Efek vitamin D terhadap respons imun adaptif penyakit graves telaah mengenai pematangan sel dendritik = Effects of vitamin D on adaptive immune responses in graves disease a study on maturation of dendritic cells

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Abstrak

Latar belakang. Pada penyakit graves (GD), konsentrasi vitamin D berbanding terbalik dengan titer antibodi dan berbanding lurus dengan status remisi. Pembentukan autoantibodi diawali dari pajanan self antigen oleh sel dendritik (DC), sebagai antigen presenting cell (APC), ke sel T naif. Kemampuan DC sebagai APC ditentukan oleh tingkat kematangannya. Sel dendritik, APC utama pada GD, bersifat lebih aktif dalam respons imun dibandingkan dengan subjek sehat. Studi pada SLE, MS, dan penyakit crohn menunjukkan efek imunoregulator vitamin D terutama melalui hambatan pematangan DC sehingga fungsi imunogenitasnya berkurang.
Tujuan. Mengetahui efek 1,25-D3 in vitro dan 1-D3 in vivo terhadap pematangan DC pasien GD
Metode. Pada periode Mei 2014 sampai dengan Maret 2015 dilakukan studi eksperimental dan klinis, masing-masing pada 12 dan 25 pasien GD fase hipertiroid. Pada studi eksperimental, dilakukan kultur monocyte derived dendritic cell (MDDC) pasien GD dengan atau tanpa intervensi 1,25-D3 in vitro pada tahap monosit dan maturasi distimulasi dengan lipopolysaccharide (LPS). Pada studi klinis, sebanyak 12 dan 13 pasien GD, masing-masing mendapatkan 1-D3 dan plasebo selama 8 minggu, di samping mendapatkan terapi standar PTU 100 mg 3 kali sehari. Kultur MDDC dilakukan sebelum dan sesudah suplementasi dan dilakukan perbandingan pematangan DC sebelum dan sesudah suplementasi pada kedua kelompok. Pematangan DC dilihat dari ekspresi penanda DC (HLA-DR, CD80, CD40, CD83, CD14, dan CD206) dan rasio sitokin IL-12/IL-10 pada supernatan kultur.
Hasil. Pada studi in vitro, pascastimulasi LPS, DC yang dikultur dengan 1,25-D3 menunjukkan ekspresi HLA-DR, CD80, CD40, dan CD83 lebih rendah serta ekspresi CD14 dan CD206 yang lebih tinggi dibandingkan dengan DC yang dikultur dengan LPS saja. Pada DC yang dikultur dengan 1,25-D3, didapatkan rasio IL-12/IL-10 lebih rendah daripada DC tanpa 1,25-D3. Pada studi klinis, apabila dibandingkan antara ekspresi penanda DC serta rasio IL-12/IL-10 sebelum dan sesudah suplementasi 1-D3 selama 8 minggu, belum didapatkan perbedaan yang bermakna pada ekspresi penanda DC dan rasio sitokin IL-12/IL-10.
Simpulan. Pemberian 1,25-D3 in vitro menghambat pematangan DC pasien GD, sedangkan efek pemberian 1-D3 in vivo terhadap pematangan DC belum dapat ditunjukkan pada penelitian ini.
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Background. In graves? disease (GD), vitamin D levels is inversely proportional to antibody titer and proportionally associated with remission status. The development of autoantibody is initiated by self-antigen exposure by dendritic cells (DC) as the antigen presenting cells (APC) to the naïve T cells. The ability of DC as APC is determined by its maturity level. Dendritic cells, the major APC in GD, have more active immune responses than those in healthy subjects. Studies on systemic lupus erythematosus (SLE), multiple sclerosis (MS) and crohn?s disease have demonstrated immunoregulator effects of vitamin D, mainly

through inhibition of DC maturation, which may lead to lower immunogenic function.
Aim. To identify the effect of 1,25-D3 in vitro and 1-D3 in vivo on DC maturation in patients with GD.
Method. Our study consisted of an experimental and a clinical study started from May 2014 until March 2015, which was conducted in 12 and 25 GD patients with thyrotoxicosis, respectively. In the experimental study, cultures of monocyte derived dendritic cell (MDDC) of GD patients were performed, with or without intervention of 1,25-D3 in vitro at monocytic phase and the maturation was stimulated by lipopolysaccharide (LPS). In the clinical study, there were 12 GD patients who received 1-D3 supplementation and 13 GD patients who received placebo for 8 weeks, in addition to the standard treatment of PTU 100 mg three times a day. MDDC cultures and comparison of DC maturation were performed before and after the supplementation for both groups. DC maturation was evaluated based on the expression of DC markers (HLA-DR, CD80, CD40, CD83, CD14 and CD206) and the ratio of cytokines IL-12/IL-10 levels in the culture supernatants.
Results. In the in vitro study and following the LPS stimulation, DC cells cultured with 1,25-D3 showed lower expression of HLA-DR, CD80, CD40 and CD83 and higher expression of CD14 and CD206 compared to DC cultured with LPS alone. DC, which were cultured with 1,25-D3 had lower ratio of IL-12/IL-10 levels than those cultured without 1,25-D3. In the clinical study, when the expression of DC marker as well as the ratio of IL-12/IL-10 levels between before and after the 8-week supplementation of 1-D3 were compared, we found no significant difference on the expression of DC markers and the ratio of IL-12/IL10.
Conclusion. In vitro 1,25-D3 supplementation inhibits DC maturation in patients with GD; while the effects of in vivo 1-D3 treatment on DC maturation have not been clearly demonstrated in the present study yet.