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Abstract

BACKGROUND AND OBJECTIVE: In-vitro performance of the PediaSat system for continuous monitoring of central venous oxygen saturation by spectrophotometry has been evaluated. METHODS: PediaSat continuous fibre-optic oximetry catheters were inserted in a black testing chamber, connected with an extracorporeal circuit and filled with human whole blood. Oxygen inflow into the cardiopulmonary bypass system was varied, and the testing chamber was perfused with blood flow of 1000 ml min. Oxygen saturation values measured by PediaSat (SPediaSatO2) were compared with cooximetry (SCO-OXO2) values from simultaneously taken blood samples by Bland-Altman and simple regression analyses. RESULTS: Fifty data pairs were obtained. SPediaSatO2 and SCO-OXO2 values ranged between 28-98 and 24.9-99.5%, respectively. Correlation between SPediaSatO2 and SCO-OXO2 was high with an r value equal to 0.96 (P < 0.0001). Overall, SPediaSatO2 only slightly overestimated SCO-OXO2 (mean bias +2.9%), and limits of agreement (+/-2 SD of bias) were acceptable (-6.8/+12.6%). Sensitivity and specificity of the first differences of SPediaSatO2 and SCO-OXO2 were 1.0 and 0.92, respectively. Subgroup analysis of SCO-OXO2 values below 70% resulted in an overestimation by SPediaSatO2, with a mean bias of +5.2% and limits of agreement of -4.7 and +15.1%. CONCLUSION: The current version of the PediaSat system does not reliably reflect SCO-OXO2 values below 70%, but it seems to be a useful tool providing an accurate trend of continuous central venous oxygen saturation.
In vitro evaluation of the PediaSat continuous central venous oxygenation monitoring system*

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Summary

Background and objective In vitro performance of the PediaSat system for continuous monitoring of central venous oxygen saturation by spectrophotometry has been evaluated.

Methods PediaSat continuous fiberoptic oximetry catheters were inserted in a black testing chamber, connected with an extracorporeal circuit and filled with human whole blood. Oxygen inflow into the cardio-pulmonary bypass system was varied and the testing chamber was perfused with blood flow of 1000 ml.min⁻¹. Oxygen saturation values measured by PediaSat (S_{PediaSatO2}) were compared with co-oximetry (S_{CO-OXO2}) values from simultaneously taken blood samples by Bland-Altman and simple regression analysis.

Results Fifty data pairs were obtained. S_{PediaSatO2} and S_{CO-OXO2} values ranged between 28 - 98% and 24.9 – 99.5% respectively. Correlation between S_{PediaSatO2} and S_{CO-OXO2} was high with $r^2 = 0.96$ (p < 0.0001). Overall, S_{PediaSatO2} only slightly overestimated S_{CO-OXO2} (mean bias +2.9%), and limits of agreement (± 2 SD of bias) were acceptable (–6.8 / +12.6%). Sensitivity and specificity of the first differences of S_{PediaSatO2} and S_{CO-OXO2} were 1.0 and 0.92, respectively. Subgroup analysis of S_{CO-OXO2} values below 70% resulted in an overestimation by S_{PediaSatO2} with a mean bias of +5.2% and limits of agreement of - 4.7 and + 15.1%.

Conclusions The current version of the PediaSat system does not reliably reflect S_{CO-OXO2} values below 70%, but it seems to be a useful tool providing accurate trend of continuous SvO₂.

Keywords: Monitoring, oxygenation, venous, central, continuous

Abstract: 224 words

Text: 1948 words
**Introduction**

Mixed venous oxygen saturation (SvO₂) assessed by a pulmonary artery catheter has been used for many years to estimate the DO₂/VO₂ balance. Recently central venous oxygen saturation (ScvO₂) has replaced SvO₂ in many clinical settings [1, 2] and is one of the core targets for early goal-directed therapy in the treatment of septic shock in adults [3-5]. The role of ScvO₂ is even more important in neonates and paediatric patients, in whom the positioning of a pulmonary artery catheter is problematic. The detection of variation of ScvO₂ values has become a point of interest particularly in the perioperative setting of cardiac and major surgery [6] in high risk patients. Standard means of monitoring ScvO₂ to assess global oxygen balance and cardiac output in paediatric patients consist of repeated blood sampling from a central venous catheter placed in the superior vena cava and analysis of the blood using co-oximetry [7]. This approach is intermittent, is attendant on increased workload and costs and results in contamination of stopcocks and iatrogenic blood loss. Additionally, haemodynamic and metabolic conditions may vary rapidly and are often not detected by intermittent blood gas analysis. Techniques providing continuous monitoring of ScvO₂ may be a real time answer to this substantial issue.

Spectrophotometry using near-infrared light [7] is one of these technologies, and several devices have been commercially introduced. Various devices has been evaluated in few clinical and experimental investigations, but the results remain controversial [8-12]. Recently a new system for paediatric patients, the PediaSat system (Edwards lifesciences, Irvine, CA 92614, USA) has become available, using central venous catheters with inbuilt fibre-optic transmission. The aim of this study was to validate its performance in an in vitro bench top model.
Methods

The PediaSat system consists of a central venous catheter with inbuilt spectrophotometric probe containing two fibre-optic lines connected proximally to the optical module of the PediaSat system. Three different catheters 4Fr 1-Lumen, 4.5 2 Lumen and 5.5 Fr. 3 Lumen central venous catheters with fibre-optic probes are available.

For the purpose of monitoring $S_{\text{PediaSatO2}}$, light of two wavelengths (660 and 800 nm) is transmitted through one of the two fibre-optic lines. Tissue chromophores, such as haemoglobin, absorb near-infrared light, depending on their oxygenation state. Changes in chromophore concentrations and oxygenation states, revealed by comparing emitted and detected near-infrared light, can therefore be quantified, using the modified Lambert-Beer law [8, 13, 14]. Light reflected from the haemoglobin in the red blood cells is detected by the second fibre-optic line of the probe and transmitted back to the sensor in the optical module. The sensor in the optical module of the PediaSat device determines light extinction and $S_{\text{PediaSatO2}}$ is calculated and displayed on the screen of the Vigileo™ Monitor (Vigileo Monitor MHM1E, Edwards Lifesciences, Irvine, CA 92614, USA).

Before starting continuous measurements, a calibrating manoeuver using a blood sample analysed by co-oximetry is required according to the manufacturer’s instructional recommendations. During continuous recording of oxygen saturation, the Vigileo monitor displays a “signal quality index (SQI)” in a 4-degree range from 1 (best quality) to 4 (worst quality). The SQI is a composite signal that expresses the signal intensity, the blood pulsatility, and the presence of outlying spikes in the re/infrared signal.
**Experimental set-up**

Two 6.0F introducer sheaths (Avanti®+ Catheter Sheath Introducer, Cordis Cooperation, East Bridgewater, NJ, USA) with a length of 7.5 cm and a distal lumen of 2.2 mm (Pulsion Medical Systems) were inbuilt into two separated chambers of a black test box of 100 cm³. The two chambers were connected to provide blood flow through both of them. Two 3 lumen - PediSat™ oximetry catheters (XT3515HS, 5.5-F, 1.83mm, 15cm; Edwards Lifesciences, Irvine, CA, USA) were introduced into the distal lumen of the introducer sheets until about 8 cm of the length of the catheter, then secured by the integrated luer-lock system. Each catheter was then connected to the optical module of one of two Vigeleo™ Monitors (Edwards Lifesciences, Irvine, CA, USA). The black box was connected to a paediatric cardiopulmonary bypass (CPB) circuit. The configuration of the CPB circuit included a roller pump and a thermoregulating device (Paediatric Pump S3, Stöckert Instruments, Munich, Germany), a Safe Mini oxygenator (Polystan/Maquet-CP, Hirlingen, Germany), a Safe Micro Reservoir (Polystan/Maquet-CP) and a real-time blood gas analyser unit (CDI 500, Terumo, Eschborn, Germany) to monitor PCO₂. Pressurized O₂, N₂ and CO₂ were connected to a fresh gas mixer (full automatic gas blender, Stöckert Instruments) (Fig 1) to provide air mixtures with various concentrations of oxygen and physiological PCO₂. The CPB circuit was filled up with 300 ml of heparinized (10’000 heparin sodium (Hoffman la Roche AG, Grenzach-Wyhlen, Germany) human full blood provided by one of the investigators; the air was completely expelled. The flow rate provided by the roller pump was kept constant at 1000 ml.min⁻¹ throughout the experiments, and blood pressure in the test chamber was held at 15 mmHg. Blood was warmed up to 37°C, and alpha-stat blood PCO₂ was held within physiological range (5-7 kPa) by external CO₂ gas source, as continuously monitored by the real-time blood gas analyser unit (CDI 500, Terumo, Eschborn, Germany) of the extracorporeal circuit and confirmed by blood gas analysis.
After obtaining steady-state values for $S_{\text{PediSatO}_2}$ at 70%, both PediaSat systems were calibrated according to the instructions of the manufacturer. If SQI was higher than two, the optical fibre was removed, cleaned and reintroduced into the introducer. Only SQI values $\leq 2$ were accepted. After initial de-saturation of the circulating blood by gradually changing the fresh gas mixture of the membrane oxygenator from oxygen to nitrogen, subsequent saturations were performed by increasing oxygenation of the fresh gas mixture.

With each change of the oxygen saturation level and under steady-state, the $S_{\text{PediaSatO}_2}$ values were recorded. Simultaneously, blood samples were taken from the distal lumen of the introducer sheet, the oxygen saturation and haemoglobin concentration (Hb) were measured by multi-wavelength co-oximetry ($S_{\text{CO}_2\text{-OXO}_2}$) (GEM®OPL™, Instrumentation Laboratory, Lexington, Massachusetts, USA) as well as pH, partial oxygen tension (PaO$_2$), partial carbon dioxide tension (PaCO$_2$), and bicarbonate base excess (GEM Premier™ 3000 with iQM, Instrumentation Laboratory, Lexington, MA, USA). Two series of measurements were done on two occasions, using identical experimental set-ups and, for each set-up, two new fibre-optic central venous catheters were used.

**Statistics**

Data were expressed as mean (±SD). Agreement between $S_{\text{PediaSatO}_2}$ and $S_{\text{CO}_2\text{-OXO}_2}$ was assessed by Bland-Altman analysis [15]. Linear regression analysis was performed to compare $S_{\text{PediaSatO}_2}$ and $S_{\text{CO}_2\text{-OXO}_2}$ and the difference values of $S_{\text{PediaSatO}_2}$ and $S_{\text{CO}_2\text{-OXO}_2}$ with $S_{\text{CO}_2\text{-OXO}_2}$. Sensitivity /Specificity of $S_{\text{PediSatO}_2}$ between two consecutive readings to indicate fall or increase of $S_{\text{CO}_2\text{-OXO}_2}$ was calculated. Intra-class correlation was computed to quantify importance of differences between the experiments. Levene’s test of equality of variances was performed to analyze the variation between the experiments. An analysis of covariance was performed to analyze the effects of the experiment and the dependence of the
difference values of $S_{\text{PediaSatO}_2}$ and $S_{\text{CO-OXO}_2}$ on $S_{\text{CO-OXO}_2}$. SPSS version 16.1 (SPSS Inc, Chicago, USA) was used from the hospital resources for this purpose.
Results

A total of fifty $S_{\text{PediaSat}O_2}$ readings and simultaneous measurements of $S_{\text{CO-OXO}_2}$ were obtained and analysed. Metabolic parameters are listed in Table 1. $S_{\text{PediaSat}O_2}$ and $S_{\text{CO-OXO}_2}$ values ranged between 28% - 98% and 24.9% – 99.5% respectively. Inter-probe reliability of $S_{\text{PediaSat}O_2}$ values detected by the two simultaneously used PediaSat catheters showed a bias of 4% and a precision of 4% ($r^2 = 0.99; p < 0.0001; \text{Fig 2}$).

Linear regression analysis demonstrated a high correlation between $S_{\text{PediaSat}O_2}$ and $S_{\text{CO-OXO}_2}$ ($r^2 = 0.96; p < 0.0001; \text{Fig 3}$). Overall, $S_{\text{PediaSat}O_2}$ only slightly overestimated $S_{\text{CO-OXO}_2}$ (mean bias +2.9%), however limits of agreement (Bias ± 2 SD of mean difference) were less acceptable with −6.8% / +12.6% (Fig 3). The differences between $S_{\text{PediaSat}O_2}$ and $S_{\text{CO-OXO}_2}$ significantly depended on $S_{\text{CO-OXO}_2}$.

$S_{\text{CO-OXO}_2}$ values above 70% resulted in a better agreement between $S_{\text{PediaSat}O_2}$ and $S_{\text{CO-OXO}_2}$ with a mean bias of 0.4% and limits of agreement of −6.0 and +6.8% (Fig 4), whereas $S_{\text{CO-OXO}_2}$ values below 70% represented an overestimation of $S_{\text{PediaSat}O_2}$ with a mean bias of +5.2% and limits of agreement of -4.7 and +15.1% (Fig 4).

Sensitivity and specificity of $S_{\text{PediaSat}O_2}$ to indicate a fall or raise of $S_{\text{CO-OXO}_2}$ between two subsequent measurements were 1.0 and 0.92, respectively.
Discussion

This bench top in-vitro set up investigated reliability of the PediaSat system for continuous monitoring central venous oxygen saturation. The main findings were that PediaSat system considerably overestimated SvO2 values at S\textsubscript{CO-OxO2} values < of 70%, however sensitivity and specificity of S\textsubscript{PediaSatO2} to indicate deterioration or improvement of S\textsubscript{CO-OxO2} were acceptable.

The PediaSat system, investigated in this study, is based on reflectance oximetry using two reference light wave-lengths and is characterised by one transmitting and one detecting fibre-optic filaments. The PediaSat system is easy to handle, does not necessitate additional invasive venous access and allows in-vivo calibration. Calibration manoeuver is recommended once a day by the manufacturer. Additionally, it is applicable in neonates, infants and children since three different sizes of the oximetry catheters are available. Disadvantages are the increased stiffness of the catheter and the necessity of updating the haemoglobin and haematocrit value if significant shifts of haemoglobin (> 1.8g/dl) or haematocrit (> 6%) occur.

Based on our findings, S\textsubscript{PediaSatO2} considerably overestimated SvO2 values at S\textsubscript{CO-OxO2} values < 70%. The reliability of ScvO2 readings is of particular importance in this lower range (< 60%), where changes become of vital interest and therapeutic interventions become necessary. Even more, during and after palliative congenital cardiac surgery in neonates and small infants with cyanotic heart diseases ScvO2 may range from 35 to 55%. Particularly in functional univentricular circulation and also following Norwood procedure or its modifications central venous saturation (ScvO2) is used to assess the ratio between pulmonary and systemic flow. Arterial oxygen saturation of 75% and ScvO2 of 50% may be adequate. In this patient population it has been demonstrated that the risk of anaerobic metabolism increased from 4.8 % to 29% when ScvO2 fell below 30%. [16]. Reliable detecting oxygen
saturation values among 50 % is therefore mandatory for systems measuring SvO₂ continuously, to support decision making for adequate treatment options. In this setting the PediaSat system did not reliably estimate SvO₂ values, and may contributes to miss necessary therapeutic interventions.

In the past, several related systems have been investigated and the most recent studies show similar variations in the SvO₂ range of interest [8, 10-13, 17]. In a previous investigation [11] we reported on a three light reference wave-length based oximetry catheter system demonstrating only a poor agreement between fibre-optically measured SO₂ and S_{CO-OX}O₂ values. Because of a nearly linear dependency of the mean difference between oxymetrically measured SO₂ and S_{CO-OX}O₂ values in this study a systematic error has been assumed. Huber and colleagues [13] reported in an in vitro setting an excellent correlation between fibre-optic measurements of two different fibre-optic catheters and S_{CO-OX}O₂. However, the Bland-Altman plots for both probes revealed high limits of agreement and demonstrated substantial overestimation of low SO₂ and underestimation at high SO₂. In a clinical investigation of a PediaSat system in neonates and paediatric patients undergoing cardiac surgery Ranucci and colleagues [17] reported a mean bias closed to zero and an acceptable value of percentage error (17.3 to 23.2%) between S_{PediaSat}O₂ and S_{CO-OX}O₂ for measurements before, during and after cardiopulmonary bypass. They concluded that the PediaSat system might be considered as an accurate tool for continuous measurement of the ScvO₂ in paediatric patients undergoing cardiac surgery. Most recently Spenceley and colleagues [12] reported in critically ill children a mean bias of 1.1% and inadmissible high limits of agreement (-15.8 and +18%) between fibre-optic measured SO₂ values of the PediaSat system and S_{CO-OX}O₂. Although the unacceptable high limits of agreement the authors deduced that the PediaSat system provided accurate trending of continuous ScvO₂ but only within physiologic range. Whereas the results of the subgroup analysis of S_{CO-OX}O₂ values above 70% in the current in-vitro set up agreed well with those by Ranucci and colleagues [17], the S_{CO-OX}O₂ values between 70 to 25% were
not sufficiently detected. Contrary to our investigation the lowest $S_{CO-OX}O_2$ values achieved in the study by Ranucci and colleagues [17], and Spenceley and colleagues [12] were only close to 50%, which may explain the considerably disagreement with the presented findings.

Although the PediaSat system demonstrated a substantial overestimation of $S_{CO-OX}O_2$ values < 70% in the current investigation, sensitivity and specificity of $S_{PediSat}O_2$ to indicate deterioration or improvement of $SvO_2$ were excellent. These findings may suggest that the PediaSat system might be a useful tool to indicate accurate trend of ScvO2.

Our bench-top model only used variations in oxygen saturation and tried to maintain other parameters constant. Consequently, there is no further information about the performance during changes of haemoglobin, use of volume expanders, temperature shifts, metabolic disturbances and coagulation disorders. However, the used 1-way bench-top model clearly demonstrated inaccuracy of the system in the clinically relevant range of ScvO2 even under otherwise constant conditions.

Based on our in-vitro findings, the new PediaSat system cannot be recommended as a reliable replacement of repeated invasive ScvO2 assessment in the clinically relevant range of ScvO2. Probably, rapid changes associated with haemodynamic deterioration and after resuscitation may be detected by the system.
References


Tables

Table 1 Metabolic parameter. Values are expressed as mean and SD
Figures

**Fig 1** Experimental set-up: position of the two PediaSat fibre-optic probes in a light-protected black box integrated into an extracorporeal circuit.

**Fig 2** Linear regression plot and Bland-Altman for interprobe comparison ($S_{\text{pediasat}O_2}$-Vigileo I and $S_{\text{pediasat}O_2}$-Vigileo II) ($n = 16$; $r^2 = 0.99$; $p < 0.0001$; bias = 4%; precision 4%)

Fig 3 Linear regression plot and Bland-Altman for comparison of $S_{\text{pediasat}O_2}$ values and $S_{\text{CO-OxO}_2}$ measured by co-oximetry ($n = 50$; $r^2 = 0.96$; bias +2.9%; 95% limits of agreement –6.8 / +12.6%)

**Fig 4** Bland-Altman plots for comparison of $S_{\text{pediasat}O_2}$ values and $S_{\text{CO-OxO}_2}$ measured by co-oximetry for SO$_2$ values > 70% and ($n = 24$; bias +0.4%; 95% limits of agreement –6.0 / +6.8%) and < 70% ($n = 26$; bias +5.2%; 95% limits of agreement –4.7 / +15.1%)
Table 1

**Parameter**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature, °C</td>
<td>36.8 (0.27)</td>
</tr>
<tr>
<td>Hb, g.dl⁻¹</td>
<td>8.0 (0.9)</td>
</tr>
<tr>
<td>Hct, %</td>
<td>23.0 (1.3)</td>
</tr>
<tr>
<td>PCO₂, kPa</td>
<td>5.54 (0.56)</td>
</tr>
<tr>
<td>pH</td>
<td>7.33 (0.03)</td>
</tr>
<tr>
<td>HCO₃, mmol/l</td>
<td>21.3 (2.5)</td>
</tr>
<tr>
<td>BE, mmol/l</td>
<td>-3.9 (0.3)</td>
</tr>
</tbody>
</table>

Abbreviations: Temp, temperature; Hb, haemoglobin; Hct, haematocrit; PCO₂, partial dioxide tension; BE, Base excess.
Fig 1

Blood Modul Tip of the fibre-optic central venous catheter

Real-Time Blood Gas Analyser

Oxygen Nitrogen

Oxygen/ Nitrogen Regulator %

Membrane Oxygenator

Introducer Sheet with Catheter

Open Venous Reservoir

Roller Pump
Fig 2:

![Graph showing the relationship between SpediaSat O2Viglieo I (%) and SpediaSat O2Viglieo II (%) with R^2 Linear = 0.993.](image)

![Graph showing the residuals of the SpediaSat O2Viglieo I (%) and SpediaSat O2Viglieo II (%).](image)
Fig 3
Fig 4.