Influence of Blood Collection Systems on Coagulation Tests

Kan Alma Sistemlerinin Koagülasyon Testleri Üzerinde Etkileri

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Abstract

Objective: Coagulation tests are influenced by pre-analytic conditions such as blood collection systems. Change of glass collection tubes with plastic ones will cause alteration of the test results.

The aim of this study was to compare three plastic blood collection tubes with a standard glass blood collection tube and each plastic collection tube with the other two for possible additional tube-to-tube differences.

Material and Methods: A total of 284 blood samples were obtained from 42 patients receiving warfarin during their routine controls, besides 29 healthy volunteers. Subgroup analyses were done according to health status.

Results: Our study demonstrated that different blood collection tubes have a statistically significant influence on coagulation tests. The magnitude of the effect depends on the tube used. However most of the tests performed on samples obtained from any tube correlated significantly with results obtained from other tube samples.

Conclusion: Although blood collection tubes with different brands or properties will have distinct effects on coagulation tests, the influence of these blood collection tubes may be relatively small to interfere with decision-making on dose prescription, therefore lack clinical importance. Correlations between the results showed that, one of these plastic blood collection tubes tested in our study, can be used interchangably for a wide variety of coagulation assays.

Key Words: Coagulation testing, Glass tubes, Plastic tubes

Özet

Amaç: Koagülasyon testleri, farklı kan alma sistemleri gibi preanalitik durumlardan etkilenirler. Kullanılan cam tüplerin, plastik olanlarla değiştirilmesi, test sonuçlarında farklılık yaratabilir.

Çalışmanın amacı 3 farklı plastik kan alma tüpünün, standart cam kan alma tüpü ile karşılaştırılmasıdır. Tüpler arası olası ek bir farklılığın saptanması açısından, plastik tüpler de ayrıca kendi aralarında karşılaştırıldı.

Gereç ve Yöntemler: Rutin kontrolleri sırasında varfarin tedavisi alan 42 hastadan ve 29 sağlıklı gönüllüden toplam 284 kan örneği alındı. Subgrup analizleri deneklerin sağlık durumlarına göre yapıldı.

Bulgular: Her ne kadar farklı marka veya özellikteki kan alma tüpleri koagülasyon testleri üzerinde belirgin etki yaratabilse de, bu etki doz ayarlamasını etkilemeyecek ve klinik önem arz etmeyecek kadar küçük olabilir. Sonuçlar

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arasındaki korelasyon, çalışmamızda kullanılan plastik kan alma tüplerinden herhangi birinin, bir çok koagülasyon testi için, diğerlerinin yerine kullanılabileceğini göstermektedir.

Sonuç: Çalışmamız farklı kan alma tüplerinin koagülasyon testleri üzerinde istatistiksel olarak anlamlı etkisi olduğunu gösterdi. Bu etkinin derecesi kullanılan tüpe göre değişmektedir. Fakat, herhangi bir tüpten alınan örneklerle gerçekleştirilen testlerin çoğunun, diğer tüplerden alınan örnekler ile belirgin korelasyon gösterdiği gözlendi.

Anahtar Sözcükler: Koagülasyon testleri, Cam tüpler, Plastik tüpler

Introduction

Siliconized glass collection tubes have traditionally been used in the coagulation tests for the determination of International Normalized Ratio (INR), prothrombin time (PT) and coagulation factor levels.[1-5] However, the potential risk of sharp injury and biohazardous exposure due to broken glass during handling or centrifugation, rendered the need of newer plastic collection tubes and clinical laboratories gradually replaced glass collection tubes with plastic ones.[1-4]

Since coagulation tests are influenced by pre-analytic conditions such as the blood collection systems, change of glass collection tubes with plastic ones raised concerns about the potential for in vitro activation of the clotting cascade, hence alteration of test results.[1-13]

Therefore, we planned to compare three different plastic blood collection tubes with a standard glass blood collection tube which is used worldwide as in our hospital, to find out whether glass and plastic blood collection tubes have significantly different influence on coagulation tests, both in patients under oral anticoagulant therapy (OAT) and in healthy volunteers. Each plastic collection tube was also compared with each other for possible additional tube-to-tube differences. To the best of our knowledge, no study in current literature has also compared the plastic collection tubes at the same time.

Patients and Methods

A total of 284 blood samples were obtained from 42 patients receiving warfarin during their routine controls, as well as 29 healthy volunteers, upon approval from Education, Planning and Coordination Committee (Ethical Committee) in our hospital. Our study was performed according to the principles outlined in the appropriate version of 1964 Declaration of Helsinki and informed consent was obtained from each subject.

Blood samples were taken using a 21G needle and BD Vacutainer reuseable standard size tube holder (Becton Dickinson, USA), allowing natural vacuum of tube to withdraw specimen into tube by clean venopuncture after 8-12 hours of fasting and prior to the daily dose of warfarin in the patient group. The test tubes contained sodium citrate 3.2%, with a ratio of one part anticoagulant to nine parts whole blood. The precedure was completed when vacuum no longer continued to withdraw. All samples were obtained from peripheral arm veins. For each case, 1 tube of blood sample was collected into a glass collection tube and 3 additional samples were collected into 3 different plastic collection tubes, in a random order. Tubes were delivered in the laboratory, checked for adequate tube filling, and centrifuged for 10 minutes at 2,000 G to prepare platelet-poor plasma (<10,000 platelets per microliter). In keeping accordance with the Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory Standards) guidelines, collection tubes were kept unopened at 18°C to 24°C before separation of cells from plasma. Hemolytic and/or lipemic samples were excluded. All samples were tested as fresh plasma and processed within 2 hours of collection to avoid the loss of activity of coagulation factors. All four samples from the same person were processed and analyzed at the same time.

Patient demographics, including sex, age, primary diseases, and medication history were recorded.

Blood collection tubes were grouped as;

Tube Group I: BD Vacutainer® Citrate Tubes - Glass (BD Vacutainer®, 9NC Sodium Citrate, 3.2%, 4.5 mL, Becton, Dickinson and Company, UK.),

Tube Group II: VACUETTE® Blood Collection Tubes (Vacuette® Coagulation Tubes, 9NC Sodium citrate, 3.2%, 4 mL, Greiner Bio-One GmbH, Germany.),

Tube Group III: BD Vacutainer® Plus Plastic Citrate Tube (BD Vacutainer® 9NC Sodium Citrate, 3.2%, 2.7 mL, Becton, Dickinson and Company, UK.),

Tube Group IV: BD Vacutainer® Plus Plastic Citrate Tube (BD Vacutainer® 9NC Sodium Citrate, 3.2%, 1.8 mL, Becton, Dickinson and Company, UK.).

Subgroup analyses were done according to health status as demonstrated below:

Group P: Patients receiving warfarin therapy (n= 42, 59.2%),

Group H: Healthy Volunteers (n= 29, 40.8%).

Mean INR, PT%, PT, activated partial thromboplastin time (APTT), activated partial thromboplastin time ratio (APTT R) and fibrinogen levels were obtained both in healthy volunteers (Group H) and patients under OAT (Group P).

D-Dimer, protein C, protein S, antithrombin, thrombin time, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, Factor XII, plasminogen, Alpha 2 antiplasmin, activated protein C resistance test (APCR), Lupus antibodies (Lupus Ab) and von Willebrand factor antigen (vWF Ag) were available only in healthy volunteers.

Statistical Analyses

The data were presented as mean and standard deviations, and percentage, where appropriate. Chi square test and Paired-Samples T test were used to compare patient characteristics and test values. Pearson correlation test was utilized to determine the correlations between groups. Probability (p) values below 0.05 were considered significant. Confidence intervals (CI) were calculated at the 95% level.

Correspondences of results between Tube Groups were undertaken using the Bland-Altman procedure, and Bland-Altman plots were performed to assess the magnitude of disagreement between the results, plotting the mean of the results for the two methods on the x axis against the arithmetic or percentage difference on the y axis [14].

Results

A total of 284 samples were obtained from 71 cases (29 men (40.8%), 42 women (59.2%)). Mean age of the patients was 44.4±14.6 years.

Without any subgrouping;

When all mean values were compared, INR, PT, APTT and fibrinogen results obtained in Tube Group II were different but not significantly from the other groups (Table 1).

Table 1: Comparison of tube groups without any subgrouping.

	Mean Values				p Values					
	I	II	III	IV	I vs II	I vs III	I vs IV	II vs III	II vs IV	III vs IV
INR (INR)	2.0±0.9	1.8±0.9	2.0±1.0	2.0±0.9	0.0001	0.594	0.297	0.0001	0.0001	0.194
PT% (%)	55.0±33.7	58.9±36.2	55.5±34.3	54.6±34.8	0.0001	0.060	0.612	0.0001	0.005	0.995
PT (Sec)	23.7±12.0	22.4±11.3	23.7±12.1	23.9±12.0	0.0001	0.372	0.344	0.0001	0.0001	0.511
APTT (Sec)	45.8±13.4	49.3±17.3	44.7±12.7	45.5±12.7	0.0001	0.002	0.176	0.0001	0.0001	0.038
APTT R (R)	1.4±0.3	1.6±0.5	1.4±0.3	1.4±0.3	0.0001	0.002	0.051	0.0001	0.0001	0.113
Fibrinogen (g/L)	3.1±0.8	3.1±0.9	3.1±0.8	3.1±0.8	0.010	0.556	1.000	0.004	0.002	0.432
D Dimer (mg/L) #	0.3±0.3	0.7±1.8	0.2±0.1	0.2±0.1	0.207	0.367	0.407	0.169	0.175	0.695
Protein C (%) #	127.4±29.0	125.9±30.3	132.7±34.8	115.4±39.9	0.730	0.356	0.067	0.310	0.087	0.019
Protein S (%) #	96.8±18.4	94.6±13.0	96.4±19.3	95.8±18.9	0.540	0.926	0.821	0.576	0.739	0.906
AntiThrombin (%) #	94.5±10.7	109.1±10.7	96.1±10.6	96.0±9.0	0.0001	0.373	0.309	0.0001	0.0001	0.939
Thrombin Time (Sec) #	18.0±1.5	19.7±2.2	18.0±4.0	20.1±5.0	0.0001	0.997	0.043	0.027	0.763	0.071
Factor V (%) #	115.5±27.8	135.4±29.3	118.6±29.1	114.7±26.3	0.002	0.640	0.788	0.008	0.003	0.441
Factor VII (%) #	104.8±26.0	121.7±42.6	107.4±28.3	107.3±32.5	0.001	0.489	0.422	0.022	0.005	0.984
Factor VIII (%) #	137.7±57.7	128.0±53.0	124.6±43.9	109.2±27.8	0.232	0.042	0.001	0.558	0.007	0.002
Factor IX (%) #	88.5±20.1	110.2±29.6	89.1±16.3	88.2±26.0	0.0001	0.843	0.961	0.0001	0.010	0.865
Factor X (%) #	100.6±16.7	115.9±23.2	102.5±17.0	95.4±20.3	0.0001	0.252	0.181	0.0001	0.0001	0.086
Factor XI (%) #	89.5±27.8	104.3±28.5	98.2±15.6	92.5±22.2	0.001	0.053	0.499	0.121	0.013	0.115
Factor XII (%) #	124.5±47.2	122.4±55.6	124.5±49.8	110.5±47.4	0.898	0.106	0.281	0.983	0.162	0.134
Plasminogen (%) #	103.8±18.4	112.6±17.6	104.8±20.4	94.5±14.8	0.0001	0.220	0.334	0.0001	0.0001	0.011
Alpha 2 antiplasmin (%) #	106.1±19.4	107.7±17.8	100.4±6.8	106.0±13.6	0.113	0.455	0.143	0.129	0.714	0.173
APCR/ FVL (NR) #	1.2±0.1	1.0±0.3	1.2±0.3	1.1±0.3	0.203	0.855	0.322	0.274	0.441	0.411
Lupus Ab (Sec) #	37.1±2.0	38.7±2.3	38.3±3.2	37.8±2.9	0.140	0.401	0.546	0.694	0.289	0.411
vWF Ag (%) #	93.1±21.7	104.7±25.3	94.4±23.6	91.9±22.3	0.0001	0.285	0.100	0.0001	0.0001	0.095

#Only in healthy volunteers not receiving warfarin.

INR: International Normalized Ratio, PT: Prothrombin time, APTT: Activated Partial Thromboplastin Time, APTT R: Activated Partial Thromboplastin Time Ratio, APCR: Activated protein C resistance test, Lupus Ab: Lupus antibodies, vWF Ag: von Willebrand factor antigen.

Table 2: Correlations and correspondences between tube groups without any subgrouping (Correlations/Correspondences).

	Pearson Correlations / Correspondences Between Groups					
	I vs II	I vs III	I vs IV	II vs III	II vs IV	III vs IV
INR (INR)	+/-	+/+	+/+	+/-	+/-	+/+
PT% (%)	+/-	+/-	+/+	+/-	+/+	+/+
PT (Sec)	+/-	+/+	+/+	+/-	+/-	+/+
APTT (Sec)	+/-	+/-	+/+	+/-	+/-	+/+
APTT R (R)	+/-	+/-	+/+	+/-	+/-	+/-
Fibrinogen (g/L)	+/-	+/+	+/+	+/-	+/+	+/+
D Dimer (mg/L) #	-/-	+/+	+/+	-/-	-/-	+/+
Protein C (%) #	+/+	+/+	+/+	+/+	+/+	+/+
Protein S (%) #	-/-	-/-	-/-	+/-	-/-	-/-
AntiThrombin (%) #	+/+	+/+	+/+	+/+	+/+	+/+
Thrombin Time (Sec) #	+/+	-/-	-/-	-/-	-/-	-/-
Factor V (%) #	+/+	-/-	-/-	+/+	-/-	+/+
Factor VII (%) #	+/-	+/+	+/+	+/-	+/-	+/+
Factor VIII (%) #	+/+	+/-	+/-	+/+	+/-	+/-
Factor IX (%) #	+/+	+/+	-/-	+/-	-/-	-/-
Factor X (%) #	+/-	+/+	+/+	+/-	-/-	-/-
Factor XI (%) #	+/+	+/-	+/+	+/-	+/+	+/+
Factor XII (%) #	+/+	+/+	+/+	+/+	-/-	+/+
Plasminogen (%) #	+/+	+/+	+/+	+/+	+/+	+/+
Alpha 2 antiplasmin (%) #	+/+	-/-	-/-	-/-	-/-	+/+
APCR #	-/-	-/-	-/-	-/-	-/-	-/-
Lupus Ab (Sec) #	-/-	-/-	-/-	-/-	-/-	+/+
vWF Ag (%) #	+/-	+/+	+/+	+/+	+/-	+/-

*INR: International Normalized Ratio, **PT:** Prothrombin time, **APTT:** Activated Partial Thromboplastin Time, **APTT R:** Activated Partial Thromboplastin Time Ratio, **APCR:** activated protein C resistance test, **Lupus Ab:** Lupus antibodies, **vWF Ag:** von Willebrand factor antigen.*

Pearson correlation test showed significant correlations between total mean values. Using Bland-Altman procedure, significant correspondences were also valid between Tube Group I, III and IV. (Table 2) Correspondences between mean INR values were shown in Figure 1 as Bland-Altman plots.

When mean D-Dimer, protein C, protein S, antithrombin, thrombin time, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, Factor XII, plasminogen, Alpha 2 antiplasmin, activated protein C resistance test (APCR), Lupus antibodies (Lupus Ab) and von Willebrand factor antigen (vWF Ag) values were compared, significant differences were observed between Tube Group II and the others, although some comparisons had significant correlations and correspondences (Table 1 and 2).

According to Group P and Group H;

Demographic data of the patients were listed in Table 3. Since Group H consisted of young healthy volunteers, the only statistically significant difference was between mean ages (p= 0.0001).

When mean values were compared, statistically significant differences existed especially between Tube Group II and the others (Table 4). When Pearson correlation test was performed, significant correlations were observed between mean values. But, Bland-Altman procedure showed poor correspondences between Tube Group II and the others (Table 5).

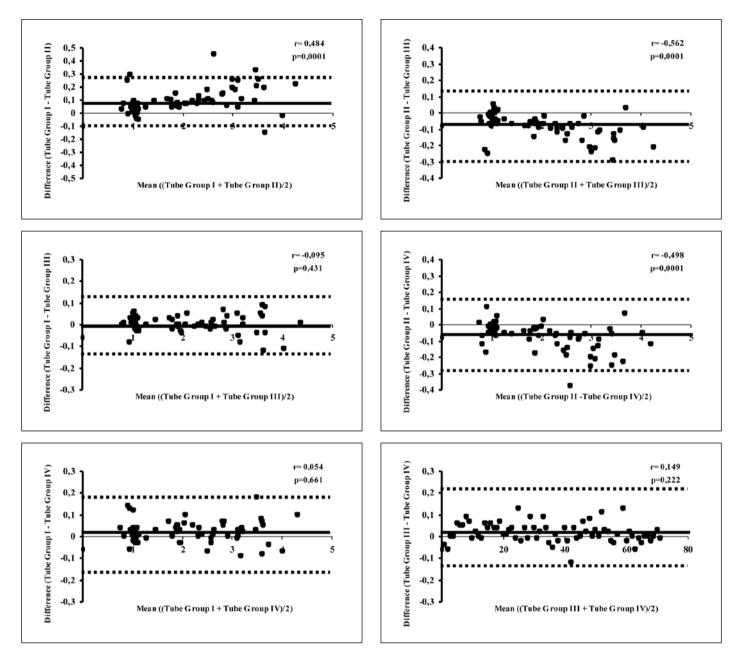Coagulation Factors were studied in Group H and variable results were obtained when mean values were com-

Figure 1: Correspondences between mean INR values according to Tube Groups without any subgrouping (Bland-Altman plots).

Upper-Left: *Tube Group I vs Tube Group II,* **Upper-Middle:** *Tube Group I vs Tube Group III,* **Upper-Right:** *Tube Group I vs Tube Group IV,*
Lower-Left: *Tube Group II vs Tube Group III,* **Lower-Middle:** *Tube Group II vs Tube Group IV,* **Lower-Right:** *Tube Group III vs Tube Group IV.*
p< 0.05: *No correspondence.*

pared (Table 1 and 2). While some of the tests were affected by plastic blood collection tubes, others were not.

Discussion

Different blood collection tubes will have an influence on laboratory tests and may result in changes in therapeutic dosage adjustment in patients receiving warfarin therapy. This may result in overdosing or underdosing which

in turn may cause bleeding or thromboembolic complications.[15]

Glass collection tubes are unblocked and have siliconized interior. On the other hand, plastic collection tubes have a double-wall technology (*sandwich tubes – plastic within plastic*) for reliable analysis results. The outer tube is made of polyethylene terephthalate and ensures a long shelf-life for the vacuum, while the inner tube is made out

Table 3: Demografic data according to Group P and H.

	Group P 59.2% (n= 42)	Group H 40.8% (n= 29)	p
Gender			
Male	37.5 (15)	48.3 (14)	0.290
Female	64.3 (27)	51.7 (15)	
Age (years)	52.5±12.9	32.7±7.2	0.0001
Warfarin dose (mg/week) #	32.8±16.8	-	-
Duration of warfarin use (months) #	57.2±59.7	-	-
DM #	9.5 (4)	-	-
HT #	31.0 (13)	-	-
HL #	7.1 (3)	-	-
CRF #	2.4 (1)	-	-
COPD #	4.8 (2)	-	-
Valve Replacement #	88.1 (37)	-	-
Atrial Fibrilation #	2.4 (1)	-	-
DVT #	9.5 (4)	-	-
Drugs #			
Warfarin	100.0 (42)	-	-
Cardiac glycosides	31.0 (13)	-	-
β Blockers	33.3 (14)	-	-
ACEI	19.0 (8)	-	-
ARB	4.8 (2)	-	-
CCB	7.1 (3)	-	-
ASA	26.2 (11)	-	-
Insulin	2.4 (1)	-	-
Oral antidiabetics	2.4 (1)	-	-
H2 receptor antagonists	11.9 (5)	-	-
Proton-pump inhibitors	4.8 (2)	-	-
Diuretics	38.1 (16)	-	-
Antihyperlipidemics	2.4 (1)	-	-
Bronchodilators	4.8 (2)	-	-

INR: International Normalized Ratio, DM: Diabetes mellitus, HT: Hypertension, HL: Hyperlipidemia, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, DVT: Deep venous thrombosis, ACEI: Angiotensin converting enzyme inhibitors, ARB: Angiotensin receptor blockers, CCB: Calcium channel blockers, ASA: Acetyl salicylic acid.

of polypropylene and prevents the citrate solution from evaporating. Polypropylene is ideal for sensitive coagulation parameters, due to its inert characteristics.[1]

There are conflicting reports about the effects of plastic blood collection tubes on coagulation testing and most are limited to PT analyses.[1,5,12,16-23] Previous studies reported significant differences in thrombin time and PT test results.[1,5,12]

The aim of our study was to determine whether conversion to plastic tubes from glass tubes would result in significant differences in laboratory results. Since no re-

port has compared plastic collection tubes at the same time, we also focused on comparing each plastic collection tube with each other.

Our study demonstrated that different blood collection tubes had a statistically significant influence on coagulation tests. The magnitude of the effect depended on the tube used.

It has been suggested that INR differences below 10% do not seriously interfere with oral anticoagulant dosage regulation.[6,23] Our study showed that the mean INR values increased or decreased by the influence of differ-

Table 4: Comparison of tube groups according to Group P and H.

		Mean Values			
		I	II	III	IV
INR (INR)	Group P	2.6±0.7*£	2.5±0.7*$€	2.6±0.7$φ	2.6±0.7£€φ
	Group H	1.0±0.1*	0.9±0.1*$	1.0±0.1$	1.0±0.1
PT% (%)	Group P	28.7±10.2*£	30.5±10.8*$€	28.7±10.2$φ	29.0±10.3£€φ
	Group H	93.0±12.2*	99.0±14.9*$€	94.3±12.6$	94.5±17.2€
PT (Sec)	Group P	31.8±9.2*£	30.0±8.8*$€	31.8±9.2$φ	31.5±9.2£eφ
	Group H	12.0±0.8*	11.5±1.2*$e	11.9±0.9$	12.1±1.7€
APTT (Sec)	Group P	54.0±11.4*#	59.8±15.2*$e	52.4±10.7#$φ	53.0±10.7€φ
	Group H	33.9±4.1	34.5±4.7	33.5±3.6	34.0±3.3
APTT R (R)	Group P	1.6±0.3*#	1.7±0.4*€	1.5±0.3#φ	1.5±0.3€φ
	Group H	1.0±0.1	1.0±0.1	1.0±0.1	0.9±0.1
Fibrinogen (g/L)	Group P	3.5±0.6*	3.7±0.7*€	3.6±0.6	3.6±0.7€
	Group H	2.4±0.4	2.3±0.4	2.3±0.4	2.3±0.4

INR: International Normalized Ratio, PT: Prothrombin time, APTT: Activated Partial Thromboplastin Time, APTT R: Activated Partial Thromboplastin Time Ratio.

(P<0.05; *I vs II, #I vs III, £I vs IV, $II vs III, €II vs IV, jIII vs IV)

Table 5: Correlations and Correspondences Between Tube Groups according to Group P and H (Correlations/Correspondences).

		Pearson Correlations[+] and Correspondences Between Tube Groups					
		I vs II	I vs III	I vs IV	II vs III	II vs IV	III vs IV
INR (INR)	Group P	+/-	+/+	+/+	+/-	+/-	+/+
	Group H	+/-	+/+	+/-	+/+	+/+	+/+
PT% (%)	Group P	+/-	+/+	+/+	+/-	+/-	+/+
	Group H	+/+	+/+	+/+	+/+	+/+	+/+
PT (Sec)	Group P	+/-	+/+	+/+	+/-	+/-	+/+
	Group H	+/-	+/+	+/+	+/+	+/+	+/+
APTT (Sec)	Group P	+/-	+/+	+/+	+/-	+/-	+/+
	Group H	-/-	+/+	+/-	-/-	-/-	+/+
APTT R (R)	Group P	+/-	+/+	+/+	+/-	+/-	+/+
	Group H	-/-	+/+	+/+	-/-	-/-	+/+
Fibrinogen (g/L)	Group P	+/+	+/+	+/+	+/+	+/+	+/+
	Group H	+/+	+/+	+/+	+/+	+/+	+/+

INR: International Normalized Ratio, PT: Prothrombin time, APTT: Activated Partial Thromboplastin Time, APTT R: Activated Partial Thromboplastin Time Ratio

ent blood collection systems. Mean INR value was lowest in Tube Group II. Values obtained in Tube Group II and IV were 4.1% and 0.3% lower, respectively, and in Tube Group III was 0.02% higher than Tube Group I. Although statistical differences not existed in INR Group I, III and IV, values were nearly equal in practice.

Although, some of the statistical analyses showed no differences for some of the assays like Alpha 2 antiplasmin, APCR, protein S or Lupus Ab between different tubes,

poor correlations were observed. It is unclear why some of the tests would be affected by plastic blood collection methods while others would not. Type or International Sensitivity Index (ISI) of the reagent used, blood-tube surface interaction, the dynamic properties of the coagulation factors, use of individual vacuum tubes or clinically insignificant differences in tube blood volume (although all samples were checked for adequate filling) are some of the factors affecting the results.[1,2,5,7,8,10,11,12,24-26]

Besides, as seen in Tube Group II, different brands may also have distinct effects on coagulation tests.

Tube Group II was the only group with a different brand, but differences related to Tube Group II did not reach clinical significance because the difference below 10% does not seriously interfere with oral anticoagulant dosage regulation. [6,23]

Correlations between the results showed that, plastic blood collection tubes can be used in place of glass tubes or instead of the other plastic tubes for a wide variety of coagulation assays but the clinicians should be aware of the fact.

The influence of blood collection tubes on a single coagulation analyzer using a single thromboplastin reagent with a constant ISI, may be insufficiently small to interfere with decision-making on dose prescription. On the other hand it must be kept in mind that probably the combination of multiple systematic variables such as different brands, reagents or analyzers may cumulatively lead to important INR differences. To reduce the resultant total error from system combinations, the influence of the blood collection systems may have to be eliminated. Detection of inter-laboratory multicenter calibration standards for the establishment of an international reference will also be helpful.

It should be a note of caution that, when any laboratory plans to change their blood collection method, clinicians must be alerted about the new method. Actually, the best way to gain experience with a new blood collection method may be the use of both the old and new tubes simultaneously for an adaptation period to avoid unmeant trouble. Since analytical or statistical significance is only numerical data, the most important judgment is clinical experience based on patient-dose-response triangle.

Conflict of Interest Statement

None of the authors have any conflicts of interest, including specific financial interests, relationships, and/or affiliations, relevant to the subject matter or materials included.

References

1. Gosselin RC, Janatpour K, Larkin EC, Lee YP, Owings JT. Comparison of samples obtained from 3.2% sodium citrate glass and two 3.2% sodium citrate plastic blood collection tubes used in coagulation testing. Am J Clin Pathol 2004;122:843-848.

2. Fiebig EW, Etzell JE, Ng VL. Clinically relevant differences in prothrombin time and INR values related to blood sample collection in plastic vs glass tubes. Am J Clin Pathol 2005;124:902-909.

3. Toulon P, Ajzenberg N, Smahi M, Guillin MC. A new plastic collection tube made of polyethylene terephtalate is suitable for monitoring traditional anticoagulant therapy (oral anticoagulant, unfractionated heparin, and low molecular weight heparin). Thromb Res 2007;119:135-143.

4. Kratz A, Stanganelli N, Van Cott EM. A comparison of glass and plastic blood collection tubes for routine and specialized coagulation assays: A comprehensive study. Arch Pathol Lab Med 2006;130:39-44.

5. Flanders M, Crist R, Rodgers G. A comparison of blood collection in glass versus plastic vacutainers on results of esoteric coagulation assays. Lab Med 2003;34:732-735.

6. van den Besselaar AM, Hoekstra MM, Witteveen E, Didden JH, van der Meer FJ. Influence of blood collection systems on the prothrombin time and international sensitivity index determined with human and rabbit thromboplastin reagents. Am J Clin Pathol 2007;127:724-729.

7. Duncan EM, Casey CR, Duncan BM, Lloyd JV. Effect of concentration of trisodium citrate anticoagulant on calculation of the International Normalised Ratio and the International Sensitivity Index of thromboplastin. Thromb Haemost 1994;72:84-88.

8. Adcock DM, Kressin DC, Marlar RA. Effect of 3.2% vs 3.8% sodium citrate concentration on routine coagulation testing. Am J Clin Pathol 1997;107:105-110.

9. Danielson CF, Davis K, Jones G, Benson J, Arney K, Martin J. Effect of citrate concentration in specimen collection tubes on the International Normalized Ratio. Arch Pathol Lab Med 1997;121:956-959.

10. Chantarangkul V, Tripodi A, Clerici M, Negri B, Mannucci PM. Assessment of the influence of citrate concentration on the International Normalized Ratio (INR) determined with twelve reagent-instrument combinations.Thromb Haemost 1998; 80:258-262.

11. Palmer RN, Gralnick HR. Cold-induced contact surface activation of the prothrombin time in whole blood. Blood 1982;59:38-42.

12. Tripodi A, Chantarangkul V, Bressi C, Mannucci PM. How to evaluate the influence of blood collection systems on the international sensitivity index. Protocol applied to two new evacuated tubes and eight coagulometer/thromboplastin combinations. Thromb Res 2002;108:85-89.

13. Rapaport SI, Vermylen J, Hoylaerts M, Saito H, Hirsh J, Bates S, Dahlbäck B, Poller L. The multiple faces of the partial thromboplastin time APTT. J Thromb Haemost 2004;2:2250-2259.

14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-10.

15. Schulman S. Clinical practice. Care of patients receiving long-term anticoagulant therapy. N Engl J Med 2003;349:675-683.

16. van den Besselaar AM, Meeuwisse-Braun J, Witteveen E, van Meegen E. Effect of evacuated blood collection tubes on thromboplastin calibration. Thromb Haemost 1998;79:1062-1063.

17. van den Besselaar AM, Bertina RM, van der Meer FJ, den Hartigh J. Different sensitivities of various thromboplastins to two blood collection systems for monitoring oral anticoagulant therapy. Thromb Haemost 1999;82:153-154.

18. van den Besselaar AM, Chantarangkul V, Tripodi A. A comparison of two sodium citrate concentrations in two evacuated blood collection systems for prothrombin time and ISI determination. Thromb Haemost 2000;84:664-667.

19. D'Angelo G, Villa C. Measurement of prothrombin time in patients on oral anticoagulant therapy: Effect of two different evacuated tubes. Haematologica 1999;84:656-657.

20. Biron-Andréani C, Mallol C, Séguret F, Schved JF. Plastic versus siliconized glass tubes: Evaluation in current laboratory practice. Thromb Haemost 2000;83:800-801.

21. Foucher K, Toulon P, Schved JF, Polack B. Suggestions for an appropriate methodological approach for the validation of an evacuated blood collection tube made in plastic material including the effect of age. Thromb Haemost 2004;91:845-847.

22. Ridyard J, Bhavnani M, Seal LH. Laboratory control of oral anticoagulant therapy: Preservation of prothrombin time specimens using a polypropylene collection system. Clin Lab Haematol 1998;20:369-372.

23. Poller L, Keown M, Chauhan N, van den Besselaar AM, Tripodi A, Shiach C, Jespersen J. European Concerted Action on Anticoagulation: A multicentre calibration study of WHO international reference preparations for thromboplastin, rabbit (RBT/90) and human (rTF/95). J Clin Pathol 2005;58:667-669.

24. Adcock DM, Kressin DC, Marlar RA. Minimum specimen volume requirements for routine coagulation testing: dependence on citrate concentration. Am J Clin Pathol 1998;109:595-599.

25. Peterson P, Gottfried EL. The effects of inaccurate blood sample volume on prothrombin time (PT) and activated partial thromboplastin time (aPTT). Thromb Haemost 1982;47:101-103.

26. Reneke J, Etzell J, Leslie S, Ng VL, Gottfried EL. Prolonged prothrombin time and activated partial thromboplastin time due to underfilled specimen tubes with 109 mmol/L (3.2%) citrate anticoagulant. Am J Clin Pathol 1998;109:754-757.