Peran mutasi gen filaggrin dan polimorfisme gen fatty acid desaturese terhadap kejadian dermatitis atopik pada bayi: kajian perubahan komposisi asam lemak tidak jenuh ganda = The Role of filaggrin gene mutation and fatty acid desature gene polymorphisms towards the composition of long chain polyunsaturated fatty acid on infant atopic dermatitis

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Abstrak

ABSTRAK
Patomekanisme dermatitis atopik melibatkan interaksi yang kompleks antara genetik dan lingkungan. Satu gen yang secara konsisten berhubungan dengan DA adalah mutasi gen Filaggrin yang dapat mengganggu agregasi sitoskeleton epidermis. Beberapa usaha pencegahan telah dilakukan antara lain dengan pemberian ASI eksklusif dan suplementasi LCPUFA, tetapi studi klinis dan meta-analisis tidak menunjukkan hasil yang konsisten. Inkonsistensi ini dapat disebabkan adanya variasi aktivitas enzim desaturase yang dapat memodulasi metabolisme PUFA, yang diatur oleh gen FADS1 dan FADS2, serta usia saat intervensi dilakukan. Diperkirakan periode in-utero memegang peran penting untuk keberhasilan intervensi.
Penelitian ini bertujuan mengetahui peran mutasi gen FLG dan polimorfisme gen FADS1 dan FADS2 terhadap timbulnya DA pada usia satu tahun. Tujuan Khusus yaitu mengetahui frekuensi mutasi gen FLG dan polimorfisme gen FADS1 dan FADS2, mengetahui peran polimorfisme gen FADS1 dan FADS2 terhadap substrat dan produk LCPUFA dan efeknya terhadap timbulnya DA, mengetahui pengaruh peningkatan rasio AA terhadap DHA di awal kehidupan terhadap timbulnya DA, mengetahui peran protektif ASI eksklusif untuk pencegahan DA.
Digunakan dua desain penelitian 1) potong lintang untuk mengetahui peran polimorfisme gen FADS1 dan FADS2 terhadap perubahan komposisi LCPUFA saat lahir, 2) analisis kesintasan untuk melihat pengaruh mutasi gen Filaggrin dan polimorfisme gen FADS1 dan FADS2 terhadap timbulnya DA, mengetahui peran peningkatan rasio AA/DHA serta mengetahui efek protektif ASI eksklusif terhadap timbulnya DA pada usia satu tahun.
Insidens DA dalam penelitian ini sebesar 15,4%. Tidak ditemukan 5 mutasi gen Filaggrin sesuai dengan data NCBI. Frekuensi alel minor pada polimorfisme gen FADS1 22−27%, sedangkan untuk FADS2 berkisar 15−48%. Dalam penelitian ini terlihat pengaruh polimorfisme gen FADS1 dan FADS2 terhadap perubahan komposisi LCPUFA, khususnya peningkatan asam arakidonat pada kelompok alel minor. Dalam penelitian ini tidak ditemukan hubungan antara komposisi LCPUFA dan polimorfisme gen FADS terhadap timbulnya DA. Pemberian ASI eksklusif selama 3−6 bulan tampaknya memberi efek proteksi terhadap DA
PeneIitian ini diharapkan dapat menjadi landasan untuk tindakan pencegahan DA.

Penelitian ini tidak berhasil menemukan common mutation yang dilaporkan NCBI. Mutasi gen Filaggrin tergantung perbedaan ras, maka untuk menemukan mutasi yang baru lebih baik digunakan sekuensing gen secara penuh. Adanya perbedaan frekuensi alel minor antara anak Indonesia dan Eropa dan aktivitas enzim yang bekerja dengan arah yang berlawanan dengan alel minor populasi Eropa, mengakibatkan peningkatan kadar AA dan DGLA pada populasi alel minor dalam penelitian ini.

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ABSTRACT

Pathomechanism of atopic dermatiis is linked to the gene-environment interactions. One genetic locus consistently linked with AD is mutations of filaggrin gene that can induce disruption in epidermal cytoskeleton aggregation. Some protective measures for the prevention of AD are breastfeeding and the provision of LCPUFA, but clinical studies and meta-analysis have shown inconsistent results, which maybe due variation in the activity of desaturating enzymes modulating PUFA metabolism, which are encoded by the FADS1 and FADS2 gene cluster and the age at which LCPUFA interventions are provided.

The general objective is to characterize the impact of genetic variation in the FLG and FADS1, FADS2 genes cluster on LC-PUFA concentration in Indonesian infants. Specific objectives including the characterization of the frequency of FLG and FADS1, FADS2 gene single nucleotide polymorphisms (SNPs), the influence of FADS gene polymorphisms on fatty acid composition and on the occurence of AD, the impact of increasing ratio of arachidonic acid to docosahexaenoic acid on the progression of AD, and to see the protective effect of exclusive breastfeeding for the prevention of AD in the first year of life in Indonesian infants.

Designs were 1) cross-sectional study to see the role of FADS1 and FADS2 gene polymorphism on the composition of LCPUFA at birth, 2) survival analysis to see the role of FLG mutation and FADS1 and FADS2 gene polymorphism on the progression of AD, the role of increasing ratio of AA/DHA and the protective effect of exclusively breastfeeding on the occurence of AD in the first year of life.

The incidence of AD in this study is 15.4%, No Filaggrin gene mutations based on 5 reported pathogenic SNP was found. The minor allele frequency of FADS1 gene polymorphism were 22−27%, whereas for FADS2 were 15−48%. We found a strong correlation between FADS gene polymorphisms with the changes of LCPUFA composition, especially for the increment of arachidonic acid. No association was found between the composition of LCPUFA and between FADS genes polymorphisms with AD. Exclusive breastfeeding until 3 months was found to be protective against AD.

In this study we did not find Filaggrin mutation that reported as pathogenic from NCBI. The frequency of FADS1 polymorphism were 22−27%, whereas FADS2 polymorphism were 15−48%. Strong correlation was seen between genetic variations of FADS genes with the alteration of LCPUFA. Arachidonic acid as the product of LCPUFA was higher in the minor allele compared with the major allele. No association were found between genetic variation of FADS genes and the increased ratio of AA/DHA with the occurence

of AD. Exclusive breastfeeding for 3−6 months seems to give protective effect