# RELATIONSHIP BETWEEN PLATELET AGGREGATION AND HS-CRP IN PATIENTS WITH PCI RECEIVING CLOPIDOGREL AND ASPIRIN

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## ABSTRAK

*Penyakit jantung koroner (PJK) adalah penyakit progresif dan berkaitan erat dengan respon inflamasi dan trombosis akut plak aterosklerotik. Penggunaan dosis muatan Klopidogrel 300 mg dan aspirin 200 mg sebagai antiagregasi platelet dilaporkan telah merespon cukup baik. Pembentukan neointimal dan restenosis merupakan komplikasi yang timbul dalam tindakan PCI, dipicu oleh proses inflamasi, IL-6 merangsang pelepasan hsCRP dalam hati. hsCRP sebagai biomarker inflamasi kejadian kardiovaskular masih kontroversial. Dari 15 pasien dengan prevalensi 80% laki-laki, dengan faktor risiko utama untuk dislipidemia, hipertensi dan merokok. Semua pasien ditemukan persen agregasi < 80% termasuk dalam hipoagregasi. Hal ini menunjukkan bahwa dosis muatan Klopidogrel 300 mg dan Aspirin 200 mg memadai sebagai antiagregasi platelet. Terlihat positif rank antara hsCRP kelompok pre (1,12 ± 1,34) dan hsCRP post PCI (2,34 ± 2,03), p = 0,001 (p < 0,05). Hal ini menunjukkan bahwa respon inflamasi terjadi karena aksi PCI. Terlihat korelasi negatif antara hsCRP dan persen agregasi r = -0,16, p = 0,56 (p > 0,05, r < 0,514). Penggunaan dosis muatan Klopidogrel 300 mg dan Aspirin 200 mg sebagai anti agregasi platelet memadai dengan respon hipoagregasi. Respon inflamasi diidentifikasi terjadi karena PCI dengan peningkatan faktor inflamasi hsCRP dan tidak ada korelasi dengan persen agregasi, sehingga hsCRP hanya disebut sebagai faktor inflamasi dan tidak biomarker inflamasi dan tidak secara langsung terkait dengan proses inflamasi dan reoklusi.* ***(FMI 2014;50:219-221)***

***Kata Kunci:*** *hsCRP, Agregasi Platelet, Klopidogrel, Aspirin, Penyakit Jantung Koroner*

## ABSTRACT

*Coronary heart disease (CHD) is a progressive disease and is closely related to the inflammatory response and acute thrombosis of atherosclerotic plaques. Use of loading dose Clopidogrel 300mg and aspirin 200 mg as anti-platelet aggregation reported to have responded quite well. Neointimal formation and restenosis are complications that arise in PCI action, triggered by the inflammatory process, IL-6 stimulates release of hsCRP in the liver. hsCRP as an inflammatory marker of cardiovascular events is still controversial. Of the 15 patients with prevalence of 80% male, with main risk factors are dyslipidemia, hypertension and smoking. All patients were found percent aggregation < 80% is included in hypoagregation. This suggests that loading dose Clopidogrel 300mg and Aspirin 200 mg is adequate as an anti-platelet aggregation. Seen positive ranks between hsCRP group pre (1.12 ± 1.34) and hsCRP post (2.34 ± 2.03), p = 0.001 (p < 0.05). This suggests that the inflammatory response occurs due to the PCI action. Seen negative correlation between hsCRP and percent aggregation r = -0.16, p = 0.56 (p > 0.05, r < 0.514). The use of Clopidogrel 300 mg loading dose and 200 mg aspirin as anti-platelet aggregation is adequate with hypoaggregation response. Identified inflammatory response occurs because of PCI with an increase in inflammatory factors hsCRP and no correlation with percent aggregation, so that hsCRP is only referred to as inflammatory factors and not a biomarkers of inflammation and is not is directly linked to the inflammatory process and reocclusion.* ***(FMI 2014;50:219-221)***

***Keywords:*** *hCRP, Platelet Aggregation, Clopidogrel, Aspirin, Percutaneous Coronary Intervention, Coronary Heart Disease*

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## INTRODUCTION

Coronary heart disease (CHD) is a progressive disease and is closely related to the inflammatory response and acute thrombosis of atherosclerotic plaques. Use of Clopidogrel 300 mg loading dose and 200 mg aspirin as anti-platelet aggregation reported to have responded quite well. PCI (Percutaneous coronary intervention) should be done as an act of invasive therapy in the management of CHD with the indication of chronic occlusion of 70% (fixed occlusion). Neointimal formation and restenosis are complications that arises, triggered by the inflammatory process, invasion of SMCs (Smooth muscle cells), T lymphocytes and macrophages, the response is an increase in the expression of VCAM-1 and ICAM-1, ROS and

proinflammatory cytokines (IL-1 and IL-6). IL-6 stimulates release of hsCRP in the liver. hsCRP as an inflammatory marker of cardiovascular events is still controversial. Sabatine et al (2007), states hsCRP > 1 mg/L lead to the risk of CHD and restenosis after PCI. American Heart Association recommendations on the use of hsCRP is > 3 mg/L are high risk, 1-3 mg/L is a moderate risk, and < 1 mg/L is a lower risk of cardiovascular events and restenosis.

## MATERIALS AND METHODS

Analysis of prospective observational studies in patients with coronary heart disease in non-probability sampling with types of purposive sampling from February to June 2014 Inclusion criteria were all patients of CHD with PCI, exclusion criteria for patients with liver disease, diabetes mellitus, inflammatory/severe trauma, or infection. Patients received loading dose of clopidogrel 300 mg and aspirin 200 mg at 2 hours before PCI. hsCRP was pre-determined at 2 hours before PCI, and hsCRP post and percent of aggregation was determined 24 hours after PCI. We examined percent aggregation of Light Transmitted Agregometry method (LTA) with agonist ADP 20 mμmol. Meaning percent aggregation is hyper aggregation with value > 99%, normoaggregation between value of 80-99% and hypo aggregation < 80%. hsCRP was examined using Chemiluminescence imunoassay method (CLIA). Comparison test was done with the Wilcoxon Signed Rank Test method. Correlation test used Pearson correlation method.

## RESULTS

Fifteen patients with prevalence of 80% male had main risk factors for dyslipidemia, hypertension and smoking. Table 1 show all patients were found percent aggregation < 80% is included in hypo aggregation. This suggests that LD Clopidogrel and Aspirin 200 mg 300 mg is adequate as an anti-platelet aggregation. Table 1 shows positive ranks between hsCRP group pre (1.12 ± 1.34) and hsCRP post (2.34 ± 2.03), p=0.001 (p < 0.05). This suggests that the inflammatory response occurs due to the PCI action. There was negative correlation between hsCRP and percent of aggregation r = -0.16, p = 0.56 (p > 0.05, r < 0.514).

Table 1. Comparison of hsCRP pre and hsCRP post

| Variable | N | Mean hsCRP | P* |
|---|---|---|---|
| hsCRP pre | 15 | 1.12 ± 1.34 | 0.001 |
| hsCRP post | 15 | 1.12 ± 1.34 | |

* Wilcoxon Signed Rank Test

Table 2. Correlation between hsCRP and Percent Aggregation

| Variable | r | P* |
|---|---|---|
| Percent of Aggregation | -0.16 | 0.001 |

* Pearson correlation
NS: negative correlation and not significant

## DISCUSSION

The use of loading dose of 300 mg Clopidogrel and Aspirin 200 mg dose has demonstrated sufficient effect as anti-platelet aggregation. Referring to the study by Montalescot et al (2006) and von Beckerath et al (2005), combination loading dose of Clopidogrel 600 mg and 900 mg with Aspirin 100 mg provides significant percent maximum aggregation at 4 hours after PCI compared dose of Clopidogrel 300 mg induced by ADP 20 µmol/L, and at doses of Clopidogrel 900mg and 600mg showed no significant difference in the percent aggregation, induced by ADP 5 µmol/L and 20 µmol/L. Use of dose Clopidogrel 300mg and Aspirin 100mg in that study resulted in percent aggregation > 80% induced by ADP 20 µmol/L. While in this study at a dose of 300mg Clopidogrel and Aspirin 200 mg resulted in percent aggregation < 80% classified into categories hypo aggregation.

In the inflammatory process associated PCI, hsCRP has several criteria as a risk factor that is > 3 mg/L: high risk, 1-3 mg/L medium risk and < 1 mg/L lower the risk of CHD and reclusion after PCI (Pearson et al, 2003, ACCF/AHA). Sabatine et al (2007) concluded in his research, that instable angina, increased hsCRP, with > 1 mg/L, is a risk factor as a significant predictor of cardiovascular events. In this study, 2 hours before PCI obtain value of pre hsCRP < 1 mg/L at 12 patients in this study showed a low risk of cardiovascular events or reclusion and three patients with value of pre hsCRP > 1 mg/L in patient no. 1, 3 and 14, which is accompanied by the risk factors of dyslipidemia, hypertension and smoking. At 24 hours after PCI obtain value of hsCRP post < 1 mg/L in four patients is no. 4, 7, 9, and 11 and > 1mg/L in 11 patients (Table 2). Seen increase in value of hsCRP for each patient, by experts has states an increase in the risk of reclusion is suspected of inflammation due to the PCI action. Therefore, several researchers of hsCRP has been referred to as inflammatory factors, not as a marker of inflammation, although some researchers suggest hsCRP as a marker of inflammation, because at inflammatory stage there are many factors involved, such as the following; atherosclerotic plaques or neointimal formation after PCI will issue several cytokines proinflamatory ie; INF-γ, TNF-α, IL-1 and IL-6. IL-6 responded to the liver produce hsCRP. hsCRP as an inflammatory factor,

increased the expression of VCAM-1 and ICAM-1 encourages the entry of a large number of monocytes and T cells, increased expression of CD40 on the surface of endothelial cells, increased ROS, increased angiotensin-receptor type 1 (AT1-R) (Paul et al, 2003). In this research, the analysis of changes in value of hsCRP 2 hours before (hsCRP pre) and 24 hours after PCI (hsCRP post) with Wilcoxon Signed Rank Test, found a significant increase in value of hsCRP ($p = 0.001$, $p < 0.05$), this means that, at this study inflammation occurs due to the PCI action. Then analyzed the relationship between changes value of hsCRP with value of percent aggregation with Pearson Correlation (bivariate), showed no correlation ($r = -0.16$; table $r = 0.514$ ($n = 15$, $p = 0.05$) with $p = 0.56$, $p > 0.05$). From these data, hsCRP as an inflammatory factor and not a marker of inflammation and is not directly related to the inflammatory process and reclusion.

## CONCLUSION

The use of Clopidogrel 300 mg loading dose and 200 mg aspirin as anti-platelet aggregation is adequate with hypo aggregation response. Identified inflammatory response occurs because of PCI with an increase in inflammatory factors hsCRP and no correlation with percent aggregation, so that hsCRP is only referred to as inflammatory factors and not a biomarkers of inflammation and is not directly linked to the inflammatory process and reclusion.

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