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ASA daily vs ASA every 3 days in healthy volunteers: effect on platelet aggregation and gastric mucosa PGE2 synthesis.

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INTRODUCTION: Substantial platelet inhibition was observed 3 days after a single administration of ASA 81 mg to healthy volunteers[1]. Here we investigate Prostaglandin E2 (PGE2) antrum concentrations and GI symptoms in two treatment groups: one receiving losartan and aspirin every day and the other receiving losartan every day and aspirin every 3 days, for 30 days.

METHODS: Twenty-eight healthy volunteers from both sexes were recruited and randomized into two different groups. Treatment A received 50 mg losartan and aspirin 81 mg daily; Treatment B received 50 mg losartan and aspirin 81 every three days with placebo on the other days. Therapy was delivered for 30 days for both groups. Gastric endoscopy was performed before and after treatment period. Only volunteers without any gastric injuries were included. Biopsies were collected for hystopathological analysis and PGE2 enzyme immunoassay. Ex vivo platelet aggregation induced by arachidonic acid (AA) 300 μg/mL and ADP 20 μM were performed using a Born aggregometer. Thromboxane B2 (TXB2) release was measured by enzyme immunoassay. Blood samples were obtained before and after 14 (D15), 15 (D16) and 16 (D17) days of treatment in both groups.

RESULTS: For volunteers that presented normal platelet aggregation with AA before therapy, it remained inhibited on D15, D16 and D17 for 12 out of 12 volunteers who received treatment A, and in 10 out of 12 volunteers who received treatment B. Percentage of total aggregation with ADP was variable between volunteers and treatment days. For both treatment groups we observed over 98% inhibition of TXB2 release, compared to basal values, after AA 300 μg/mL stimulation on PRP samples on D15, D16 and D17. TXB2 release after ADP 20 μM was at least 85.7% abolished for both treatment groups, in this same period. At the end of 30-day treatment, 7 out of 28 volunteers presented some type of gastric lesion. Two of them received treatment A and 5 received treatment B. The worst outcome observed was 3 erosions on antrum. We understand that these injuries can normally occur in population, since we observed similar lesions on volunteers during recruitment phase which had no gastrointestinal complaints. Histhopathological analysis showed no significant difference between both treatment groups, however when dividing the 28 volunteers by the prevalence of *H. pylori* on GI tract, the positive group presented a worsening of inflammatory characteristics on biopsies collected from body and antrum.

We found a 50% suppression of antrum PGE2 content on volunteers randomized in treatment A (Basal = 1402.0 ng/mg, Post-treatment = 703.70 ng/mg, p=0.0025), while for treatment B there was no significant difference between pre and post-treatment antrum PGE2 dosages (Basal = 1853.0 ng/mg, Post-treatment = 1925.7 ng/mg, p=0.4193).

CONCLUSIONS: 1) The every 3 day low-dose aspirin regimen produced sufficient inhibition of platelet aggregation compared to the daily treatment, while maintained PGE2 levels on antrum after 30 days of therapy. Since PGE2 is involved in gastric protection, we conclude that this proposed therapy scheme is as effective as daily administration and safer.

1. Mendes GD et al. 2013. *Proceedings of the British Pharmacological Society* at http://www.pa2online.org/abstract/abstract.jsp?abid=31400&author=de%20nucci&cat=-1&period=-1