DISERTASI

EFEK SUPLEMENTASI VITAMIN D TERHADAP KEJADIAN INFEKSI TUBERKULOSIS PADA ANAK BAWAH LIMA TAHUN SEHAT YANG TERPAPAR *Mycobacterium tuberculosis*

Tinjauanterhadapkadarvitamin D,IFN-γ,katelisidin, aktivitas fagositosis makrofag dan polimorfisme genetik reseptor vitamin D secara in vivo dan in vitro

FINNY FITRY YANI
NIM. 103 120 2005

Nama Pembimbing :

1. **Prof. dr. Nur Indrawati Lipoeto, MSc, PhD, SpGK**
2. **Prof. Dr. dr. Bambang Supriyatno, SpA (K)**
3. **Prof. Dr. dr. Eryati Darwin, PA (K)**

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ABSTRAK

Efek Suplementasi Vitamin D terhadap Kejadian Infeksi Tuberkulosis pada Anak Bawah Lima Tahun Sehat yang Terpapar *Mycobacterium tuberculosis*

Tinjauan terhadap kadar vitamin D, IFN-γ, katelisidin, aktivitas fagositosis makrofag dan polimorfisme genetik reseptor vitamin D secara in vivo dan in vitro

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Latar belakang. Peningkatan prevalensi tuberkulosis (TB) di Indonesia juga akan meningkatkan risiko tertular pada anak balita, yang memiliki sistem imun belum sempurna. Hal ini akan berisiko menjadi penyakit berat, cacat dan meninggal. Saat ini upaya intervensi untuk meningkatkan sistem imun pada balita belum menjadi perhatian pada program penanggulangan TB. Vitamin D diketahui dapat meningkatkan imunitas alamiah, menghambat invasi bakteri, sehingga melindungi dari terjadinya infeksi tuberkulosis.

Tujuan. Penelitian ini bertujuan menilai efek suplementasi vitamin D terhadap kejadian infeksi tuberkulosis pada anak balita sehat kontak *Mycobacterium tuberculosis* melalui tinjauan terhadapkadar vitamin D, IFN-γ, katelisidin, aktivitas fagositosis makrofag dan polimorfisme genetik reseptor vitamin D secara in vivo dan in vitro.

Metode. Disain penelitian adalah studi intervensi secara acak terkontrol buta ganda dengan pengamatan berulang. Skrining awal pada 225 anak balita kontak TB di 22 puskesmas kota Padang, dan didapatkan anak yang memenuhi kriteria sebanyak 136 dan dapat dianalisis adalah 66 subjek penelitian. Kriteria inklusi anak balita kontak TB dengan hasil uji tuberkulin negatif (sehat). Intervensi berupa suplementasi vitamin D3 2 x @ 25.000 IU, dengan interval 6 minggu, dan dipantau sampai 12 minggu. Dilakukan pengukuran pada awal dan diulang setelah 12 minggu, terhadap indikator kadar vitamin D, IFN-**γ,** katelisidin (ELISA) dan aktivitas makrofag. Dilakukan juga pemeriksaan gen RVD (PCR). Analisis statistik dilakukan dengan chi-square untuk perbedaan proporsi kejadian infeksi dan uji t-independent untuk perbedaan rerata semua indikator pada data akhir intervensi. Persetujuan etik telah didapatkan dari Fakultas Kedokteran Universitas Andalas.

Hasil. Tidak terdapat perbedaan infeksi TB pada kedua kelompok intervensi dan plasebo (p=0,855). Data awal menunjukkan pada semua subjek, rerata kadar vitamin D <30 ng/ml, IFN-γ rendah, katelisidin normal, aktivitas fagositosis >80%. Sebagian besar memiliki gen mutan untuk jenis gen FokI (93,9%), ApaI (72,7%), TaqI (94%), gen BsmI mutan lebih sedikit (25,8%). Suplementasi vitamin D secara bermakna meningkatkan kadar vitamin D dengan rerata 28,47±7,19 dengan p= 0,003. Tidak terdapat perbedaan bermakna rerata kadar vitamin D, IFN-γ, katelisidin dan aktivitas fagositosis makrofag antara kedua kelompok intervensi dan plasebo. Terdapat

perbedaan bermakna pada gen BsmI terhadap perubahan kadar vitamin D antar ke dua kelompok intervensi dan plasebo (p = 0,003).

Kesimpulan. Suplementasi vitamin Dselama 12 minggu tidak memberikan pengaruh terhadap kejadian infeksi TB pada anak balita sehat kontak TB, akan tetapi sudah meningkatkan kadar vitamin D dalam serum. Terdapat peran gen BsmI mutan dalam peningkatan kadar vitamin D.

ABSTRACT

Effect of Vitamin D Supplementation on Tuberculosis Infection among Under-Five Healthy Children Exposed to Mycobacterium tuberculosis

Focus on analyze of vitamin D, IFN-γ, and cathelicidin levels, phagocytic activity of macrophages and genetic polymorphisms of vitamin D receptor based on in vivo and in vitro

Finny Fitry Yani

***Background**. Prevalence of tuberculosis (TB) in Indonesia remains high that directly increase the risk of infection among under-five healthy children, whose immune systems are not fully developed. This children can suffer severe illness, disability, and death. It is important to boost the immune system among under-five healthy children, but it has not yet be a concern in the TB control program now. Vitamin D is known to affect innate and adaptive immunity, inhibit bacterial invasion, therefore will protect from tuberculosis infection.*

***Aim**. This study aims to evaluate the effects of vitamin D supplementation towards the incidence of tuberculosis infection among under-five healthy children with Mycobacterium tuberculosis contact through levels of vitamin D, IFN-γ, cathelicidin, phagocytic activity of macrophages, and vitamin D receptor genetic polymorphisms in vivo and in vitro.*

***Method**. A randomized, double-blind, placebo-controlled trial was conducted. Initial screening among 225 under-five children with TB contact in 22 primary health cares in Padang was done. Among 136 children were eligible for this study, only 66 of them were analyzed. The inclusion criteria was under five children whose tuberculin skin test were negative (healthy). Vitamin D3 supplementation was given two times, each 25.000 IU, with an interval of 6 weeks, and monitored until 12 weeks. Measurements were performed at baseline and repeated after 12 weeks towards the indicators levels of vitamin D, IFN-γ, cathelicidin (ELISA) and macrophage phagocytosis activity. RVD gene was also assessed (PCR). Categorical variableswere assessed with chi-square test and continuousvariables were compared by using independent t-test. Ethics approval was obtained from the Ethics Committee from Faculty of Medicine, Andalas University.*

***Results**. There were no difference ofTB infectionbetween intervention and placebo groups(p=0.855). Baseline characteristics showed, the mean levels of vitamin D <30 ng / ml, low IFN-γ, normal cathelicidin, and phagocytic activity > 80%. Most of the subjects have mutant FokI(93.9%), ApaI (72.7%), TaqI (94%), and mutant BsmI was found fewer (25.8%). Vitamin D supplementation significantly increasedvitamin D level with the average of 28.47 ± 7.19, p = 0.003. There were no significant differences in mean levels of vitamin D, IFN-γ, cathelicidin, and macrophage activity*

between the two groups. BsmI has a role in the alteration of vitamin D level, this study showed significant differences between the two groups (p = 0,003).

***Conclusion**. Supplementation of vitamin Dfor 12 weeks among under-five healthy children with TB contacts did not affect to the incidence of TB infection, but it has increased of vitamin D serum levels. There was an association between mutant genes of VDR BsmIto the rise of vitamin D levels.*


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