Efektivitas dan Keamanan Vitamin D Oral dan Topikal sebagai Terapi Adjuvan pada Akne Vulgaris Sedang dan Berat: Kajian terhadap Ekspresi VDR, IL-1, IL-6, IL-10, dan IL-17 = Effectiveness and Safety of Oral and Topical Vitamin D as Adjuvant Therapy in Acne Vulgaris: Study of VDR, IL-1ï¢, IL-6, IL-10, IL-17 expression

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Abstrak

Akne vulgaris (AV) adalah penyakit inflamasi kronik kelenjar pilosebasea kulit yang memengaruhi kualitas hidup dan psikologis. Baku emas terapi AV sedang hingga berat masih menghadapi tantangan terkait efek samping dan resistensi. Proses inflamasi dilaporkan terjadi sebelum hiperkeratinisasi, dan Cutibacterium acnes memicu inflamasi. Sebosit dan keratinosit menjadi target terapi potensial, tetapi bukti klinisnya terbatas. Studi menunjukkan vitamin D berpotensi sebagai agen antiinflamasi melalui reseptor vitamin D (VDR) pada sebosit. Penelitian ini bertujuan menilai efektivitas dan keamanan vitamin D oral dan topikal pada akne vulgaris sedang dan berat. Penelitian ini adalah studi eksperimental acak tersamar ganda. Sebanyak 105 subjek dengan AV inflamasi sedang hingga berat menjalani terapi di Poliklinik Divisi Dermatologi Kosmetik, Departemen Dermatologi dan Venereologi RSUPN Dr. Cipto Mangunkusumo, dan pemeriksaan biomarker di Laboratorium Terpadu FKUI selama delapan minggu. Subjek dibagi menjadi tiga kelompok: Kelompok eksperimen: vitamin D oral 2000 IU + vitamin D topikal + adapalene topikal (Do+Dt). Kelompok plasebo oral + vitamin D topikal + adapalene topikal (Plo+Dt). Kelompok kontrol: plasebo oral + plasebo topikal + adapalene topikal (Plo+Plt). Kadar serum 25-hidroksivitamin D (25(OH)D) diukur dengan ELISA. Ekspresi VDR pada lesi dievaluasi menggunakan flow cytometry, dan sitokin inflamasi (IL-1b, IL-6, IL-10, IL-17) dianalisis dengan Luminex. Perubahan klinis dinilai setiap kunjungan (minggu ke-0, 1, 2, 4, 6, dan 8). Hasil analisis flow cytometry menunjukkan proporsi VDR (+) monosit lebih tinggi dibandingkan sebosit dan keratinosit. Kadar 25(OH)D sebelum perlakuan memiliki korelasi positif lemah dengan proporsi VDR (+) monosit ($r = 0,27$; $p = 0,004$) dan VDR (+) sebosit ($r = 0,18$; $p = 0,04$). Korelasi positif lemah juga ditemukan antara proporsi VDR (+) monosit dan total lesi AV sebelum perlakuan ($r = 0,28$; $p = 0,007$). Terdapat penurunan lesi AV inflamasi, non-inflamasi dan lesi total yang bermakna setelah intervensi pada setiap kelompok ($p < 0,05$), namun tidak terdapat perbedaan yang bermakna antara ketiga kelompok ($p > 0,05$). Perbaikan klinis lesi inflamasi terbesar ditemukan pada kelompok Do+Dt (63%), diikuti Plo+Dt (57,1%) dan Plo+Plt (54,5%).
Pada kunjungan kedua, IL-1b menurun bermakna pada semua kelompok ($p = 0,016$, $p = 0,012$, $p = 0,004$), sementara IL-6 tidak menunjukkan perubahan bermakna. IL-10 meningkat bermakna pada kelompok Do+Dt ($p = 0,012$) dan Plo+Dt ($p = 0,047$). IL-17 juga meningkat bermakna pada kelompok Do+Dt ($p = 0,003$) dan Plo+Dt ($p = 0,046$). Korelasi negatif moderat antara kadar 25(OH)D dan total lesi ditemukan pada kelompok Do+Dt ($r = 0,375$; $p = 0,027$), tetapi tidak pada kelompok lain. Tidak ada perbedaan efek samping bermakna di antara kelompok perlakuan ($p = 0,301$). Vitamin D, melalui reseptor pada sebosit dan monosit, terbukti efektif sebagai terapi adjuvan pada AV inflamasi. Kombinasi vitamin D oral dan topikal selama delapan minggu dapat mengurangi derajat keparahan AV inflamasi, terutama melalui peningkatan IL-10. Temuan ini mendukung potensi vitamin D sebagai terapi alternatif untuk AV.

.....Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous glands of the skin that affects quality of life and psychology. The gold standard therapy for moderate to severe AV still faces challenges related to side effects and resistance. The inflammatory process has been reported to occur before hyperkeratinization, and Cutibacterium acnes triggers inflammation. Sebocytes and keratinocytes are potential therapeutic targets, but clinical evidence is limited. Studies have shown that vitamin D has the potential as an anti-inflammatory agent through the vitamin D receptor (VDR) on sebocytes. This study aims to assess the Efficacy and Safety of Oral and Topical Vitamin D in Acne Vulgaris: A Study on the Expression of VDR, IL-1, IL-6, IL-10, and IL-17. This study was a double-blind randomized experimental study. A total of 105 subjects with moderate to severe inflammatory AV underwent therapy at the Cosmetic Dermatology Division Polyclinic, Department of Dermatology and Venereology, Dr. Cipto Mangunkusumo National Hospital, and biomarker evaluation in the Integrated Laboratory of the Faculty of Medicine, University of Indonesia for eight weeks. The subjects were divided into three groups: Experimental group: oral vitamin D 2000 IU + topical vitamin D + topical adapalene (Do+Dt). Oral placebo group + topical vitamin D + topical adapalene (Plo+Dt). Control group: oral placebo + topical placebo + topical adapalene (Plo+Plt). Serum 25-hydroxyvitamin D (25(OH)D) levels were measured by ELISA. VDR expression in lesions was evaluated using flow cytometry, and inflammatory cytokines (IL-1b, IL-6, IL-10, IL-17) were analyzed by Luminex. Clinical changes were assessed at each visit (weeks 0, 1, 2, 4, 6, and 8). Flow cytometry analysis results showed that the proportion of VDR (+) in monocytes was higher than in sebocytes and keratinocytes. Pre-treatment 25(OH)D levels had a weak positive correlation with the proportion of VDR (+) monocytes ($r = 0,27$; $p = 0,004$) and VDR (+) sebocytes ($r = 0,18$; $p = 0,04$). A weak positive correlation was also found between the proportion of VDR (+) monocytes and total AV lesions before treatment ($r = 0,28$; $p = 0,007$).

Significant reduction of inflammatory lesions, non inflammatory lesions, and total lesions was found in each group ($p < 0,05$), however, there is no significant difference between each group ($p > 0,05$). The greatest clinical improvement was found in the Do+Dt group (63%), followed by Plo+Dt (57,1%) and Plo+Plt (54,5%). However, the difference in lesion reduction was not statistically significant ($p < 0.30$). At the second visit, IL-1b decreased significantly in all groups ($p = 0.016$, $p = 0.012$, $p = 0.004$), while IL-6 showed no significant change. IL-10 increased significantly in the Do+Dt ($p = 0,012$) and Plo+Dt ($p = 0,047$) groups. IL-17 also increased significantly in the Do+Dt ($p = 0.003$) and Plo+Dt ($p = 0,046$) groups. A moderate negative correlation between 25(OH)D levels and total lesions was found in the Do+Dt group ($r = 0.375$; $p = 0,027$), but not in the other groups. There was no significant difference in side effects between treatment groups ($p = 0,301$). Vitamin D, through receptors on sebocytes and monocytes, has been shown to be effective as an adjuvant therapy for inflammatory AV. A combination of oral and topical vitamin D for eight weeks can reduce the severity of inflammatory AV, mainly through increasing IL-10. These findings support the potential of vitamin D as an alternative therapy for AV.