Short-term bleeding events observed with clopidogrel loading in acute ischemic stroke patients.

INTRODUCTION: The Fast Assessment of Stroke and Transient Ischemic Attack to Prevent Early Recurrence trial raised concern that loading doses of clopidogrel may increase hemorrhagic complications. We investigated if similar rates of hemorrhage occur in patients with acute ischemic stroke (AIS) of varying severity.

METHODS: Patients meeting inclusion criteria were divided into 2 groups: the LOAD group and non-LOAD group. The LOAD group was defined as patients who were administered a loading dose of 300 mg or more of clopidogrel with or without aspirin within 24 hours of admission. The non-LOAD group was devised using propensity score (PS): 55 patients who received a loading dose of clopidogrel of 300 mg or more were matched on PS to 55 patients who did not receive loading doses. These patients were taken from a pool of 341 consecutive ischemic patients ineligible for intravenous or intra-arterial fibrinolysis, 162 of whom received a clopidogrel loading dose and the remainder of whom did not. The frequency of hemorrhage was compared between the 2 groups using Student t test and chi-square. Logistic regression was used to assess the relationship between loading dose and serious bleeding events (symptomatic intracerebral hemorrhage [sICH] or transfusion for systemic bleeding).

RESULTS: AIS patients (N = 596) were screened during the 31-month period of this retrospective study. Of this sample, 170 patients were excluded: 149 patients were excluded because
they were treated with intravenous tissue plasminogen activator (IV t-PA) alone, 11 were excluded because they were treated with IV t-PA combined with intra-arterial therapy (IAT), and 10 were excluded for treatment with IAT alone. An additional 85 patients were excluded because they were not admitted to the stroke service or because they had an in-hospital stroke. Baseline characteristics of the groups were well matched. There were no significant differences in the rates of sICH, transfusion, hemorrhagic transformation, or systemic bleeding. Clopidogrel loading was not associated with increased odds of serious bleeding events in the crude model (odds ratio [OR] .92, 95% confidence interval [CI] .27-3.13) or after adjusting for covariates and confounders of interest (OR 1.06, 95% CI .28-4.04).

**DISCUSSION:** Contrary to our original hypothesis, patients with AIS receiving clopidogrel loading doses within 24 hours of symptom onset did not appear to experience a higher rate of new serious bleeding events during acute hospitalization when compared with patients who did not receive loading doses. The Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke trial is expected to provide insight into the safety of clopidogrel loading as an acute intervention after cerebral ischemia.

DOI 10.1016/j.jstrokecerebrovasdis.2013.03.001
Alternate Journal J Stroke Cerebrovasc Dis
PubMed ID 23541421
Grant List 3 P60 MD000502-08S1 / MD / NIMHD NIH HHS / United States
5 T32 HS013852-10 / HS / AHRQ HHS / United States