비침습적 혈색소 검사법 2종의 성능 평가

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Evaluation of Two Noninvasive Hemoglobin Testing Devices

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Background: Determination of the hemoglobin (Hb) levels of prospective blood donors has been performed on capillary blood obtained by finger prick using a gravimetric CuSO₄ method. Noninvasive Hb testing devices based on pulse oximetry technology have recently been developed. This study was conducted to evaluate the performance of two noninvasive Hb testing devices, NBM 200 and Pronto-7 as a predonation Hb screening test.

Methods: Hb levels of 993 blood donors (727 males, 266 females) were measured using five methods: two noninvasive methods, CuSO₄ method, HemoCue, and hematology analyzer (Sysmex KX-21N). The hematology analyzer was considered as the reference method.

Results: Compared with Hb levels of the hematology analyzer, the bias was 0.7 g/dL for NBM 200, 0.1 g/dL for Pronto-7, and 0.4 g/dL for HemoCue. The intraclass correlation coefficients of Hb measurements compared to the hematology analyzer were 0.57 (95% CI: 0.25~0.73) for NBM 200, 0.73 (95% CI: 0.69~0.75) for Pronto-7, and 0.87 (95% CI: 0.69~0.93) for HemoCue. The ability to detect Hb <12.5 g/dL and ≥12.5 g/dL was 16.4% and 99.2% for NBM 200, 55.8% and 95.9% for Pronto-7, 60.0% and 98.6% for HemoCue and 81.8% and 95.2% for the CuSO₄ method, respectively.

Conclusion: Unsatisfactory results were obtained using the noninvasive Hb testing devices for a predonation Hb screening test, although they have the apparent advantage of reducing pain and stress in donors thereby increasing donor satisfaction. However, for application in the blood donation setting, performance of these devices should be improved. (Korean J Blood Transfus 2015;26:273-281)

Key words: Blood donors, Hemoglobin, Noninvasive

Introduction

Hemoglobin (Hb) determination before blood do-

nation is required in most countries to prevent phlebotomy of anemic individuals, and to ensure adequate Hb content of blood units. A predonation Hb

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screening is routinely performed in blood donation centers on capillary blood obtained by finger prick using a gravimetric CuSO₄ method^{1,2)} or a portable hemoglobinometer such as HemoCue.^{3,4)} To date, all methods imply finger stick samples, leading to blood donor discomfort. In populations with high deferral rates due to low Hb, such as high school and university students, this issue is especially burdensome.

Recently, there are available methods for noninvasive Hb measurement, based on the occlusion spectroscopy.⁵⁻¹⁰⁾ The OrSense NBM 200 (OrSense Co., Petah-Tikva, Israel) is a noninvasive Hb measurement system using occlusion spectroscopy by OrSense. It is composed of a reusable ring-shaped sensor probe that fits on the subject's finger, and a portable desktop monitor that calculates and displays the measurement results. Another noninvasive point-of-care Hb measurement device based on spectrophotometric method is the Pronto-7 (Masimo Co., Irvine, CA, USA). The Pronto-7 is a palm-sized hand-held device with a wider range of finger sizes sensor.

The introduction of noninvasive Hb measurements in predonation Hb screening could prevent prospective donors likely to be deferred from having to proceed through additional testing, including an invasive blood test. This has the potential to improve efficiency and the donor experience, which can contribute to increase repeated donation and minimizing the infection risk for donors and health care staffs. The objective of this study was to evaluate the new two noninvasive methods comparing its results with a current invasive method as a predonation Hb screening test and an autoanalyzer as a reference method.

Materials and Methods

All data were collected under institutional review board approval of the Korean Red Cross Blood Services and all participants provided written, informed consent. A total 993 blood donors (727 males, 266 females) were participated from July 2013 to January 2014 in the trial. In consecutive trial, blood donors from three donation sites of Korean Red Cross Seoul-Dongbu Blood Center were tested before routine donation procedure by the NBM 200 device, and by Pronto-7 according to the manufacturer's instruction.

Immediately following the noninvasive testing, a capillary blood sample was obtained by finger prick with a 2.25 lancet. Hb determination from capillary blood was analyzed with gravimetric CuSO₄ method and with a point-of-care hemoglobinometer HemoCue (HemoCue AB, Angelholm, Sweden).

A venous sample was also obtained by venipuncture of the median cubital vein of the non-dominant arm with a disposable syringe and then transferred to 3 mL EDTA Vacutainers (BD, Franklin Lakes, NJ, USA). Venous blood samples were transported at room temperature and analyzed for reference Hb with a laboratory analyzer (KX-21N, Sysmex, Kobe, Japan). The correlation between Hb measurements taken by laboratory analyzer and noninvasive Hb testing devices was assessed using intraclass correlation coefficients (ICCs). The ICCs were interpreted as follows: <0, poor; 0.01~0.20, slight; 0.21~0.40, fair; 0.41~0.60, moderate; 0.61~0.80, substantial; and 0.81~1.00, almost perfect agreement. For agreement between methods across the range of the Hb, Bland-Altman graphs¹¹⁾ with limits of agree-

ment were also plotted. Sensitivity (ability to detect Hb < 12.5 g/dL) and specificity (ability to detect ≥ 12.5 g/dL) were calculated as the percentage of ineligible donors who were correctly identified as ineligible to donate whole blood and the percentage of eligible donors who were correctly identified as eligible to donate whole blood, respectively. All statistical analyses were performed using R software version 2.13 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Hb was measured in 993 donors (727 males, 266 females) in this study. The average Hb measurements using the Sysmex KX-21N, NBM 200, Pronto-7, and HemoCue were 14.0 ± 1.5 g/dL, 14.7 ± 1.1 g/dL, 14.1 ± 1.5 g/dL and 14.4 ± 1.5 g/dL, respectively (Table 1). The Hb measurements of the Sysmex KX-21N showed a normal distribution, while those of the NBM 200, Pronto-7 and HemoCue were slightly left-skewed (Fig. 1).

Scatter plots of the Hb measured using NBM 200 or Pronto-7 vs. Sysmex KX-21 showed wider distribution than that of the HemoCue vs. the Sysmex KX-21N (Fig. 2). The ICCs of Hb measurements between NBM 200, Pronto-7 or HemoCue with

Sysmex KX-21N were 0.57 (95% CI: 0.25~0.73), 0.73 (95% CI: 0.69~0.75) and 0.87 (95% CI: 0.69~0.93) respectively (Table 2). The mean difference between NBM 200 and reference analyzer was 0.7 g/dL, while that between Pronto-7 and Sysmex KX-21N was 0.1 g/dL. The mean difference of HemoCue compared to the reference analyzer was 0.4 g/dL. A Bland-Altman plot showed that the 2SD difference of Hb measurements between the Sysmex KX-21N and the NBM 200 was >2.0 g/dL, while that between the Sysmex KX-21N and Pronto-7/HemoCue was <2.0 g/dL (Fig. 3).

Of the 165 donors who have unacceptable Hb for blood donation by the Sysmex KX-21N, the percentage of donors correctly screened for blood donation (sensitivity) by NBM 200 was 16.4%, by Pronto-7 was 55.8%, by HemoCue was 60.0% and by CuSO₄ was 81.8% (Table 3). On the other hand, the numbers of donors who were acceptable for blood donation by Sysmex KX-21N were 828 donors. Among those the percentage of donors classified as acceptable by the methods (specificity) was 99.2% for NBM 200, 95.9% for Pronto-7, 98.6% for HemoCue and 95.2% for CuSO₄, respectively (Table 3).

Table 1. Statistical difference between hemoglobin point-of-care testing devices and the reference analyzer

	NBM 200	Pronto-7	HemoCue	Sysmex KX-21N
Number of Samples	993	993	993	993
Mean (g/dL)	14.7	14.1	14.4	14.0
Standard Deviation (g/dL)	1.1	1.5	1.5	1.5
Mean Difference (g/dL)	0.7	0.1	0.4	-
SD of the Difference (g/dL)	0.8	0.7	0.5	-

Fig. 1. Distribution of hemoglobin levels measured using the Sysmex KX-21 (A), the NBM 200 (B), Pronto-7 (C), and the HemoCue (D) in this study.

Discussion

Introduction of pulse oximetry¹²⁾ dramatically improved patient care, particularly in the emergency room, the recent development of devices allowing noninvasive and almost immediately measurement of Hb by spectrophotometry (SpHb) is promising. Continuous and noninvasive hemoglobin testing with the SpHb spectrophotometric method has been clin-

ically evaluated in multiple studies in hospital operating rooms and intensive care units¹³⁻¹⁵⁾ with some studies also comparing HemoCue measurements with the reference device.¹⁶⁾ Many of these studies have found acceptable accuracy and precision of SpHb measurement in comparison with laboratory hematology analyzer or CO-oximetry.

The method currently used for Hb screening for blood donors is an invasive with all risks of invasive

Fig. 2. Scatter plots of the hemoglobin levels measured using the Sysmex KX-21N vs. the NBM 200 (A) Pronto-7 (B) and the HemoCue (C).

Table 2. Hemoglobin measurements and intraclass correlation coefficients (ICCs) between NBM 200, Pronot-7 or HemoCue with Sysmex KX-21N according to blood donation eligibility

Testing Devices	Hemoglobin level (g/dL)	Donors	ICC (95% CI)	Mean±SD	Median (IQR)	Minimum	Maximum
NBM 200	Total	993	0.57 (0.25 ~ 0.73)	14.7±1.1	14.8 (14.1 ~ 15.6)	10.7	16.7
	< 12.0	108	0.09 (-0.06 ~ 0.29)	13.2±1.0	13.4 (12.5 ~ 13.9)	10.7	14.8
	12.0 ~ 12.4	57	0.00 (-0.03 ~ -0.06)	13.7±0.7	13.7 (13.2 ~ 14.2)	12.1	14.9
	≥ 12.5	828	0.46 (0.26 ~ 0.60)	15.0±0.9	15.1 (14.4 ~ 15.7)	11.7	16.7
Pronto-7	Total	993	0.73 (0.69 ~ 0.75)	14.1±1.5	14.3 (13.1 ~ 15.1)	7.1	17.9
	< 12.0	108	0.33 (0.11 ~ 0.52)	11.9±1.4	12.0 (11.1 ~ 13.0)	7.1	14.7
	12.0 ~ 12.4	57	-0.00 (-0.23 ~ 0.24)	12.6±1.0	12.6 (11.9 ~ 13.3)	10.9	14.6
	≥ 12.5	828	0.56 (0.51 ~ 0.61)	14.5±1.2	14.5 (13.7 ~ 15.2)	10.8	17.9
HemoCue	Total	993	0.87 (0.69 ~ 0.93)	14.4±1.5	14.6 (13.4 ~ 15.5)	8.6	18.6
	< 12.0	108	0.59 (0.09 ~ 0.80)	11.8±1.0	11.9 (11.5 ~ 12.5)	8.6	14.3
	12.0 ~ 12.4	57	0.09 (-0.09 ~ 0.30)	12.6±0.6	12.8 (12.3 ~ 13.0)	11.2	13.8
	≥ 12.5	828	0.78 (0.55 ~ 0.87)	14.9±1.1	14.9 (14.1 ~ 15.7)	11.2	18.6

methods and quite uncomfortable for the donor. A noninvasive method would have several advantages: minimized use of consumables, reduced stress of the donor and avoidance of complications at the puncture site. Therefore, in this study, we attempt to evaluate the performance of two noninvasive Hb testing devices (NBM 200 and Pronto-7) for Hb screening in prospective blood donors. The correla-

tion between the Sysmex KX-21N and the NBM 200 was fair (ICC=0.57) while that between the Pronto-7 agreed substantially (ICC=0.73). HemoCue showed the best agreement with venous Hb determination that agreed almost perfectly (ICC= 0.87) in this study (Table 2). The percentage of donors correctly screened for blood donation by the Hb testing methods was 16.4%, 55.8%, 60.0% and 81.8% for

Fig. 3. Bland-Altman plot of the difference between the hemoglobin point-of-care testing devices with laboratory reference (A) NBM 200 (B) Pronto-7 (C) HemoCue.

NBM 200, Pronto-7, HemoCue and CuSO_4 method, respectively (Table 3). Interestingly, in general it demonstrated that HemoCue is suitable for Hb determination of blood donors,⁴⁾ however, in the present study, gravimetric CuSO_4 method was more precise than the HemoCue in use with regards to excluding ineligible donors. There are reports indicating that Hb values are higher in capillary blood than in venous blood.¹⁷⁾ Therefore, this may cause using a capillary blood for HemoCue instead of venous blood. Determination of Hb by CuSO_4 method in prospective blood donors is routine performed before

donation, and donors who failed to satisfy Hb criteria using CuSO_4 method have a further test on capillary sample using a HemoCue at blood donation centers in Korea. This strategy should be confirmed the effectiveness in terms of preventing ineligible donors to be accepted, although testing venous blood Hb in a blood donation centers is impractical as it is time-consuming and donor's complaining.

Comparing noninvasive SpHb from the NBM 200, Pronto-7, and HemoCue with a laboratory hematology analyzer, we showed that neither noninvasive hemoglobin detection nor the HemoCue can

Table 3. Ineligible sensitivity and eligible specificity of the Hb measurement methods

		Reference Measurement (g/dL)		Sensitivity*	Specificity [†]
		< 12.5 (165)	≥ 12.5 (828)		
NBM 200	< 12.5 g/dL	27 (16.36%)	7 (0.85%)	16.4%	99.2%
	≥ 12.5 g/dL	138 (83.64%)	821 (99.15%)		
Pronto-7	< 12.5 g/dL	92 (55.76%)	34 (4.11%)	55.8%	95.9%
	≥ 12.5 g/dL	73 (44.24%)	794 (95.89%)		
HemoCue	< 12.5 g/dL	99 (60.00%)	12 (1.45%)	60.0%	98.6%
	≥ 12.5 g/dL	66 (40.00%)	816 (98.55%)		
CuSO ₄	< 12.5 g/dL	135 (81.82%)	40 (4.83%)	81.8%	95.2%
	≥ 12.5 g/dL	30 (18.18%)	788 (95.17%)		

*Sensitivity, the ability to detect < 12.5 g/dL; [†]specificity, the ability to detect ≥ 12.5 g/dL.

replace the laboratory test in a venous sample as a way of preventing inappropriate donation. An important issue in the measurement of capillary hemoglobin seems to be the pre-analytical variability of sampling related not only to anatomical differences at finger pulp circulation but also difference between venous and capillary blood has to be taken into account.¹⁸⁾

Although NBM 200 had the highest specificity, having a very low sensitivity, more than 80% of donors who did not satisfy the Hb criteria would have been accepted for blood donation (Table 3), which was a finding similar to that of other studies in which NBM 200 fail to over half of the ineligible donors.¹⁰⁾ Performance of Pronto-7 was also not considered to be acceptable for implementation. Similar to our results, some previous studies also reported that noninvasive methods do not ameliorate the percentage of donors correctly screened for blood donation, due to photometric methods such as NBM 200 and Pronto-7 are influenced by a variety factors, including skin color, perfusion index of the finger, fin-

ger temperature, position of donors (standing or sitting) and ambient light.^{9,13,19)} However, other studies suggested otherwise in that inaccuracy of noninvasive Hb measurement is not because of the quality of the measurement technique, but because of the capillary sample itself, this is not always the same quality as a venous sample.²⁰⁾

Taken together these results, the data in this study demonstrated that the measurement of Hb by non-invasive methods does not replicate the results of laboratory hematology analyzer. Meanwhile, the gravimetric CuSO₄ method for Hb screening showed nearly comparable results for specificity (95.2%) and for sensitivity (81.8%). The noninvasive Hb testing devices have the apparent advantage of reducing pain and stress in donors thereby increasing donor satisfaction. However, the noninvasive Hb measurement could be inaccurate, thus potentially affecting both donor safety and the blood supply. Noninvasive Hb measurement remains a conflictive issue in routine donor acceptance procedures and these devices needs to be improved prior to apply in the blood

donation setting.

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요 약

배경: 헌혈 전 혈색소 농도는 손가락 모세혈을 채취한 후 황산구리용액에 의한 혈액비중검사로 측정하고 있다. 최근에는 맥박산소측정법(pulse oximetry)에 의한 비침습적 혈색소 검사 장비가 개발되어 있어, 본 연구에서는 헌혈 전 혈색소 농도 사전 검사를 위하여 NBM 200, Pronto-7 등 두 종의 비침습적 혈색소검사 장비 성능을 평가하였다.

방법: 헌혈자 993명(남성 727명, 여성 266명)을 대상으로 비침습적 혈색소 검사법 2종, 황산구리용액에 의한 혈액비중검사, HemoCue 및 혈액자동분석기 Sysmex KX-21N에 의한 혈색소 농도 검사 등 총 5가지 방법으로 혈색소 검사를 실시하였으며, 혈액자동분석기에 의한 혈색소 측정값을 참고치로 하였다.

결과: 혈액자동분석기에서 측정된 혈색소 측정치를 참고치로 했을 때, NBM 200, Pronto-7, HemoCue의 바이어스는 각각 0.7 g/dL, 0.1 g/dL,

0.4 g/dL이었다. 급내상관계수(ICCs)는 NBM 200이 0.57 (95%CI: 0.25~0.73), Pronto-7이 0.73 (95%CI: 0.69~0.75), HemoCue가 0.87 (95%CI: 0.69~0.93)로 나타났다. Hb <12.5 g/dL를 검출하는 능력과 Hb ≥12.5 g/dL를 검출하는 능력은 각각 NBM 200 16.4%와 99.2%, Pronto-7 55.8%와 95.9%, HemoCue 60.0%와 98.6% 그리고 황산구리용액에 의한 혈액비중 측정법은 81.8%와 95.2%였다.

결론: 비침습적 혈색소 검사방법은 헌혈자의 고통과 스트레스를 경감시켜 헌혈자 모집 측면에서 긍정적인 측면이 있을 것으로 보이나, 현재로서는 이들 검사가 헌혈 현장에 적용되기 위해서는 장비의 성능 개선이 필요한 것으로 보인다.

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