Insights on the Mechanism of Platelet Inhibition by Omega-3 Polyunsaturated Fatty Acids. Results of the LEAP trial.

Abstract Body*

Background: Omega-3 polyunsaturated fatty acid (PUFA) supplements may inhibit platelet function, but the mechanism is poorly defined. We evaluated the effect of escalating doses of omega-3-PUFA using electrophoretic quasi-elastic light scattering (EQELS), a novel method that measures electrophoretic mobility of platelets by virtue of the surface charge density. Methods: LEAP was a prospective non-randomized pilot study. A total of 30 subjects received escalating doses of omega-3-PUFA (from 2 to 8 g daily). Ten subjects were on no background antiplatelet therapy (Group A), 10 subjects on aspirin alone (group B), and 10 subjects on aspirin and clopidogrel (group C). Blood samples were collected at baseline and at 6, 12, 18 and 24 weeks. Platelet function was assessed by bleeding time and EQELS. Results: EQELS showed a significant stepwise increase in the magnitude of negative surface charge density compared to baseline with increasing doses of omega-3-PUFA up to 4g/day. The median electrophoretic mobility for all patients was -0.72 mobility units at baseline, -1.33 mobility units at 6 weeks, and -1.47 mobility units at 12 weeks ($p<0.001$). This effect was marked in patients that were not on background clopidogrel therapy. Standard bleeding time increased among patients not taking background antiplatelet therapy (median 150 sec at baseline vs. 240 sec at week 12 in Group A, $p<0.05$). Conclusions: This pilot study suggests that the mechanism for platelet inhibition by omega-3-PUFA is by increasing the magnitude of negative platelet surface charge density and, therefore, attenuating platelet activation. Measuring omega-3-PUFA platelet inhibition may have important implications in cardiovascular disease management.