## INTERNATIONAL JOURNAL OF MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2023.19042 Int J Med Biochem 2023;6(3):165-172

**Research Article** 



# The use of new generation small-volume blood collection tubes for complete blood count

® Ahmet Erkin Bozdemir<sup>1</sup>, ® Fatma Demet Arslan², ® Banu Isbilen Basok<sup>1</sup>, ® Sukran Copur³, ® Nisel Ozkalay Yilmaz³, ® Harun Akar⁴

<sup>1</sup>Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkiye <sup>2</sup>Department of Medical Biochemistry, Bakircay University, Cigli Training and Research Hospital, Izmir, Turkiye <sup>3</sup>Department of Medical Microbiology, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkiye <sup>4</sup>Department of Internal Medicine, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkiye

#### Abstract

**Objectives:** Newborns and especially patients with malignancy develop frequently iatrogenic anemia based on phlebotomy. The use of blood collection tubes with small-volume may reduce the need for blood transfusion and the associated risks due to frequent phlebotomy. Therefore, we evaluated the reliability and accuracy of the complete blood count (CBC) using new generation small-volume blood collection tubes (SV-BCT) instead of large-volume blood collection tubes (LV-BCT).

**Methods:** Venous blood samples were taken from 40 adult in-patients and collected to SV-BCT/LV-BCT pairs of three different brand (Microtainer®MAP-0.5 ml/Vacutainer®-2.0 ml; Becton, Dickinson and Company, USA) ([Microvette®-0.5 mL/S-Monovette®-2.6 ml; Sarstedt Ag and Co. KG, Germany]) ([MiniCollect®Complete-0.5 ml/Vacuette®-2.0 ml; Greiner Bio-One GmbH, Austria]). All tubes contained K2EDTA except Microvette®. Sixteen parameters of CBC were analyzed using a DxH 800 (Beckman Coulter Inc., USA). CBC results in tube pairs were compared in terms of statistical and clinical (bias%) significance.

**Results:** There were statistically significant differences between the results of SV-BCT and LV-BCT pairs of the same brands for some parameters. However, bias% between tubes for 16 parameters was within the desirable limits, the differences were not clinically significant.

**Conclusion:** Health personnel and phlebotomists can safely prefer SV-BCT which is a new generation and technically useful for CBC, especially in patients requiring frequent phlebotomy. Thus, the volume of blood sampling may be reduced to prevent iatrogenic blood loss.

Keywords: Blood collection tube, complete blood count, latrogenic anemia, phlebotomy

How to cite this article: Bozdemir AE, Arslan FD, Isbilen Basok B, Copur S, Ozkalay Yilmaz N, Akar H. The use of new generation smallvolume blood collection tubes for complete blood count. Int J Med Biochem 2023; 6(3):165-172.

One of the important factors in patient blood management is minimizing "iatrogenic" blood loss. Nowadays, there is an increasing tendency for more laboratory analyzes to diagnose and treat patients. It has been known that blood samples taken for laboratory tests cause iatrogenic anemia for more than 35 years [1]. Especially, patients suffer more blood loss in pediatric, oncologic, and chronic diseases that need frequent

laboratory tests. Premature infants who have critically ill undergo multiple erythrocyte suspension transfusions in the early weeks of life because of frequent blood testing [2].

However, measures against iatrogenic anemia are being taken to reduce the amount of blood samples taken from patients. The researchers had some success in finding ways to reduce transfusions significantly in this patient population in the past

Address for correspondence: Ahmet Erkin Bozdemir, MD. Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkiye

Phone: +90 532 372 46 50 E-mail: ahmeterkin@yahoo.co.uk ORCID: 0000-0001-9542-1454

Submitted: October 02, 2022 Revised: January 03, 2023 Accepted: January 12, 2023 Available Online: March 10, 2023 OPEN ACCESS This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).



years [3, 4]. In addition, it is shown that costs, length of stay, and need for transfusion are significantly decreased by reducing the number of ordered unnecessary laboratory tests [5].

Pediatric small-volume blood collection tubes (SV-BCT) were produced in the late 1970s due to their advantages in patients who had difficulty in collecting blood samples and required frequent blood sampling. Nevertheless, pediatric blood sampling tubes were not suitable for directly use in auto analyzers. There were some obstacles to the widespread use of SV-BCT. SV-BCT had disadvantages such as their labeling difficulties, and manual loading and running to the devices. In addition, it could rise injury risk, loss of time, and over workload. The innovations such as manufacturing SV-BCT or micro-collection tubes, we believe those disadvantages no longer exist.

Complete blood count (CBC) is one of the most preferred laboratory tests for many diseases and frequently used for diagnosis and follow-up. The type and amount of anticoagulants used may affect the analysis results. The Clinical and Laboratory Standards Institute (CLSI) recommends EDTA as an anticoagulant for whole blood analysis and reports that the amount should be 1.4–2.0 mg for 1 mL of blood sample [6, 7]. However, while reducing the collected amount of blood samples, the quality and efficiency of the results should not compromise. Thus, CLSI documents and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) recommend the clinical validation for new blood collection tubes [8]. As following these recommendations, the local clinical validation of the tubes has begun to be carried out widely [9–11].

Now SV-BCT that can be load with no manual processing in auto-analyzers are produced. In the study, we evaluated whether novel SV-BCT instead of large-volume blood collection tubes (LV-BCT) can be safely used in automated CBC analyzers due to their advantages. Thus, we planned to provide ease of use in the laboratory by ensuring the commonly using of SV-BCTs.

## **Materials and Methods**

#### Participants

A total of 40 adult inpatients at Internal Medicine Clinics were randomly selected in this study. As possible, especially in patients with different chronic diseases (diabetes mellitus, hyperlipidemia, anemia, blood cancer, thyroid, liver disorders etc.) were included in the study to obtain data covering the clinical decision limits or analytical range for each test simultaneously. This analytical comparison study conducted under the Helsinki Declaration [12] and with the approval of the local ethics committee. Informed consent obtained from the patients.

#### **Collecting of blood samples**

Venous blood samples were collected in three different brand tubes (six tubes overall) both SV-BCT and LV-BCT tubes within 5 consecutive days, and all samples were simultaneously analyzed on the collection day. This study was designed according to the "EFLM Working Group for Preanalytical Phase" recommendation, except for the blood sampling process [13]. Blood samples were taken by syringe following CLSI GP41-A6 standard [14], because SV-BCT were vacuum-free. Blood samples were discharged from the syringe into the tubes in random order. No visible clot was seen in any of the tubes.

#### **Blood collection tubes**

SV-BCT and LV-BCT of the same brand were compared. Becton, Dickinson, and Company (BD) and Greiner Bio-One GmbH (GBO) tube pairs contained K2EDTA, while Sarstedt AG and Co tube pairs have K3EDTA. All tubes have been validated by the manufacturers. It was considered that the tube pairs have the same EDTA content and that would not create an obstacle for peer-to-peer comparison. All tubes are as follows;

- a. Vacutainer<sup>®</sup> (Reference number: 367842, 2 ml, 13×75 mm) and Microtainer<sup>®</sup>MAP (Reference number: 363706, 0.5 mL, 13×75 mm); (Becton, Dickinson and Company (BD), NJ, USA).
- b. Vacuette<sup>®</sup> (Item No.: 454047, 2 ml, 13×75 mm) and MiniCollect<sup>®</sup>Complete (Item No.: 450547, 0.25–0.5 ml, 13×75 mm); (GBO GmbH, Kremsmünster, Austria).
- c. S-Monovette<sup>®</sup> (Order Number: 04.1901.100, 2.6 ml, 13×65 mm) and Microvette<sup>®</sup> (Order number: 20.1341.100, 0.5 mL, 10.8×47.6 mm); (SARSTEDT AG & Co. KG, Nümbrecht, Germany). External tube adapter (13×75 mm) used for Microvette<sup>®</sup> tubes.

#### **CBC** parameters and its analysis

White blood cell (WBC), red blood cell (RBC), hemoglobin (Hb), platelet (PLT), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular Hb (MCH), MCH concentration (MCHC), red cell distribution width (RDW), mean platelet volume (MPV), neutrophil (NE), lymphocyte (LYM), monocyte (MO), eosinophil (EO), basophil (BA), and plateletcrit (Pct) were analyzed by an automated hematology analyzer using impedance and multi-angle laser scatter method (DxH 800, Beckman Coulter Inc., USA). The commercial internal and external quality control materials were run to ensure the reliability of test results throughout the study.

All blood samples were run on the same analyzer. To simultaneously analyze CBC within six different blood collection tubes, they were automatically loaded using a rack system to an automated blood counter device. Blood samples were run in a random order in duplicate.

#### **Statistical analysis**

Statistical analysis was performed using MedCalc statistical program (MedCalc Software, Belgium). The duplicate results were averaged. The mean values between the tube pairs were statistically and clinically compared. The normal distribution of data was analyzed using Shapiro–Wilk test.

Table 1. Comparison results of BD brand tubes								
	Vacutainer®	Microtainer®MAP	r	bias%	bias <sub>d</sub> %	р	Slope (95% Cl)	Intercept (95% CI)
WBC (×10 <sup>9</sup> /L)	7.7 (3.3–19.7)	7.7 (3.3–19.7)	0.998	-0.41	4.59	0.210	0.992-1.008	-0.075-0.056
RBC (×10 <sup>12</sup> /L)	3.95±0.87	3.97±0.88	0.998	0.52	1.56	0.005*	0.987-1.021	-0.058-0.081
Hb (g/L)	106 (70–148)	106 (71–150)	0.997	0.46	1.61	0.005*	1.000-1.037	-0.309-0.05
PLT (×10 <sup>9</sup> /L)	216 (75–733.5)	211 (71–738.5)	0.997	-1.34	2.55	0.003*	0.970-1.015	-7.251-4.989
Hct (%)	32.7±6.5	32.9±6.5	0.998	0.46	1.34	0.045*	0.978-1.014	-0.212-0.916
MCV (fl)	84.1±9.3	83.9±9.4	0.999	-0.24	1.01	0.018*	0.995–1.031	-2.688-0.258
MCH (pg)	28.3±3.9	28.2±4.0	0.998	-0.41	0.75	0.006*	0.987–1.029	-0.962-0.267
MCHC (g/L)	336±14	336±15	0.967	-0.14	0.47	0.429	0.957–1.150	-5.085-1.419
RDW (%)	15.1 (12–37.6)	15.0 (12.2–37.5)	0.992	0.01	0.69	0.915	0.981-1.004	-0.057-0.331
MPV (fl)	9±1	8±1	0.990	0.16	1.54	0.660	0.951-1.031	-0.277-0.430
NE (×10 <sup>9</sup> /L)	4.9 (1.3–18)	4.9 (1.3–18)	0.998	-0.21	5.08	0.519	0.986-1.015	-0.083-0.057
LYM (×10 <sup>9</sup> /L)	1.6±0.6	1.6±0.6	0.996	-0.75	5.65	0.343	1.000-1.000	0.000-0.000
MO (×10 <sup>9</sup> /L)	0.6 (0.1–1.6)	0.6 (0.15–1.6)	0.962	-1.01	5.07	0.083	1.000-1.000	0.000-0.000
EO (×10 <sup>9</sup> /L)	0.1 (0.0–0.6)	0.1 (0.0–0.6)	0.978	-4.42	17.8	0.564	1.000-1.000	0.000-0.000
BA (×10 <sup>9</sup> /L)	0.0 (0.0-0.1)	0.0 (0.0–0.1)	0.573	-1.25	6.21	0.531	0.500-2.000	0.000-0.000
Pct (%)	0.22 (0.07–0.57)	0.21 (0.07–0.55)	0.988	-1.07	2.97	0.004*	0.954–1.000	-0.005-0.007

The results were represented as mean ± standard deviation for normally distributed data or median (minimum-maximum) for non-normal distributed data. \*: Statistically significant difference between tubes was considered as p<0.05. P value of the correlation coefficient for all parameters between paired tube was <0.001. BD: Becton, Dickinson; r: Correlation coefficient; bias%: Calculated bias; bias; %: Desirable specification for the inaccuracy European Biological Variation Study (EuBIVAS) (15); CI: Confidence interval; WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; PLT: Platelet; Hc: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCH: CMCH concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; NE: Neutrophil; UYM: Lymphocyte; MO: Monocyte; EO: Eosinophil; Bc: Platelet; Flatelet; Fla

The results were represented as mean±standard deviation for normally distributed data or median (minimum-maximum) for non-normal distributed data. The statistical difference between the results of paired tubes (SV-BCT and LV-BCT) according to the normal distribution was evaluated by Wilcoxon or paired t-test. P<0.05 was considered statistically significant. The correlation between tubes was analyzed by Spearman or Pearson test according to the normal distribution.

To evaluate clinical difference between tubes, the bias% of WBC, RBC, Hb, PLT, Hct, MCV, MCH, MCHC, RDW, MPV, NE, LYM, MO, EO, BA, and Pct parameters between SV-BCT and LV-BCT of same brand was calculated. LV-BCT was accepted as reference tubes, that LV-BCT are the tube currently in use in our lab. Bias% was calculated using the following formula: bias%=100\*([SV-BCT]–[LV-BCT])/LV-BCT. All bias% values were evaluated according to the desirable specification for bias% based on the European Biological Variation Study (EuBIVAS) [15].

Passing-Bablok regression analysis was performed to determine the presence of systematic or proportional error between the results of paired tubes. Bland-Altman plots were generated to ascertain areas of bias between paired tubes. The mean difference was also assessed with Bland-Altman plots and then compared with the bias.

## Results

When we compared SV-BCT and LV-BCT of each brand; RBC, Hb, PLT, Hct, MCV, MCH, and Pct levels in BD (Table 1); MCV and MCH levels in GBO (Table 2); WBC, RBC, PLT, MCV, NE, and Pct levels in Sarstedt (Table 3) were found statistically different. Correlation coefficients between all paired tubes were greater than 0.900 for all parameters, except BA. For BA, while the relationship between paired tubes of BD was found moderate (r=0.573, p<0.001), GBO and Sarstedt paired tubes had high relationships (r=0.683, p<0.001 and r=0.800, p<0.001).

According to the regression analysis, systematic, and proportional errors were detected for PLT in GBO tubes. PLT in Vacuette<sup>®</sup> were statistically higher than in MiniCollect<sup>®</sup>Complete, but the difference was not clinically significant (Table 2). In Sarstedt tubes, there was systematic error for RBC, Hb, and Hct; both systematic and proportional errors were detected for MCHC parameters (Table 3). Only Hb and PLT in S-Monovette<sup>®</sup> were statistically less than in Microvette<sup>®</sup>, but not clinically significant. However, bias% values between SV-BCT and LV-BCT of three different brands for all parameters were within desirable limits (Tables 1-3), and the clinical difference (based on the EuBIVAS) was not found [15].

Bland-Altman plots comparing the difference between the results of paired tubes were shown in Figures 1-3, respectively, except for EO and BA parameters. Since the mean of EO and BA were zero, the difference as % of the mean could not be expressed in the Bland-Altman charts. In general, bias% between paired tubes was decreased by the increasing values of all parameters. It was seen bias% values up to 20% in NE, MO, LYM, Plt, and Pct values, up to 8% in RBC, Hb, Hct, and WBC values, and up to 3% in MCV, MCH, and MCHC values. However, the mean bias% values were not exceeded 2%.

Table 2. Comparison results of GBO brand tubes									
	<b>Vacuette</b> <sup>®</sup>	MiniCollect® Complete	r	bias	bias <sub>d</sub> %	р	Slope (95% Cl)	Intercept (95% CI)	
WBC (×10 <sup>9</sup> /L)	7.7 (3.3–19.65)	7.5 (3.4–19.9)	0.997	-0.24	4.59	0.203	0.983–1.007	-0.086-0.104	
RBC (×10 <sup>12</sup> /L)	3.94±0.87	3.96±0.88	0.999	0.34	1.56	0.095	0.995–1.015	-0.039-0.040	
Hb (g/L)	105 (70–148)	106 (71–150.5)	0.996	0.05	1.61	0.165	1.000-1.017	-0.160-0.050	
PLT (×10 <sup>9</sup> /L)	211 (83–743)	207 (71–759)	0.997	-0.89	2.55	0.472	1.011-1.061+	-14.561-(-3.524)†	
Hct (%)	32.8±6.5	32.8±6.6	0.998	0.12	1.34	0.485	0.989–1.017	-0.463-0.401	
MCV (fl)	84.2±9.4	84.0±9.4	0.999	-0.21	1.01	0.006*	0.984–1.015	-1.439-1.130	
MCH (pg)	28.4±4.0	28.3±4.0	0.999	-0.35	0.75	0.013*	0.977-1.017	-0.550-0.529	
MCHC (g/L)	336±15	336±15	0.983	-0.08	0.47	0.561	0.978–1.097	-3.205-0.746	
RDW (%)	15.1 (12.2–37.8)	15.0 (12.1–37.8)	0.991	0.07	0.69	0.589	0.993–1.024	-0.377-0.155	
MPV (fl)	9±1 (8–9)	9±1 (8–9)	0.994	0.41	1.54	0.108	0.956–1.031	-0.233-0.427	
NE (×10 <sup>9</sup> /L)	4.9 (1.3–18.1)	4.9 (1.3–18.2)	0.999	-0.56	5.08	0.057	0.987-1.008	-0.071-0.035	
LYM (×10 <sup>9</sup> /L)	1.6±0.7	1.6±0.7	0.988	-0.68	5.65	0.558	1.000-1.032	-0.058-0.000	
MO (×10 <sup>9</sup> /L)	0.6 (0.15–1.55)	0.6 (0.15–1.5)	0.970	2.00	5.07	0.174	1.000-1.100	-0.050-0.000	
EO (×10 <sup>9</sup> /L)	0.1 (0.0–0.6)	0.1 (0.0–0.6)	0.960	1.79	17.8	0.851	1.000-1.000	0.000-0.000	
BA (×10 <sup>9</sup> /L)	0.0 (0.0–0.15)	0.0 (0.0–0.15)	0.683	0.83	6.21	0.751	1.000-1.000	0.000-0.000	
Pct (%)	0.21 (0.08–0.55)	0.21 (0.07–0.58)	0.988	-0.85	2.97	0.586	1.000-1.083	-0.017-0.000	

The results were represented as mean ± standard deviation for normally distributed data or median (minimum-maximum) for non-normal distributed data. \*: Statistically significant difference between tubes was considered as p<0.05. P value of the correlation coefficient for all parameters between paired tube was <0.001. ': The values for which 95% CI of the slope and 95% CI of the intercept did not include 1 and 0 (respectively). GBO: Greiner Bio-One GmbH; r: Correlation coefficient; bias%: Calculated bias; bias%: Desirable specification for the inaccuracy European Biological Variation Study (EuBIVAS) (15); CI: Confidence intervai; WBC: White blood cell; RBC: Red blood cell; BL: Hb: Hemoglobin; PLT: Platelet; Hct: Hemoscrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCHC: MCH concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; NE: Neutrophil; LYM: Lymphocyte; HO: Monocyte; EO: Eosinophil; BA: Basophil; Pct: Plateletcrit

#### Table 3. Comparison results of Sarstedt brand tubes

	S-Monovette®	Microvette®	r	bias%	bias <sub>d</sub> %	р	Slope (95% Cl)	Intercept (95% CI)
WBC (×10 <sup>9</sup> /L)	7.7 (3.3–20.2)	7.7 (3.3–19.8)	0.994	-1.09	4.59	<0.001*	0.975-1.000	-0.100-0.957
RBC (×10 <sup>12</sup> /L)	3.96±0.89	3.98±0.88	0.998	0.61	1.56	0.030*	0.971-1.006	0.007-0.147 <sup>+</sup>
Hb (g/L)	106 (69.5–151)	107 (70.5–148.5)	0.994	0.51	1.61	0.062	0.967-1.000	0.050-0.402 <sup>+</sup>
PLT (×10 <sup>9</sup> /L)	212 (72–747.5)	211 (70–763.5)	0.995	-1.49	2.55	0.013*	0.962-1.023	-6.428-5.359
Hct (%)	32.5±6.7	32.6±6.5	0.998	0.39	1.34	0.229	0.963-1.000	0.125–1.388†
MCV (fl)	83.2±9.3 (79.2-87.9)	83.1±9.3 (78.8–88.1)	0.999	-0.24	1.01	0.003*	0.986-1.020	-1.861-0.926
MCH (pg)	28.3±3.9 (26.0-30.1)	28.3±4.0 (26.2–30.2)	0.998	-0.01	0.75	0.883	1.000-1.044	-1.247-0.000
MCHC (g/L)	339±14 (332–346)	340±15 (330–346)	0.973	0.22	0.47	0.161	1.019–1.240†	-8.087-(-0.571) <sup>+</sup>
RDW (%)	15.1 (12.1–37.7)	15.1 (12.2–37.9)	0.988	-0.38	0.69	0.151	0.963-1.012	-0.306-0.507
MPV (fl)	9±1 (8–9)	9±1 (8–9)	0.984	0.26	1.54	0.602	0.960-1.065	-0.545-0.360
NE (×10 <sup>9</sup> /L)	5.1 (1.3–18.6)	4.9 (0.0–17.9)	0.994	-1.10	5.08	0.006*	0.957-1.000	-0.100-0.139
LYM (×10 <sup>9</sup> /L)	1.6±0.7 (1.2–2)	1.6±0.6 (1.2–1.9)	0.995	-0.88	5.65	0.068	0.938-1.000	0.000–0.859
MO (×10 <sup>9</sup> /L)	0.6 (0.15–1.6)	0.6 (0.0–1.55)	0.945	-1.62	5.07	0.205	1.000-1.000	0.000-0.000
EO (×10 <sup>9</sup> /L)	0.1 (0.0–0.65)	0.1 (0.0–0.6)	0.961	-0.19	17.8	0.627	1.000-1.000	0.000-0.000
BA (×10 <sup>9</sup> /L)	0.0 (0.0-0.1)	0.0 (0.0–0.2)	0.800	-3.75	6.21	0.629	1.000-2.000	0.000-0.000
Pct (%)	0.21 (0.06–0.58)	0.21 (0.06–0.58)	0.991	0.88	2.97	0.044*	0.973-1.027	$0.004 - 0.008^{\dagger}$

The results were represented as mean±standard deviation for normally distributed data or median (minimum-maximum) for non-normal distributed data. \*: Statistically significant difference between tubes was considered as p<0.05. P value of the correlation coefficient for all parameters between paired tube was <0.001. ': The values for which 95% CI of the slope and 95% CI of the intercept did not include 1 and 0 (respectively). r: Correlation coefficient; bias<sub>3</sub>%: Desirable specification for the inaccuracy European Biological Variation Study (EuBIVAS) (15); CI: Confidence interval; WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; PLT: Platelet; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCHC: MCH concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; NE: Neutrophil; LYM: Lymphocyte; RO: Eosinophil; BA: Basophil; Pct: Plateletrit

## Discussion

Although there are some studies where different SV-BCT were compared or validated [16–20], our study is the first to compare SV-BCT and LV-BCT of three different brands in au-

tomated blood counter analyzers under the same conditions. The crucial result of this comparison is that CBC results in SV-BCT on automated blood-counting devices may be clinically reliable. In our study, the new generation SV-BCT is automatically processed, centrifuged, and labeled like a standard large-







RBC: Red blood cell; Hb: Hemoglobin; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCHC: MCH concentration; RDW: Red cell distribution width; PLT: Platelet; Pct: Plateletcrit; WBC: White blood cell; NE: Neutrophil; LYM: Lymphocyte; MO: Monocyte; BD: Becton, Dickinson; LV-BCT: Large-volume blood collection tubes; SV-BCT: Small-volume blood collection tubes.

volume tube. It fits in instrument racks, thus, transferring to a secondary tube or manual pipetting is eliminated.

When the pairs of SV-BCT and LV-BCT were compared, the adaptation of the existing SV-BCT to the automated systems would be advantageous for both the patient and laboratorian. By reducing blood loss due to phlebotomy, the risk of iatrogenic anemia, the need for transfusion, and the resulting complications and cost burden may be reduced [21]. It has also been shown that reducing the amount of blood taken from patients shortens the length of hospital stay [22–24]. Thus, instead of dealing with side problems that may arise from phlebotomy, clinicians will be able to deal more with the patient and other issues related to the disease during hospitalization. As the blood volume taken from the patients will decrease by approximately 75% (0.5 mL/2.0 mL), it can be estimated that

the rate and cost of medical waste will decrease. In a recent study, a cost analysis was performed over an infant who was hospitalized for 40 days. During the period, 2 mL of blood was taken from the baby for each CBC and a total of 4 units of ery-throcyte suspension were given for a total of 26 mL of blood loss. When the costs of the erythrocyte suspension and blood collection tubes were calculated together and the reduction in expenses was tried to be estimated according to the estimated erythrocyte suspension need in case of using a pediatric tube. Accordingly, it has been calculated that using SV-BCT instead of LV-BCT can cost almost 74% reduced cost in total [4].

The new generation SV-BCT for the automated process is the one-piece microtube to offer compatibility with most automated blood counter devices. These SV-BCT offer the extra advantage of having the carrier tube permanently attached, fur-



RBC: Red blood cell; Hb: Hemoglobin; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCHC: MCH concentration; RDW: Red cell distribution width; PLT: Platelet; Pct: Plateletcrit; WBC: White blood cell; NE: Neutrophil; LYM: Lymphocyte; MO: Monocyte; GBO: Greiner Bio-One GmbH; LV-BCT: Large-volume blood collection tubes; SV-BCT: Small-volume blood collection tubes.

ther reducing the need for separate accessories. They can be automatically handled, processed, centrifuged, and labelled as a primary tube as a standard LV-BCT. They fit in instrument racks and eliminate the need for manual processing. Thus, extra procedures such as transfer to a secondary tube or manual pipetting will be eliminated. This is an opportunity and convenience for a large-scale clinical laboratory. One can speculate that employee safety can increase by automating laboratory tests compared to manual work on analyzers. In addition to these speculations, reduced medical waste or decreased cost would be among the possible positive outcomes of the study. In addition to the advantages of SV-BCT, it few disadvantages, such as being vacuum-free, and not being able to run a test a 3<sup>rd</sup> time. However, running a CBC a 3<sup>rd</sup> time is a rare situation according to our clinical experiences. We can

MO (10 ML)

strongly recommend the use of these tubes, in patients (especially in newborns, pediatric oncology and hematology, and other pediatric units) collecting blood with the needle tip or syringe. SV-BCT will provide benefit when the use of tubes with vacuum is limited, especially due to structural vascular disorders, etc.

## Limitations

In our study, patients from the Internal Medicine service were included in the study so that the outcome range of the parameters could be particularly wide. However, due to ethical concerns, blood was not drawn from patients with extreme CBC values. In addition, the advantages of SV-BCT in terms of patients, employees, costs, and medical waste could not be determined and remained speculative. A long-term study with more detailed plan can address these limitations.



RBC: Red blood cell; Hb: Hemoglobin; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular Hb; MCHC: MCH concentration; RDW: Red cell distribution width; PLT: Platelet; Pct: Plateletcrit; WBC: White blood cell; NE: Neutrophil; LYM: Lymphocyte; MO: Monocyte; LV-BCT: Large-volume blood collection tubes; SV-BCT: Small-volume blood collection tubes.

## Conclusion

New generation SV-BCT can be automatically processed, centrifuged, and labeled like a standard large-volume tube. It fits in instrument racks, thus, transferring to a secondary tube or manual pipetting will be eliminated.

However, clinical validation is required to prove that SV-BCT does not compromises on quality. This clinical validation study can contribute to advancing knowledge about SV-BCT, so to widely use of these.

latrogenic anemia and its risks may be prevented by reducing the blood volume collected for CBC. These tubes may provide convenience for phlebotomists who use a needle or syringe. The safety of laboratory staff may be increased by removing the manual process, such as transferring the sample to another tube. We showed that the SV-BCT can be safely used instead of the LV-BCT of the same brand. Today, in an era when the test systems can be worked with a drop of blood samples and the test adapters developed for mobile phones are discussed, it is not considered sustainable for patients and employees to perform blood testing with such high sample volumes. We also recommend developing new blood tubes suitable for automated systems and demonstrating their clinical relevance to encourage the use of SV-BCT for other laboratory tests.

**Acknowledgements:** Here, we thank the Nurse Supervisor of the Department of Internal Medicine, Ecmel Ozen, for the efforts during the sampling process.

**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Ethics Committee Approval:** The study was approved by The Dokuz Eylul University Non-interventional Research Ethics Committee (No: 2016/26-32, Date: 06/10/2016).

**Financial Disclosure:** The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept – F.D.A.; Design – F.D.A.; A.E.B.; Supervision – F.D.A., A.E.B., B.I.B.; Funding – F.D.A., A.E.B., B.I.B.; Materials – H.A.; Data collection &/or processing – F.D.A., A.E.B., B.I.B., S.C., N.O.Y.; Analysis and/or interpretation – F.D.A., A.E.B., B.I.B., H.A., S.C., N.O.Y.; Literature search – F.D.A., A.E.B., B.I.B., H.A., S.C., N.O.Y.; Writing – F.D.A., A.E.B., B.I.B.; Critical review – F.D.A., A.E.B., B.I.B., H.A., S.C., N.O.Y.

### References

- Henry ML, Garner WL, Fabri PJ. latrogenic anemia. Am J Surg 1986;151(3):362–63. [CrossRef]
- Whitehead NS, Williams LO, Meleth S, Kennedy SM, Ubaka-Blackmoore N, Geaghan SM, et al. Interventions to prevent iatrogenic anemia: a Laboratory Medicine Best Practices systematic review. Crit Care 2019;23(1):278. [CrossRef]
- Widness JA, Madan A, Grindeanu LA, Zimmerman MB, Wong DK, Stevenson DK. Reduction in red blood cell transfusions among preterm infants: results of a randomized trial with an in-line blood gas and chemistry monitor. Pediatrics 2005;115(5):1299–306. [CrossRef]
- Ince FD, Aksit MZ, Sipahi M, Tatli M, Aksun S. The relation between the requested tests and the transfusion requirement in newborn patients. TBD Preanalytical Phase Symposium. Turk J Biochem 2016;41:S2.
- Faisal A, Andres K, Rind JAK, Das A, Alter D, Subramanian J, et al. Reducing the number of unnecessary routine laboratory tests through education of internal medicine residents. Postgrad Med J 2018;94(1118):716–19. [CrossRef]
- Bull BS. Reference and selected procedures for the quantitative determination of hemoglobin in blood - Third Edition; Approved Standard. CLSI document H15-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2000.
- Wiseman JD. Evacuated tubes and additive for blood specimen collection - Fourth Edition; Approved Standard. CLSI document H1-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 1996.
- Dubrowny N. Validation and verification of tubes for venous and capillary blood specimen collection; Approved Guideline. CLSI document GP34-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
- Demet Arslan F, Karakoyun I, Isbilen Basok B, Zeytinli Aksit M, Baysoy A, Kilic Ozturk Y, et al. The local clinical validation of a new lithium heparin tube with a barrier: BD Vacutainer<sup>®</sup> Barricor LH Plasma tube. Biochem Med 2017;27:535–45. [CrossRef]
- 10. Lima-Oliveira G, Lippi G, Salvagno GL, Montagnana M, Picheth G, Guidi GC. Preanalytical management: serum vacuum

tubes validation for routine clinical chemistry. Biochem Med 2012;22(2):180–86. [CrossRef]

- Kocijancic M, Cargonja J, Delic-Knezevic A. Evaluation of the BD Vacutainer<sup>®</sup> RST blood collection tube for routine chemistry analytes: clinical significance of differences and stability study. Biochem Med 2014;24(3):368–75. [CrossRef]
- 12. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191–94.
- Lippi G, Cornes MP, Grankvist K, Nybo M, Simundic AM. EFLM WG-Preanalytical phase opinion paper: local validation of blood collection tubes in clinical laboratories. CCLM 2016;54(5):755–60. [CrossRef]
- 14. Slockblower JM. Procedures for the collection of diagnostic blood specimens by venipuncture - Sixth Edition; Approved Standard. CLSI document GP41-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2007.
- 15. Coşkun A, Carobene A, Kilercik M, Serteser M, Sandberg S, Aarsand AK, et al. European Biological Variation Study of the EFLM Working Group on Biological Variation. Within-subject and between-subject biological variation estimates of 21 hematological parameters in 30 healthy subjects. Clin Chem Lab Med 2018;56(8):1309–18. [CrossRef]
- 16. Unal K. Comparison of small-volume tubes with vacuum blood tubes for complete blood count. Int J Med Biochem 2019;2(1):24–9. [CrossRef]
- 17. Sanchez-Giron F, Alvarez-Mora F. Reduction of blood loss from laboratory testing in hospitalized adult patients using small-volume (pediatric) tubes. Arch Pathol Lab Med 2008;132(12):1916–19. [CrossRef]
- Inal S, Kelleci M. Relief of pain during blood specimen collection in pediatric patients. MCN Am J Matern Child Nurs 2012;37(5):339–45.
- 19. Smoller BR, Kruskall MS, Horowitz GL. Reducing adult phlebotomy blood loss with the use of pediatric-sized blood collection tubes. Am J Clin Pathol 1989;91(6);701–3.
- 20. Dillman C, Sandhaus L, Natali R, Baffa A, Forsythe P. A joint pediatric-laboratory quality improvement initiative to reduce pediatric blood sample volumes for laboratory testing. Int J Lab Hematol 2007;29:37–8.
- 21. Whitehead NS, Williams LO, Meleth S, Kennedy SM, Ubaka-Blackmoore N, Geaghan S, et al. Interventions to prevent iatrogenic anemia: a Laboratory Medicine Best Practices systematic review. Crit Care 2019;23(1):278. [CrossRef]
- 22. Lewandrowski K. Managing utilization of new diagnostic tests. Clin Lab Man Rev 2003;17(6):318–24.
- 23. Chant C, Wilson G, Friedrich JO. Anemia, transfusion, and phlebotomy practices in critically ill patients with prolonged ICU length of stay: a cohort study. Crit Care 2006;10(5):R140.
- 24. Kurniali PC, Curry S, Brennan KW, Velletri K, Shaik M, Schwartz KA, et al. A retrospective study investigating the incidence and predisposing factors of hospital-acquired anemia. Anemia 2014;2014:634582. [CrossRef]