

## PENGARUH MAKANAN RINGAN KAYA PATI RESISTEN TERHADAP METILASI PROMOTER GEN MCP-1 DAN KADAR TRIGLISERIDA PASIEN DIABETES MELITUS TIPE 2

Synta Haqqul Fadlilah<sup>1</sup>, Sunarti<sup>2</sup>, Arta Farmawati<sup>2</sup>

1) Mahasiswa Program Pascasarjana FK UGM Yogyakarta Prodi Ilmu Kedokteran Dasar & Biomedis Minat Biokimia

2) Dosen Bagian Biokimia, FK UGM Yogyakarta

**Intisari.** Diabetes melitus tipe 2 (DM tipe 2) berkaitan erat dengan kondisi inflamasi. Salah satu marker inflamasi pada DM tipe 2 ini adalah kemokin *monocyte chemoattractant protein-1* (MCP-1). Modifikasi epigenetik merupakan salah satu mekanisme yang berpotensi dalam meregulasi ekspresi MCP-1. Penelitian sebelumnya menunjukkan bahwa metilasi promotor gen MCP-1 berkorelasi signifikan dengan kadar trigliserida (TG) plasma pasien DM tipe 2. Beberapa studi menyebutkan bahwa kadar TG pada penderita DM tipe 2 dapat dikendalikan melalui konsumsi diet yang mengandung pati resisten. Asam lemak rantai pendek hasil fermentasi pati resisten tersebut diketahui dapat menurunkan lipolisis pada jaringan adiposa, meningkatkan  $\beta$ -oksidasi lemak di hati, dan meningkatkan sensitivitas insulin, sehingga dapat menurunkan kadar trigliserida sirkulasi. Tujuan penelitian ini yaitu untuk mengetahui pengaruh pemberian *snack* kaya pati resisten terhadap metilasi promotor gen MCP-1 dan kadar trigliserida plasma subjek DM tipe 2. Desain penelitian ini adalah *cross-over trial*. Sebanyak 19 subjek DM tipe 2 dipilih dalam penelitian ini dengan kriteria kadar gula darah puasa (GDP) > 126 mg/dL, berusia 40-60 tahun, dan lama menderita DM minimal 1 tahun. Subjek mengkonsumsi *snack* sebanyak 32 g/hari dengan kandungan pati resisten 4,25 g selama 4 minggu, kemudian dilakukan washout 1 bulan untuk menghilangkan efek dari intervensi. Selanjutnya dilakukan pengambilan data kontrol selama 4 minggu. Pengambilan darah dilakukan 4 kali, yaitu sebelum dan sesudah intervensi serta sebelum dan sesudah pengambilan data kontrol. Analisis metilasi promotor gen MCP-1 dilakukan dengan metode *methyalted specific-PCR* (MS-PCR) menggunakan sampel DNA yang diekstraksi dari sel mononuklear, sedangkan analisis kadar TG dilakukan dengan metode kolorimetri enzimatis (*DiaSys Kit*) menggunakan plasma darah. Analisis data metilasi dilakukan dengan uji *Fisher Exact*, sedangkan kadar TG dianalisis menggunakan uji t berpasangan dan uji t tidak berpasangan. Uji korelasi dilakukan menggunakan *Spearman test*. Signifikansi ditandai dengan nilai  $p < 0,05$ . Hasil analisis metilasi menunjukkan bahwa frekuensi status tidak termetilasi (52,6%) dan termetilasi (47,4%) sebelum maupun setelah intervensi sama, sehingga tidak terdapat perbedaan yang bermakna ( $p > 0,05$ ). Kadar trigliserida plasma setelah intervensi mengalami penurunan, namun tidak signifikan. Korelasi antara status metilasi promotor gen MCP-1 dan kadar trigliserida plasma signifikan pada kelompok intervensi, namun tidak signifikan pada kelompok kontrol. Kesimpulan penelitian ini yaitu pemberian makanan ringan kaya pati resisten tidak mempengaruhi perubahan metilasi promotor gen MCP-1 secara signifikan. Pemberian intervensi ini dapat menyebabkan penurunan kadar trigliserida plasma subjek DM tipe 2, namun tidak signifikan secara statistik.

**Kata kunci:** Diabetes melitus tipe 2, pati resisten, metilasi DNA, MCP-1, trigliserida, *methyalted specific-PCR* (MS-PCR)

## EFFECT OF RICH RESISTANT STARCH SNACK ON MCP-1 PROMOTER METHYLATION AND TRIGLYCERIDES LEVELS IN TYPE 2 DIABETES MELLITUS

Synta Haqqul Fadlilah<sup>1</sup>, Sunarti<sup>2</sup>, Arta Farmawati<sup>2</sup>

- 1) Student of Postgraduate Program of Faculty of Medicine UGM Yogyakarta, Program of Basic Medical Sciences and Biomedics, Department of Biochemistry  
2) Lecturer of Biochemistry Department, Faculty of Medicine UGM Yogyakarta

**Abstract.** Type 2 diabetes mellitus (T2DM) is closely related to inflammation. One of inflammation marker in T2DM is monocyte chemoattractant protein-1 (MCP-1). Epigenetic modification is a potensial mechanism of MCP-1 expression regulation. Previous research suggests that MCP-1 promoter methylation correlated significantly with plasma triglycerides levels (TG) in T2DM. Some studies state that TG levels in T2DM can be controlled through consumption of diets containing resistant starch. Short chain fatty acids as the results of resistant starch fermentation is known to decrease lipolysis in adipose tissue, increase  $\beta$ -oxidation of fat in liver, and improving insulin sensitivity, thus lowering circulating triglyceride levels. This study aimed to investigate the effect of high resistant starch snack on MCP-1 promoter methylation and triglycerides levels in type 2 diabetes mellitus. This study was a cross-over trial. A total of 19 T2DM subjects have been selected with the criteria of fasting blood glucose levels (GDP)>126 mg/dL, aged 40-60 years, and duration of DM at least 1 year. Subject consume snack as much as 32 g/day with resistant starch content 4.25 g for 4 weeks, then washout 1 month to eliminate the effects of the intervention. Furthermore, the control data collection for 4 weeks. Blood sampling performed four times, before and after the intervention and before and after taking control data. The analysis of MCP-1 promoter methylation was performed by methylated specific-PCR (MS-PCR) using DNA samples extracted from mononuclear cells, whereas TG levels analysis performed by the enzymatic colorimetric method (DiaSys Kit) using blood plasma. Statistic analysis was performed by Fisher Exact test for methylation data, paired t-test and unpaired t test for TG levels, and Spearman correlation test for the correlation between variabls ( $p < 0.05$ ). Methylation result showed that frequency of “methylated” (52.6%) and “unmethylated” (47.4%) status before and after intervention were same, so there was no significant difference ( $p > 0.05$ ). Plasma triglyceride levels after intervention decreased, but not significant statistically. The correlation between MCP-1 promoter methylation and plasma triglyceride levels was significant in the intervention group, but not significant in the control group. This study concludes that the giving of rich resistant starch snacks intervention does not affect MCP-1 promoter methylation changes significantly. This intervention can lead to decrease plasma triglyceride levels subjects, but not statistically significant.

**Keyword:** Type 2 diabetes mellitus, resistant starch, DNA methylation, MCP-1, triglyceride, methylated specific-PCR (MS-PCR)