Stability of TGA Parameters in Patients Treated with Anticoagulants Using the Fully Automated ST-Genesia System

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PB 445 | Use of a Synthetic Collagen to Monitor Platelet Function in Patients Receiving Dual Antiplatelet Therapy

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Background: Patients with coronary artery disease (CAD) are treated with aspirin and a P2Y12 antagonist to prevent myocardial infarction or stent thrombosis. Variable clinical response to both types of agents has been reported. Existing assays to identify sub-optimal response to anti-platelet therapy do not meet reported medical needs.

Aims: To characterize the utility of a synthetic collagen (SynC) to monitor platelet function in patients on dual-antiplatelet therapy.

Methods: Blood samples from healthy individuals (n=5) and CAD patients treated with clopidogrel (75-600 mg) with or without aspirin (75-325 mg) (n=51) were centrifuged to produce plasmas for aggregometry studies (PAP 8E, Bio/Data Corp. Horsham, PA). The aggregation response to 20 µM ADP, 500 µg/ml arachidonic acid and 190 µg/ml Type 1 biologic collagen was compared to that induced by SynC (2-200 ng/ml; JNC Corp., Yokohama, Japan). The aggregation response was characterized in terms of % aggregation, slope and AUC.

Results: Using plasmas from healthy individuals and CAD patients, two lots of SynC produced a concentration-dependent aggregation response over a concentration range of 16 to 128 ng/ml. Patients treated with 81 mg aspirin and 75 mg clopidogrel (33 of 51 patients) were stratified into two groups based on their % aggregation response to SynC, using the median % aggregation as the cut point. While the two groups had a distinct response to SynC, the median responses to ADP, arachidonic acid and biologic collagen were nearly the same and there was a strong overlap between the responses to these agonists in the two sub-groups. This is most evident at the lower concentrations of SynC.

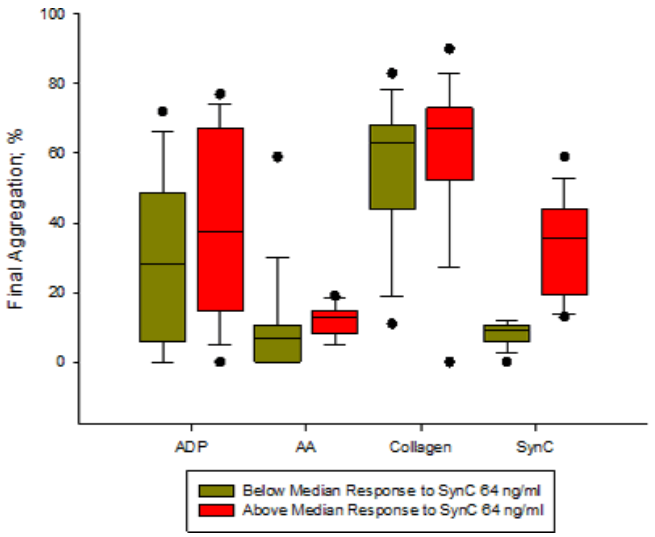

FIGURE 1

Conclusions: SynC-induced platelet aggregation may identify subgroups of patients with sub-optimal response to dual antiplatelet therapy that go undetected with traditional platelet agonists. Studies to clarify why biologic and synthetic collagens have different sensitivities to aspirin and clopidogrel are warranted.

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Background: Current thrombin generation assay (TGA) systems are semi-automated with samples tested in batch. Thus, the method lacks automation and standardization for homogeneity in results from study to study. TGA may be more informative than plasma concentration to assess the intensity of anticoagulation in a particular individual. A new automated and standardized TGA assay (i.e: ST-Genesia) has been recently developed by Stago.

Aims: To assess if TGA results in healthy subjects and patients treated by DOACs (dabigatran, rivaroxaban, apixaban), vitamin K antagonist (acenocoumarol) or LMWH (enoxaparin) are stable along time on samples stored at around -80°C during 10 months.

Methods: 6 healthy individuals and 30 samples of patients treated with anticoagulants were planned to be collected according to standard pre-analytical conditions. Samples were taken at peak and anticoagulant activity was measured according to current recommendations. Each sample were planned to be tested fresh (D0) and after storage at -80°C during 1 day (D1), 1 month (M1), 2 months, 3 months, 6 months, 9 months and 10 months. Impact of freezing (D1 vs D0) was to be assessed through paired-sample analysis (Student or Wilcoxon test) and stability through evaluation of trends overtime vs D1.

Results: Currently 6 healthy subjects, 7 apixaban, 3 dabigatran, 6 rivaroxaban, 5 VKA and 6 LMWH patients were included. Only results for D0, D1 and M1 are currently available. Table 1 summarizes, the mean difference relative to D0 or D1 and the range of relative deviations.

Conclusions: Freezing slightly affects all TG parameters. Once plasmas are frozen, TG parameters are also slightly influenced during the first month of storage. As it is frequently impossible to ensure that storage duration of samples is strictly equivalent throughout a study on a plasma bank, working with fresh samples would help in avoiding the outliers observed. This demonstrates the utility of a fully automatized TGA analyzer that could be integrated in the routine lab.

TABLE 1 Stability of TGA parameters after 1 day and 1 month storage at -80°C.

		Lag time (min)		Peak Height (nM)		Time to Peak (min)		ETP (nM.min)	
		D1 vs D0	M1 vs D1	D1 vs D0	M1 vs D1	D1 vs D0	M1 vs D1	D1 vs D0	M1 vs D1
Healthy subjects	Mean diff. (range)	-1% (-15 to 11%)	-8% (-12 to 4%)	-8% (-12 to 4%)	5% (0 to 7%)	-1% (-19 to 20%)	-7% (-10% to -3%)	-6% (-27% to 24%)	-2% (-8% to 3%)
Apixaban	Mean diff. (range)	0% (-10% to 12%)	1% (-20% to 33%)	15% (-4% to 28%)	-2% (-12% to 9%)	-4% (-12% to 6%)	1% (-8% to 15%)	2% (-9% to 7%)	0% (-23% to 18%)
Dabigatran	Mean diff. (range)	-10% (-14% to -4%)	-10% (-19% to 2%)	2% (-3% to 6%)	3% (-2% to 8%)	-7% (-12% to 1%)	-9% (-16% to -2%)	2% (1% to 3%)	-6% (-8% to -3%)
Rivaroxaban	Mean diff. (range)	-7% (-11% to -4%)	-6% (-12% to 7%)	13% (-5% to 25%)	-1% (-14% to 16%)	-7% (-12% to -3%)	-4% (-12% to 2%)	6% (-9% to 20%)	-2% (-6% to 5%)
VKA	Mean diff. (range)	-1% (-6% to 1%)	-3% (-13% to 2%)	1% (-4% to 5%)	-1% (-11% to 10%)	-1% (-4% to 2%)	-1% (-11% to 5%)	3% (-3% to 11)	-2% (-16% to 8%)
LMWH	Mean diff. (range)	-1% (-9% to 6%)	-9% (-20% to 3%)	15% (-5 to 69%)	0% (-26% to 18%)	1% (-8% to 10%)	-6% (-15% to 3%)	14% (-1% to 54%)	-3% (-18% to 17%)

PB 447 | First European Evaluation of ClarityCor Plasma Set for Instrument to Instrument Reproducibility Assessment

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Background: In Accreditation context, labs have to manage reproducibility between instruments.

To perform such testing, the lab can archive patient samples spanning the reportable range or can purchase pre-assayed validation plasma sets from commercial suppliers.

In this context, Stago (Asnières, France) has developed the ClarityCor (CC) Plasma Set, a set of frozen plasmas enabling to verify the correlation between different coagulation analysers.

Aims: Evaluation of CC Plasma Set to assess between-instrument reproducibility in comparison to locally selected frozen plasma samples.

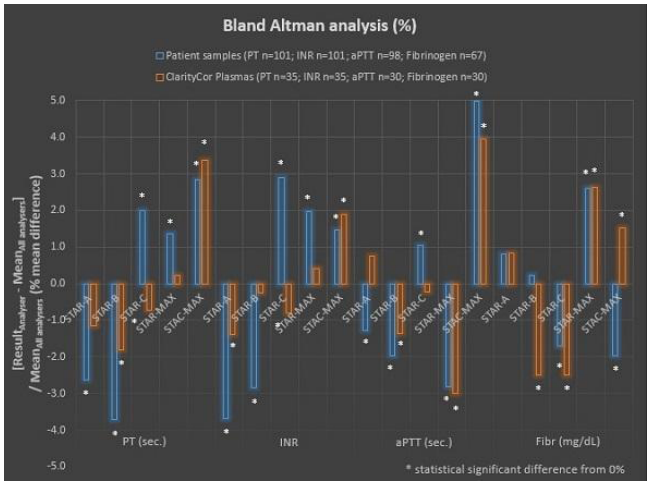

FIGURE 1 Overview of %mean bias comparing a single analyser (3 STAR Evolutions [A,B,C],STAR-MAX,STAC-MAX) with the mean of all analysers for routine parameters

Methods: One CC Plasma Set (n=30 for PT, INR, aPTT and Fibrinogen (Fibr) + n=5 for INR across the reportable range) was used for each instrument in the lab (Figure 1). In addition, citrated patient plasmas were collected. Method comparison to the mean of all analysers was done by Passing-Bablok (PB) regression and Bland-Altman (BA) analysis. Comparison was made between CC Plasma and patient sample datasets.

Results: Rank correlations (Rs) were between 0.967 and 0.999. PB slopes revealed no proportional bias for PT(sec) and INR of patient samples and CC Plasma Set except for STAR-MAX. 2/5 and 3/5 analysers showed concordant slope results between both data sets for aPTT and fibrinogen.. The %mean difference was ≤5% and ≤3.7% for all analyser/parameter combinations as compared to the mean and between datasets respectively (figure 1). All manufacturer's criteria were met (Rs>0.95, proportional(slope:0.9< x< 1.1) and systematic bias(BA %bias: 5-10%)).

Conclusions: Between instrument evaluation with CC Plasma Set results in sufficient data across the measuring range of PT, INR, aPTT and Fibrinogen. No major deviations were noted between frozen samples and CC Plasma Set. Given the advantages of sufficient plasma volume for all 3 parameters on a multitude of analysers and no need for time-consuming selection of suitable patient samples, the CC Plasma Set is a good alternative for local patient samples to evaluate between-instrument reproducibility.

PB 448 | Comparison of Activated Clotting Time Measured by I-STAT, Sonoclot and ACTPlus and Correlation with Anti-Xa during Cardiopulmonary Bypass Procedures

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Background: Activated clotting time (ACT) is used to monitor anticoagulation therapy with high heparin concentrations.