Research Article

Comparison of central venous saturation by standard ABG machine versus co-oximeter: Is 18 carat as good as the 24 carat gold standard?

Gayathri Subramanian, Anitha V. P.[1], Suchitra Ranjit[2]

Abstract

Aims: Aggressive therapy aimed at desired end-points of Early Goal Directed Therapy (EGDT) is the cornerstone of septic shock management. A key endpoint that improves outcomes is achieving central venous saturation ($ScvO_2$) >70%. The gold standard to measure $ScvO_2$ is by a co-oximeter (co-ox). **Settings and Design:** This prospective, observational study from a multidisciplinary pediatric intensive care unit (PICU) was conducted to assess the validity of $ScvO_2$ levels by standard ABG (stand ABG) machine in comparison with co-ox in conditions that shifted the oxygen dissociation curve (ODC) to the right or left in sick children and controls. **Materials and Methods:** Data from paired samples was tested for correlation coefficient for pH, $paCO_2$, paO_2, and $ScvO_2$. Tests for correlation (Pearson's coefficient) and agreement (Bland–Altman analysis) were performed on $ScvO_2$ values obtained in various subgroups. Sensitivity and specificity for $ScvO_2$ values determined by standard ABG machine versus co-ox were calculated in reference to EGDT endpoints. **Results:** A total of 141 paired samples were collected from 82 children. Despite a statistically significant difference in the pH and $ScvO_2$, there was good linear correlation between these parameters. Limits of agreement between $ScvO_2$ measured by standard ABG machine and co-ox by Bland–Altman gave 2.3% bias with 95% CI of -24.2% to 19.5%. Sensitivity and specificity of standard ABG machine in detecting low $ScvO_2$ in shock was 84.21% and 93.18% respectively, while it was false positive in 4 samples. **Conclusions:** The less expensive standard ABG machine showed satisfactory correlation with gold standard co-ox over a range of patient conditions; however, the wide range for agreement was of concern and it performed particularly poorly in anemic patients.

Keywords: Central venous saturation, co-oximeter, goal directed therapy, septic shock

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Introduction

Shock due to any reason carries a significant risk of mortality and morbidity, especially if the therapy is inappropriate. Aggressive fluid and/or vasoactive therapy aimed at achieving the desired end-points of early goal directed therapy (EGDT) is the cornerstone of management of both adults and children with septic shock,[1,2] and also following cardiac surgery.[3] Specifically, achieving a central venous saturations ($ScvO_2$) >70% is one of the key therapeutic goals that has been shown to improve outcomes,[1,2] as this reflects tissue oxygenation and oxygen delivery.[4]

Although the true value of mixed venous oxygen may be obtained by obtaining a sample from the pulmonary artery by Swan Ganz catherization, a $ScvO_2$ from an appropriately sited central venous catheter (CVC) is an acceptable surrogate.[5,6] The gold standard to measure $ScvO_2$ is analysis of the venous blood gas sample by a co-oximeter (co-ox). This is because the

From:
Pediatric, Neonatal and Cardiac Intensive Care Services, Great Ormond Street Hospital For Children, National Health Service Trust, London, United Kingdom, [1]Mehta Children's Hospital, [2]Apollo Children's Hospital, Chennai, India

Correspondence:
Dr. Suchitra Ranjit, Apollo Children's Hospital, Shafee Mhd Rd, Thousand Lights, Chennai - 600 006, India. E-mail: suchitraranjit@yahoo.co.in

saturation is directly *measured* in a co-ox, whereas this value is *calculated* (with many assumptions) in a standard blood gas machine.[7,8] In sick patients, binding of hemoglobin (Hb) to oxygen cannot be assumed to be normal, and, furthermore, the position of the oxyhemoglobin curve may be shifted due to multiple reasons.[7,8]

However, due to the cost constraints, many intensive care units (ICU) in India measure $ScvO_2$ by a standard ABG (stand ABG) machine, which is significantly less expensive. This prospective, observational study from a multidisciplinary (medical, cardiac, and surgical) pediatric ICU (PICU) of a tertiary level hospital (Apollo Hospitals, Chennai) was conducted to assess the validity of $ScvO_2$ levels obtained by stand ABG in comparison with co-ox. In particular, with reference to reaching EGDT endpoints in septic shock, we aimed to elucidate the false positive rates ($ScvO_2$ >70% by stand AB standard ABG machine G but <70% on co-ox) that could potentially lead to inadequate resuscitation of this group, resulting in morbidity and mortality of these critically ill patients. We also wanted to study the correlation of $ScvO_2$ obtained by the two methods under common conditions that shifted the oxygen dissociation curve (ODC) to the right or left (acidosis and alkalosis, temperature variations), as these conditions are frequent occurrences in critically sick ICU patients. Sensitivity and specificity of standard ABG machine against gold standard (co-ox) for $ScvO_2$ values in patients with shock was determined.

Materials and Methods

This was a prospective, observational study that included consecutive children over a period of 12 months from Jan 2008 to 2009 who were admitted to a PICU with central line *in situ*. Those with hemoglobinopathies and inappropriate central line placement (as detected radiographically) were excluded from the study.

Paired central venous blood gas samples were taken with a maximum time interval of 1 min between sampling. Both blood samples were analyzed by stand ABG (Bayer 248 blood gas analyzer) and co-ox (Bayer Diagnostics Mfg Ltd., Sudbury, UK) simultaneously. The machines were located in the ICU premises and, hence, there was minimal time delay in processing the sample. The standard ABG machine quality control of the stand ABG and co-ox machines were maintained to reduce calibration errors. Both machines were calibrated by the Biomedical Department as per the hospital and concerned company policies. Some patients had venous gas performed more than once. All samples were collected in preconfigured heparinized syringes for blood gases (BD India). The cost per test in each modality was Rs 450/- for standard ABG test and Rs 750/- for ABG by co-ox.

At the time of sampling, general patient demographics including diagnosis, clinical condition (vitals, core temperature, need for inotropes, ventilation), and laboratory data (Hb level, lactate) were recorded. After the sample was processed, the blood gas values were entered on a spreadsheet and cross-checked by two authors (GS and VPA). Data was analyzed using SPSS package by an independent statistician. Data obtained from paired samples was tested for correlation coefficient for pH, $paCO_2$, paO_2 (measured values), and $ScvO_2$ (measured in co-ox and calculated by stand ABG). A correlation coefficient does not measure the agreement between variables. A perfect agreement requires that all points obtained by plotting data pairs lie along the line of equality, while excellent correlation is obtained when the points lie along any straight line. Data that is high in correlation can be widely discrepant for agreement. In addition, a difference in scale of values between two parameters does not affect correlation, but affects agreement.[9] For these reasons, Bland–Altman assessment for agreement was used to compare the $ScvO_2$ measured by the two methods. A range of agreement was defined as mean bias ± 95% CI.[10]

The patient data was further subdivided into six groups, based on predefined criteria. The groups included patients in shock, those with abnormalities in factors that shift the ODC, viz. pH, temperature, and Hb levels and those without any abnormalities (normal). Acidosis and alkalosis were defined as venous pH < 7.32 and pH > 7.42, respectively. Temperature abnormality included patients with both hypothermia (≤97ºF) and hyperthermia (≥99ºF). Anemia was defined as Hb <10 gm%. Patients were said to be in shock if they had at least three of the following clinical and laboratory evidence of shock: Disproportionate tachycardia, low blood pressure for age, prolonged capillary refill time (>3 sec), poor peripheral pulses, core to peripheral temperature difference of >2ºC, low urine output, or elevated lactate (>4 mmol/L).

Tests for correlation (Pearson's coefficient) and agreement (Bland–Altman analysis) were further performed on $ScvO_2$ values obtained in these subgroups. Sensitivity (true positive) and specificity (true negatives) for $ScvO_2$ values determined by stand ABG versus the gold standard (co-ox) were calculated with particular reference to reaching EGDT endpoints in septic shock. False positives ($ScvO_2$ <70% on co-ox, but >70% by stand ABG) were determined in the sample population. A $P < 0.05$ was considered significant.

Results

The baseline characteristics of the study population are summarized in Table 1. From 82 patients, 141 paired samples were collected. Forty-four paired samples were collected in patients in shock, 54 in acidemic patients, 29 in alkalemic patients, 34 anemic patients, 32 in patients with either hypothermia or hyperthermia, and 31 in patients who did not fall in any of these categories (normal).

Results obtained on blood gas analysis for the two groups are tabulated in Table 2. Despite a statistically significant difference in the pH and $ScvO_2$ values measured by both the methods, there was good linear correlation between these parameters [Table 2, Figures 1 and 2]. Among the blood gas parameters, pH, $paCO_2$, and paO_2 showed positive good correlation when obtained by either method [Figures 1 and 2]. In the case of $ScvO_2$, a positive correlation was obtained when the $ScvO_2$ was analyzed by either machine (r = 0.69, P = 0.001) [Figure 3]. Limits of agreement between $ScvO_2$ measured by standard ABG machine and co-ox by Bland–Altman methodology gave 2.3% bias with 95% CI of − 24.2% to 19.5% [Figure 4].

The sensitivity of the standard ABG machine machine in detecting $ScvO_2$ in patients with shock was 84.21%, while the specificity was 93.18%. In 4 (2.84%) samples, the standard ABG machine gave false positive results, indicating that that shock endpoint had been reached ($ScvO_2$ >70% when it was <70% on co-ox). The $ScvO_2$ values obtained by the two methods in various subgroups are tabulated in Table 3. All the subgroups, including patients with shock, had substantial correlation of the $ScvO_2$ values (0.6 - 0.8, P = 0.001) whether it was analyzed by standard ABG machine or co-ox. In those

Table 1: Baseline characteristics

Age (Median and inter-quartile range)	4 years (2-7)
Sex ratio (Male: Female)	42:40
Medical: Surgical	21:61
Mechanical ventilation instituted (*n*)	58
Vasoactive medications received (*n*)	55
Mean hemoglobin in gm% (±2 SD)	11.34 (4.3)

Table 2: Comparison of blood gas parameters between standard blood gas machine (stand ABG) and co-oximeter (co-ox)

	Stand ABG	Co-ox	P
ph	7.37 (0.9)	7.34 (0.9)	<0.001
$PaCO_2$	44.3 (8.5)	44.6 (7.4)	0.44
PaO_2	42.8 (13.9)	44.6 (7.4)	0.87
HCO3	24.5 (5.2)	25.3 (6.5)	0.7
$ScvO_2$	74.3 (11)	71.8 (15.5)	0.01

Results are expressed as mean (±SD); *P* value is calculated by students *t* test, ABG: Arterial blood gases

Table 3: $ScvO_2$ obtained in subgroups

	Number	Stand ABG	Co-ox	P
Temperature abnormalities	32	70.9 (17.2)	73.1 (12.1)	0.29
Shock	44	72.0 (15.7)	73.6 (12.3)	0.30
Anemia	34	68.2 (17.7)	73.1 (10.8)	0.08
Alkalosis	29	73.1 (13.4)	73.8 (11.7)	0.57
Acidosis	54	73.0 (16.1)	74.3 (12.7)	0.42
Normal	31	72.3 (13.8)	74.3 (11.6)	0.20

Results are expressed as mean (±SD); *P* value is calculated by students *t* test, ABG: Arterial blood gases

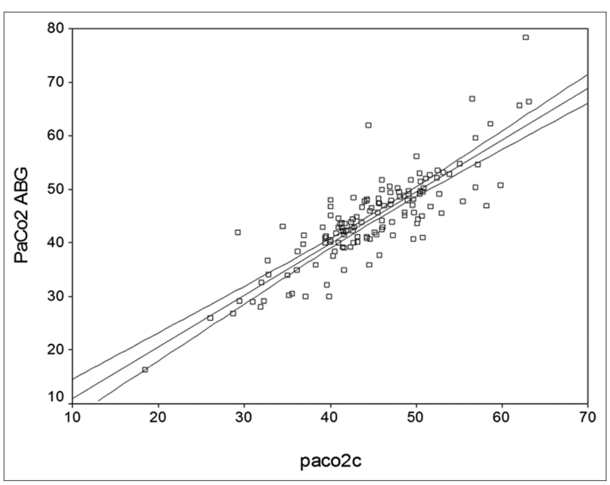

Figure 1: Correlation between $paCO_2$ measured by stand ABG and co-ox. Scatter diagram with regression estimate shows the positive good correlation between $paCO_2$ by stand ABG and co-ox (r = 0.84, P = 0.001); $paCO_2$ ABG = stand ABG; $paCO_2$ c = co-ox

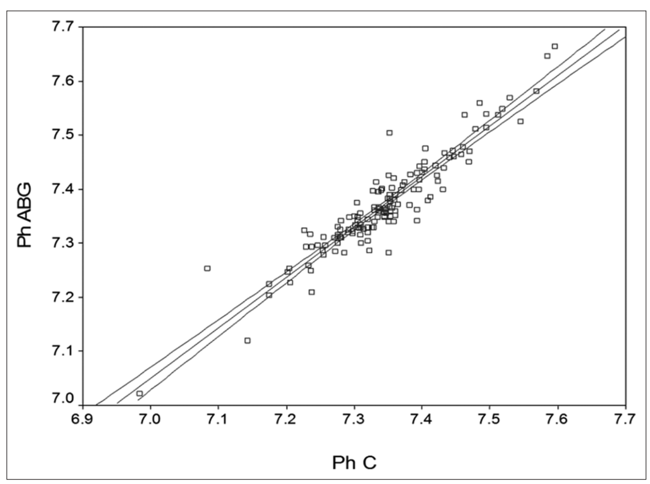

Figure 2: Scatter diagram correlation between pH by stand ABG and co-ox (pH C). Scatter diagram with regression estimate shows the positive good correlation between pH by stand ABG and co-ox (r = 0.94, P = 0.001); pH ABG = pH analyzed by stand ABG; pH C = pH analyzed by co-oximeter)

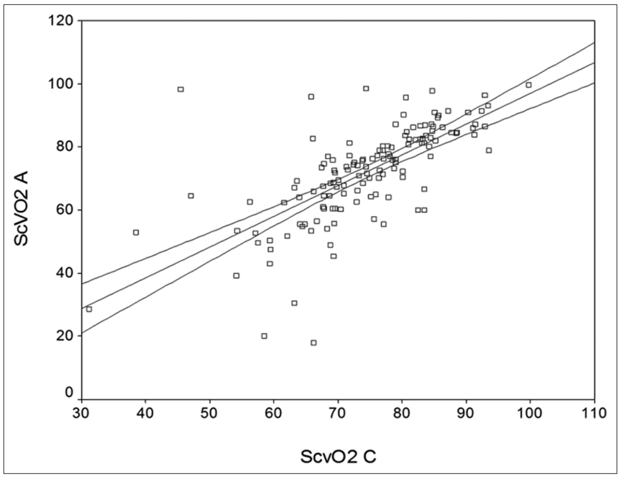

Figure 3: Correlation between $ScvO_2$ by stand ABG and co-ox. Scatter diagram with regression estimate shows the positive good correlation between $ScvO_2$ by stand ABG and co-ox (r = 0.69, $P = 0.001$). ($ScvO_2$ A = Central venous saturation measured by Standard Blood Gas machine; $ScvO_2$ C = Central venous saturation measured by co-oximeter)

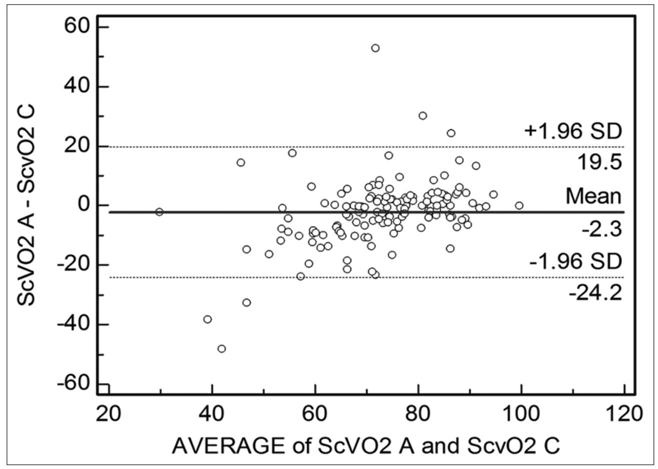

Figure 4: Agreement between $ScvO_2$ values obtained by the two machines. The dotted lines represent 95% CI. $ScvO_2$ A = Central venous saturation measured by Standard Blood Gas machine, $ScvO_2$ C = Central venous saturation measured by co-oximeter

with alkalosis, the $ScvO_2$ values had good substantial correlation (0.90, $P = 0.001$). However, presence of anemia showed only moderate correlation (0.49, $P = 0.001$). However, when analyzed by Bland–Altman plot, poor agreement was noted in all subgroups.

Discussion

Aggressive fluid and/or vasoactive therapy aimed at achieving the desired end-points of EGDT, including $ScvO_2$ >70%, is one of the key therapeutic goals that has been shown to improve outcomes.[1,2] The gold standard to measure $ScvO_2$ is analysis by a co-ox. There have been no previous published studies comparing $ScvO_2$ values obtained by standard ABG machine and co-ox.

In our study, a positive good correlation (r = 0.69) was obtained in the $ScvO_2$ values measured by both the machines in a heterogeneous group of critically sick children, i.e., there is a strong, linear relationship unlikely to happen by chance ($P = 0.001$). Factors affecting the ODC did not affect this linear positive co-relation. However, in patients with Hb <10 gm%, the correlation co-efficient showed only moderate positive correlation (r = 0.49, $P = 0.001$). The standard ABG machine, which is widely used for blood gas analysis in many hospitals across India, *measures* the $paCO_2$, paO_2, and pH of the sample. All other values are *calculated* by the algorithm inbuilt in the machine. As against this, most ICUs in the western world use the co-ox, which considered the gold standard. The advantage of a co-ox compared to a standard blood gas machine is its capability to *measure* concentrations of oxygenated Hb, reduced Hb, carboxyhemoglobin, methemoglobin, and bicarbonate. The co-ox is intuitively considered more reliable, especially in sick patients, where an algorithm-based calculation of $ScvO_2$ by a standard blood gas machine may be prone to fallacies.

Knowledge regarding the limits of agreement and correlation of $ScvO_2$ values analyzed by stand ABG versus co-ox across a wide range of typical ICU conditions is important for critical care practitioners. Limits of agreement between $ScvO_2$ obtained by stand ABG versus co-ox showed 2.3% bias with 95% CI of − 24.2% to 19.5% by Bland–Altman methodology. The same methodology was used in the subgroups with none, except the group with alkalosis showing agreement. Thus, although there was good correlation, the agreement levels were wide, suggesting that the wide difference is possibly machine related.

Hemodynamic monitoring is a standard of care in the management of critically sick children to identify cardiovascular insufficiency, determine its cause, and evaluate the response to treatment. Global tissue oxygen delivery is commonly monitored using mixed venous oxygen saturation ($ScvO_2$) level, which reflects the cardiac output, oxygen delivery (DO_2), peripheral extraction of oxygen, and consumption (VO_2). Its value is related to four determinants: VO_2, cardiac output, Hb, and oxygen saturation of Hb. $ScvO_2$ trends measured with the central venous catheter tip in right atrium is more easily measurable than the mixed venous saturations and is an acceptable surrogate.[1,3] Inadequate DO_2 is presumed to be occurring if tissue oxygen extraction is markedly increased, as manifested by a decrease in $ScvO_2$ <70 in any kind of shock.[1-4] Hence, our particular focus of interest was to determine whether the stand ABG performed adequately when assessing $ScvO_2$ in patients with shock.

In samples where the sample was analyzed by stand ABG and the $ScvO_2$ was >70%, the false positive rates were low and the degree of specificity and sensitivity was high, suggesting that the chance of missing a patient with uncorrected shock was low. Two of the 4 patients who had $ScvO_2$ < 70% on co-ox, but >70% on stand ABG were febrile. However, given the small sample size of false positives, we are underpowered at this stage to conclusively comment if fever tends to increase the rate of false positives. Overall, $ScvO_2$ obtained by the stand ABG machine showed good overall correlation with the $ScvO_2$ obtained by co-ox, except in anemic patients who had Hb <10 gm%, where it consistently performed poorly.

Our study was limited by the rather small number of paired samples in each subgroup. Larger number of samples would have eliminated the small margins of error and improved the strength of relationship (determined by the *P* value) occurring during the statistical evaluation. It was a single-centre observational study. Furthermore, we did not process phosphate levels (another variable that affects the ODC). It may be argued that even missing a single patient with $ScvO_2$ < 70% increases the probability of that patient being under-resuscitated with a higher chance of mortality. However, in practice, the patient's condition is considered in totality and is not based on a single variable (in this case, $ScvO_2$). Therefore, if other parameters in EGDT for septic shock are not achieved, an ICU physician is unlikely to consider an isolated $ScvO_2$ value of >70% as the end point of treatment.

Intensive care is making a foray in a big way in the developing world with several institutes offering tertiary level care. Cost is a major constraint for the hospital management that invests in equipment purchase. Most ICUs use a standard ABG machine for blood gas analysis. This machine is relatively "cheaper" (approximately Rs 400,000) as compared to the much more expensive co-ox (approximately Rs 10,00,000-14,00,000) and the cost per ABG carried out by a stand ABG is half of that performed by a co-ox. While it was encouraging that the less expensive equipment showed satisfactory correlation with the gold standard co-ox over a wide range of patient conditions, the wide range for limits of agreement was of concern.

Tertiary care ICUs in developing nations may prefer the stand ABG as the co-ox is much more expensive and there was a general perception that the accuracy of the readings from a stand ABG are "in sync" with the co-ox. This decision is not based on scientific studies and is often intuitive. Our study indicates that the stand ABG can be a satisfactory and cost-effective surrogate for the more expensive co-ox when assessing $ScvO_2$ for patients with shock. Although the correlation was good over a range of conditions, the limits of agreement were wide and it performed particularly poorly in anemic patients.

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