not found significantly in CAo or CAt usage compared to the other two groups. Conclusion: In well controlled blood glucose, improvement of SSRC and SCap in CAo + CAt were greater than Plo + Plt. In partially controlled blood glucose, increment of SOD in CAo + CAt was greater than Plo + Plt. There was moderate to strong correlation between CML or IL-1 and SOD in well controlled blood glucose. There were no significant adverse events found due to CAo + CAt compared to the other 2 group in the study. Keywords: CML, diabetes mellitus, dry skin, IL-1a, SCap, SOD, SRRC