Dose-Dependent Clopidogrel-Atorvastatin Drug-Drug Interaction Determined by Light Transmission Aggregometry

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Introduction:

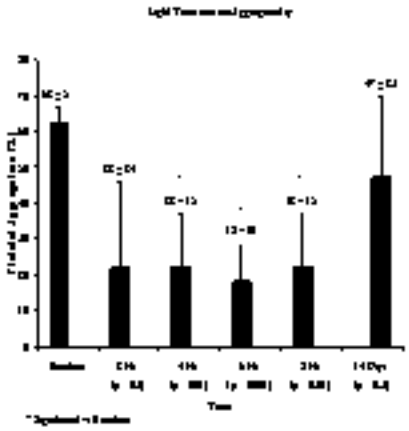
Previous reports suggest that atorvastatin decreases the ability of a loading dose of clopidogrel 300mg, but not 600mg, to optimally inhibit platelet aggregation. Whether the attenuation was a clopidogrel dose-dependent observation, overcome by higher loading doses is currently unknown.

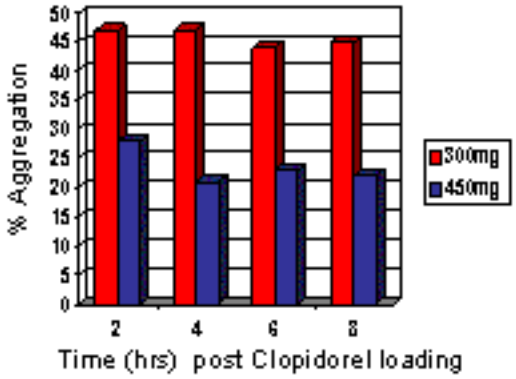
Methods:

Thirty three clopidogrel responders (relative decrease in platelet aggregation >30% after dosing with clopidogrel at 450mg) after a 14 day washout period were treated for 28 days with atorvastatin 40mg and received either: 1) clopidogrel 300mg (n=15), 2) clopidogrel 450mg (n=15), or 3) clopidogrel 600mg followed by 75mg/d for 14 days (n=3). Platelet aggregation was measured at 0, 2, 4, 6, 8 hours, and 14 days in group 3.

Results:

Clopidogrel 450mg and 600mg similarly inhibited platelet aggregation. Clopidogrel 300mg, compared with 450mg at 2, 4, 6, and 8 hours, was less successful in inhibiting platelet aggregation (47%±18 V's 28%±9, 47%±17 V's 21%±6, 44%±17 V's 23%±6, and 45%±16 V's 22%±9, respectively – Figure 1). Platelet aggregation was initially inhibited by clopidogrel 600mg, but returned toward normal at day 14 despite the





Conclusion:

A clopidogrel 450mg loading dose is as effective as 600 mg in initially overcoming the clopidogrel-atorvastatin interaction seen with clopidogrel 300mg. However, the clopidogrel 75mg/d maintenance dose does not maintain platelet aggregation inhibition when co-administered with atorvastatin 40mg/d. Whether this remains a clinical phenomenon when additional subjects have been recruited to this group remains to be evaluated.