Prevalence of platelet Non-responsiveness to aspirin by Thromboelastography in children with congenital heart disease

Fernando M. Berganza MD, Ghaele S. MD, Gonzalez de Alba C. MD, Bartakian S. MD, Brownlee J. MD, FAAP, FACC
Driscoll Children’s Hospital

ABSTRACT

Rationale: Aspirin resistance (AR) using thromboelastography platelet mapping (TEGPM) has been reported in up to 80% of pediatric patients with congenital heart disease and systemic to pulmonary artery shunts (1). A patient at Driscoll Children’s Heart Center who had hypoplastic left heart syndrome (HLHS) had embolic stroke while on standard therapeutic aspirin doses. Aspirin resistance was present on his TEGPM. Because of this unexpected finding, we chose to obtain a TEGPM on cardiac patients on aspirin antplatelet therapy coming to our center to assess the efficacy of their aspirin treatment.

Objectives: This study evaluates AR noted in these patients and their characteristics

Methods and Results: A retrospective review was performed of TEGPM on 25 cardiac patients taking aspirin for at least a month at therapeutic dose. Eleven females were enrolled. Age ranges for these patients were 5 months to 27 years. Nineteen had Fontan surgery. Three had cavo pulmonary anastomosis, 1 had a hybrid procedure for HLHS and two had coronary anomalies. Compliance was assessed at the time of the clinic visit. AR was defined as platelet inhibition by aspirin below 50% on TEGPM. Variables evaluated were: percentage of platelet inhibition, age, Body mass index (BMI), gender, clinical and echocardiographic diagnosis, and thrombus. Statistical analysis using Chi Square, Man-Whitney test was performed. AR was present in 72% of these patients (73% in post Fontan and 67% in the remaining patients). It was not affected by gender (P=0.54), age (P>0.54) or BMI (P=0.28).

Conclusions: The TEGPM shows aspirin resistance is present in the majority of children taking aspirin at standard doses for antplatelet prophylaxis. A larger cohort is needed to confirm our findings. There is currently no evidence supporting dosing guidelines in aspirin therapy in children with cardiac disease.

Key Words: Aspirin resistance, Thromboelastography (TEG) plus platelet mapping, congenital heart disease.

BACKGROUND

• The incidence of aspirin resistance (AR) has been reported to range from 2.3% up to 80% in children in the medical literature through different laboratory tests (1-2). No laboratory assay has been recognized to be effective to monitor aspirin therapy in children (3).

• The evidence supporting most recommendations for antithrombotic therapy in neonates and children remains weak and most recommendations are based on extrapolation from adults (4,5). Children are at increased risk for thrombosis after cardiac surgery. Eight to 33% of patients after a Fontan surgery are reported to develop thrombosis (6).

• TEGPM has been previously proposed to function as a test for platelet function of patients taking aspirin to assess AR (1).

METHODS AND MATERIALS

• A retrospective chart review of 24 patients with surgically repaired congenital heart disease and one patient with an acquired heart condition (coronary aneurysm due to Kawasaki disease) who had a standard TEGPM done to evaluate aspirin therapy.

• Inclusion criteria: aspirin therapy for more than one month. The aspirin dosage was 5 mg/kg/day, not to exceed 81 mg per day.

• A board certified cardiologist assessed the compliance of aspirin therapy during the patient’s one-month follow-up visit.

• Charts reviewed were from July 2014 to June 2015.

• A complete blood count drawn within a week from the TEGPM sample was also extracted from the patients’ charts to measure hemoglobin and platelet levels for quality control.

• All study patients had an echocardiogram performed within a week of their standard TEGPM test collection.

• TEG 500 Haemometrics ® analyzer was utilized and AR was defined as level of platelet inhibition by aspirin below 50%.

OBJECTIVE

To evaluate the effectiveness of platelet inhibition in children taking aspirin for this purpose in the Driscoll Children’s Heart Center

RESULTS 1

Our study population consisted of eleven females (mean age 10.7 ± 8.9 years) and 14 males (mean age 9.4 ± 4.4 years). Aspirin resistance was found in 72% of all patients (18/25). An intra-cardiac thrombus was identified in 1 patient with cavo-pulmonary anastomosis with a level inhibition of platelet of 33%. A Second thrombus was noted in another patient after Fontan surgery with level of platelet inhibition of 54%.

RESULTS 2

CONCLUSION AND DISCUSSION

• These results are similar to those previously published by Mir et al, who evaluated aspirin therapy with TEGPM in the immediate post-operative period in systemic to pulmonary shunt dependent 1 month old post operative patients, finding an AR of 80% (1). Our results suggest that this high aspirin non-responsiveness persists long after surgery. Despite this finding only one of our patients (index case) who had AR by TEGPM had a thrombus.

• Adult patients post-Fontan have demonstrated to have a 23% increase of Von Willebrand factor levels as well as P-selectin in the platelet’s surface (7). This increase activation on P-selectin in platelets has also been found in healthy children when compared to healthy adults (8), pointing to a multi factorial cause that combines specific characteristics of a developing hemostatic system in children and the physiology after a vascular surgery that might predispose to AR.

• Our findings show that aspirin resistance is present in our congenital heart population. The accuracy of the TEGPM to predict clinical disease (thrombosis) is in question given the published data that sets the standard for aspirin resistance. However, our patient numbers are not high enough to reach a conclusion on this. Further research is needed to assess the appropriate therapy for anticagulation/antplatelet therapy on patients with congenital heart disease.

REFERENCES


