



External Quality Assessment Scheme for Laboratory Monitoring of Anticoagulation with Heparins and Direct Thrombin Inhibitors

Peetz D¹, Dick A², Spannagl M²

¹Johannes Gutenberg University Mainz, Institute of Clinical Chemistry and Laboratory Medicine, Mainz, Germany,

²Ludwig-Maximilians-University, City Center Clinics, Medical Hospital, Haemostaseology/Angiology, Munich, Germany

Aims

Monitoring of anticoagulation with sophisticated laboratory methods is of growing interest for the medical community as there is an expanding use of low molecular weight (LMWH) heparins and direct thrombin inhibitors (DTI) in therapeutic concentrations. Possible issues of internal quality control are availability and traceability of adequate control materials. Therefore, external quality assessment (EOA) schemes are an important part of the quality control system. Since 2006, EOA for LMWH and DTI is available through the Institute for Standardization and Documentation in the Medical Laboratory (INSTAND). Systematic evaluation of these EOA results will help to improve the existing assay systems. Data of first year experience with these anticoagulation EOA schemes are presented.

Methods

Two kinds of surveys were offered four times a year: a) heparins/sulfated glycosaminoglycans (EOA Heparins) and b) direct thrombin inhibitors (EOA DTI). Each survey consisted of two plasma samples (covering two concentration levels in most surveys). Evaluation of EOA data were performed taking method or/and reagent into account.

Survey	EOA Heparins		EOA DTI	
	Sample 1	Sample 2	Sample 1	Sample 2
Jan 06	UFH (0.63 IU/mL)	LMWH (0.41 IU/mL)	Hirudin (0.49 µg/mL)	NP
May 06	LMWH (0.5 IU/mL)	LMWH (1.0 IU/mL)	Hirudin (4.0 µg/mL)	Hirudin (1.1 µg/mL)
Aug 06	Danaparoid (0.5 IU/mL)	Danaparoid (1.0 IU/mL)	Argatroban (0.5 µg/mL)	Argatroban (0.5 µg/mL)
Oct 06	UFH (0.5 IU/mL)	UFH (1.0 IU/mL)	Argatroban (0.5 µg/mL)	NP

Results

Number of participants per survey ranged between 51 and 72 for EOA Heparin and between 18 and 27 for EOA DTI. Total passing rates (=both samples correctly assigned) ranged from 82 to 100% using anti-Xa-activity (aXa) for LMWH, from 87 to 97% using aXa or APTT for UFH and from 67 to 100% using different methods for hirudin determination. Detailed passing rates for each sample and method are listed in Table 1 (results for normal plasma samples are not shown).

Overall there were few problems in EOA Heparins. In EOA DTI for Hirudin outliers or systematic deviations were observed for some methods. The number of participants for Argatroban (determination of concentration) was low, therefore only a qualitative interpretation is given.

Table 1: Passing rates

Sample	Anti-Xa	APTT	TZ	Heptest	PICT	ECT	DTI chromogen	ECA-H/T
UFH Jan 06 (Sample 1)	88.6% (n=35)	97.2% (n=36)	92.3% (n=26)	n.a. (n=2)	n.a. (n=1)	-	-	-
UFH Oct 06 (Sample 1)	86.7% (n=59)	77.8-100% (n=5/8/9/2/4)	82.6-100% (n=5/6/2/3)	100% (n=4)	100% (n=4)	-	-	-
UFH Oct 06 (Sample 2)	93.2% (n=59)	91.7-100% (n=5/8/8/2/4)	83.3-100% (n=5/6/2/3)	100% (n=4)	100% (n=3)	-	-	-
LMWH Jan 06 (Sample 2)	88.6% (n=35)	97.2% (n=36)	92.3% (n=26)	n.a. (n=2)	n.a. (n=1)	-	-	-
LMWH May 06 (Sample 1)	90.0% (n=60)	88.9-100% (n=9/14/2/3)	n.a. (n=38)	100% (n=5)	(n=0)	-	-	-
LMWH May 06 (Sample 2)	93.1% (n=58)	80-100% (n=9/14/2/0)	n.a. (n=38)	100% (n=5)	(n=0)	-	-	-
Danaparoid Aug 06 (Sample 1)	93.2% (n=44)	n.a. (n=28)	n.a. (n=24)	50% (n=4)	passed (n=1)	-	-	-
Danaparoid Aug 06 (Sample 2)	88.6% (n=44)	n.a. (n=28)	n.a. (n=24)	50% (n=4)	passed (n=1)	-	-	-
Hirudin Jan 06 (Sample 2)	-	85.7% (n=14)	-	-	n.a.* (n=1)	[100%]** (n=3)	100% (n=36)	87.5% (n=8)
Hirudin May 06 (Sample 1)	-	100% (n=7/9)	-	-	-	33.3% (n=3)	87.5% (n=8)	75% (n=8)
Hirudin May 06 (Sample 2)	-	88.9-100% (n=7/9)	-	-	-	66.7% (n=3)	87.5% (n=8)	87.5% (n=8)
Argatroban Aug 06 (Sample 1)	-	100% (n=11)	-	-	passed*** (n=1/2)	n.a.* (n=1)	passed (n=1)	-
Argatroban Aug 06 (Sample 2)	-	100% (n=11)	-	-	passed*** (n=1/2)	n.a.* (n=1)	passed (n=1)	failed (n=1)
Argatroban Oct 06 (Sample 1)	-	100% (n=17)	-	-	passed*** (n=1/3)	50% (n=2)	passed (n=1)	passed (n=1)

*no concentration reported (only seconds), **due to statistical procedure 100% passing rate at n=3: wide spreading of results, *** only one participant reported concentration

Conclusions

Overall, monitoring of anticoagulants in this EOA scheme resulted in satisfactory results for most methods. However, some methods for DTI monitoring require improvements in calibration and/or methodology. Additionally, more experience has to be achieved with methods for determination of Argatroban concentration.