Original Article

Utility of non-invasive haemoglobin monitoring in oncosurgery patients

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Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_707_16

Quick response code

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ABSTRACT

Background and Aims: Oncosurgeries may incur massive blood loss demanding frequent blood sampling to assess blood loss and the need for intraoperative blood transfusions. Accuracy of non-invasive spectrophotometric haemoglobin (hereafter to be referred as SpHb) monitoring has been studied in various perioperative settings. The intraoperative use of Radical-7®, Masimo Corp., (Radical-7®) for SpHb monitoring may be useful during cancer surgery. The aim of this study is to evaluate the intraoperative utility of SpHb monitoring by the Radical-7® to guide intraoperative transfusion in oncosurgeries. **Methods:** Fifty adult patients, undergoing oncosurgery with anticipated blood loss of more than 20% of blood volume, were selected. Continuous SpHb monitoring was performed intraoperatively and blood transfusion was based on SpHb values. Simultaneous laboratory haemoglobin (LabHb) samples were taken for validation. The accuracy of intraoperative blood transfusions based on SpHb was analysed using Error Grid Analysis. Paired measurements of SpHb and LabHb were compared using Bland–Altman plot analysis. **Results:** There were 66 paired data points for blood transfusion from fifty patients with a correlation of 73% ($P < 0.001$) between SpHb and LabHb. In the Bland–Altman analysis, the bias was – 0.313 g/dl with ~ 95% of values within the limits of agreement of 1.81 g/dl to –2.44 g/dl. In the Error Grid Analysis, most data points were in the least error zone (Zone A). **Conclusion:** The Radical-7® has the advantage of providing SpHb value continuously to take prompt decision regarding blood transfusion intraoperatively.

Key words: Blood loss, blood transfusion, haemoglobinometry, surgical, transcutaneous oximetry

INTRODUCTION

Cancer is on a rising trend in India and is projected to increase by 17% from 2010 to 2020.[1] Surgery, whether curative or palliative, is an important management option in cancer patients. Intraoperative blood loss depends on the type of surgery, experience of surgeon, duration of surgery and diagnosis which defines the type of tissue a surgeon must cut through. Owing to characteristics of the cancer tissue and extended surgical time, massive blood loss is inevitable. All modes of treatment (chemotherapy and radiotherapy) in such patients can cause anaemia by varying pathological process, making them prone for repeated haemoglobin measurements and multiple venous punctures.[2] Oncosurgeries are of long duration and may be associated with large blood loss, requiring repeated haemoglobin estimation for deciding the need for intraoperative blood transfusion. Along with rough estimates of blood loss by gravimetric method, repeated blood samples are sent for laboratory assessment of haemoglobin to decide the time and amount of blood to be transfused. We designed a study so as to improve the intraoperative management of oncosurgeries using continuous non-invasive haemoglobin (SpHb) monitoring to guide intraoperative blood transfusions.

How to cite this article: Gupta N, Kulkarni A, Bhargava AK, Prakash A, Gupta N. Utility of non-invasive haemoglobin monitoring in oncosurgery patients. Indian J Anaesth 2017;61:543-8.

Radical-7® provides non-invasive continuous haemoglobin assessment in contrast to that of laboratory haemoglobin (LabHb) which is invasive and intermittent.

The utility of SpHb assessment with Radical-7® to guide intraoperative blood transfusion based on SpHb was studied (at the discretion of an attending anaesthesiologist) and validated with the decision that would have been taken if LabHb was used as an indicator for blood transfusion during intra-operative period of oncosurgeries.

METHODS

After approval of Institutional Ethics Committee and written informed consent from each patient, fifty adult patients, posted for elective oncosurgery under general anaesthesia with anticipated blood loss of >20% of blood volume, were included. Exclusion criteria included patients with cardiac pathology, documented peripheral vascular disease, hyperbilirubinaemia and haemoglobinopathies.

Continuous SpHb measurement was done using Radical-7® throughout intra-operative period. Radical-7® probe was placed on the middle finger of hand opposite to non-invasive blood pressure monitoring and covered with company provided black cover. Using Radical-7®, following parameters were continuously monitored: SpHb, perfusion index (PI), pleth variability index (PVI) and oxygen content. PVI was maintained below 14 and CVP between 10–14 mmHg with the help of appropriate fluid management (crystalloid and colloid). Any SpHb readings during severe hypotension (mean arterial pressure [MAP] <65 mmHg) or PI <1.0 were excluded from the analysis (device reliability is not proven in lower PI). Blood sampling for laboratory method was done using a previously inserted central venous catheter. Designated haemoglobin monitoring using Beckman Coulter, which was used as laboratory method (LabHb), was done at just after induction, and whenever ~500 ml blood loss was suspected, and final sampling just before reversal of neuromuscular blockade. Transfusion of blood products was made based on SpHb, at the discretion of the attending anaesthesiologist. Blood loss was estimated both using gravimetric (weighing surgical swab) and volumetric method (blood collected in suction bottle). Total blood loss, total blood transfused and fluid administered were documented.

This study was a pilot clinical trial where decision to transfuse blood using SpHb was validated against the LabHb reading using patients' blood sample. Minimum three sets of observations of SpHb and LabHb were collected for every patient.

Descriptive statistics was analysed with Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA). Continuous variables are presented as mean ± SD g/dl, and categorical variables are presented as absolute numbers and percentage. The comparison of normally distributed continuous variables between the groups was performed using Student's *t*-test. For two-tailed tests, a $P < 0.05$ was considered statistically significant. Following the approach recommended by Bland and Altman,[3] we summarise bias as the mean of difference between measures and the 95% limits of agreement by the interval defined by the observed bias ± 1.96 the observed SD of the observed differences. Paired haemoglobin values provided by Radical-7® and the LabHb was also plotted using the Error Grid Zone Analysis proposed by Morey *et al*.,[4] which accounts for the clinical significance of the difference.

The primary sample size calculation was based on the expected difference in SpHb and LabHb values and the confidence interval (CI) for the 95% limits of agreement as described by Bland and Altman. Based on a previously reported standard deviation (SD) of the difference between measurements of 1.45 g/dl, we calculated that a sample size of 45 patients would provide a 95% CI for detecting difference between two means of 0.5 g/dl. Based on an estimated 10% patient dropout rate, we aimed to include fifty patients for our study.

RESULTS

There were 29 females out of 50 patients, and 70% of all patients were within age group of 20–60 years; demographics and surgical characteristics are given in Table 1. Twenty-seven surgeries (54%) were gynae-uro-oncosurgeries. There were total of 141 paired (SpHb and LabHb) data points. Four paired measurements were discarded because of low MAP (<60 mmHg). Of remaining 137 points, packed cell transfusions were made at 66 data points. Mean pre-operative haemoglobin was 11.6 g/dl. Mean of estimated blood loss intraoperatively was found to be 1440 ml, and mean of transfused packed cells intraoperatively was 750 ml (3 units each of 250 ml in our hospital).

Mean ± SD for SpHb was 9.67 ± 1.72 g/dl and mean ± SD for LabHb was 10.05 ± 1.76 g/dl at all data points. Minimum SpHb was 5.1 g/dl and maximum was 14.1 g/dl. Minimum LabHb was 6.7 g/dl and maximum SpHb was 16.2 g/dl.

SpHb was within 1 g/dl of the LabHb value in 66% and within 1–1.5 g/dl in 17% of paired measurements [Table 2]. In 8–10 g/dl group, 68% of the bias values were within ± 1.0 g/dl range. For <8 g/dl group, 64% of bias values were within ±1.0 g/dl group. Paired SpHb and LabHb values showed a correlation coefficient to be 0.727 at all data points and 0.73 at all packed cell transfusion data points, with $P < 0.001$ for both cases.

There were a total of 66 paired measurements when packed cell transfusion was done. There was a 73% ($P < 0.001$) correlation between the two sets of data points, with a mean bias of − 0.313 g/dl as shown in Figure 1. Negative value of bias shows that SpHb is lower than LabHb on an average. The 95% CIs are −2.44g/dl to 1.81 g/dl [Figure 1]. Performing Morey's Error Grid Analysis on all transfusion points, as majority of data points (~95%) are in Zone A, we can say that SpHb and LabHb are in strong agreement [Figure 2]. Two values are in Zone B showing higher difference but without any effect on decision-making regarding packed cell transfusion. Only two data points lie in Zone C, showing significant difference in values, but decision to transfuse has been taken based on clinical condition of the patient. There were no values in critical Zone D.

We found a correlation of 72.7% ($P < 0.001$) between LabHb and SpHb. Bland–Altman analysis of agreement between SpHb and LabHb of all paired measurements was also performed and is shown in Figure 3. Mean bias between SpHb and LabHb was −0.376 g/dl with SD of ±1.27 g/dl. The 95% confidence limits of agreement were −2.92 g/dl to 2.16 g/dl [Figure 3].

Performing Morey's Error Grid Analysis for all data points, among seven values of Zone C, there were five values where no transfusion was done. Of five values, at two points (LabHb, SpHb; point 1:11.6 g/dl, 8.3 g/dl; point 2:12.5 g/dl, 8.3 g/dl), PI was very low (<0.3). Among other three data points, two data points (LabHb, SpHb; point 1:8.2 g/dl, 10.9 g/dl; point 2:8.9 g/dl, 11.8 g/dl) were just after induction and the other one was the last paired measurement (LabHb, SpHb; 8.8 g/dl, 13.5 g/dl); decision for not transfusing was based on pre-operative haemoglobin and haemodynamics of the patient [Figure 4].

Among seven data points in Zone C, at two points, transfusion was done (LabHb, SpHb; point 1:8.0 g/dl, 5.1 g/dl; point 2:8.3 g/dl, 10.8 g/dl) in view of on-going losses.

Table 1: Patient demographics and surgical characteristics

Demographics/Surgical characteristics	Values
Age (year)	45 (18-75)
Gender (male/female)	21/29
Weight (kg)	62 (13)
Pre-operative Hb (g/dl)	11.6 (1.9)
ASA class	
I	6
II	41
III	3
Blood loss (ml)	1440 (200-5200)
Packed cells transfused (units)	3 (0-7)
Type of resection	
Gynae-uro-oncosurgeries	27
Ortho-oncosurgeries	11
Gastro-oncosurgeries	10
Oro-maxillary oncosurgeries	2

Values are reported as mean (SD), median (range) or absolute numbers. Hb – Haemoglobin; SD – Standard deviation; ASA – American Society of Anaesthesiologists

Table 2: Categorical analysis of non-invasive haemoglobin and laboratory haemoglobin

LabHb range	SpHb-LabHb			
	All values, *n* (%)	<±1.0 g/dl, *n* (%)	±1.1-±1.5 g/dl, *n* (%)	>±1.5 g/dl, *n* (%)
>12 g/dl	12 (8.8)	7 (58)	3 (25)	2 (17)
10-12 g/dl	44 (32.2)	29 (66)	7 (16)	8 (18)
8-10 g/dl	59 (43)	40 (68)	10 (17)	9 (15)
<8 g/dl	22 (16)	14 (64)	3 (14)	5 (22)
Total	137 (100)	90 (66)	23 (17)	24 (17)

LabHb – Laboratory haemoglobin; SpHb – Non-invasive haemoglobin

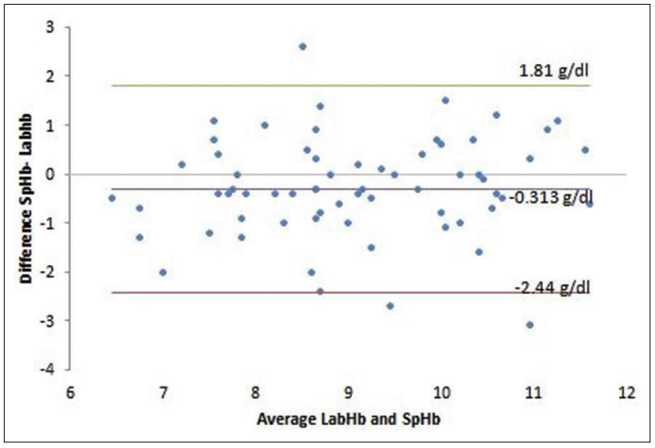

Figure 1: Bland–Altman plot for all transfusion, line above the X-axis shows upper limit of agreement (1.81 g/dl), line below shows lower limit of agreement (–2.44 g/dl). Line just adjacent to X-axis is bias (–0.313g/dl)

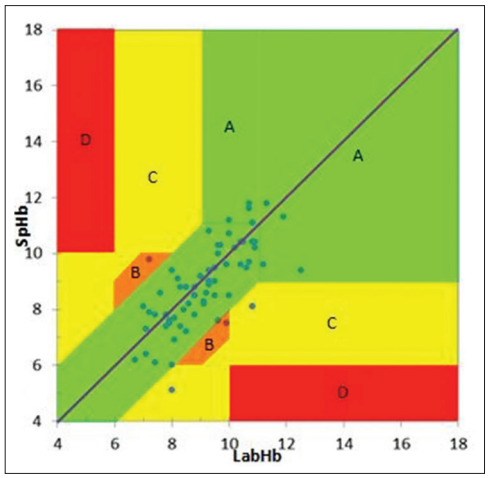

Figure 2: Error Grid Analysis for all transfusion figure is divided into four zones, Zone A is maximum agreement area, Zone B is better agreement area, Zone C is error area, Zone D is danger area (X-axis LabHb; Y-axis SpHb). SpHb – Non-invasive haemoglobin; LabHb – Laboratory haemoglobin

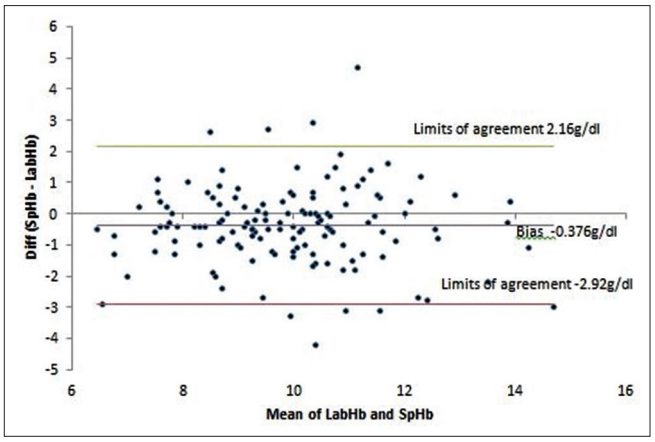

Figure 3: Bland–Altman of all SpHb values, line above the X-axis shows upper limit of agreement (2.16 g/dl), line below shows lower limit of agreement (−2.92 g/dl), line just adjacent to X-axis is bias (−0.376 g/dl). SpHb – Non-invasive haemoglobin

Mean bias for values <11 g/dl is less as compared to values higher than 11 g/dl. Bias in <11 g/dl group of values was found to be −0.33 g/dl and SD of ±0.89 g/dl. Mean bias in pre- and post-bleed and packed cell transfusion was of −0.314 g/dl and with SD of ±1.28 g/dl and − 0.774 g/dl and with SD of ±1.40 g/dl, respectively, and correlation decreased from 77% ($P < 0.05$) in pre-packed cell transfusion group to 54% ($P < 0.001$) in post-bleed and packed cell transfusion group. As our decision to transfuse PRBCs was based on SpHb and clinical assessment, we did a separate Bland–Altman analysis for first transfusion decision, all transfusion decisions and all non-transfusion decisions. We found a correlation of 62% in first transfusion group (33 paired measurements) with only two outliers (beyond limits of agreement) [Figure 1]. In all transfusions group (66 paired measurements), there was correlation of 73% and three outliers. For non-transfusion group (71 paired measurements), correlation was 64% with four outliers.

DISCUSSION

In this clinical trial, we evaluated the utilisation of Radical-7® in deciding the intra-operative packed cell transfusions in oncosurgical patients using the SpHb values to do blood transfusions, and these decisions were also validated against the gold standard LabHb values. We found a correlation of 73% between SpHb and LabHb when blood transfusions were done with mean difference (bias) being −0.313 g/dl and SD ± 1.06 g/dl. Causey *et al*.[5] also reported correlation of 77% and a bias of 0.29 g/dl. However, only 25 out of 70 patients in their study were surgical patients. They have found an 86% correlation in post-bleeding values, but only five patients were given packed cell transfusions after which correlation has not been studied. Lamhaut *et al*.[6] showed mean bias of −0.02 ± 1.39 g/dl and a correlation of 77%. They studied 85 measurements in 44 patients. Blood transfusion in their study was based on LabHb.

Applegate *et al*.[7] studied 360 values in 91 surgical patients showed a bias 0.50 ± 1.44 g/dl. The bias was larger in patients with blood loss of more than 1000 ml, when haemoglobin was <9.0 g/dl and when any intra-operative transfusion was administered. In our study, there was no significant difference in bias for loss more than 1000 ml. We have found that haemoglobin monitoring with the Radical-7 Pulse Co-oximeter gives lower readings than compared with automated haemoglobin measurement in the laboratory. Considering an acceptable difference to be <±1 g/dl with the laboratory measurement, 66% of SpHb values in our study were within this range. In 8–10 g/dl group, 68% of the values are within <±1.0 g/dl range. For <8 g/dl group, 64% of values are in <±1.0 g/dl group.

A separate analysis done for haemoglobin values before any blood loss and packed cell transfusion and after blood loss and packed cell transfusion were also performed and we found an increased bias in the latter group. Correlation between SpHb and LabHb reduced towards the end of surgery (from 77% to 54%) which can be explained by effects of intra-operative fluid on accuracy of SpHb. These changes might have been because of unexplained effect of crystalloid or colloid which needs to be studied further.

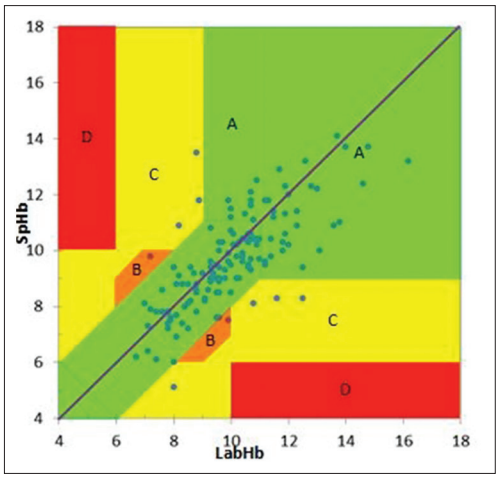

Figure 4: Error Grid Analysis of all SpHb values, figure is divided into four zones, Zone A is maximum agreement area, Zone B is better agreement area, Zone C is error area, Zone D is danger area (X-axis LabHb; Y-axis SpHb). SpHb – Non-invasive haemoglobin; LabHb – Laboratory haemoglobin

Clinical measurement of haemoglobin values requires analysis of a blood sample with an automated laboratory device, similar to co-oximeter, usually performed in the haematology department. However, as spectrophotometric-based LabHb measurement represents the reference method for haemoglobin estimation, their accuracy range in the clinical setting is often wider than the official specification. For example, comparing two identical devices of five different manufacturers, Gehring *et al*.[8] reported significant intra-device and inter-device variations in haemoglobin measurements. It is also important to note that there is no standard procedure for testing the measurement error of co-oximeter, and both the reference device and the test device have inherent errors. In addition, from the Bland–Altman comparison, we must bear in mind that both reference device and test device could be responsible for inherent errors. Finally, the expected percentage difference between several instruments measuring haemoglobin in a laboratory is estimated to be ±7% of the target value as suggested by the Clinical Laboratories Improvement Act of 1988.[9]

Based on Bland–Altman plot analysis of only transfusion points, we concluded that decision to transfuse blood was correct for 95% cases if it was taken just on the basis of SpHb readings. The same can be said about non-transfusion group. Our results were different from the Gayat *et al*.[10] study that showed transfusion errors of 38%. They did a spot checking on emergency department patient with non-invasive and invasive methods. Till date, there are no studies which have validated the accuracy of SpHb as an aid to guide packed cell transfusion in oncosurgery patients. Moreover, SpHb has varied in the opposite direction of reference haemoglobin in 9.5% of assessments in our study. Similar findings were also reported intraoperatively by other authors, with inverse haemoglobin variations displayed in 6, 7, 11 and 16% measurements.

As Morey *et al*. described the flaws of Bland–Altman plot analysis, we also did Error Grid Analysis on our data. Error grid helps with better visualisation of the relation between SpHb and LabHb readings. It helps the reader visualise the higher density of points lying closer to the perfect agreement line. Error Grid Analysis of all paired data points in our study showed Zone A has maximum data points [Figure 4]. Only two values in Zone B, though the difference between LabHb and SpHb is higher, the decision taken to transfuse (or not transfuse) comes out the same whether SpHb or LabHb readings were used to guide the packed cell transfusion. The only difference is the strength of the 'advocacy' to transfuse (or not transfuse). There were seven points in Zone C and no data points in Zone D.

The paired measurements in Zone C could not be explained collectively by single reason. If transfusion was based solely on SpHb values, seven values in Zones C could be taken as an error and this is 4.96% (which is fairly within 95% of CI).

Hence, after analysing the error grid, we found that none of the SpHb readings could have contributed to wrong decision in blood transfusion, especially if decision is taken wisely considering haemodynamics of patient. There was no direct correlation between the bias (SpHb-LabHb) and PI.

The main benefits of SpHb monitoring are the non-invasiveness (no blood sample is required) and the continuous online assessment of haemoglobin concentration. Indeed, continuous online monitoring of SpHb enables the instantaneous (time-critical) detection of a haemoglobin drop, whereas a physician had not yet scheduled an invasive haemoglobin measurement by analysis in the haematology laboratory (delayed result). In this situation, by the time the result arrived from an invasive measurement, acute anaemia might be responsible for coronary ischaemia, especially in patients with pre-existing cardiovascular diseases. Thus,

continuity and non-invasiveness of online SpHb monitoring undoubtedly represent an advancement for transfusion management during perioperative patient care. In practice, we took transfusion decisions based on live SpHb readings and validated them later against LabHb readings. The SpHb readings turned out to be very important for high blood loss and time critical operations.

Finally, more than the absolute and instantaneous haemoglobin value displayed by the Radical-7®; its continuous measurement allows the physician to focus on the haemoglobin trend and detect either a slow decrease or a significant rapid drop in haemoglobin and therefore decide the appropriate time to perform an invasive measurement of haemoglobin.

We note few limitations in our study. First, we collected venous blood sample from central venous line rather arterial blood. Haemoglobin concentration has been reported to be higher in venous blood than arterial blood though precision for haemoglobin estimation is higher for venous blood.[11] We have tried our best to maintain factors such as colloid administration[12] and skin temperature[13] at probe site which has been reported to affect the SpHb accuracy. Our study has shown the transfusion decision to be correct for 95% of values. Thus, even these factors would not have affected the decision significantly although further study on association with these factors can be warranted. Our study includes the group of patients which involves the massive but steady blood loss over a long time, thus cannot be extrapolated to the patients with differing blood loss rates. Further studies need to be done in this regard, although numerous studies have been done to find the reliability of the device in more acute and severe haemorrhage conditions such as trauma.

We would also like to add that our sample was randomly chosen and normally distributed, because of which we can say that our sample is a reasonably good representative of the entire population, and hence, likelihood of population-mean lying close the sample mean is quite high. There will certainly be data points (or patients) for which the SpHb and LabHb may be farther away from the mean bias, but likelihood of such observations appearing is lower than the likelihood otherwise. These are the cases where the discretion of attending anaesthesiologist becomes important.

CONCLUSION

Continuous SpHb monitoring can aid us regarding early blood transfusion decisions in oncosurgical patients along with other measures such as clinical judgement by attending consultant and haemodynamic variables. It may improve the intraoperative management of oncosurgeries by helping in real time and continuous decision-making for blood transfusion.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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