The utility of thrombo-elastography in the monitoring of aspirin therapy

E Mayne, B Jacobson, S Louw, P Bernstein, A Mayne

To assess the utility of the thrombo-elastogram in monitoring of aspirin therapy 25 healthy volunteers were selected and given low-dose aspirin therapy. Thrombo-elastography and platelet aggregometry were conducted at baseline and 1 week later. After 1 week of aspirin therapy, thrombo-elastogram data failed to demonstrate a significant change in the clotting profile. Platelet aggregometry identified significant changes in the clotting profile in response to stimulation with arachidonic acid, adrenaline and ADP.

We conclude that thrombo-elastography may not have utility in monitoring of response to aspirin.

S Afr Med J 2007; 97: 1289-1291.

Aspirin therapy is widely used in patients with arterial disease to prevent platelet aggregation. Currently aspirin therapy is monitored using platelet aggregation to measure the dose-response curve to diverse platelet activators including adrenaline, ADP, arachidonic acid and collagen.

Thrombo-elastography measures the shear elastic strength of a clot and gives information on the clotting process from its initiation to fibrinolysis.[1,2] The thrombo-elastogram is currently used primarily in the context of liver transplantation in order to measure the fibrinogen output of the graft.[2,3]

Multiple parameters are measured by the thrombo-elastogram (Fig. 1), which gives information about various properties of the clot (Table I).

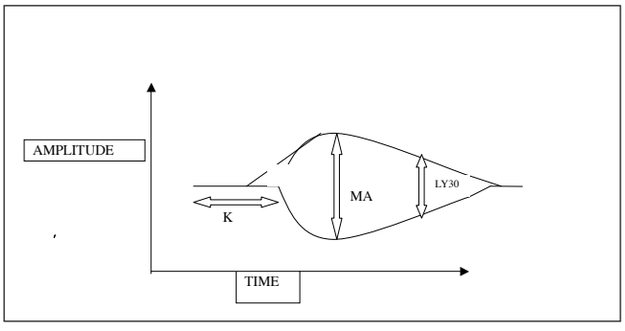

Fig. 1. Diagram of thrombo-elastogram.

Department of Molecular Medicine and Haematology, University of the Witwatersrand and National Health Laboratory Service, Johannesburg
E Mayne, MB BCh
B Jacobson, MB ChB, FRCS, MMed, PhD
S Louw, MB BCh
P Bernstein, MB BCh

Department of Statistics, UNISA
A Mayne, CA (SA), MSc (Statistics), MCom

Corresponding author: *E Mayne (esm24@mweb.co.za)*

The measure of maximal amplitude of a clot has been shown to correlate best with platelet number and function.

The purpose of this study was to assess the effect of low-dose aspirin therapy on the parameters of the thrombo-elastogram and to compare these results with platelet aggregometry.

Methods

This study was approved by the Ethics Committee of the University of the Witwatersrand.

Twenty-five healthy subjects (mean age 53 years) with no history or signs of cardiovascular disease were recruited from among colleagues in the laboratory. Thrombo-elastograms were performed at baseline on a sub-population (*N*=11) using the Haemoscope Corporation TEG Hemostasis analyser. The volunteers were treated with Ecotrin (coated aspirin) 75 mg for 7 days. A second thrombo-elastogram was performed in conjunction with platelet aggregation studies on samples from selected patients (*N*=13) after 7 days.

Thrombo-elastography

Approximately 1 ml of fresh blood was taken, analysed in its original state and then activated with arachidonic acid (AA) and kaolin. Heparinase was added to the kaolin preparation to neutralise the effects of original heparins which may have altered the thrombo-elastogram readings. A subpopulation were of subjects was re-analysed 2 hours later to exclude time as a confounding variable in analysis. Appropriate controls were utilised according to the manufacturer's instructions.

Platelet aggregometry

Platelet aggregometry was performed using the ON Helena Aggregometer. The citrated blood was separated into platelet-rich plasma and then activated using the following reagents in two concentrations according to the manufacturer's instructions:

Table I. Properties of the clot measured by the thrombo-elastogram

Reaction time	Latency to initial fibrin formation
K	Measure of speed taken to reach clot stability (measure of clot kinetics)
Angle (α)	Speed of fibrin build-up and cross-linking (fibrinogen level)
Maximal amplitude (MA)	Measure of peak strength of a clot (representative of platelet aggregation)
LY30	Measure of the loss of clot strength after 30 minutes (clot lysis)

Table II. Thrombo-elastogram analysis before aspirin therapy

	Arachidonic acid				Kaolin			
Sample No.	R value	K value (min)	Angle (deg)	MA (mm)	R value	K value (min)	Angle (deg)	MA (mm)
C040A	0.8	1.5	71.6	63.7	11.8	6.7	27.0	43.5
C041A	0.6	1.8	67.6	50.3	14.4	11.2	18.2	36.4
C042A	0.8	2.0	65.4	50.7	42.4			
C045A	1.1	5.0	43.7	25.6	15.4	11.8	19.5	44.0
C046A	1.4	4.2	45.4	33.5	22.0		4.7	8.1
C049A	0.6	1.7	70.2	51.4	21.3	21.7	10.5	23.8
C052A	0.7	1.4	72.6	59.1	18.1	9.0	22.6	44.3
C053A	0.7	1.8	68.7	62.9	22.0	11.3	18.2	28.7
C054A	0.7	1.6	70.5	59.8	14.8	8.5	24.2	41.1
C055A	0.6	1.3	74.1	63.4	13.3	9.7	22.0	45.3
C056A	0.8	1.5	71.1	60.4	32.3		3.6	6.9

Reagent: high concentration	**Reagent: low concentration**
Arachidonic acid high – 1.5 mM	Arachidonic acid low – 0.187 mM
ADP high – 2 mM	ADP low – 0.1 mM
Adrenaline high – 10 mM	Adrenaline low – 0.05 mM
Collagen high – 2 mM	Collagen low – 0.02 mM

Response to the reagents was measured as a percentage of platelet aggregation and reported as normal, reduced or flat.

Results

Analysis was conducted using a two-factor analysis of variance (ANOVA) without replication.

Thrombo-elastogram analysis failed to show any significant difference between measured parameters at baseline and 1 week later at a significance level of p=0.05 (Tables II and III). A decrease in maximal amplitude was noted consistently between the pre-aspirin and post-aspirin samples, but this failed to reach significance (p=0.09).

Analysis of the same data with platelet aggregometry showed a highly significant reduction of platelet aggregation in response to activation with arachidonic acid (p=0.000), adrenaline (p=0.001) and ADP (p=0.000), but no significant response to collagen. In only 1 patient did platelet aggregometry demonstrate no response to arachidonic acid – in this case, aspirin resistance was suspected. This patient failed to show a significant change on thrombo-elastography.

Discussion

Maximal amplitude is considered to be the most sensitive parameter for assessment of platelet function in thrombo-elastography. The maximal amplitude is dependent on the strength of the clot following initial fibrin formation – this strength is almost entirely dependent on the interaction between the GP IIb/IIIa receptors on platelets and platelet aggregation which plays an integral part in this interaction. Previous reports have shown mixed data with regard to the decreased MA in response to aspirin therapy – certain authors demonstrated that in the setting of thrombocytopenia, this measurement was a sensitive measure of platelet function,[4] in particular in the context of pre-existing vascular bed damage and reperfusion injury.[3] A previous study on healthy controls given low-dose aspirin failed to show a significant change in the maximal amplitude.[5] Our study concurred with these

Table III. Thrombo-elastogram analysis after aspirin therapy

	Arachidonic acid				Kaolin			
Sample No.	R value	K value (min)	Angle (deg)	MA (mm)	R value	K value (min)	Angle (deg)	MA (mm)
C041B	0.7							
C042B	0.7	1.5	71.6	63.7	11.8	6.7	27.0	43.5
C043B	0.7	1.8	67.6	50.3	14.4	11.2	18.2	36.4
C045B	0.8	2.0	65.4	50.7	42.4			
C046B	0.6	5.0	43.7	25.6	15.4	11.8	19.5	44.0
C049B	1.1	4.2	45.4	33.5	22.0		4.7	8.1
C050B M42	0.8	1.7	70.2	51.4	21.3	21.7	10.5	23.8
C051B M48	0.8	1.4	72.6	59.1	18.1	9.0	22.6	44.3
C052B	0.7	1.8	68.7	62.9	22.0	11.3	18.2	28.7
C054B	0.7	1.6	70.5	59.8	14.8	8.5	24.2	41.1
C057B	0.7	1.3	74.1	63.4	13.3	9.7	22.0	45.3
C058B	0.8	1.5	71.1	60.4	32.3		3.6	6.9
C059B	0.7	1.7	70.2	59.1	18.1	10.45	18.85	34.9

findings – despite evidence of aspirin response on platelet aggregometry, there was no significant change in parameters measured using thrombo-elastography. Limitations of this study were the small sample size and the short period of the intervention. These data show that it is not possible to consider thrombo-elastography for routine monitoring of aspirin therapy.

References

1. McNulty S, Maguire D, Thomas R. Effect of heparin-bonded pulmonary artery catheterisation on the activated coagulation time. *J Cardiothorac Vasc Anesth* 1998; 5: 533-535.
2. Stensrud P, Nuttall G, De Castro M, *et al*. A prospective, randomized study of cardiopulmonary bypass temperature and blood transfusion. *Ann Thorac Surg* 1999; 67: 711-715.
3. Pivalizza E, Abramson D, Harvey A. Perioperative hypercoagulability in uremic patients: A viscoelastic study. *J Clin Anesth* 1997; Sep-Oct; 9(6): 442-445.
4. Beilin Y, Arnold I, Hossain S. Evaluation of the platelet function analyzer (PFA-100) vs. the thromboelastogram in the parturient. *Int J Obstet Anesth* 2006; 15: 7-12.
5. Trentalange M, Walts L. A comparison of thromboelastogram and template bleeding time in the evaluation of platelet function after aspirin ingestion. *J Clin Anesth* 1991; 5: 377-381.

Accepted 5 July 2007.