

ANALISIS SUPLEMENTASI SENG TERHADAP RESPONS IMUN NARAKONTAK KUSTA YANG SEROPOSITIF

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ABSTRACT

Incidence of leprosy showed no decline; it happened since there was no prevention or preventive medicine for seropositive contact of leprosy patients. Zinc supplementation was expected to improve their cell mediated immunity response

The aim of this research was to analyze the influence of zinc supplementation toward immunity response of seropositive contact of leprosy patients.

This research was experiment with pre post control group design. Research sample was seropositive contact of leprosy patients with marginal zinc deficiency. The amount was 22 people, 11 people for each group treatment and control. Seropositive leprosy was determined by examining IgM anti PGL – 1 level using Elisa method. Zinc plasma level was measured with atomic absorption spectrophotometer. Zinc supplementation dosage was 40 mg/per day as zinc sulphate given for 90 days. IFN gamma and IL – 2 level were measured with Elisa method.

The result showed no significant increase of IFN gamma and IL – 2. However, a major decline of IFN gamma and IL – 2 happened on control group. There was significant change of IL-2 level between both groups.

Zinc supplementation could modulate T – Cell to maintain IFN gamma and IL – 2 level productions since zinc took part in intracellular signal to produce cytokine. Zinc supplementation ineffectiveness happened since *Mycobacterium leprae* could impair host immune response, high ratio of phytate:zinc, *Mycobacterium leprae* capability to compete the host by zinc acquisition, supplementation length, and zinc interaction with other nutrients.

Further research needs to be done by increasing the length of supplementation and giving others micronutrient.

Key word: seropositive leprosy, zinc supplementation, IFN gamma, IL - 2

RINGKASAN

ANALISIS SUPLEMENTASI SENG TERHADAP RESPONS IMUN NARAKONTAK KUSTA YANG SEROPOSITIF

Sampai saat ini penyakit kusta masih merupakan salah satu masalah kesehatan masyarakat di Indonesia karena penderita baru kusta cenderung meningkat, hal ini kemungkinan karena adanya narakontak kusta yang seropositif telah berubah menjadi kusta manifes. Salah satu metoda untuk mendeteksi adanya subyek yang sudah masuk seropositif kusta adalah dengan memeriksa kadar *Imunoglobulin M (IgM) anti Phenolic Glycolipid (PGL)-1*.

Pencegahan dengan menggunakan pengobatan sedini mungkin seperti kemoprofilaksis, akan lebih baik pada penyakit kusta. Namun pengobatan pencegahan membutuhkan biaya yang sangat besar dengan operasional lapangan yang sangat sulit, sedangkan hasil yang diperoleh sangat terbatas. Sehingga pencegahan tanpa obat kemungkinan lebih efisien.

Penyakit kusta juga dianggap sebagai penyakit imunologik karena peranan imunitas seluler pada pasien sangat besar. Derajat respon imunitas seluler akan menentukan spektrum penyakit kusta. Beberapa penelitian menunjukkan bahwa respon imun dipengaruhi oleh asupan gizi mikro, misalnya seperti seng.

Kadar seng serum pada pasien kusta sesuai dengan spektrum penyakit kusta yang merupakan gambaran derajat respons imunitas seluler. Beberapa laporan penelitian menunjukkan penurunan kadar seng serum pada pasien kusta secara bertahap mulai dari tipe Pausi Basiler sampai Multi Basiler, dengan kadar terendah pada tipe Multi Basiler.

Seng juga berpengaruh pada produksi sitokin seperti interferon (IFN)- γ , dan interleukin (IL)-2. Sitokin produk sel T *helper* 1 (Th1) seperti IFN- γ dan IL-2 menurun pada penelitian dengan *cell lines* yang dibuat defisiensi seng. Produksi IFN- γ dan IL-2 kembali membaik setelah suplementasi seng.

Narakontak kusta yang seropositif sering kelak menjadi penderita kusta dengan manifes tipe multibasiler (MB). Kekebalan seluler penderita kusta tipe MB menunjukkan penurunan bahkan sudah anergi dan berubah menjadi kekebalan humoral (tipe Th2), yang justru memperburuk kondisi penderita. Agar kekebalan seluler penderita seropositif tetap bekerja dengan baik, maka suplementasi seng diharapkan mampu memperbaiki kekebalan seluler (tipe Th1). Indikator kekebalan seluler (tipe Th1) yang baik dapat diukur dengan kadar sitokin yang dihasilkan oleh sel Th1 yaitu IFN- γ dan IL-2.

Penelitian menggunakan eksperimen dengan *pre post control group design*. Penelitian dilakukan di Kecamatan Brondong, Kabupaten Lamongan tahun 2009. Sampel penelitian adalah mereka yang memenuhi kriteria inklusi berusia 20 – 40 tahun (laki-laki maupun perempuan) dengan hasil uji *screening* menunjukkan serologi positif kusta (kadar IgM anti PGL – 1 antara 600 unit/ml-1500 unit/ml) dengan status seng marjinal (kadar seng plasma 10,7 - 13,0 $\mu\text{mol/L}$); Secara anamnestik dan klinis tidak menunjukkan ada gejala penyakit kusta dan tidak minum obat anti kusta serta tidak menderita penyakit yang dapat mempengaruhi status seng; Anamnestik tidak pernah menderita batuk darah dan tidak minum obat anti tuberkulosa; Tidak minum obat anti imunosupresan dalam tiga bulan terakhir sebelum pemeriksaan darah; Indeks massa tubuh di atas 18 kg/m^2 .

Dosis seng yang diberikan adalah 40 mg/hari dengan lama pemberian 90 hari. Kepatuhan mengkonsumsi suplemen dipantau oleh peneliti dan petugas kesehatan setempat

(Puskesmas). Kunjungan kerumah untuk memantau telah dilakukan dua kali dalam seminggu.

Pengukuran kadar IgM anti PGL – 1 (dengan metode ELISA) dan kultur sel limfosit dilakukan di Laboratorium Institut Tropical Disease, Univ Airlangga, Surabaya. Pengukuran kadar seng plasma dilakukan dengan metode *Atomic Absorbion Spectrophotometer* dikerjakan Balai Besar Laboratorium Kesehatan Surabaya. Pengukuran kadar IFN- γ dan IL-2 dilakukan dengan metode ELISA dikerjakan di laboratorium patologi klinik Rumah Sakit Dr. Soetomo, Surabaya. Asupan makanan sehari-hari telah diukur dengan metode *recall* dan frekuensi makanan.

Kadar IFN- γ dan IL – 2 setelah diberi lepromin mengalami penurunan pada kelompok kontrol, sedangkan pada kelompok perlakuan relatif tetap. Hal ini menunjukkan bahwa suplementasi seng dapat menahan penurunan kadar IFN- γ dan IL – 2. Sebaliknya pada kelompok kontrol, terjadi penurunan yang lebih besar. Pada kelompok kontrol, hal tersebut dapat dijelaskan karena bakteri *Mycobacterium leprae* telah mengganggu respon imun penjamu. Sebaliknya kemampuan seng menahan penurunan kadar IFN- γ dan IL – 2 dapat dijelaskan karena seng berperan dalam sinyal intraseluler untuk memproduksi ke dua sitokin tersebut.

Pemberian hanya satu zat gizi saja (seng) pada penelitian ini, kemungkinan hanya mampu menahan penurunan IFN- γ dan IL – 2, belum mampu meningkatkannya. Kemungkinan lain adalah kemampuan bakteri berkompetisi dengan penjamu dengan mengakuisisi seng. Lama suplementasi seng selama tiga bulan pada penelitian ini kemungkinan juga masih belum cukup untuk melihat efek terhadap peningkatan IFN- γ dan IL – 2. Defisiensi seng *in vivo* secara umum merupakan proses yang lama dan dapat berlangsung dari hitungan hari bahkan sampai tahunan, demikian juga proses perbaikan respon imun akibat defisiensi seng kemungkinan juga membutuhkan waktu yang tidak sebentar. Hal ini mengingat terdapat lebih dari 1000 gen yang merespon terhadap seng dan banyak diantara gen tersebut terlibat dalam transduksi sinyal dan fungsi sitokin.

Saran penelitian ini adalah penelitian lebih lanjut dengan jangka waktu suplementasi yang lebih lama dan ditambah dengan beberapa zat gizi mikro lainnya.

SUMMARY

ANALYSIS OF ZINC SUPPLEMENTATION ON IMMUNE RESPONSES IN SEROPOSITIVE CONTACT OF LEPROSY PATIENT

Up to now Leprosy is still one of public health problems in Indonesia since new leprosy patient is increasing. It happens because seropositive contact of leprosy patient has changed into manifest leprosy. Detecting subject seropositif leprosy can be done by using various methods; one of them is by examining *Immunoglobulin M (IgM) anti Phenolic Gliko Lipid (PGL)-1* level.

Early treatment prevention with chemoprophylaxis will be better for leprosy. Preventive treatment, however, will cost much money and huge operational cost whereas the result is very limited. Therefore, prevention without drugs is more likely to be efficient.

Leprosy is considered as immunologic disease since the role of cellular immunity is immense. Cellular immunity respond level will determine leprosy spectrum. Some researches show that immunity respond is influenced by micro nutrient such zinc.

Zinc serum level which is appropriate with leprosy spectrum describes cellular immunity respond level. Some research results show gradual decrease of zinc serum level on leper type PB to MB. The lowest level is found on MB type.

Zinc gives influence for cytokine product such as interferon (IFN)- γ , interleukin (IL)-2. Cytokine product of T-helper 1 (Th1) cell, such as IFN- γ and IL-2, weaken on research with zinc deficiency cell lines. They are improving after zinc supplementation.

Seropositive contact of leprosy patient has a tendency to change into leprosy multibacilar type (MB). Cellular immunity of Leprosy MB is decreasing or even anergy and it turns into humoral immunity (Th2) which makes patient's condition worse. To make cellular immunity seropositive leprosy works, zinc supplementation is expected to cure cellular immunity (type Th1). A good indicator of cellular immunity (type Th1) can be examined by cytokine level which is produced by Th1 cell namely IFN- γ and IL2.

This research was an experiment with pre post control group design. The research was conducted in Kecamatan Brondong, Kabupaten Lamongan year 2009. Research samples were those who meet the inclusion criteria on the age of 20 to 40 years old (both male and female) whom proven to be positive with serology leprosy (IgM anti PGL-1 level is 600 - 1500 unit/ml) and have marginal zinc status (zinc plasma level 10,7 - 13,0 $\mu\text{mol/L}$). They were not clinically shown any leprosy symptoms and they don't consume anti-leprosy medicine. They also don't have any disease which influenced their zinc status; they don't suffer from tuberculosis and don't consume any anti-tuberculosis medicine; they don't consume any anti-immunosupresan in the last three months before blood samples are taken; their body mass indexes are more than 18 kg/m^2 and are willing to join the research by signing *informed concern*.

Zinc dosage given was 40 mg/day for about 90 days. The obedience of consuming supplement was monitored by the researcher and local health staff (Puskesmas). Home visit was conducted twice a week.

The measurement of IgM anti PGL-1 level (using ELISA method) and lymphocytes cells culture was done in the Institute Tropical Disease Laboratory, Airlangga University, Surabaya. The measurement of zinc plasma level is accomplished by Atomic Absorption Spectrophotometer method in Balai Besar Laboratorium Kesehatan Surabaya. The measurement of IFN- γ and IL-2 level is performed using ELISA method in Laboratorium patologi Dr. Soetomo hospital, Surabaya. Daily intake was measured using *recall* method and food frequency.

IFN- γ and IL - 2 levels weaken on control group after lepromin given, whereas on treatment group is relatively stable. This shows that zinc supplementation is able to maintain IFN- γ and IL - 2 decreases. On the other hand, on control group, there was a significant decrease. It could be explained that on control group, *Mycobacterium Leprae* has interfered the host immunity respond. On the contrary, zinc ability to endure the decrease of IFN- γ and IL-2 level could be clarified since zinc takes part in intracellular signal to produce both cytokines.

Providing only one type of nutrition namely zinc on this research can bear the decrease of IFN- γ and IL-2; however, it cannot yet increase the level. Other possibility is the bacteria ability to compete with the host by zinc acquisition. Three months of giving

supplementation in this research is not enough to find out the effect toward the increase of IFN- γ and IL-2 level. Zinc deficiency *in vivo* in general is quite a long process and can last for days or even years; so does the recovery process of immunity respond caused by zinc deficiency since there are more than 1000 genes which respond toward zinc and many of them take part in transduction of cytokine signal and function.

Further research needs to be done by increasing the length of supplementation and giving others micronutrient.

