ADENOSINE MAY MEDIATE TICAGRELOR-INDUCED DYSPNEA

ACC Oral Contributions
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Authors: Li-ming Gan, Ann Wittfeldt, Hakan Emanuelsson, Sven Nylander, Jenny Jonasson, Institute of Clinical and Molecular Medicine, Sahlgrenska Academy at Göteborg University, Göteborg, Sweden

Background: Ticagrelor (T) is a reversibly binding, direct-acting, oral P2Y12 antagonist used for prevention of atherothrombotic events in patients with acute coronary syndrome. One of its known potential side-effects is dyspnea. In addition to its antiplatelet effects, T also blocks cellular adenosine reuptake through inhibition of ENT-1. Since adenosine induces dyspnea, this exploratory analysis aimed to determine if T might augment adenosine-induced dyspnea.

Methods: Healthy volunteers (N=39) received T 180 mg or placebo in a crossover fashion, separated by a washout period of 1-2 weeks. Increasing doses of adenosine were infused using a stepwise protocol (0, 50, 80, 110 and 140 μg/kg/min for 2 min each) predose, 2h after study drug, and after a 20 min infusion of theophylline (5 mg/kg). Dyspnea was measured at each adenosine dose at each time using the modified Borg scale.

Results: As expected there was a clear trend for increasing severity of dyspnea with increasing adenosine doses (before study drug dosing). Adenosine-induced dyspnea was more severe with T than placebo for 3 of the 4 adenosine doses: p<0.01 for 80, 110 and 140 μg/kg/min. Theophylline reduced dyspnea in both groups (for T, before vs. after theophylline: p<0.01 for all adenosine doses).

Conclusion: T increased the severity of dyspnea induced by adenosine infusions in healthy volunteers. This effect was reversed (at least partially) by theophylline, suggesting that adenosine may mediate the dyspnea reported by some patients treated with T.

Figure. Histogram of Borg value during adenosine infusion (110 μg/kg/min) by treatment group, pre- and post-ticagrelor or placebo, and following theophylline infusion.