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Research Article

Comparison of Hb Measurements between POCT and Laboratory Hb Measurements in Pediatric Intensive Care Unit

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Abstract

Background: The analysis of biochemical parameters at or near the bedside is a rapidly evolving field in laboratory diagnosis. We studied whether hemoglobin measurements by noninvasive pulse co-oximetry (SpHb) and blood gas analyzer could provide clinically acceptable absolute accuracy in critically ill children compared to the reference standard, the automated laboratory analyzer, in a pediatric intensive care unit.

Methods: Data were prospectively collected in critically ill patients at metropolitan teaching hospital in Sydney, Australia. Hemoglobin measurements by two point-of-care tests i.e. noninvasive hemoglobin measurements (SpHb) and blood gas analyzer were recorded and were then compared with hemoglobin measured via reference standard laboratory automated analyzer. The agreement between these methods were evaluated by linear regression and Bland and Altman analysis.

Results: Data was collected on 84 patients aged from 1 day and 17.99 years (median 1.93 years). The overall correlation of the SpHb (Masimo Radical 7) and the laboratory Hemoglobin (Sysmex XE-5000) was 0.81 ($P < 0.0001$) with a mean difference of 0.37 g/dL (95% confidence interval, -2.23 - +2.98), which may affect the utility of using co-oximetry values alone to guide clinical management. Almost perfect correlation was observed when comparing results from blood gas analyzer (Radiometer ABL800 FLEX) and the laboratory hemoglobin analyzer with coefficient of correlation 0.98 ($P < 0.0001$) with a mean difference of 0.04 g/dL (95% confidence interval, -0.81 - +0.73).

Conclusion: SpHb monitoring is a novel technology and the results correlate well but with large confidence interval. Further studies are needed in critically ill pediatric patients and in children with severe anemia. In the meantime, blood gas analyzer is a good alternative to the reference standard laboratory hemoglobin for the rapid assessment of Hb among critically ill children.

Keywords: *Hemoglobin; Co-Oximeter; Masimo Radical-7; Blood Gas Analyzer; Point-of-Care test; Pediatric Intensive Care*

Introduction

Medical testing at or near the site of patient care or point of care testing (POCT) can help physicians to make immediate decisions in the clinical management of their patients. Measurement of hemoglobin is one of the most frequent tests performed in intensive care units (ICU) and operating theaters. In a patient with significant blood loss, timely and accurate assessment of hemoglobin concentration is required. An automated analyzer is considered the gold standard for hemoglobin measurements in a laboratory and photometric cyanmethemoglobin is the most widely used assay for this test [1,2]. Automated analyzers have the advantage of not only providing a reliable

hemoglobin measurement but also contributing additional information such as platelet counts which are important during management of the patient with active bleeding. However, there are several limitations to this method and one of the most important of which is the time taken to obtain the blood result. The process of a blood test by automated analyzer in the laboratory involves collecting the blood specimen and then transporting it to the laboratory. The results are then analyzed and validated and then made available to the physician, and this entire process can take from minutes to hours [3,4]. In addition, repeated measurements result in a cumulative blood loss, which may be clinically significant in pediatric and neonatal patients.

Blood gas analyzers measure hemoglobin level accurately and are located within intensive care units, in contrast to automated analyzers, which are usually situated in centralized hospital laboratories [5,6]. Blood gas analyzers also have the advantage of providing results immediately without the need to transport specimens to the laboratory [7-9]. Additionally, blood gas analyzers require a smaller blood volume for analysis and are more economical compared to automated laboratory analyzers.

Noninvasive hemoglobin measurement by spectrophotometry is a recent technology and has the advantage of providing immediate and continuous hemoglobin (SpHb) measurement [10]. Pulse co-oximetry utilizes a sensor with various light-emitting diodes that pass light through the site to a diode (detector). Signal data is obtained by passing various visible and infrared lights (500 to 1400nm) through a capillary bed and measuring changes in light absorption during the blood pulsatile cycle. The detector receives the light, converts it into an electronic signal and utilizes extraction technology to calculate the patient's total hemoglobin concentration (SpHb (g/dl)) [11-13]. However, data are limited on the reliability of this device in children, and no reports exist of use in children in pediatric intensive care. This study tests the hypothesis that the two POCT-SpHb monitoring and blood gas hemoglobin measurement are equivalent to that of the gold standard method of hemoglobin measurement in the laboratory in children's ICU patients.

Materials and Methods

This prospective, observational study was conducted in a 17 bed surgical and medical ICU at Sydney Children's Hospital, Randwick. Approval for this study was obtained from the Sydney Children's Hospitals Network ethics committee (agreement number AU/6/DE2D013). The two point-of-care tests studied were hemoglobin measurements by the ICU blood gas analyzer (Radiometer ABL800 FLEX) and percutaneous hemoglobin concentration (SpHb) measured by Radical-7 pulse co-oximeter. Hemoglobin measurement in the laboratory (Sysmex XE-5000) is considered the gold standard test and was used as a reference for analyzing the results of two point-of-care tests. Hemoglobin measurements in the laboratory and by blood gas analyzer are performed as routine care for our patients in intensive care unit. SpHb is a noninvasive test and there were no additional blood tests required, so the ethics committee determined that consent could be waived for subjects in this study.

A convenience sample of patients admitted to the children's ICU between December 2012 and April 2013 were enrolled in the study. Medical record number, age, capillary refill time, blood pressure, weight, date and time blood test, clinical diagnosis, percutaneous oxygen saturations and perfusion index were recorded for each subject. Blood samples for hemoglobin measurement by formal laboratory and blood gas analyzer were performed as needed for intensive care at the discretion of the attending physician. A single SpHb measurement for each patient was obtained at the same time of blood collection for hemoglobin measurement by formal laboratory and blood gas analyzer. Only single blood gas hemoglobin, SpHb and laboratory hemoglobin measurement was recorded for each patient to avoid sampling bias.

SpHb monitoring was carried out using a Radical-7 pulse co-oximeter, software version 7.8.0.1, with disposable adhesive SpHb finger sensor version G. Sensors were applied to the patient's skin in accordance with the instructions from the manufacturer as well as using general principles involved in measurements by oximetry. The emitter and detector were appropriately aligned to get the signals and the sensors were covered with an opaque shield to prevent any optical interference. SpHb and Perfusion index (PI) were recorded from pulse co-cximeter device. The Perfusion Index (PI) display provides a numeric indication of the pulse strength at the measurement site. It is a

calculated percentage between the pulsatile signal and non-pulsatile signal of arterial blood moving through the site. PI displays an operating range of < 0.02 percent to 20 percent. A percentage greater than 1.00 percent is desired during the study.

Statistical analysis

Hemoglobin measurements in the laboratory were considered as the reference standard and hemoglobin measurements by blood gas analyzer and SpHb were methods of comparison. Relationship between standard laboratory hemoglobin, SpHb and blood gas analyzer hemoglobin were analyzed by Bland and Altman method [14-16]. Statistical analysis was performed using SPSS Version 17.0 (SPSS Inc., Chicago, IL) and MedCalc Version 12.1.4 (Mariakerke, Belgium). *P*-values less than 0.05 were considered to be statistically significant.

Results

A total of 94 patients were enrolled over a five month study period. Ten patients were excluded. In 2 patients we were unable to obtain a SpHb reading with the pulse co-oximeter despite careful sensor positioning and good skin perfusion (among the two, one had cyanotic congenital heart disease with oxygen saturations 75 - 80% and the other patient had tricyclic antidepressant poisoning with the SpHb monitor reading "low SpHb Signals"). For 5 patients formal laboratory hemoglobin were not performed, and only blood gas analyzer hemoglobin values were available. In 3 patients the blood samples were clotted, and results were not available for simultaneous correlation.

The remaining 84 subjects were aged between 1 day and 17.99 years (median 1.93 years), weight 2.1 - 67.0 kg (median 11.25 kg) and divided almost equally between medical (n = 43) and surgical (n = 41) cases. Oxygen saturations at the time of SpHb measurement ranged from 76 - 100% (median 97%). Hemoglobin values ranged from 6.9 g/dL to 18.5 g/dL (mean 11.0 g/dL) on the laboratory hematology analyzer, 6.5 g/dL to 18.6 (mean 11.0 g/dL) on the blood gas analyzer and 7.4 g/dL to 17.6 g/dL (mean 11.4 g/dL) on the Pulse CO-Oximeter.

The agreement between the laboratory automated analyzer hemoglobin and pulse CO-Oximetry hemoglobin was analyzed by Bland-Altman plot (Figure 1). Although the mean difference between measurements was 0.37 g/dL, the standard deviation of 1.33 g/dL generates a relatively large range of -2.23 - +2.98 g/dL to encompass 95% of the values (mean +/- 1.96 SD), which may affect the utility of using co-oximetry values alone to guide patient's clinical management.

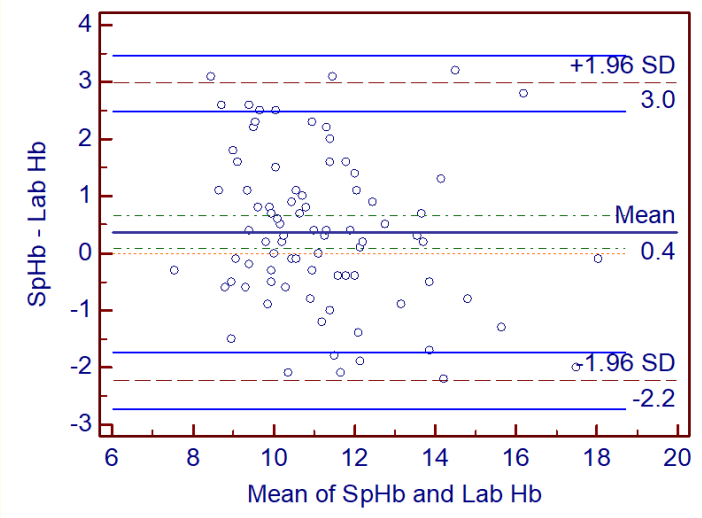

Figure 1: *Comparison analysis performed between the hemoglobin measurements by the laboratory automated analyzer and the pulse co-oximeter, illustrated by Bland-Altman plot. The mean difference (solid dark blue line) and the limits of agreement (dotted lines, bias ± 1.96 SD) are represented on the graph (n = 84).*

SpHb and the laboratory Hemoglobin were closely correlated, with r = 0.81 (p<0.0001) (Figure 2). There were 13 patients with perfusion index < 1 and 71 patients with perfusion index ≥1. There was no significant difference in between the correlation coefficient in patients with perfusion index <1 (r = 0.84, n = 13) and patients with perfusion index ≥ 1 (r = 0.80, n = 71).

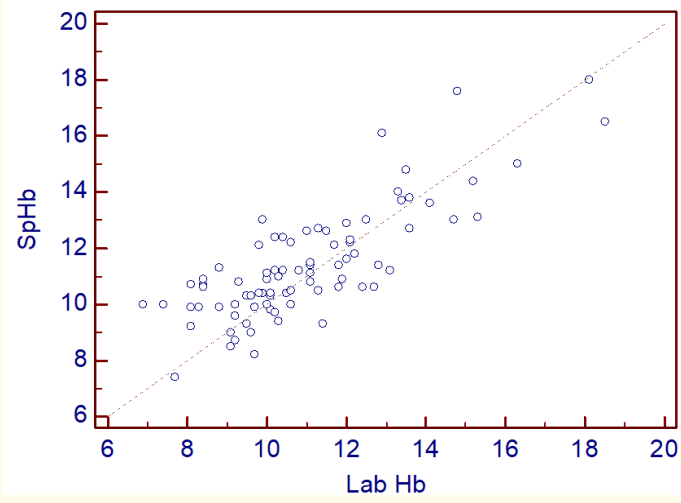

Figure 2: *Scatter plot demonstrating a correlation between hemoglobin measurements with a laboratory automated analyzer and a pulse co-oximeter. The dotted line is the line of equality.*

Close agreement was observed when comparing results from the blood gas analyzer and the laboratory gold standard. Bland-Altman plots are shown in figure 3. The mean difference was 0.04 g/dL with a standard deviation of 0.39 g/dL, giving a relatively tight 95% CI of -0.81 - +0. 73 g/dL.

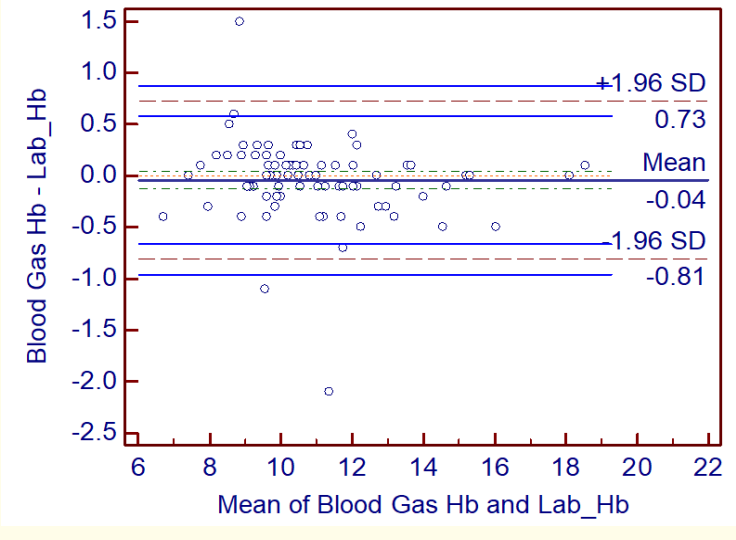

Figure 3: *Comparison analysis performed between the hemoglobin measurements by the laboratory automated analyzer and the blood gas analyzer, illustrated by Bland-Altman plot. The mean difference (solid dark blue line) and the limits of agreement (dotted lines, bias ± 1.96 SD) are represented on the graph (n = 84).*

Blood gas analyzer hemoglobin and laboratory hemoglobin measurements demonstrated an almost perfect correlation ($r = 0.98$, $p < 0.0001$) (Figure 4).

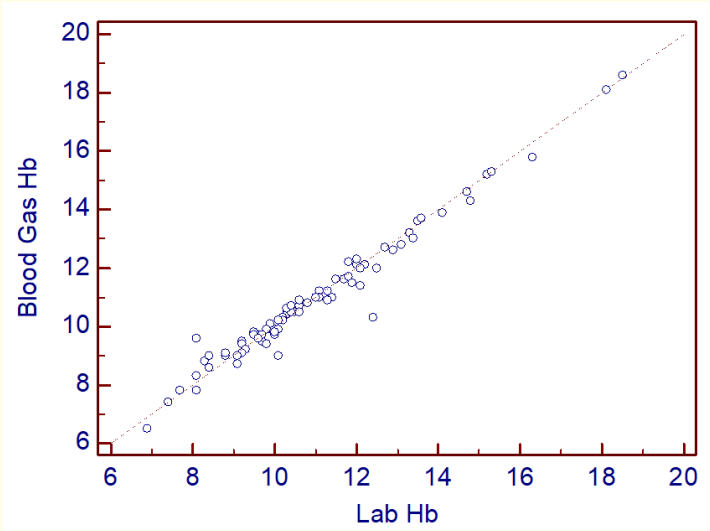

Figure 4: *Scatter plot demonstrating a correlation between hemoglobin measurements with a laboratory automated analyzer and a blood gas analyzer. The dotted line is the line of equality.*

Discussion

For critically ill children, immediate laboratory results can be a strategic necessity. When a child's clinical condition is changing rapidly, it may be prudent to sacrifice clinically insignificant differences to achieve more real-time data. We compared hemoglobin measurements by two point of care tests i.e. noninvasive pulse co-oximetry and blood gas analyzer, with laboratory hemoglobin measurements in 84 critically ill children.

SpHb monitoring can provide immediate hemoglobin results utilizing the principles of photospectrometry and its initial results were presented in 2007 by Macknet., *et al* [17]. The ability to measure hemoglobin noninvasively via Pulse CO-Oximetry has significant potential to facilitate timely clinical care. It provides immediate and continuous information about hemoglobin levels without the discomfort, expense, infection risk and blood loss necessitated by repeated invasive measurements. It is the first device of this kind and it provides significant expansion in the field on monitoring technology [18-20].

Our study is unique as it compares the performance of Pulse CO-Oximetry and central laboratory device to determine actual hemoglobin levels in pediatric patients admitted to intensive care unit. Our data demonstrates that SpHb monitoring with Radical-7 Pulse CO-Oximetry gives comparable results to formal hemoglobin measurements in pediatric ICU patients, albeit with a potentially clinically significant 95% CI of -2.23 - +2.98 g/dL [21]. Our results are consistent with findings reported in post-operative pediatric and neonatal intensive care patients [20,22].

One limitation of our study is that only 29% (28/84) hemoglobin values were ≤ 10 g/dL, and none was less than 6.9 g/dL. Clearly it is most important that the device is accurate in moderate to severe anemia, and the majority of patients in our cohort had hemoglobin

values in the mild to moderate anemia range [23]. Nevertheless, within the limitations of our study the performance of the device appears acceptable and the data clinically useful [24,25]. Further research should be performed to address specifically the issue of accuracy in a larger cohort of anemic patients. Another limitation of our study was a lack of continuous SpHb data and trend monitoring as reported by Patino., et al. in perioperative pediatric patients [10,20]. Continuous non-invasive monitoring will be helpful in the management of patients with ongoing bleeding.

Our data also demonstrate excellent correlation and agreement between hemoglobin values measured by blood gas analyzer when compared to a laboratory reference [5,7,8]. Given that almost all ICUs have an onsite blood gas analyzer, this provides strong evidence that should enable a reduction in the number of samples sent for a formal laboratory estimation of hemoglobin [6,7,26].

SpHb monitoring has potential benefits that include reducing phlebotomy induced anemia in critical care, hastening detection of post operative bleeding and providing safety and comfort to patients needing Hb monitoring [17]. SpHb monitoring is an innovative technology and is still developing, it is expected that advances in both hardware and software will lead to improved performance, especially during conditions of hypothermia, vasoconstriction, and hypoperfusion.

Conclusion

The goal of POCT is to provide accurate, reliable and cost-effective information about the patient condition in a short period. Noninvasive hemoglobin monitoring is a new technology with the potential to provide immediate clinical information on hemoglobin values allowing for more rapid and appropriate medical intervention [22,27]. Our study found the SpHb measured by CO-Oximetry to have clinically acceptable accuracy across a broad range of pediatric intensive care patients. Larger studies will need to be undertaken before clinical decisions can be based solely on hemoglobin values obtained by CO-Oximetry [28,29]. A blood gas analyzer present in intensive care unit provides a valid alternative method to the gold standard laboratory hemoglobin for the immediate assessment of hemoglobin concentration in a pediatric intensive care unit.

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Conflicts of Interest

The authors declare no conflicts of interest.

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