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Acute Coronary Syndromes

COMPARISON OF 600MG VERSUS 300MG LOADING DOSE OF CLOPIDOGREL FOR PATIENTS WITH STEMI: A META-ANALYSIS

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Background: The optimal loading dose (LD) of clopidogrel in ST-elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PCI) is not well established. The current AHA/ACC STEMI guidelines recommend 300-600mg as LD.

Methods: We undertook a meta-analysis of controlled trials and observational studies comparing 600mg and 300mg clopidogrel LDs. The efficacy end point was major adverse cardiac events (MACE), and the safety end point was major bleeding. Data were extracted on an intention to treat basis. The chi-squared (χ 2) test was used to evaluate heterogeneity and a p-value <0.05 was deemed significant. A random effects model was used and odds ratios (OR) were calculated using the Mantel-Haenszel method.

Results: 9 studies involving 18,623 patients were included in the efficacy analysis. Mean duration of follow-up was 8 months. Only 4 studies were eligible for the safety analysis. The MACE risk was lower with 600mg LD (7.0%; 650/9,231) compared to 300mg LD (9.2%; 867/9,392) [OR 0.75; 95% CI (0.63-0.91)] (Fig. 1). On the other hand, there was no significant difference in the major bleeding events between the two groups (2.5%; 89/3,551 with 600 mg vs. 2.3%; 63/2,796 with 300 mg) [OR 0.84; 95% CI (0.60-1.16)].

Conclusion: In STEMI patients treated with primary PCI, the administration of 600mg of clopidogrel LD was associated with lower risk of MACE compared to 300mg without causing an increase in the risk of major bleeding.

Figure 1. MACE

	Clopidogr	el 600	Clopidogr	el 300		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Jung 2009	1	73	11	98	0.8%	0.11 [0.01, 0.87]	
Patti 2011(ARMYDA-6 MI)	6	103	15	98	3.1%	0.34 [0.13, 0.92]	
Fefer 2009	19	116	26	97	6.1%	0.53 [0.27, 1.04]	
Mangiacapra 2010	26	157	26	98	6.8%	0.55 [0.30, 1.02]	
Song 2012	50	381	38	310	10.4%	1.08 [0.69, 1.70]	+
Dangas 2009(HORIZONS-AMI)	93	2158	81	1153	15.3%	0.60 [0.44, 0.81]	+
Choi 2011	155	1217	198	1447	18.9%	0.92 [0.73, 1.15]	+
Steg 2010(PLATO)	128	1357	282	2433	19.1%	0.79 [0.64, 0.99]	-
CURRENT-OASIS 7 2008	172	3669	190	3658	19.5%	0.90 [0.73, 1.11]	4
Total (95% CI)		9231		9392	100.0%	0.75 [0.63, 0.91]	•
Total events	650		867				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 17.07$, $df = 8$ (P = 0.03); $l^2 = 53\%$							box o'x 1 10 100
Test for overall effect: Z = 2.95 (P = 0.003)							Eavours 600 Eavours 300
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