Hubungan faktor metabolik dengan respons inflamasi pada sindrom koroner akut pasien diabetes melitus tipe 2. Kajian efek kurkumin terhadap faktor metabolik dan respons inflamasi pada sindrom koroner akut

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Abstrak

Diabetes mellitus (DM) is one of the public health problems worldwide, including in Indonesia. Cardiovascular disease was the main cause of death (75-80%) in DM, three-fourths of this death was caused by coronary heart disease (CHD). Approximately 34.2% of patients with acute coronary syndrome (ACS) receiving care at ICCU of Dr. Cipto Mangunkusumo General Hospital (RSCM) suffered from DM. Mortality rates of ACS in DM patients were still high and ACS prognosis in DM patients were still unfavorable. There are many factors playing a part in atherosclerosis and ACS incidence in DM patients, such as metabolic disorders due to hyperglycemia and the fomration of advanced glycation end product (AGE), oxidative stress, atherogenic dyslipidemia in DM in the form of high triglyceride level and low HDL cholesterol as well as an increase in small dense LDL, and insulin resistance. In addition, other risk factors of CHD frequently encountered with DM were hypertension, obesity, thrombocytc hyperaggregation and hypercoagulation. The management ofthis disease which was based on the control of risk factors was not yet satisfactory.

Inflammatory response played an important role in pathogenesis of atherosclerosis, beginning with early lesion up to acute coronary syndrome. Increase in inflammatory responses (hsCRP) could predict cardiovascular event and predict post-ACS prognosis. Studies in DM population showed an increase in inflammation. ln-depth studies on inflammatory responses in ACS DM patients have not yet been reported. In normal condition, there was a balance of proinflammatory and antiinflammatory cytokines. The ratio of proinflammatory and antiinflammatory cytokines in ACS, particularly DM patients has not been studied. The relationship between metabolic factor (blood glucose, glyco Hb and lipid) and inflammatory response in ACS DM patients has not yet also been studied.

Currently, the effort to decrease inflammatory response is made, among others, by aspirin, statin hypolipidemic medication and insulin sensitizer. Although aspirin and statin were used routinely in ACS patients and have proved to reduce inflammation, morbidity and mortality rates of ACS patients were still high. Thus, we would like to observe whether an addition of other medications in standard therapy could reduce inflammation better. Curcumin in experimental animals-and humans) showed -hypolipidemic effect (decrease 'in absorption and increase in catabolism) and hypoglycemia (effect on PPAR-7). Curcumin also demonstrated antiinflammatory effect. In this study we would like to observe the effects of curcumin on both metabolic factors and inflammatory responses in ACS patients.

PROBLEM IDENTIFICATION
The above elaboration showed a discrepancy associated with inflammatory response in DM ACS patients.

Up to now, the relationship of metabolic factor and inflammatory response in DM ACS has not been clear yet. Likewise, the effects of curcumin on metabolic factor and inflammatory response in ACS have not yet been identified.

OBJECTIVES

To evaluate inflammatory responses in DM ACS and its relationship with metabolic factors (glucose, blood; glyco Hb, total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride); to evaluate the ratio of proinflammatory and antiinflammatory cytokines (IL-6/IL-10) in ACS DM patients, and to identify the effects of curcumin on metabolic factors and inflammatory responses in ACS patients.

SETTING

The study was conducted at ICCU of RSCM, ICCU of Persahabatan, ICCU of RS MMC and ICCU of Medistra Hospital, Cardiology Polyclinic, Department of Internal Medicine, Faculty of Medicine University of Indonesia! RSCM and Integrated Cardiac Service Poiyclinic of RSCM.

STUDY SUBJECTS

ACS patients (DM and non-DM) and CHD (DM and non-DM).

DESIGN

There were two studies: l. Observational design to observe inflammatory responses (hscRP, IL-6, IL-IO, VCAM and ICAM) in DM ACS, non-DM ACS, DM CI-ID, and non-DM CHD; to evaluate the relationship between metabolic factors (fasting blood glucose, blood glucose 2 hours PP, glyco Hb, total cholesterol, LDL cholesterol, HDI.. cholesterol and triglyceride) and inflammatory responses (hsCRP, IL-6, IL-10, VCAM and ICAM) in ACS DM. 2. Interventional study which was a double-blind randomized trial to evaluate the effects of curcumin at escalating doses (low dose 3:-:IS mglday, moderate dose 3x30 mg/day and high dose 3x60 mg/day on metabolic factors (fasting blood glucose. blood glucose 2 hours PP and glyco Hb) and the effects of curcumin at escalating doses on inflammatory responses (hsCRP, ll.-6, VCAM and ICAM) in ACS patients.

RESULTS

In observational study, |46 subjects were analyzed, consisting of 84 ACS patients, (30 DM ACS patients and 54 non-DM ACS), and 62 CHD (25 DM CHD patients and 37 non-DM CHD patients). The results of the study in the four groups of patients showed: 1. Inflammatory response in DM ACS was higher than in DM CHD (hsCRP, p=0.00; II..-6, p=0.00; IL-10, p=0.00) and non-DM ACS (ICAM, P=0.03). 2. The ratio of proinflammatory and antiinflammatory cytokines (IL-6/II..-10) in DM ACS did not differ from that of DM CHD (p=0.2l) and non-DM ACS (p=0.5 l). 3. There was a relationship between metabolic factors and inflammatory responses in DM ACS: triglyceride and ll.-6 (r=O.39, p=0.03) and II..-I0 (r=0.37, p=o.o4).

In interventional study we performed randomization in 75 ACS patients divided into four groups, consisting of low-dose curcumin group of 15 patients, moderate-dose curcumin group of 15 patients, high-dose curcumin group of IS patients, and placebo group of 30 patients. The results of the study in these four groups showed: l. Low-dose curcumin showed a decrease in hsCRP in one week ofthe first month after

intervention, there was a significant difference liom that of placebo (p=0.04). Low-dose, moderate-dose, high-dose curcumin groups showed a decrease in IL-6, but was not significantly different from placebo. Low-dose, moderate-dose, high-dose curcumin did not show a decrease in VCAM and ICAM after intervention of 2 months. 2. Low-dose curcumin group tended to experience a decrease in glyco Hb level after intervention of 2 months (p=0.06); however, it was not significantly different from that of placebo. 3. There was a tendency that low-dose curcumin reduced total cholesterol and LDI. cholesterol; however, it was not significantly different from that of placebo. There was a tendency that low-dose curcumin increased HDL cholesterol; however, it was not significantly different from that of placebo. 4. There was a tendency that the pattern of escalating doses had some effects in inflammatory responses and metabolic factors, in which low-dose curcumin showed the best effects, followed by moderate-dose and finally high- dose curcumin.

CONCLUSIONS

In this study, inflammatory responses in DM ACS patients were higher than those in DM CHD and non-DM ACS patients. There was no difference in the ratio of proinflammatory and antiinflammatory cytokines (IL-6fIL-IO) in DM ACS compared with DM CHD and non-DM ACS. ln addition, the present study identified some of the relationships between metabolic factors and inflammatory responses. Low-dose curcumin reduced hsCRP in one week of the first month after the intervention in ACS patients. There was a tendency that low-dose curcumin reduced glyco Hb level in ACS.