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The Efficacy of Noninvasive Hemoglobin Measurement by Pulse CO-Oximetry in Neonates

신생아에서 Pulse CO-Oximetry 를 통해 비침습적으로 측정한 혈색소의 유효성

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by

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학위논문 원문제공 서비스에 대한 동의서

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1. 동의사항
① 본인의 논문을 보존이나 인터넷 등을 통한 온라인 서비스 목적으로 복제할 경우 저작물의 내용을 변경하지 않는 범위 내에서의 복제를 허용합니다.
② 본인의 논문을 디지털화하여 인터넷 등 정보통신망을 통한 논문의 일부 또는 전부의 복제.배포 및 전송 시 무료로 제공하는 것에 동의합니다.

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논문 제목: **The Efficacy of Noninvasive Hemoglobin Measurement by Pulse CO-Oximetry in Neonates**

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ABSTRACT

The Efficacy of Noninvasive Hemoglobin Measurement by Pulse CO-Oximetry in Neonates

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Objective: To evaluate clinical applicability of noninvasive hemoglobin (Hb) measurement with a pulse CO-oximetry in neonates.

Materials and Methods: We conducted a prospective study for preterm or term neonates admitted to NICU of Seoul National University Children's Hospital, Seoul, Korea. After IRB approval and informed consents from their parents, 56 neonates were enrolled in the study. Hb measurements by the Masimo Radical-7™ (Rainbow Pulse CO-Oximeter®, Masimo Corp., Irvine, CA, USA) were recorded just prior to venous samplings and the collected data was compared with the corresponding venous Hb value by laboratory test.

Results: The collected data were compared with the corresponding venous Hb level obtained in laboratory testing, and a total of 137 data pairs were analyzed. Noninvasive Hb values measured with a pulse CO-Oximetry were significantly correlated with the venous Hb levels (correlation coefficient, *r*

= .758; $p < .001$). Hb values measured with a pulse CO-Oximetry were higher than those measured with a laboratory hematology analyzer (13.3 ± 2.6 g/dL vs. 12.5 ± 3.1 g/dL). In terms of the agreement between the laboratory analyzer and the pulse CO-oximetry, 94.8% of the measurements fell within two standard deviations of the mean difference.

Conclusion: Noninvasive Hb measurements with pulse CO-Oximetry provide clinically acceptable accuracy, and they were significantly correlated with laboratory Hb measurement in neonates. In terms of the clinical applicability, noninvasive Hb monitoring with a pulse CO-Oximetry could be useful in the early detection of Hb changes in neonates.

Keywords : hemoglobin; hemoglobinopathy; monitoring; neonatal intensive care; premature infant

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INTRODUCTION

Total hemoglobin (Hb) measurement is one of the most important laboratory tests during intensive care. Hb measurement using an automated analyzer in a clinical laboratory is the gold standard method (1). However, a limitation of this method is the time delay for physicians to obtain the results. In addition, serial measurements are frequently needed during intensive care periods for the assessment of disease progression, the early detection of acute blood loss, or the evaluation of the effectiveness of transfusions. However, repeated measurements may induce significant blood spoliation (2), which could be of utmost importance in the intensive care for preterm or term neonates. Recently, a new noninvasive spectrophotometry-based monitoring technology that provides immediate and continuous Hb measurement(Masimo Radical-7 running board software version 7211; Masimo Corp., Irvine, CA) has been introduced (3). Macknet et al (4) reported that the device provided validated Hb values compared with Hb measured with an automated analyzer in adult patients and healthy volunteers. However, data are limited on the reliability of this device in children, and no reports exist for neonates. The purpose of this study was to evaluate the usefulness of noninvasive Hb measurement (SpHb) with pulse CO-Oximetry in neonates.

MATERIALS AND METHODS

Patients. This prospective study was conducted in the neonatal ICU (NICU) of Seoul National University Children's Hospital from March to April 2011. After approval from the Seoul National University Hospital Institutional Review Board, informed consent was obtained from the parents of each neonate prior to their enrollment. On the basis of the previous study performed in adult patients by Allard et al (5), we planned to acquire 150 measurement pairs to test the equivalence between laboratory Hb and SpHb. Assuming that one patient can undergo Hb measurements at least three times during a NICU admission, the required sample size was 50 infants. Therefore, with a 10% dropout rate, we estimated that we would need to enroll 56 subjects. Patients who were under the postmenstrual age of 45 wks were included, and patients with congenital hematologic diseases or skin problems were excluded. Gestational age, birth weight, postmenstrual age, postnatal age, weight on the study day, and vital signs were collected for each subject.

Hb Measurements. Blood samples for Hb measurement in the laboratory were performed as needed for intensive care according to the attending physician's discretion. Hb measurements in the laboratory (laboratory Hb) were performed using a Sysmex SE-9000 hematology analyzer (TOA Medical Electronics Co. Ltd, Kobe, Japan). Monitoring with Radical-7 Pulse CO-Oximetry (Masimo Radical-7 running board software version 7211; Masimo Corp.) was performed immediately before blood sampling. The pulse CO-

Oximetry method discerns the distinctive light absorption characteristics of different hemoglobin species and applies proprietary algorithms to determine Hb levels (24). A Rainbow R1-20L adhesive sensor (Rev C; Masimo Corp.) connected to Radical-7 Pulse CO-Oximetry was placed on the wrist of the neonate's right hand and covered with an opaque probe cover to eliminate interference from ambient light.

Statistical Analysis. Statistical analysis was performed to determine the relationship between the SpHb and the standard laboratory Hb. Wilcoxon signed-rank tests were used for analyzing the correlation; we calculated the correlation coefficient (r) and the coefficient of determination (r^2). Ninety-five percent confidence intervals were calculated when required. Agreement between the laboratory Hb and SpHb was evaluated as described by Bland and Altman (6). The accuracy of the SpHb compared with that of the laboratory Hb was calculated using the accuracy root mean square (Arms) with the formula $\sqrt{([Mean\,bias]^2 + [SD]^2)}$ (7, 8). Bivariate correlation analysis was also performed to determine the impact of demographic and physiologic variables. All statistical analysis was performed with SPSS Version 19.0 (SPSS, Inc., Chicago, IL) and Bland-Altman plot with MedCalc Version 12.1.4 (MedCalc Software, Inc., Mariakerke, Belgium), with the statistical significance set at $p < .05$.

RESULTS

During the 2 months of the study period, Hb measurements were performed in 56 patients, and 158 data pairs were obtained. Twenty-one pairs were excluded due to inability to obtain a SpHb reading with the pulse CO-Oximetry; therefore, a total of 137 data pairs were analyzed.

The characteristics of the patients are presented in **Table 1**. The gestational age range was 24^{+1} to 40^{+5} wks, and the birth weight range was 370 to 4,230 g. Body weight range on the day of the study was 530 to 4,230 g, and the postnatal age range was 1 to 98 days. The mean laboratory Hb value was 12.5 ± 3.1 g/dL with a range of 7.4 to 23.7 g/dL. The SpHb was higher than the laboratory Hb (13.3 ± 2.6 g/dL vs. 12.5 ± 3.1 g/dL). The correlation coefficient (r) was .758 ($p < .001$), which represented a good correlation between the SpHb and the laboratory Hb (Fig. 1). The calculated coefficient of determination (r^2) was .58 (95% confidence interval 0.53–0.72). To assess the agreement between the laboratory automated analyzer and the pulse CO-Oximetry a Bland-Altman plot was applied. Figure 2 depicts the SpHb compared with the laboratory Hb. The bias and limits of agreement was 0.86 ± 3.40 g/ dL. Using this method, 94.8% of the measurements fell within two standard deviations of the mean difference. The accuracy was obtained with an Arms of 2.21 g/dL. Table 2 shows the relevance between the SpHb and laboratory Hb according to the Hb range. The highest accuracy (lowest Arms) was obtained for the Hb levels from 12 to 18 g/dL, with an Arms of 1.68 g/dL.

The laboratory Hb was significantly correlated with SpHb if the Hb concentration was <18 g/dL. For the subgroup with Hb values >18 g/dL, the Arms was 3.28 g/dL, and the laboratory Hb and SpHb were not significantly correlated.

To assess the correlation given the impact of demographic factors and clinical data, bivariate correlation analysis was performed between the bias and birth weight, body weight, postnatal age, and postmenstrual age and showed no significant correlation.

Table1. Patient characteristics

Patients	n = 56
Birth data	
Male /Female	30 / 26
Gestational age, median (range), week	31^{+1} (24^{+1}-40^{+5})
Birth weight, median (range), g	1,440 (370-4,230)
Study day data	
Postnatal age, median (range), day	20 (1-98)
Postmenstrual age, median (range), week	34^{+5} (24^{+1}-44^{+6})
Weight, median (range), g	1,765 (530-4,230)
Laboratory hemoglobin, mean ± SD (range), g/dL	12.5 ± 3.1 (7.4-23.7)

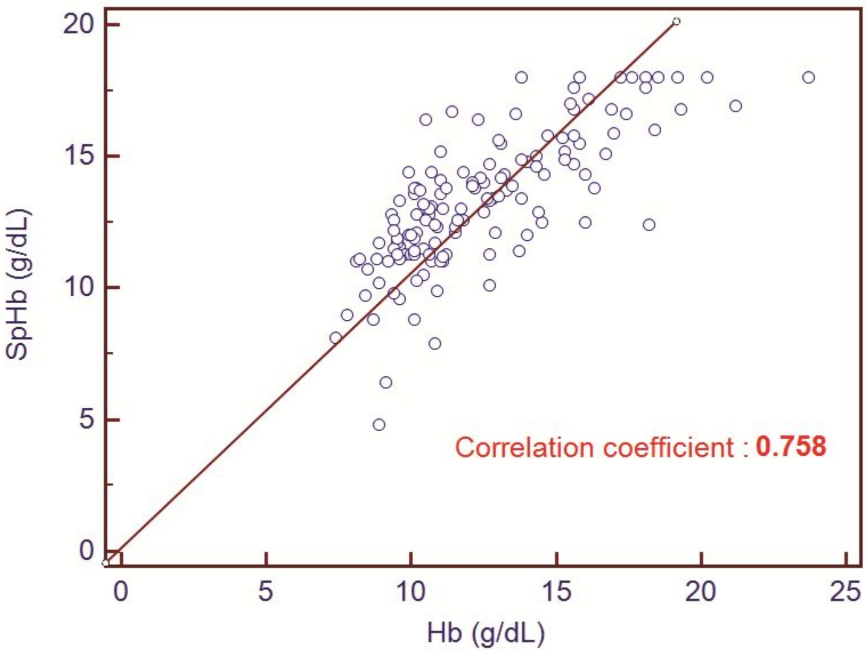

Figure 1. The correlation between hemoglobin measurements with a laboratory analyzer and a pulse CO-Oximetry. Scatter plot of hemoglobin measurements with a laboratory automated analyzer and corresponding hemoglobin values measured with a pulse CO-Oximetry. The solid line is the line of identity. (n=137)

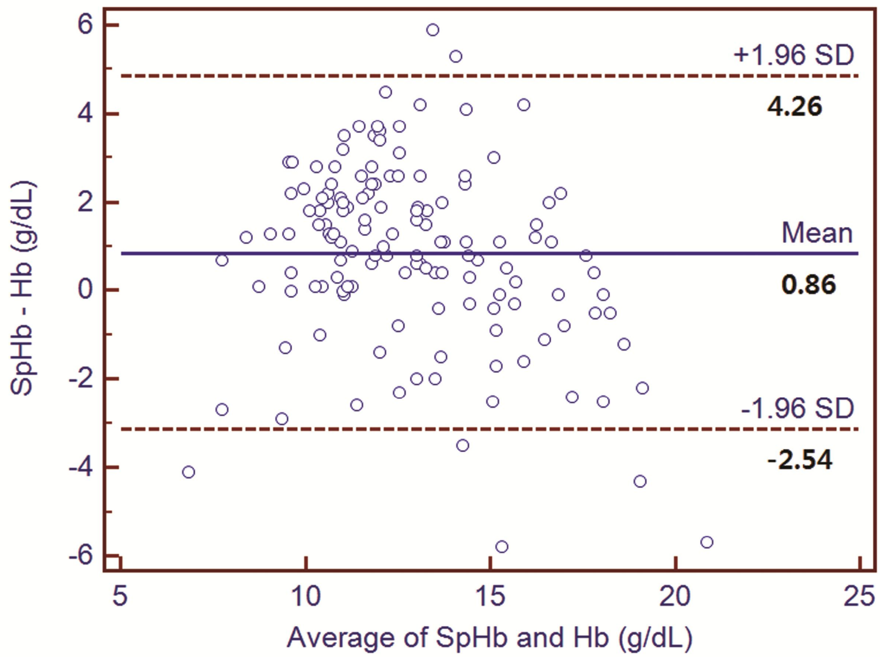

Figure 2. Bland-Altman representation of comparison analysis between the hemoglobin measurements performed on a laboratory automated analyzer and a pulse CO-Oximetry. The bias (solid line) and the limits of agreement (dotted lines, Bias ± 1.96 SD) are represented on the graph. (n=137)

Table 2. Accuracy and Correlation of Pulse CO-Oximetry ™ based on Laboratory Hemoglobin Ranges

Hemoglobin range	N	Correlation coefficient	Arms	*P* value
<12 g/dL	73	0.513	2.50	<0.001
12 to <18 g/dL	54	0.550	1.68	<0.001
≥18 g/dL	10	0.294	3.28	0.41

DISCUSSION

The accuracy of the pulse CO-Oximetry device in measuring Hb was firstly evaluated in adults in 2007 by Macknet et al (4), and the SpHb provided clinically acceptable accuracy compared with the laboratory Hb, and they were well correlated (9). In addition, there were several reports suggesting that the SpHb was significantly correlated with the laboratory Hb during surgical procedures with substantial blood loss (8, 10–13). However, there are no reports on its use in neonates. To the best of our knowledge, this is the first prospective study designed for neonates to evaluate the applicability of this noninvasive technology in the measurement of Hb, and the present study revealed that noninvasive Hb monitoring with Radical-7 Pulse CO-Oximetry was significantly correlated with the laboratory measurement of Hb in neonates, including preterm infants.

Hb monitoring for neonates who require intensive care or surgery is very important to evaluate hemodynamic states (14–16). Noninvasive Hb monitoring allows for the detection of acute bleeding or disease progression without invasive procedures (17). Furthermore, noninvasive Hb monitoring can reduce the risk of infection related to invasive monitoring catheters and recurrent blood sampling (9).

Currently, point of care devices are commonly used in hospital environments because they provide portability and allow the collection of small volume blood samples from skin punctures. Several studies have demonstrated that the sufficiently high accuracy of the point of care devices justifies the routine use of these devices in clinical practice (18). Both Hb measured with a pulse CO-Oximetry and that with a point of care device were significantly correlated with laboratory Hb, but the point of care devices still require an invasive sampling procedure (8, 19–21). Thus, SpHb monitoring might be a very useful and complementary method in the NICU setting for providing noninvasive and continuous clinical information on Hb trends, allowing for more rapid and appropriate medical interventions in neonates who are particularly vulnerable to hemodynamic changes.

There are several considerations in this study because the accuracy of the device varied based on the Hb ranges. As shown in Table 2, at Hb values >18 g/dL, the SpHb measurements were less accurate whereas the Hb values <18 g/dL showed significant correlation between the SpHb values and the Hb values obtained with a laboratory analyzer. A previous report stated that the difference between Hb levels measured with a noninvasive pulse CO-Oximetry and those measured with a laboratory hematology analyzer would be greater in low perfusion states (22). The hemodynamic status of sick neonates, especially preterm infants, fluctuates sharply and may cause problems with the peripheral circulation. Besides polycythemia can be observed in those sick infants with perinatal distress, and high viscosity of the blood in polycythemia

might also affect the peripheral circulation and interfere with the detection of the signals. SpHb measurements should be interpreted with caution, and confirmation with laboratory-based Hb measurements will be necessary.

However, the number of our patients with Hb >18 g/dL was relative small because that condition is not common. Therefore, further data accumulation of SpHb measurement in patients with Hb over 18g/dL would be necessary to verify the accuracy of SpHb in that condition. In addition, our study population included infants with body weight <3 kg and the sensor was placed on the wrist of the neonate's right hand; however the Rainbow R1-20L adhesive sensor (Rev C, Masimo Corp.) that we used in the present study is designed for infants who weigh >3 kg. Developing more reliable finger probes for small infants might improve the accuracy. Furthermore, the effect of HbF on noninvasive spectrophotometry-based monitoring technology has not studied yet, and the studies to assess the influence of HbF on SpHb might be necessary for further understanding of the technology in neonates.

Because of the limited number of devices, we could not perform the continuous SpHb monitoring on each patient. Larger scale studies with continuous Hb monitoring are needed to verify the applicability of the pulse CO-Oximetry in neonates.

Conclusion

SpHb measurements with pulse CO-Oximetry provides clinically acceptable accuracy and correlation compared with laboratory Hb measurement in neonates, and because of the advantages afforded with noninvasive continuous monitoring, its application for infants in the NICU would be very meaningful.

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국문 초록

목표: 정맥혈 검사와 비교하여 신생아에서의 pulse CO-Oximetry를 이용한 비침습적인 혈색소 측정의 정확성을 평가하고, 신생아 중환자 치료에 있어 비침습적인 혈색소 측정의 임상적 유효성을 확인하고자 한다.

방법: 서울대학교 어린이병원 신생아중환자실에 입원한 환아 중, 교정 재태주령 44주 미만의 신생아로 보호자로부터 informed consent를 받은 환아, 총 56명을 대상으로 하였으며, 정기적으로 시행하는 혈액검사 직전에 Masimo Radical-7™ (Rainbow Pulse CO-Oximeter®, Masimo Corp., Irvine, CA, USA)를 이용하여 혈색소를 측정하고 이를 정맥혈 검사에서 측정된 혈색소 수치와 비교하였다.

결과: 평균 재태주령은 31.2 ± 0.72 wk, 출생 후 나이는 중간값 20 days(range = 1-98 days), 출생 체중의 중간값은 1,440g(range = 530-4,230g)이었으며, 총 137쌍의 검사 결과가 분석에 이용되었다. 비침습적으로 측정된 혈색소 값은 정맥혈 혈색소 값과 유의한 상관관계를 보였고(correlation coefficient, r=.758; $p<.001$), pulse CO-Oximetry로 측정한 혈색소의 값이 정맥혈 혈색소의 값보다 높게 측정되었다(13.3 ± 2.6 g/dL vs. 12.5 ± 3.1 g/dL). 정맥혈 분석을 통한 혈색소의 측정과 비침습적인 혈색소 측정 간에는 ± 2 SD의 범위 내에서 94.8%의

일치도를 보였다.

결론: 신생아에서 pulse CO-Oximetry를 이용한 비침습적인 혈색소 수치는 정맥혈로 측정한 혈색소와 유의한 상관관계를 보였으며 94.8%의 정확성을 보였다. 신생아, 특히 미숙아에서 pulse CO-Oximetry를 이용한 비침습적인 혈색소 수치의 지속적 모니터링은 혈색소의 변화를 일찍 발견 함으로써 신생아 중환자의 집중 치료에 유용하게 사용될 수 있을 것이다.

주요어 : 혈색소; 혈색소측정법; 신생아 집중 치료; 모니터링; 산소측정법; 미숙아

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