Impact of repeated clopidogrel reloading doses and increased maintenance dose in patients with acute coronary syndrome and persistent low response to clopidogrel in 30-day follow-up

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Objectives: Platelet response to clopidogrel is not uniform.¹ It is known that inadequate effect of clopidogrel on platelets increases the risk for new ischemic events²⁻³. We aimed to investigate whether repeated clopidogrel reloading regimen and increased maintenance dose in persistent low responders is an effective and a safe strategy.

Patients and Methods: Patients with acute coronary syndrome who underwent coronary stenting were tested with impedance aggregometer — Multiplate[®] function analyzer. This is a point of care instrument which measures residual platelet reactivity (RPR) in small quantities of the whole blood. Low clopidogrel responders received another loading dose and underwent aggregometry testing the following day. The remaining low responders on repeated aggregometry received the third loading dose followed by a maintenance dose of 150 mg/day. On day 7, we repeated aggregometry testing and patients who remained low responders were assigned to a clopidogrel maintenance dose of 300 mg/day. After one month follow-up we conducted control interview and Multiplate[®] testing.

Results: Persistent low response to clopidogrel was found in 12 patients out of 43 initially low responders (27.9%). After one month of follow-up no patient had a major bleeding

event. Furthermore, three patients sustained a new ischemic event: non fatal myocardial infarction, ischemic (fatal) stroke and in-stent thrombosis. After 30 days, seven patients (63.6%) still had high RPR.

Conclusion: Our study showed that repeated clopidogrel reloading doses and very high maintenance doses can be safe in persistent low responders in terms of bleeding complications. However, certain number of patients are still inadequately treated and sustain new ischemic events. Changing clopidogrel by a new thienopyridine like ticagrelor or prasugrel should be considered for those patients, if available.

KEYWORDS: acute coronary syndrome, clopidogrel, residual platelet reactivity.

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Table 1. Demographic data.

Patient	Gender	Age	ACS	HLP	HA	DM2	Smoking	Aspirin resistance	Multivessel disease	CYP2C19*2	MACCE	HRPR after 30 days
1	F	64	STEMI	yes	yes	no	no	yes	yes	no	no	yes
2	F	81	STEMI	yes	no	yes	no	no	no	no	no	yes
3	F	45	STEMI	yes	yes	yes	no	no	no	yes	no	yes
4	F	57	STEMI	yes	yes	yes	no	yes	yes	no	no	yes
5	M	63	STEMI	yes	yes	yes	yes	yes	no	no	isch. CVI, death	N/A
6	M	57	NSTEMI	no	no	no	no	no	yes	yes	no	yes
7	M	54	STEMI	yes	yes	yes	yes	no	yes	yes	non fatal MI	no
8	M	60	NSTEMI	yes	yes	no	no	no	yes	no	no	no
9	M	60	NSTEMI	yes	yes	yes	no	no	yes	no	no	no
10	F	68	STEMI	yes	yes	no	yes	no	yes	no	no	yes
11	M	52	STEMI	yes	yes	no	yes	yes	no	yes	IST	yes
12	F	70	STEMI	yes	yes	yes	no	no	yes	no	no	no

HLP = hyperlipidemia, HA = arterial hypertension, DM2 = diabetes mellitus type 2, MACCE = major adverse cardiac and cerebrovascular event, CVI = stroke, MI = myocardial infarction, HRPR = high residual platelet reactivity.

Literature

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