Usporedba reagensa Pathromtin SL, Dade Actin FS i STA Cephascreen za određivanje aktiviranog parcijalnog tromboplastinskog vremena

Comparability of Pathromtin SL, Dade Actin FS i STA Cephascreen reagents for activated partial thromboplastin time measurement

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Sažetak

Cilj: Ispitati korelaciju vrijednosti APTV dobivenih korištenjem triju reagensa: Pathromtin SL i Dade Actin FS na analizatoru Berichrom Coagulation System (BCS), odnosno STA Cephascreen na analizatoru STA Compact.

Materijali i metode: APTV je određen u 114 uzoraka svježe plazme ispitanika, od kojih je 46 liječeno niskomolekularnim heparinom, a ostalih 68 nije bilo na antikoagulantnoj terapiji. Vrijednosti APTV određene su koagulometrijskom metodom usporedno pomoću sva tri reagensa neposredno nakon donošenja uzoraka u koagulacijski laboratorij. Vrijednosti APTV određene su i u komercijalnim kontrolnim pripravcima Lypocheck Coagulation Control proizvođača Bio-Rad (Bio-Rad Laboratories, SAD), koji obuhvaćaju tri različita raspona vrijednosti.

Rezultati: Vrijednosti komercijalnih kontrolnih uzoraka Bio-Rad kretale su se unutar raspona što ga navodi proizvođač za sva tri ispitivana reagensa. Korelacijom reagensa Pathromtin SL i Dade Actin FS, Pathromtin SL i STA Cephascreen, te Dade Actin FS i STA Cephascreen dobivene su izvrsne povezanosti (R = 0,9485, 0,9353 i 0,9072). Ispitana je razlika između dobivenih koeficijenata korelacije i nađena je statistički značajna razlika između koeficijenata korelacije rezultata dobivenih reagensima Pathromtin SL i Dade Actin FS. Passing-Bablok regresijom vrijednosti nagiba i odsječka na osi y obuhvaćale su 1 odnosno 0 samo u kombinaciji reagensa Dade Actin FS i STA Cephascreen.

Zaključak: Ispitivanje je pokazalo da su najbolje usporedive vrijednosti dobivene reagensima Dade Actin FS i STA Cephascreen. Unatoč izvrsnoj povezanosti Passing-Bablok regresija pokazala je da su reagensi Pathromtin SL i Dade Actin FS te Pathromtin SL i STA Cephascreen slabije usporedivi. Kako dobiveni rezultati potvrđuju opažanja iz svakodnevnog rada, bitno je da se bolesnici izloženi heparinskom liječenju ne prate istodobno različitim reagensima zbog različite osjetljivosti reagensa prema terapiji niskomolekularnim heparinom.

Ključne riječi: aktivirano parcijalno tromboplastinsko vrijeme, usporedba metoda, koagulacijski analizatori

Abstract

Aim: Aim of the study was to investigate correlation of activated partial thromboplastin time (APTT) measured with three different reagents: Pathromtin SL and Dade Actin FS reagents on Berichrom Coagulation System analyzer, and by STA Cephascreen reagent on STA Compact analyzer.

Material and methods: APTT was determined in parallel by Pathromtin SL and Dade Actin FS reagents, and by STA Cephascreen reagent in 114 fresh plasma samples from subjects administered low-molecular-weight heparin and in subjects known to receive no anticoagulant therapy. APTT values were determined by coagulometry method immediately upon the material receipt at coagulation laboratory. APTT values were also determined in Bio-Rad Lypocheck Coagulation Control samples (Bio-Rad Laboratories, USA) covering three different value ranges.

Results: The values recorded in Bio-Rad controls were within the range declared by the manufacturer for all three reagents used. Correlation of APTT values obtained by use of Pathromtin SL *vs.* Dade Actin FS, Pathromtin SL *vs.* Cephascreen and Dade Actin FS *vs.* STA Cephascreen yielded strong correlations (R = 0.9485, 0.9353 and 0.9072, respectively). A statistically significant difference was recorded between the results obtained by Pathromtin SL and Dade Actin FS reagents. Passing-Bablok regression slope and y-axis intercept included 1 and 0 only for Dade Actin FS *vs.* STA Cephascreen.

Conclusion: Study results showed the best compliance of values obtained by Dade Actin FS and STA Cephascreen reagents. In spite of strong correlations, Passing-Bablok regression indicated lower comparability between Pathromtin SL and Dade Actin as well as between Pathromtin SL and STA Cephascreen reagents. As the study results confirmed the observations from daily routine, it is of utmost importance that individual patients receiving heparin therapy be not monitored by use of different reagents due to the variable reagent sensitivity to low molecular weight heparin.

Key words: activated partial thromboplastin time, coagulation analyzers, method comparison

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Uvod

Aktivirano parcijalno tromboplastinsko vrijeme (APTV) je probirni test za praćenje unutarnjeg puta zgrušavanja krvi, kao i za praćenje heparinskog liječenja te otkrivanje hemoragijskih poremećaja (1). Za pokretanje unutarnjeg puta rabi se tzv. parcijalni tromboplastin koji se sastoji samo od fosfolipida kojem je dodan određeni površinski aktivator negativno nabijene površine (silicijev dioksid, kaolin, elaginska kiselina, cefalin itd.). Vrijeme potrebno za stvaranje fibrinskog ugruška mjeri se u sekundama.

Na tržištu se nalazi veći broj različitih reagensa za određivanje APTV koji se međusobno razlikuju po osjetljivosti parcijalnog tromboplastina i izboru površinskog aktivatora. Osjetljivost parcijalnog tromboplastina ovisi o njegovom podrijetlu i koncentraciji. Fosfolipidi od kojih se sastoji parcijalni tromboplastin mogu biti izdvojeni iz tkiva životinjskog podrijetla (posteljica ili mozak), a mogu biti i biljnog podrijetla. Pathromtin SL i Dade Actin FS sadrže fosfolipide biljnog podrijetla, dok je fosfolipidni udio reagensa STA Cephascreen životinjskog podrijetla (cefalin iz tkiva zečjeg mozga). Reagensi se razlikuju i po vrsti aktivatorskih površina: silikon dioksid (Pathromtin SL), elaginska kiselina (Dade Actin FS) i polifenoli (STA Cephascreen). Ovisno o sastavu reagensa proizvođači predlažu različite referentne raspone. Za Pathromtin SL predložene vrijednosti su 25,9–36,6 sekunda, za Dade Actin FS 23,0–31,9 sekunda i za STA Cephascreen 24–35 sekunda. Preporuka je da svaki laboratorij, ovisno o primijenjenom reagensu, sam odredi svoj referentni raspon za APTV (1).

Različitost u sastavu reagensa uzrokuje neujednačena mjerenja APTV u istoj plazmi, naročito ako se radi o heparinoziranoj plazmi, budući da heparin vezan za antitrombin III inhibira ključne aktivirane faktore u unutarnjem putu zgrušavanja (7).

Ova problematika potaknula nas je na uspoređivanje vrijednosti APTV dobivenih reagensima Pathromtin SL i Dade Actin FS na analizatoru Behring Coagulation System (BCS) te reagensom STA Cephascreen na analizatoru STA Compact.

Kako bi se smanjile razlike u određivanju APTV između različitih reagensa, kao jedinica izražavanja vrijednosti APTV uveo se omjer. Omjer APTV predstavlja količnik između broja sekunda ispitivanog APTV i srednje vrijednosti referentnog raspona za primijenjeni reagens. Prema preporuci Hrvatske komore medicinskih biokemičara on iznosi od 0,8 do 1,2 za osobe starije od šest mjeseci (8).

U ovom smo se radu odlučili na usporedbu vrijednosti APTV u sekundama zbog dosljednosti u prikazu rezultata budući da su vrijednosti komercijalnih pripravaka kontrola što ih navodi proizvođač izražene u sekundama, a i zbog činjenice da analizatori mjere sekunde.

Materijali i metode

Ukupno je ispitano je 114 uzoraka svježih citratnih plazmi ispitanika od kojih 68 nije bilo na antikoagulantnoj terapi-

Introduction

Activated partial thromboplastin time (APTT) is a screening test used to assess the intrinsic pathway of coagulation, to monitor heparin treatment and to detect hemorrhagic disorders (1). Partial thromboplastin consists only of phospholipids to which a certain surface activator with negative surface charge (silicon dioxide, kaolin, ellagic acid, cephalin, etc.) has been added to activate the intrinsic pathway. The time to the fibrin clot formation is measured in seconds.

A number of different reagents for APTT determination are commercially available. They differ according to the partial thromboplastin sensitivity and choice of surface activator. The sensitivity of partial thromboplastin depends on its origin and concentration. The phospholipids comprising partial thromboplastin may be isolated from the placental or brain tissue, or may be of plant origin. The reagents also differ according to the type of surface activator: silicon dioxide (Pathromtin SL), ellagic acid (Dade Actin FS) and polyphenols (STA Cephascreen). Depending on the reagent composition, manufacturers suggest different reference ranges. The suggested values for Pathromtin SL are 25.9–36.6 seconds, for Dade Actin FS 23.0–31.9 seconds and for STA Cephascreen 24–35 seconds. It is recommended that each laboratory determine its own reference range of APTT in dependence of the reagent used (1).

Different composition of reagents results in variable APTT values measured in the same plasma sample, especially in heparinized plasma, because heparin binds to antithrombin III, thus precipitating its inhibitory action upon activated factors in the intrinsic pathway (7).

This observation stimulated us to compare the APTT values obtained by Pathromtin SL and Dade Actin FS reagents on Behring Coagulation System analyzer, and by STA Cephascreen reagent on STA Compact analyzer.

APTT ratio has been introduced as a unit to express the measured values in order to reduce differences in APTT results due to different reagents. APTT ratio is a quotient between the number of seconds of the APTT measured and the mean reference range of the reagent used. According to recommendations issued by the Croatian Chamber of Medical Biochemists, the reference range for individuals older than six months is 0.8–1.2 (8).

In this study, we compared APTT values in seconds because the values of commercial control materials are declared in seconds and analyzer's units are also expressed seconds.

Materials and methods

The study included 114 fresh citrated plasma samples from 68 subjects without heparin therapy, with APTT values within the reference range of Pathromtin SL reagent

ji i čije su vrijednosti APTV bile unutar referentnih vrijednosti za reagens Pathromtin SL (26–37 s) i 46 ispitanika za koje se znalo da su liječeni niskomolekularnim heparinom. Vrijednosti APTV određene su usporedno pomoću reagensa Pathromtin SL i Dade Actin FS na analizatoru Behring Coagulation System (BCS) (Dade Behring Marburg GmbH, Njemačka) i reagensom STA Cephascreen na analizatoru STA Compact (Roche Diagnostics GmbH, Mannheim, Njemačka). Uzorci su analizirani koagulometrijskom metodom pomoću sva tri reagensa i na oba analizatora neposredno nakon donošenja uzoraka u koagulacijski laboratorij tijekom ožujka 2006.
Neprekidno tijekom 31 dana određivane su i vrijednosti APTV u kontrolama Lypocheck Coagulation Control (Level 1, 2 and 3) proizvođača Bio-Rad pomoću gore navedenih reagensa.

Statistička obrada

Načinjena je korelacija rezultata APTV, pričem statistički značajnom razlikom smatrala vrijednost P < 0,01. Razlike između koeficijenata korelacije testirane su na statističku značajnost.
Za usporedbu vrijednosti APTV rabili smo Passing-Bablok regresiju uz Cusum test linearnosti. Za opisnu statistiku kao i cjelokupnu navedenu statističku obradu rabili smo program MedCalc 9.2.0.0 (MedCalc, Mariakerke, Belgija).

Rezultati

Izmjerene vrijednosti komercijalnh kontrolnih uzoraka Bio-Rad kretale su se unutar vrijednosti što ih navodi proizvođač za sve tri razine kontrola (Level 1, 2, 3). U tablici 1. prikazane su vrijednosti što ih navodi proizvođač kontrolnih uzoraka i dobivene vrijednosti u istim uzorcima, te njihovo međusobno odstupanje. Najveće odstupanje od deklariranih vrijednosti, 14%, dobiveno je primjenom reagensa STA Cephascreen.
Medijan vrijednosti APTV dobivenih u 114 uzoraka plazme za sva tri primijenjena reagensa kretao se između 30,55 i 36,70 sekunda. Cjelokupna deskriptivna statistika prikazana je u tablici 2.
Napravljena je korelacija vrijednosti APTV dobivenih u uzorcima plazme svih 114 ispitanika načinjenih pomoću triju reagensa: Pathromtin SL, Dade Actin FS i STA Cephascreen. Usporedbom rezultata dobivenih reagensima Pathromtin SL i Dade Actin FS, Dade Actin FS i STA Cephascreen te Pathromtin SL i STA Cephascreen dobiveni su koeficijenti korelacije od 0,9485, 0,9353 i 0,9072 (tablica 3).
Ispitivana skupina od 114 ispitanika podijeljena je na dvije skupine – skupinu ispitanika koji nisu bili na antikoagulantnoj terapiji (N = 68) i skupinu koja je primala niskomolekularni heparin (N = 46). Za novo podijeljene skupine

(26–37 s), and from 46 subjects known to receive therapy with low molecular weight heparin. APTT values were determined in parallel by use of Pathromtin SL and Dade Actin FS reagents on a Behring Coagulation System analyzer (Dade Behring GmbH, Marburg, Germany) and by use of STA Cephascreen reagent on an STA Compact analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Samples were analyzed by the coagulometry method with all three reagents and on both analyzers immediately upon the receipt at coagulation laboratory during March 2006.
APTT values were determined continuously for 31 days in the Bio-Rad Lypocheck Coagulation Control samples (Level 1, 2 and 3) by use of the mentioned reagents.

Statistical analysis

Correlation of the APTT results was performed. The level of significance was set at P < 0.01. Differences between correlation coefficients were tested for the statistical significance.
Passing-Bablok regression was used on APTT value comparison, including the Cusum test for linearity. Statistical analysis including descriptive statistics was performed by use of the MedCalc 9.2.0.0 software (MedCalc, Mariakerke, Belgium).

Results

The values recorded in Bio-Rad controls were within the range reported by the manufacturer at all three control levels (Level 1, 2 and 3). The APTT values obtained in Bio-Rad controls (Level 1, 2 and 3), the values declared by the manufacturer and the bias are presented in Table 1. The largest bias of 14% was recorded with STA Cephascreen reagent.
The median of APTT values measured in 114 plasma samples was from 30.55 to 36.70 s for all three reagents used. Complete descriptive statistics is shown in Table 2. Correlation of APTT values obtained by use of different reagents yielded the following correlation coefficients: Pathromtin SL *vs*. Dade Actin FS 0.9485; Dade Actin FS *vs*. STA Cephascreen 0.9353; and Pathromtin SL *vs*. Cephascreen 0.9072 (Table 3).
The study population of 114 subjects was categorized into two groups: without heparin or heparin derivative therapy (N = 68) and the group on therapy with low molecular weight heparin (N = 46). Correlation coefficients and presence of statistically significant between-group differences were determined in these two groups (Table 4).
A statistically significant difference in correlation coefficients was recorded between the results obtained by use of Pathromtin SL and Dade Actin FS reagents in the groups with and without heparin therapy (P = 0.001). Passing-Bablok regression was performed for each group in separate.

Tablica 1. Usporedba deklariranih vrijednosti APTV kontrola Bio-Rad s dobivenim vrijednostima za sve primijenjene reagense

Table 1. Comparison of declared APTT values of Bio-Rad controls and measured values for all reagents used

Reagent	Bio-Rad Level 1 Control N = 31 LOT-78131			Bio-Rad Level 2 Control N = 31 LOT-78132			Bio-Rad Level 3 Control N = 31 LOT-78133		
	Declared value (s)	Measured value (s)	Bias%	Declared value (s)	Measured value (s)	Bias %	Declared value (s)	Measured value (s)	Bias %
APTT Pathromtin SL	38.2 (30.6-45.8)	36.5 (35.2-40)	4.5	98.6 (78.9-118)	96 (92.3-98.8)	2.6	139 (111-167)	141.5 (138.1-145.8)	1.8
APTT Dade Actin FS	29.2 (23.3-35.0)	27.7 (27-28.6)	5.1	63.8 (51.0-76.6)	64.1 (62.3-66.4)	0.5	89.2 (71.4-107)	89.5 (87.7-90.9)	0.3
*APTT STA Cephascreen	32.9 (26.3-39.5)	28.3 (27.4-29.8)	14	67 (53.6-80.5)	60.5 (52-62.9)	9.7	88.6 (70.9-106)	76.1 (73.8-78.4)	14.1

Values are presented with median and range
*Declared values refer to all Roche STA APTT (Diagnostica Stago PTT Automate) reagents without kaolin

Tablica 2. Opisna statistika dobivenih vrijednosti APTV za sva tri primijenjena reagensa

Table 2. Descriptive statistics for APTT values obtained with the three reagents

Reagent	N	Median value	95% CI	Min	Max
STA Cephascreen	114	34.650	32.016-39.284	23.700	136.600
Dade Actin FS	114	30.550	28.748-33.600	20.600	136.000
Pathromtin SL	114	36.700	32.748-40.780	21.300	145.000

Tablica 3. Koeficijenti korelacije za sve tri kombinacije reagensa u svim ispitivanim uzorcima

Table 3. Correlation coefficients for all three reagent combinations in all study samples

Reagent combination	R	P
Pathromtin SL *vs.* Dade Actin FS	0.9485	< 0.001
Dade Actin FS *vs.* STA Cephascreen	0.9353	< 0.001
Pathromtin SL *vs.* STA Cephascreen	0.9072	< 0.001

određeni su koeficijenti korelacije te je testirano postoji li među njima statistički značajna razlika (tablica 4).
Statistički značajna razlika dobivena je među koeficijentima korelacije rezultata dobivenih reagensima Pathromtin SL i Dade Actin FS u skupinama s heparisnkom terapijom i bez nje (P = 0,001) te je Passing-Bablok regresija napravljena za svaku skupinu zasebno. Za ostale kombinacije reagensa (Dade Actin FS i STA Cephascreen te Pathromtin SL i STA Cephascreen) nije nađena značajna razlika između

Other reagent combinations (Dade Actin FS *vs.* STA Cephascreen and Pathromtin SL *vs.* STA Cephascreen) yielded no statistically significant difference in correlation coefficients, thus being considered as a homogeneous group.
The Cusum linearity test performed on Passing-Bablok regression showed that there was no significant deviation from linearity for any of the above reagent combinations (P > 0.10).

Tablica 4. Koeficijenti korelacije rezultata APTV za skupine bez terapije i s terapijom određenih pomoću sva tri primijenjena reagensa

Table 4. Correlation coefficients of APTT results in groups without and with therapy determined with all three reagents used

Reagent combination	Without therapy N = 68 R	With therapy N = 46 R	P
Pathromtin SL *vs.* Dade Actin FS	0.7256	0.9161	0.0010
Dade Actin FS *vs.* STA Cephascreen	0.8229	0.8852	0.2348
Pathromtin SL *vs.* STA Cephascreen	0.796	0.8129	0.8074

Tablica 5. Podaci dobiveni Passing-Bablok regresijom – nagib i odsječak na osi y uz 95% interval pouzdanosti

Table 5. Passing Bablok regression data – slope and intercept with 95% confidence interval

Reagent combination	N	Slope (95% CI)	Intercept (95% CI)
Pathromtin SL vs. Dade Actin FS (without therapy)	68	0.6170 (0.5000–0.7422)	8.5723 (4.7500–12.0250)
Pathromtin SL *vs.* Dade Actin FS (with therapy)	46	0.8249 (0.6828–0.9746)	–2.9283 (–10.9106–(–4.7741))
Pathromtin SL *vs.* STA Cephascreen	114	0.7060 (0.6551–0.7787)	8.6698 (6.5606–10.3423)
Dade Actin FS *vs.* STA Cephascreen	114	1.1231 (1.0061–1.2452)	–0.2230 (–3.8022–(–3.4309))

koeficijenta korelacije i stoga je ispitivana skupina promatrana kao jedna cjelina. U sklopu Passing Bablok regresije učinjen je Cusum test linearnosti koji je za sve gore navedene kombinacije reagensa pokazao da nema značajnog odstupanja od linearnosti (P > 0,10).

Nagib i odsječak na osi y, kao i 95% intervali pouzdanosti dobiveni Passing-Bablok regresijom različitih kombinacija reagensa prikazani su u tablici 5.

Svi podaci iz Rezultata u sekundama preračunati su u omjer s obzirom na referentne vrijednosti za svaki reagens. Te vrijednosti nisu prikazane u ovom radu, jer statističke značajke, vrijednosti testova, kao i njihovo tumačenje odgovaraju onima primijenjenim za sekunde. S obzirom na to da komercijalne pripravke kontrola proizvođač deklarira u sekundama, kako je napomenuto u Uvodu, zbog dosljednosti izražavanja odlučili smo se za prikaz naših rezultata u sekundama.

Rasprava

Provedenim ispitivanjem željelo se istražiti koliko su utemeljene naše praktične spoznaje iz svakodnevnog rada o usporedivosti različitih reagensa za određivanje APTV.

Pathromtin SL, Dade Actin FS i STA Cephascreen pokazali su različitu osjetljivost prema komercijalnim pripravcima

The slope and y-axis intercept as well as 95% confidence intervals yielded by Passing-Bablok regression for various reagent combinations are presented in Table 5.

All data in the Results section that were presented in seconds were re-calculated as ratio depending on the reference range for each reagent used. These data are not shown because the statistical features, values of tests and their interpretation correspond to those in seconds. Considering that the values of commercial control materials are declared in seconds, as mentioned in the Introduction, we decided to express all study results in seconds in order to sustain consistency of the result presentation.

Discussion

The aim of the study was to verify our daily routine experience with comparability of different reagents used on APTT determination. Pathromtin SL, Dade Actin FS and STA Cephascreen showed variable sensitivity according to the commercial control samples, Bio-Rad Level 1, 2 and 3. All three reagents performed well in terms of preset values declared by the manufacturer but differed between each other. The largest bias from the declared values was observed with STA Cephascreen reagent. It should be noted that the manufacturer of the commercial controls

kontrola, Bio-Rad Level 1, 2 i 3. Sva tri reagensa odlično se odnose prema deklariranim vrijednostima proizvođača, ali se međusobno razlikuju. Najveće odstupanje od deklariranih vrijednosti primijećeno je kod reagensa STA Cephascreen. Međutim, treba napomenuti da proizvođač kontrola reagense Roche STA APPT (Diagnostica Stago PTT Automate) dijeli u skupine s kaolinom i bez njega, tj. nema određene vrijednosti za reagens STA Cephascreen. Na osnovi toga STA Cephascreen nalazi se u skupini reagensa bez kaolina.

Važno je naglasiti da su koeficijenti korelacije za sve ispitivane kombinacije reagensa pokazali izvrsnu povezanost, te da je kod svih kombinacija zadovoljen uvjet linearnosti. Daljnjom analizom Passing-Bablok regresije uočena su razilaženja.

Usporedba reagensa Dade Actin FS i Pathromtin SL pokazala je da se unatoč odličnoj korelaciji skupina ispitanika ne može ispitivati kao cjelina ako je prisutna terapija niskomolekularnim heparinom. U skupini bez terapije koeficijent korelacije je značajno niži od koeficijenta korelacije skupine na terapiji, iako se prije podjele skupina očekivala daleko veća razlika rezultata kada se radi o višim vrijednostima APTV.

Iz podataka dobivenih Passing-Bablok regresijom vidljivo je da rezultati nisu usklađeni i ne slijede jednaku linearnost (nagib i odsječak na osi y ne obuhvaćaju 1 odnosno 0). Uz to, nagib pravca u skupinama bez terapije i s terapijom nije podjednak, što dodatno upućuje na lošu podudarnost. Iz navedenih podataka može se zaključiti kako nema proporcionalnog odstupanja među rezultatima, dakle, usporedivost ipak nije zadovoljavajuća.

Činjenica da su se rezultati ispitivanja reagensima Pathromtin SL i Dade Actin FS morali ispitati prema pripadnosti skupini bez terapije ili s terapijom upućuje na relativno lošu usporedivost ovih dvaju reagensa.

Za reagense Pathromtin SL i STA Cephascreen Passing-Bablok regresija također upućuje na neusklađenost rezultata koji pokazuju različitu linearnost.

Reagensi Dade Actin FS i STA Cephascreen jedini zadovoljavaju postavke Passing-Bablok regresije, odnosno nagib pravca je vrlo blizu 1, a odsječak na osi y je malen. Dakle, rezultati dobiveni reagensima Dade Actin FS i STA Cephascreen su dobro usklađeni i slijede istu linearnost.

Iz svih navedenih podataka može se zaključiti da su međusobno najjače povezani rezultati APTV dobiveni reagensima Dade Actin FS i STA Cephascreen. Najslabija međusobna povezanost rezultata APTV pokazala se između vrijednosti dobivenih reagensima Pathromtin SL i Dade Actin FS. Vidljivo je da su veća odstupanja među rezultatima u skupini uzoraka bez terapije, što je proizvođač vjerojatno želio ispraviti različitim preporučenim rasponom referentnih vrijednosti.

Bez obzira na to što su za sve reagense dobivene vrlo dobre i odlične korelacije, vidljivo je da postoje razlike u vri-

divides Roche STA APTT (Diagnostica Stago PTT Automate) reagents into groups with or without kaolin, meaning there are no specific values for STA Cephascreen reagent. According to this, STA Cephascreen reagent is in the "without kaolin" group.

It should be noted that correlation coefficients yielded high correlation for all the reagent combinations tested, with the condition of linearity met in all of these combinations. However, additional analysis by use of Passing-Bablok regression revealed some discrepancies. Comparison of Dade Actin FS and Pathromtin SL reagents indicated that, in spite of the high correlation, patients should not be tested as a homogeneous group if receiving low molecular weight heparin therapy.

A significantly lower correlation coefficient was obtained in the group without heparin therapy than in the group of patients administered heparin therapy, although the result difference recorded prior to group categorization seemed to be by far greater relative to high APTT values.

The slope 95% confidence interval did not include 1 in either group, whereas the y-axis intercept 95% confidence interval in the group without therapy did not include 0 for difference from the group with heparin therapy, where it included 0. Also, the slope was not comparable in the two groups, thus additionally indicating low compatibility level. These data show that there was no proportional result deviation, i.e. the level of comparability was rather low.

The fact that the results obtained by use of Pathromtin SL and Dade Actin FS reagents had to be tested according to categories of patients with or without heparin therapy points to the relatively poor comparability of the two reagents. The slope and y-axis intercept obtained by Passing-Bablok regression for Pathromtin SL and STA Cephascreen did not include 1 and 0, respectively, also pointing to discrepancy of the results showing variable linearity. Dade Actin FS and STA Cephascreen were the only combination meeting the conditions of Passing-Bablok regression, i.e. the slope was very close to 1, while the y-axis intercept was small. Thus, the results obtained by Dade Actin FS and STA Cephascreen reagents were quite compatible and followed the same linearity pattern.

Accordingly, the highest correlation was observed between the results of APTT measurement by use of Dade Actin FS and STA Cephascreen reagents, whereas the results obtained by use of Pathromtin SL and Dade Actin FS yielded lowest correlation. Greater result deviation was observed in the group of samples without heparin therapy, which the manufacturer had probably tried to correct by proposing different reference ranges.

Thus, although very good correlations were obtained for all three reagents, the APTT values determined by different reagents showed differences that could not be disregarded.

jednostima APTV određenih različitim reagensima koje se ne smiju zanemariti.
Važno je napomenuti da su Pathromtin SL i Dade Actin FS reagensi istog prozvođača i da su fosfolipidi obaju reagensa biljnog podrijetla, dok je fosfolipidni udio reagensa STA Cephascreen životinjskog podrijetla (cefalin iz tkiva zečjeg mozga). Budući da se reagensi bitno razlikuju po vrsti aktivatorskih površina: silikon dioksid (Pathromtin SL), elaginska kiselina (Dade Actin FS) i polifenoli (STA Cephascreen), možda je upravo vrsta aktivatorske površine presudna u osjetljivosti pojedinog reagensa za određivanje APTV.
Iz svega prikazanog može se zaključiti da je veoma važno pratiti APTV pojedinog bolesnika istim reagensima na istom analizatoru.

It should be noted that Pathromtin SL and Dade Actin FS reagents come from the same manufacturer and the phospholipids found in the two reagents are of plant origin, whereas the phospholipid moiety of the STA Cephascreen reagent is of animal origin (cephalin from rabbit brain tissue). As the reagents differ substantially according to the type of activator surfaces, i.e. silicon dioxide (Pathromtin SL), ellagic acid (Dade Actin FS) and polyphenols (STA Cephascreen), the type of activator surface may play a decisive role in the particular reagent sensitivity on APTT determination.
All these data suggest that it is of great importance to follow APTT results of each individual patient using the same reagents on the same analyzer.

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Literatura/References

1. *Wagner C, Dati F. Activated partial thromboplastin time (APTT) test. In: Thomas L. Clinical Laboratory Diagnostics. Frankfurt/Main: TH-Books Verlagsgesellschaft mbH; 1998. str. 602-4.*
2. *Labar B, Hauptman E et al. [Sustav zgrušavanja i fibrinolize]. In: Labar B, Hauptman E, et al, eds. [Hematologija]. Zagreb: Školska knjiga; 1998. p. 48-52. (in Croatian)*
3. *Proctor RR, Rappaport SJ. The partial thromboplastin time with kaolin: a simple screening test for first stage plasma clotting factor deficiencies. AJCP1961;36:212-9.*
4. *Suchman L, Griner PF. Diagnostic uses of the activated partial thromboplastin time and prothrombin time. Ann Intern Med 1986;104:810-6.*
5. *Strekerud FG, Abilgaard U. Activated partial thromboplastin time in heparinized plasma: influence of reagent, acute phase reaction, and interval between sampling and testing. Clin Appl Thrombosis Hemostasis 1996;2:169-76.*
6. *Kohler M, Dati F, Kolde HJ. Activated partial thromboplastin time position finding. Standardization of the method, interpretation of results and limits of applicability. Lab Med 1995;19:162-6.*
7. *Hirsh J, Fuster V. Guide to anticoagulant therapy. Part I: Heparin. Circulation 1994;98:1449-68.*
8. *Harmonizacija laboratorijskih nalaza u području opće medicinske biokemije. Available at: http://www.hkmb.hr/novosti/Harmonizacija%20laboratorijskih%20nalaza.htm; Accesed: March 2007.*