Shock, Publish Ahead of Print

DOI : 10.1097/SHK.0000000000000949

Evaluation of non-invasive hemoglobin monitoring in trauma patients with low hemoglobin levels

Medhat Gamal[1], Bassant Abdelhamid[1], Dina Zakaria[1], Omnia Abd El Dayem[2], Ashraf Rady[1], Maher Fawzy[1], Ahmed Hasanin[1,3].

[1] Department of anesthesia and critical care medicine, Cairo university, Egypt.

[2]Department of clinical and chemical pathology, Cairo university, Egypt.

[3]Department of critical care medicine, Elameen hospital, Taif, KSA.

Corresponding author

Ahmed Hasanin

Assistant professor of anesthesia and critical care medicine, Cairo university, Egypt.

Department of anesthesia and critical care medicine, 01 Elsarayah street, Cairo11559, Egypt

ahmed.hasanin@kasralainy.edu.eg

+201095076954

Running title: Masimo hemoglobin measurement in trauma patients

Abstract

Objective

Bleeding is a leading cause of death among trauma patients. Delayed assessment of blood hemoglobin levelmight result in either unnecessary blood transfusion in non-indicated patients or delayed blood transfusion in critically bleeding patients. In this study, we evaluate the precision of non-invasive hemoglobin monitoring in trauma patients with low hemoglobin levels.

Methods

We included trauma patients with low hemoglobin levels (less than 8g/dL) scheduled for surgical intervention. Blood samples were obtained on admission and after each blood unit with concomitant measurement of serum hemoglobin using radical-7 Masimo device. The change in blood hemoglobin after every transfused blood unit was also assessed by both methods (Delta-Sp-Hb and Delta-Lab-Hb). The precision of Masimo hemoglobin level (Sp-Hb) compared toLaboratory hemoglobin level (Lab-Hb) was determined using both Bland-Altman and Pearson correlation analyses.

Results

One hundred and eighty-four time matched samples were available for final analysis. Bland-altman analysis showed excellent accuracy of Sp-Hb compared to Lab-Hb with mean bias of 0.12 g/dL and limits of agreement between -0.56 g/dL to 0.79 g/dL. Excellent correlation was reported between both measures with Pearson correlation coefficient of 0.872. Excellent agreement was also reported between both Delta-Sp-Hb and Delta-Lab-Hb with mean bias of -0.05 and limits of agreement from -0.62 to 0.51

Conclusions

Sp-Hb showed accurate precision in both absolute values and trend values compared to Lab-Hb measurement in trauma patients with low hemoglobin levels.

Keywords:

Trauma, Hemoglobin,Masimo, Pulse co-oximetry, Non-invasive.

Introduction

Trauma is a leading cause of death all over the world. Haemorrhage is the most frequent cause of preventable death accounting for 50% of preventable deaths within the first 24 hours after major trauma[1]. Early recognition of haemorrhage would allow proper transfusion decision and improve patient outcome. Clinical signs of haemorrhage are usually delayed and affected by many confounding factors. Invasive laboratory testing is considered the gold standardfor measurement of serum hemoglobin; however, laboratory testing is time wasting and unsuitable for remote locations.

Non-invasive continuous hemoglobin monitoring (Sp-Hb) is evolving nowadays; Radical 7 (Masimo corporation, Irvine, CA) is one of the popular devices used for Sp-Hb. The accuracy of Sp-Hb monitor was previously investigated in different various population[2]. Few studies have examined Sp-Hb in trauma patients[3][4][5]; however, the evidence for Sp-Hb in trauma patients with low hemoglobin levels is not consistent. The aim of this study is to evaluate the accuracy of non-invasive Masimo hemoglobin monitor in trauma patients with hemoglobin levels lower than 8 gm/dL.

Methods

A prospective observational study was conducted in the emergency department (ER) at Cairo university hospital; a large 5500-bedded tertiary center. The Study was approved by the institutional research ethics committee. A written informed consent was obtained from either the participant or from the next-of-kin if the participant was unable to sign.

The study included trauma patients admitted to the ER with major hemorrhage requiring surgical intervention. We included patients aged 18 years or above with hemoglobin levels < 8 g/dL. Patients who received cardiopulmonary resuscitation > 5 minutes, patients on high doses of vasopressors, and patients with hand injuries hindering the application of the device probe were excluded. Patients were monitored during resuscitation in both ER and operating room.

Baseline blood samples were obtained as a part of standard care. Patients received whole blood transfusion if: 1- The obvious estimated blood loss was more than 20% of blood volume. 2- Serum hemoglobin levels < 7 g/dL. 3- Ongoing intraoperative blood loos with mean arterial blood pressure < 60 mmHg.

Sp-Hb was continuously measured using Radical-7 device pulse co-oximeter (Masimo corporation, Irvine, CA) via a pulse oximeter probe applied to the third or fourth digit of left hand. The probe was covered with an opaque shield to avoid any error by external light sources. A baseline reading for Sp-Hb was obtained followed by a reading after each unit of blood. Simultaneous laboratory hemoglobin levels (Lab-Hb) were measured through venous samplesas a part of standard care.

For blood sampling, two millilitres of venous blood were obtained through a sterile venepuncture, and then drawn into an ethylene diamine tetra acetic acid (EDTA) vacutainer tube. Each sample was thoroughly mixed and sent immediately to the central laboratory of the hospital for measuring hemoglobin by automated Hemoglobin analyser (Coulter LH 750 Beckman). In the laboratory, the performance of the analyser was daily monitored and calibration was verified using stable reference controls. The samples were processed and the analysed Hemoglobin values were returned according to the standard practice of the hospital.

Collected data included: demographic data (age, race, and gender), operative data, type of injury, injury severity score, serum lactate, time to operating room admission, Lab-Hb, Sp-Hb, vital signs (blood pressure and heart rate), and number of transfused blood units. The change in blood hemoglobin (delta-Hb) after transfusion of every blood unit was calculated as follows: Delta-Hb = hemoglobin level after transfusion – hemoglobin level before transfusion. We calculated delta Hb measured by both methods (laboratory and Masimo). Evaluation of themean bias and level of agreement between both methods to determine the accuracy of Masimo as a trend monitor.

Statistical analysis

As the previous data for the correlation between Lab-Hb and Sp-Hb are not consistent, we made a conservative assumption for the sample size to detect any correlation. We calculated a minimum number of 164 pairs to detect a correlation coefficient (r) of 0.25 with a study power of 90% and alpha error of 0.05.

Data were presented as means (standard deviations), medians (quartiles), and frequencies (%) as appropriate. Data analysis was done using SPSS 18 and Medcalc software. Data were tested for normality using Shapiro-Wilk test. The accuracy of Sp-Hb in comparison to Lab-Hb was assessed usingBland-Altman analysis. Pearson's correlation coefficient was used for correlation between both variables as the data was normally distributed.

Results

One hundred and thirteen patients were available for screening. Forty-three patients were excluded because the initialblood hemoglobin level was above 8 gm/dL and 70 patients were included in the study. All our patients were Caucasian and all of them were admitted after road-traffic accidents. Mean age was 37±9, 59% of our patients were males,54(77%) patients underwent abdominal exploration with subsequent intervention (splenectomy, liver repair, intestinal repair) and 16(23%) patients underwent orthopedic procedures. The median injury severity score was 18 with quartiles of (17-26). Demographic data are presented in table 1. We obtained 194 blood samples, 6 samples (from the samples obtained after blood transfusion) were excluded because serum hemoglobin was above 8 g/dL, 4 samples were excluded due to poor device signals, and 184 samples were available for final analysis. We had a poor device signal at 10% of the monitoring time. Patient were enrolled in the study at 90±12 minutes before surgical intervention.Thirty-one samples (17%) were obtained during hypovolemic shock state.

Mean lab-Hb for all samples was 6.7±0.7 g/dL and mean Sp-Hb was 6.58±0.6 (table 2). Twenty samples (11%) had Lab-Hb below 6 g/dL,97(53%) samples and 67(36%) samples had Lab-Hb of (6-7g/dL) and (7-8g/dL) respectively (table 3). Mean bias between Lab-Hb and Sp-Hb was 0.12 with 95% confidence interval of (-0.56 to 0.79) (figure 1). Astrong correlation was observed between both hemoglobin measures with Pearson correlation coefficient (r) of 0.872 (figure 2). Mean bias between Delta-Lab-Hb and Delta-Sp-Hb was -0.05 with 95% confidence interval of (-0.62 to 0.51) (figure 3).

Discussion

We demonstrated low bias andstrong correlation between Sp-Hb and Lab-Hb in a cohort of trauma patients with low hemoglobin levels. Using non-invasive monitors for hemoglobin measurement is a promising technology that would save both time and effort during patient management in addition to avoiding hazards of infection. Radical-7 device is a small sized, simple, non-invasive device. Radical-7 technology is based on co-oximetry with emergingpopularity in both emergency [6] and critical care settings [7].

Being commonly managed in remote unequipped areas and vulnerable to frequent blood transfusion, trauma patients would be the highest group that might benefit from non-invasive hemoglobin measurement technology. Sp-Hb have been previously validated in various groups of patients; however, the impressions for its precision are not clear. In the special group of trauma patients, few studies have reported the accuracy of non-invasive hemoglobin measurement; none of them was conducted in the special population with low hemoglobin levels.

Our results agreed with other previous reports. In a large cohort of trauma patients, Joseph et al[3] reported a bias of 0.3 g/dL between invasive and non-invasive hemoglobin measurement; this bias is near to ours (0.11 g/dL). They also reported good correlation between both measurements with correlation coefficient of 0.77. A similar bias (0.3 g/dL) was reported by Bridges et al [4] in combat casualties; however, the wide limits of agreement (-2.4 to 3.4 g/dL) impaired its precision in transfusion.Another study supporting our findings was conducted in pediatric trauma patients with a mean bias of -0.49 g/dL[8]. Only one systematic review and meta-analysis has investigated the accuracy of Sp-Hb in both perioperative and critical care settings [2]. The pooled mean bias in the perioperative settings was 0.39 g/dL; however, the limits of agreement reported in the meta-analysis was wider than our limits (-2.2 to 2.9 g/dL).

In a large cohort of trauma patients, Galvano et al[5] reported that Sp-Hb measurement did not improve the ability to predict the need to blood transfusion; However, Galvano study was designed in a different way than our study as they evaluated 18 regression models with different combinations of variables for the accuracy of prediction of blood transfusion where they found that adding Sp-Hb did not improve the accuracy of any model. Moreover, they did not analyze the correlation and the agreement between both methods as we did. Another study by Tsuei at al reported poor performance for Sp-Hb (bias: 1.5 g/dL, limits of agreement: -2 to 5 g/dL); However, many differences are present between Tsuei study and our study: 1- Type of patients: We included only trauma patients; whereas, they included surgical patients, trauma patients, and liver transplant patients. Liver transplant patients are characterized by frequent need to vasopressors in addition to massive blood loss that would impact the accuracy of co-oximetry2- They included ICU patients who are subjected to many factors that would impair the co-oximeter accuracy such as vasopressors.Another study by Moore et al[10] showed wide limit of agreement between -4 and 2 g/dL between invasive and non-invasive hemoglobin measurement in trauma patients.

With interpretation of our findings and comparing to the available data, we assume that there is a clear conflict of evidence when dealing with the precision of Sp-Hb in trauma patients. This conflict is also obvious in other groups of patients especially in critically ill patients [2][11].Our study is uniquely designed to investigate the precision of Sp-Hb in patients with low hemoglobin levels as these patients are the most vulnerable for decision of transfusion. We included pairs of measures in various stages in patient management (during resuscitation, preoperative, and intraoperative). Moreover, we conducted a conservative sample size calculation assumption targeting a study power of 90%. Nevertheless, our findings are not enough to impact the most debatable question: Can we transfuse blood relying solely on Sp-Hb or not? However, our findings would impact the current evidence and raise the need for larger studies in the same population to reach more accurate results.Our findings (if validated in more studies) would enhance more research with a higher level of evidence such as randomized controlled trials investigating the use of Masimo in blood transfusion decision. Only two randomized controlled trials were conducted for this purpose with promising results in neurosurgical[12] and orthopedic patients[13]. Using non-invasive hemoglobin monitor for blood transfusion resulted in lower number of transfused blood[12,13] in addition to shorter time to transfusion decision[12].We also encourage more research to compare Radical-7 device to other non-invasive devices such as Pronto-7 device.Although all patients in our study are bleeding patients, a low number of them was shocked; this might be an important limitation that warrants more research. It was previously reported thatMasimo device is more accurate in patients with adequate perfusion[14].

The value of non-invasive measurement of hemoglobin is not only limited to its absolute accuracy, but it also depends on many other factors: 1- Its performance as a trend monitor that would alert the physician to any sudden bleeding mishaps. 2- Being a continuous monitor that provide a good confidence even if the reading was within 1-1.5 g/dL limits of accuracy (which is the lowest level of accuracy reported by some previous studies) 3- The variability in hemoglobin level is also present in laboratory measurement devices. 4- Sp-Hb could be a good supplementary measure that would help Lab-Hb in the decision rather than totally replacing it. 5- Sp-Hb is a continuous real-time measure that would save time and effort. 6- The normal evolution in monitoring devices would raise the hope in development of more accurate sensors with more precision.

In conclusion, Sp-Hb showed accurate precision in both absolute values and trend values compared to Lab-Hb measurement in trauma patients with low hemoglobin levels.

Acknowledgment

We would like to thank Dr. Wael Nabil Awada for his help in this study.

Conflict of interest

The authors declare that they have no conflict of interest with this work.

Funding

This study was funded by departmental resources.

References

(1) Acosta JA, Yang JC, Winchell RJ, Simons RK, Fortlage DA, Hollingsworth-Fridlund P, Hoyt DB. Lethal injuries and time to death in a level I trauma center. *J Am Coll Surg* 186:528–33, 1998.

(2) Kim S-H, Lilot M, Murphy LS-L, Sidhu KS, Yu Z, Rinehart J, Cannesson M. Accuracy of Continuous Noninvasive Hemoglobin Monitoring: a systematic review and meta-analysis. *Anesth Analg* 119:332–46, 2014.

(3) Joseph B, Pandit V, Aziz H, Kulvatunyou N, Zangbar B, Tang A, O' Keeffe T, Jehangir Q, Snyder K, Rhee P. Transforming hemoglobin measurement in trauma patients: noninvasive spot check hemoglobin. *J Am Coll Surg* 220:93–8, 2015

(4) Bridges E, Hatzfeld JJ. Noninvasive Continuous Hemoglobin Monitoring in Combat Casualties. *Shock* 46:55–60, 2016.

(5) Galvagno SM, Hu P, Yang S, Gao C, Hanna D, Shackelford S, Mackenzie C. Accuracy of continuous noninvasive hemoglobin monitoring for the prediction of blood transfusions in trauma patients. *J Clin Monit Comput*29:815–21, 2015.

(6) Rasmy I, Mohamed H, Nabil N, Abdalah S, Hasanin A, Eladawy A, Ahmed M, Mukhtar A. Evaluation of Perfusion Index as a Predictor of Vasopressor Requirement in Patients with Severe Sepsis. *Shock*44:554–9, 2015.

(7) Hasanin A, Mohamed SA, El-adawy A. Evaluation of perfusion index as a tool for pain assessment in critically ill patients. *J Clin Monit Comput* 2016 [Epub ahead of print].

(8) Ryan ML, Maxwell AC, Manning L, Jacobs JD, Bachier-Rodriguez M, Feliz A, Williams RF. Noninvasive hemoglobin measurement in pediatric trauma patients. *J Trauma Acute Care Surg* 81:1162–6, 2016.

(9) Tsuei BJ, Hanseman DJ, Blakeman MJ, Blakeman TC, Yang SH, Branson RD, Gerlach TW. Accuracy of noninvasive hemoglobin monitoring in patients at risk for hemorrhage. *J Trauma Acute Care Surg* 77:S134–9, 2014.

(10) Moore LJ, Wade CE, Vincent L, Podbielski J, Camp E, Junco D del, Radhakrishnan H, McCarthy J, Gill B, Holcomb JB. Evaluation of noninvasive hemoglobin measurements in trauma patients. *Am J Surg* 206:1041–7, 2013.

(11) Xu T, Yang T, Kim JB, Romig MC, Sapirstein A, Winters BD. Evaluation of Noninvasive Hemoglobin Monitoring in Surgical Critical Care Patients*. *Crit Care Med* 44:e344–52, 2016.

(12) Awada WN, Mohmoued MF, Radwan TM, Hussien GZ, Elkady HW. Continuous and

noninvasive hemoglobin monitoring reduces red blood cell transfusion during neurosurgery: a prospective cohort study. *J Clin Monit Comput* 29:733-740, 2015.

(13) Ehrenfeld JM, Henneman J. Impact of continuous and noninvasive hemoglobin monitoring on intraoperative blood transfusions. J Blood DisordTransfus. 2014;5:9.

(14) Isosu T, Obara S, Hosono A, Ohashi S, Nakano Y, Imaizumi T, Mogami M, MurakawaM. Validation of continuous and noninvasive hemoglobin monitoring by pulse CO-oximetry in Japanese surgical patients. *J Clin Monit Comput* 27:55–60, 2013.

Figure legends

Figure 1: Bland-Altman blot demonstrating excellent agreement between Sp-Hb and Lab-Hb. Mean bias: 0.12, 95% confidence interval:(-0.56 to 0.79). Sp-Hb: Non-invasive Masimo hemoglobin, Lab-Hb: Laboratory hemoglobin.

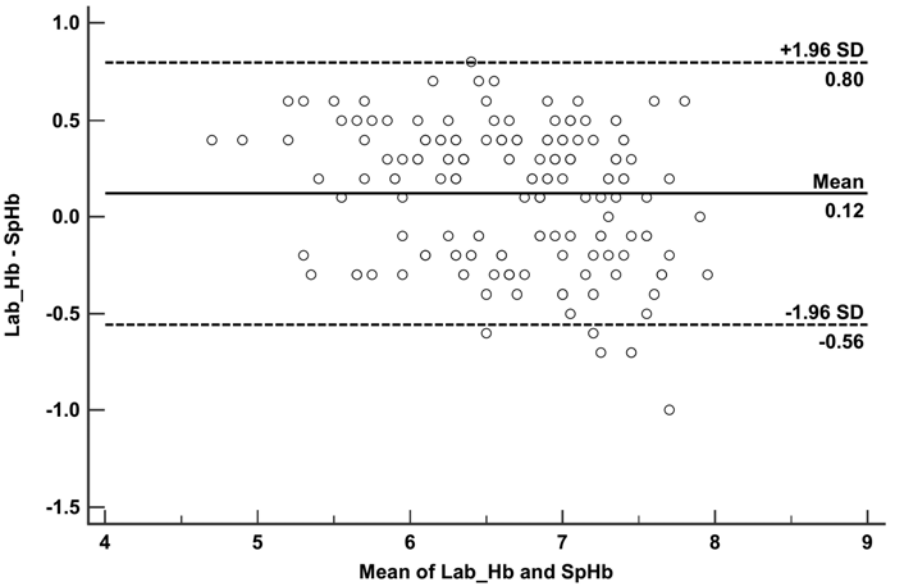

Figure 2: Pearson correlation plot showing strong correlation between Sp-Hb and Lab-Hb. Pearson correlation coefficient r = 0.872. Sp-Hb: Non-invasive Masimo hemoglobin, Lab-Hb: Laboratory hemoglobin.

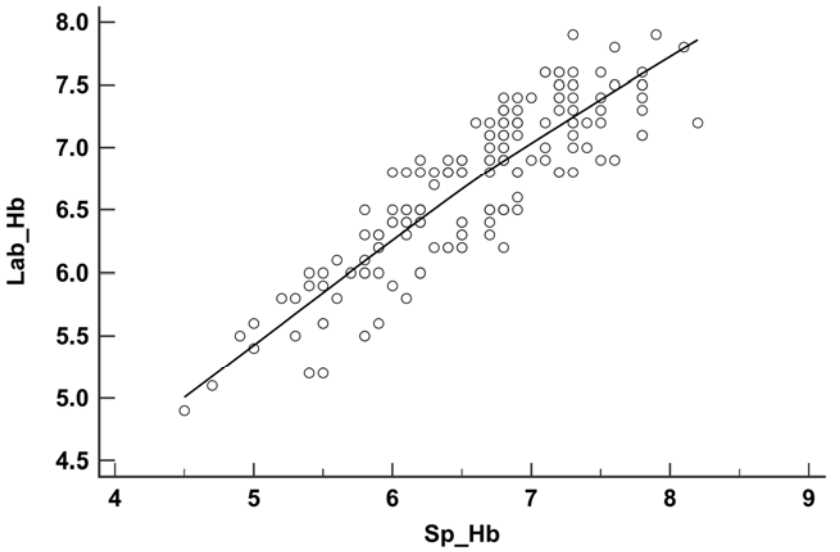

Figure 3: Bland-Altman blot demonstrating excellent agreement between Delta-Sp-Hb and Delta-Lab-Hb. Mean bias: -0.05, 95% confidence interval:(-0.62 to 0.51). Delta-Sp-Hb: Change in non-invasive Masimo hemoglobin, Delta-Lab-Hb: Chnege in laboratory hemoglobin.

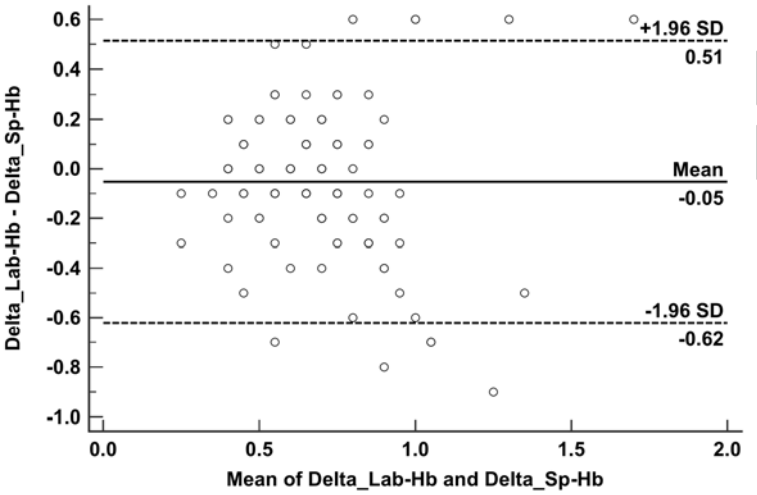

Table 1: Demographic data and patient characteristics (n=70). Data are presented as mean ± Standard deviation, median (quartiles), and frequency (%).

Variables	
Age (years)	37±9
Weight (Kg)	86±10
Male gender	41(59%)
Baseline heart rate (bpm)	102±18
Baseline systolic blood pressure (mmHg)	106±17
Baseline Lactate level (mmol/L)	1.2±0.4
Operation - Abdominal exploration - Orthopedic procedures	 54(77%) 16(23%)
Infused blood units	1.5(1-2)
Patients who received: - One blood unit - Two blood units - Three blood units - Four blood units	 35(50%) 20(28%) 11(16%) 4(6%)
Patients with obtained - Two samples - Three samples - Four samples - Five samples	 70(100%) 35(50%) 15(21%) 4(6%)

Table 2: Hemoglobin readings. Data are presented as mean ± standard deviation and median (quartiles).

Baseline reading - Lab-Hb (g/dL) - Sp-Hb (g/dL)	 6.2±0.5 6.1±0.5
After first blood unit - Lab-Hb (g/dL) - Sp-Hb (g/dL)	 6.9±0.6 6.8±0.6
After second blood unit - Lab-Hb (g/dL) - Sp-Hb (g/dL)	 7.2(6.8-7.5) 7.2(6.7-7.6)
After third blood unit - Lab-Hb (g/dL) - Sp-Hb (g/dL)	 7.3±0.3 7.1±0.4
After fourth blood unit - Lab-Hb (g/dL) - Sp-Hb (g/dL)	 7.5±0.3 7.1±0.2

Lab-Hb: laboratory hemoglobin, Sp-Hb: non-invasive Masimo hemoglobin.

Table 3: Blood sample categories according to hemoglobin levels. Data are presented as frequency (%).

Category	Number (%)
Samples with hemoglobin 7-8 gm/dL	20 (%)
Samples with hemoglobin 6-7 gm/dL	97 (%)
Samples with serum hemoglobin <6 gm/dL	67(%)