THE SENSITIVITY OF TWO NEW APTT REAGENTS TO FACTORS VIII, IX AND XI

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INTRODUCTION

- The APTT is used as a screening test for deficiencies of factors VIII, IX and XI. It is recommended that a prolongation to the APTT should be observed when the clotting factor is below 30 IU/dL [1].
- APTT reagents may demonstrate different sensitivities to these clotting factors because of their composition.

AIM

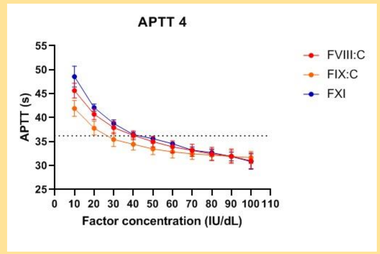
- To compare the APTT sensitivity to clotting factors VIII, IX and XI of two new APTT reagents, **Yumizen G APTT 4** and **Yumizen G APTT Liq 4**, (HORIBA Medical, Montpellier, France), with 6 commonly used APTT reagents.

METHOD

- FVIII deficient plasma (Siemens, Marburg, Germany), FIX and FXI deficient plasma (Precision Biologic, Halifax, Canada) was spiked with normal plasma (CCNRP, Precision Biologic) to obtain plasmas with factor concentrations of 0-90 IU/dL.
- APTT were performed on 5 different days with the 8 APTT reagents.
- Local reference ranges were generated for each reagent using 30 normal donors.
- The intersection of the upper limit of the APTT reference range and concentration of clotting factor determined the reagent sensitivity.
- All testing was performed on Sysmex CS5100i instrumentation (Kobe, Japan).

RESULTS

- Sensitivity to **FVIII** ranged from 31.5- 67.3 IU/dL (Synthasil, Actin FS), median of 43.8 IU/dL.
- Sensitivity to **FIX** ranged from 15.9-36.1 IU/dL (APTT SP, Synthasil), median 27.2 IU/dL. Sensitivity to FIX was greater than 30 IU/dL with Synthasil only.
- Sensitivity to **FXI** from 28.3-55.2 IU/dL (Actin FSL, Synthafax), median 46.1 IU/dL.
- Sensitivity to FVIII and FXI was greater than 30 IU/dL with all reagents, with the exception of FXI using Actin FSL (28.3 IU/dL).
- The sensitivity of **Yumizen G APTT 4** ranged from 26.8-43.3 IU/dL.
- The sensitivity of **Yumizen G APTT Liq 4** ranged from 29.7-48.9 IU/dL.
- Inter assay CV was less than 5.5% for all reagents and clotting factors measured.
- Average inter assay CV for **Yumizen G APTT 4** was 3.7%, 3.9%, 2.6% and **Yumizen G APTT Liq4** was 0.9%, 1.3%, 0.9% for FVIII, FIX, FXI respectively.



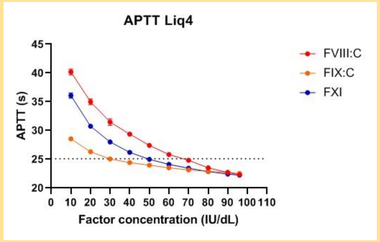


Figure 1: The sensitivity of APTT4 and APTT Liq4 to FVIII:C (•), FIX:C (•) and FXI (•) in IU/dL as determined by the intersection between the lower limit of normal (dotted line) and the individual curves. Mean APTT and standard deviation of each point are shown.

APTT REAGENT	COMPOSITION EA –ellagic acid RB-rabbit brain PL-phospholipid	SENSITIVITY (IU/dL)		
		FVIII	FIX	FXI
Yumizen G APTT 4	Micronised silica RB PL	40.9	26.8	43.3
Yumizen G APTT Liq 4	EA, RB PL	37.4	29.7	48.9
Actin FS	EA purified soy phosphatides	67.3	25.5	49.3
Actin FSL	EA soy/RB phosphatides	46.7	22.6	28.3
APTT SP	Silica synthetic PL	38.4	15.9	35.6
STA-PTTA	Silica, RB PL	47.6	29.0	35.7
Synthafax	EA synthetic PL	62.8	27.5	55.2
Synthasil	Silica synthetic PL	31.5	36.1	49.0

CONCLUSIONS

- A normal APTT does not always indicate normal haemostasis.
- The sensitivity to FVIII and FXI of most APTT reagents included in this study was considered acceptable however sensitivity to FIX was lower.
- **Yumizen G APTT 4** and **Yumizen G APTT Liq 4** results were reproducible and a prolongation to the APTT was observed above 30 IU/dL for FVIII and FXI.
- The source of activator did not appear to affect sensitivity but the phospholipid source, type and concentration influenced the ability to diagnose reduced factor activities, particularly FIX.

REFERENCES

1. Clinical Laboratory Standards Institute. One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test; Approved Guideline - Second Edition H47-A2. 2008.

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