293 256

Pediatric Anesthesia 2004 **14**: 989–995

Tissue oxygenation monitoring during major pediatric surgery using transcutaneous liver near infrared spectroscopy

MARKUS WEISS *, GABRIELE SCHULZ†, IAN TELLER‡, ALEXANDER DULLENKOPF*, ANNA KOLAROVA‡, HERRMANN SAILER§, CLAUDIA M. DILLIER*, HANS U. BUCHER†, ANDREAS C. GERBER* AND OSKAR BAENZIGER‡

**Department of Anaesthesia, University Children's Hospital, †Department of Neonatology, University Hospital, ‡Department of Intensive Care and Neonatology, University Children's Hospital, and §Department of Craniofacial Surgery, University Hospital, Zurich, Switzerland*

Abstract

Background: The aim of the study was to compare liver tissue oxygenation determined by near infrared spectroscopy (NIRS) with central venous oxygen saturation (SvO_2) and intestinal perfusion as measured by gastric intramucosal pH (pHi) in pediatric surgical patients.

Methods: Twenty children undergoing craniofacial surgery with expected major intraoperative blood loss were studied. NIRS tissue oxygenation index (TOI_{Liver}) and pHi values were recorded. Arterial blood gas analysis and SvO_2 were assessed from periodically taken blood samples. Data are presented as ranges (median) and were compared using linear regression analysis. Sensitivity and specificity of the intra-individual changes in TOI_{Liver} to predict falling SvO_2 or pHi values were calculated.

Results: Patients age ranged from 0.79 to 8.27 years (1.92 years). TOI_{Liver} ranged from 41.5 to 77.4% (61.5%), gastric pHi from 7.13 to 7.60 (7.37) and SvO_2 from 51 to 86% (74%). Among patients only moderate correlation was found between TOI_{Liver} and SvO_2 ($r = 0.594$, $P < 0.0001$) and gastric pH_i ($r = 0.502$, $P < 0.0001$). Intra-individual measured TOI_{Liver} values, however, demonstrated close correlation with SvO_2 values ($r = 0.680$ to 0.976) but a varying correlation with gastric pHi values ($r = 0.055$ to 0.972). Sensitivity/specificity of TOI_{Liver} to predict decreasing SvO_2 or gastric pHi values were 76.4/73.4% and 67.4/62.7% respectively.

Conclusions: TOI_{Liver} provided a better trend monitor of central venous oxygen saturation than gastric intramucosal pH. Because of its limited sensitivity and specificity to indicate deterioration of SvO_2, liver tissue oxygenation measured by transcutaneous NIRS does not provide additional practical information for clinical management.

Correspondence to: Markus Weiss, Department of Anaesthesia, University Children's Hospital, Steinwiesstrasse 75, CH-8032 Zürich, Switzerland (email: markus.weiss@kispi.unizh.ch).

© 2004 Blackwell Publishing Ltd

Keywords: near-infrared spectroscopy; liver; tissue oxygenation; gastric tonometry; children; monitoring

Introduction

Adequacy of global tissue oxygenation during major pediatric surgery is monitored by periodic assessment of acid–base state, central venous oxygen saturation and serum lactate concentration. These parameters represent intermittent but not continuous monitors and require invasive central-venous and/or arterial catheterization. Near-infrared spectroscopy (NIRS) is a well-described, noninvasive technique which allows continuous monitoring of tissue oxygenation (1, 2). The technique of NIRS depends on the transparency of biological tissue to light in the near-infrared region and also on the fact that the main chromophores (oxygenated and deoxygenated hemoglobin) exhibit distinct spectral features in this spectral region. Hemoglobin absorbs near-infrared light depending on the oxygenation state and changes in hemoglobin oxygenation can be quantified using the modified Lambert–Beer Law (2). Newer generations of NIRS spectrometers such as the NIRO 300 (Hamamatsu Phototonics, Hamamatsu City, Japan) using spatially resolved spectroscopy allow the measurement of a quantitative tissue oxygenation value (3, 4). NIRS has been extensively tested in cerebral tissue and is well accepted to monitor cerebral oxygenation during general anesthesia (5, 6).

Recently, we reported on the close association between NIRS liver tissue oxygenation and central venous oxygen saturation (SvO_2) in critically ill children obtained by single point measurements (7). However, large interindividual differences between NIRS liver tissue oxygenation and SvO_2 single point assessments limits its clinical usefulness and continuous NIRS liver tissue oxygenation measurement has been suggested to be more useful to monitor global tissue oxygenation (7).

The aim of the present study was to compare the course of continuously recorded NIRS liver tissue oxygenation with global tissue oxygenation as measured by SvO_2, and with splanchnic oxygenation assessed by gastric tonometry (8, 9) in children undergoing major surgery.

Materials and Methods

With approval of the local Hospital Ethics Committee and informed parental consent, 20 children from birth up to 8 years of age scheduled for craniofacial surgery with expected major blood loss were studied. A standard anesthesia technique and identical patient positioning was used in all patients including general anesthesia using sevoflurane in nitrous oxide/oxygen, tracheal intubation and intermittent positive pressure ventilation with PEEP, continuous intravenous infusion of alfentanil and muscle paralysis with pancuronium. In all patients an arterial cannula and a central venous catheter were established for continuous invasive pressure monitoring and periodic blood sampling. Central venous catheters were placed with the tip in the upper right atrium, as confirmed by the intracardiac electrocardiogram from the catheter tip. In addition, body temperature was measured by a rectal probe and a urinary catheter was inserted for control of urine output.

Near infrared spectroscopic measurements

On each patient a NIRO 300 NIRS probe consisting of a near-infrared light emitter optode and a receiver optode, was placed below the right costal margin on the skin overlying the palpable liver. Emitter and receiver optode were inserted into a soft black probe receptacle (Probe Holder S: A 7928; Hamamatsu Phototonics) to provide an interoptode distance of 4 cm and to shield the optodes from ambient light (10). The emitter optode (Ø 8 mm) provides laser light of 775, 810, 847 and 919 nm wavelength and the detector optode (Ø 18 mm) placed 4 cm from the emitter probe, comprises three spatially separated detectors (three-segment photodiode chip) within one detector probe. Multi-distance measurement of light attenuation by the three-segment photodiode chip allows the calculation of a quantitative tissue oxygenation index [TOI (%)] representing the ratio of oxygenated hemoglobin (HbO_2) to total hemoglobin [HbO_2 + HHb)]. The penetration depth of the NIR light is close to the interoptode distance (4 cm)

and therefore in children most of the region investigated is liver tissue.

The receptacle was secured to the skin by adhesive tapes and bandages wrapped around the patient for stable close sensor–skin contact. The NIRS emitter and receiver optodes were connected to a precalibrated measuring unit of the NIRO 300 spectrometer. Proper signal quality was checked by means of the initialization procedure. NIRS measurements were performed at a sample rate of 2 s. TOI_{Liver} was calculated as the mean value of 30 measurements (1 min) during the period of blood sampling from the arterial and central venous catheter.

Tonometric measurements

After tracheal intubation, an 8-F tonometry catheter (Tonometrics™ Catheter; Datex Ohmeda Division, Helsinki, Finland) was orally inserted into the stomach. Correct gastric placement was confirmed by auscultation and aspiration of gastric fluid. Gastric fluid was allowed to drain through the feeding channel of the tonometer catheter into a reservoir bag. The tonometer sampling line was connected to an automated air tonometer (TONOCAP®; Datex-Engstrom, Tonometrics Division, Helsinki, Finland). The automated air tonometer fills the tonometer balloon with air (11). Following an equilibration period, the air is automatically sampled and analyzed for CO_2 concentration by means of an infrared sensor. In order to avoid depletion of gastric luminal CO_2 and to reduce equilibration times, the aspirated gas mixture is refilled into the sampling balloon (11). Measurements were performed at intervals of 10 min and intramucosal pH (pHi) was calculated by the TONOCAP® from gastric luminal PCO_2, arterial PCO_2 and arterial pH (12).

Arterial and venous blood was sampled every hour starting prior to surgery or if required at shorter intervals according to the patients clinical conditions. Blood samples were analysed for arterial pH, PCO_2, BE, PO_2, SO_2, lactate concentration, hemoglobin concentration (cHb) and central venous oxygen saturation by means of a blood gas analyzer with oximeter (ABL 700; Radiometer Medical A/S, Copenhagen, Denmark). Mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP), and body temperature (BT) were noted from the anesthesia monitor (A/S 5, Datex Ohmeda, Helsinki, Finland). Patient characteristics (age, weight, gender) and intraoperative data (duration of surgery, estimated blood loss) were taken from the patient anesthesia chart.

Data analysis

Patients' characteristics and measured data are presented as median (range). Pearson's correlation coefficients and *P*-values from linear regression analysis were calculated between TOI_{Liver} and SvO_2, gastric pHi and the following covariables: mean arterial pressure, heart rate, central venous pressure, body temperature, arterial pH, PCO_2, BE, lactate concentration, PO_2, SO_2 and hemoglobin concentration.

To compare the time course of variables and to overcome interindividual and age-related differences among patients, proportional changes (Δ%) between TOI values ($\Delta\%TOI_{Liver}$) and corresponding proportional changes of gastric pHi, SvO_2 and the above mentioned co-variables were calculated between two subsequent measurements. Sensitivity and specificity of the $\Delta\%TOI_{Liver}$ to indicate decreasing SvO_2 or gastric pHi values were calculated for proportional levels of ≥0, ≥5 and ≥10% ($\Delta\%TOI_{Liver}$).

A multivariable regression model with TOI_{Liver} as the dependent variable and the variables listed above as independent variables was calculated to elucidate which variables retained a significant association with TOI_{Liver}. Statistical calculations were performed using StatView for Windows (Version 5.0.1; SAS Institute Corp., Cary, NC, USA). A *P*-value of 0.01 was considered to be statistically significant for all tests.

Results

Twenty children aged 1.92 years (0.79–8.27 years) were studied. Intraoperative blood loss ranged from 36 to 282 $ml \cdot kg^{-1}$ (115 $ml \cdot kg^{-1}$). One hundred and twenty-eight blood samples were drawn [seven samples per patient (3–9)]. Patient characteristics and surgical data are shown in Table 1.

The TOI_{Liver} values ($n = 20$) before surgery ranged from 47.4 to 77.4% (66.0%), gastric pHi from 7.32 to 7.60 (7.42) and SvO_2 from 56 to 86% (80%). TOI_{Liver} values prior to surgery and blood loss demonstrated a well correlation with SvO_2

Table 1
Demographic and intraoperative data (n = 20 patients; 128 blood samples)

	Median (range)
Age (years)	1.92 (0.79–8.27)
Body weight (kg)	12.05 (8.1–23.0)
Gender (male/female)	N = 12/8
Duration of surgery (h)	4.7 (2.2–8.0)
Blood samples (n)	7 (4–10)
Interval time (min)	60 (20–71)
Blood loss (ml)	1062 (400–5700)
Blood loss/weight ($ml \cdot kg^{-1}$)	110 (36–282)

($r = 0.727$; $P < 0.001$), and gastric pHi ($r = 0.528$: $P < 0.02$).

Overall values for TOI_{Liver} ranged from 41.5 to 77.4% (61.5%), for gastric pHi from 7.13 to 7.60 (7.38) and for SvO_2 from 51 to 86% (75%). Measured values are summarized in Table 2. TOI_{Liver} values demonstrated significant association but moderate correlation with SvO_2 ($r = 0.594$; $P < 0.0001$), gastric pHi ($r = 0.502$: $P < 0.0001$) (Figure 1; Table 2). Intra-individual TOI_{Liver} values demonstrated a closer correlation with SvO_2 ($r = 0.680$ to 0.976; median 0.798) (Figure 2) but a considerably varying correlation to gastric pH_i ($r = 0.055$ to 0.972; median 0.458). Correlation between SvO_2 and gastric pHi was weak ($r = 0.472$: $P < 0.0001$). In the multivariable regression model SvO_2 alone explained 35.3% of the observed variance of TOI_{Liver} ($P < 0.0001$). No further variable retained a significant association with TOI_{Liver}.

For 108 samples, proportional changes between two measurements were calculated. Comparison between $\Delta\%TOI_{Liver}$ and proportional changes of other variables revealed significant association and improved correlation for $\Delta\%SvO_2$ ($r = 0.664$; $P < 0.0001$) but not for $\Delta\%$pHi ($r = 0.493$; $P < 0.0001$) (Figure 3). In the multivariable regressions analysis, variance of $\Delta\%TOI_{Liver}$ was explained 66.4% by $\Delta\%SvO_2$ ($P < 0.0001$). Significant association with $\Delta\%TOI_{Liver}$ was demonstrated for $\Delta\%SaO_2$ ($P = 0.0023$) and ΔCVP ($P = 0.0027$). Adding these parameters only slightly improved the explained portion of variance to 46.4%. Sensitivity and specificity of $\Delta\%TOI_{Liver}$ to detect decreasing SvO_2 values were 76.4 and 73.4%, and 67.4 and 62.7% for gastric pHi respectively. Sensitivity and specificity were higher if only larger proportional changes of $\Delta\%TOI_{Liver}$ between two measurements were considered (Table 3; Figure 3).

Discussion

In this study we investigated transcutaneously measured NIRS liver tissue oxygenation with an optode placed over the palpable liver as a noninvasive tool to continuously monitor global and splanchnic tissue oxygenation in children undergoing major surgery.

The main finding was that the time course of transcutaneously measured NIRS liver tissue oxygenation using the NIRO 300 near-infrared spectrometer provided a better trend monitor of global oxygenation state measured by SvO_2 than of intestinal perfusion as indicated by gastric tonometry.

Measurement of NIRS liver tissue oxygenation represents a modern approach to assess hepatosplanchnic oxygenation in animal studies (13–18). NIRS

Parameters (units)	*Median (range)*	*Absolute values (r/P) (n = 128)*	*Δ% values (r/P) (n = 108)*
TOI_{Liver} (%)	61.5 (41.5–77.4)	–	–
MAP (mmHg)	56 (29.0–74.0)	0.356/<0.0001	0.426/<0.0001
HR ($b \cdot min^{-1}$)	110.0 (82.0–152.0)	0.275/0.0017	0.162/0.0948
CVP (mmHg)	10.0 (3.0–22.0)	0.121/0.1753	0.151/0.1439
Body temperature (°C)	36.4 (34.5–38.4)	0.129/0.1598	0.228/0.0175
pH_a	7.38 (7.19–7.49)	0.366/0.0001	0.144/0.1369
$PaCO_2$ (kPa)	4.74 (4.04–8.7)	0.049/0.5817	0.099/0.3063
BE_a ($mmol \cdot l^{-1}$)	−3.2 (−12.4–3.8)	0.347/<0.0001	0.050/0.5657
PaO_2 (kPa)	23.3 (10.8–68.0)	0.064/0.4707	0.003/0.9762
SaO_2 (%)	100.0 (97.9–100)	0.104/0.2406	0.184/0.0566
SvO_2 (%)	74.0 (51–86)	0.594/<0.0001	0.664/<0.0001
cHb ($g \cdot l^{-1}$)	87.5 (47.0–140.0)	0.209/0.0179	0.303/0.0014
Lactate concentration ($mmol \cdot l^{-1}$)	1.9 (1.0–4.0)	0.099/0.2741	0.060/0.5405
pHi	7.37 (7.13–7.60)	0.502/<0.0001	0.493/<0.0001

Table 2
Measured parameters presented as median (range). Pearson correlation coefficient and P-values are provided from simple regression analysis for the comparison of absolute TOI_{Liver} values and the other measured parameters and for procentual changes (Δ%) as well (n = 20 patients)

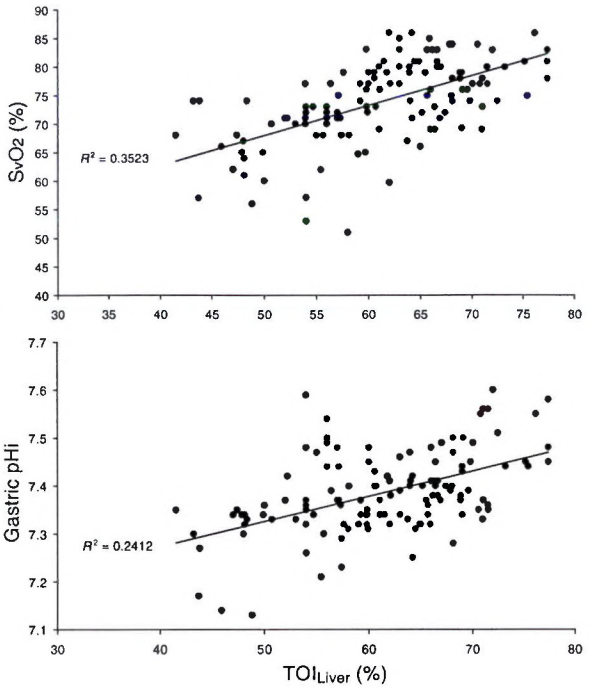


Figure 1
Linear regression plot for the comparison of NIRS liver tissue oxygenation index (TOI_{Liver}) with central venous oxygen saturation (SvO_2; top) and gastric intramucosal pH (pHi; bottom) ($n = 20$ patients, 128 blood samples) ($r = 0.72$; $P < 0.0001$).

liver tissue oxygenation directly measured on the liver surface in animal studies has been reported to correlate well with cardiac output and oxygen delivery (DO_2) during hemorrhagic shock (13–15) hepatic venous oxygenation during graded liver hypoxia (16, 17). Whereas transcutaneous NIRS measurement of tissue oxygenation is validated for the brain, only limited data are available about its transcutaneous application for the liver (7, 18). The rational to use transcutaneous NIRS for hepatic oxygenation monitoring in children was that the liver represents a homogeneous and easily accessible organ for transcutaneous NIRS, being palpable in neonates, infants and children below the costal arch. Our clinical data obtained in children demonstrate that transcutaneously measured NIRS liver tissue oxygenation with an optode placed over the palpable liver correlated moderately with central venous oxygen saturation, as previously reported for single-point measurements in critically ill children (Figure 1) (7).

Continuous measurement of TOI_{Liver} in this study allowed the comparison of proportional changes of

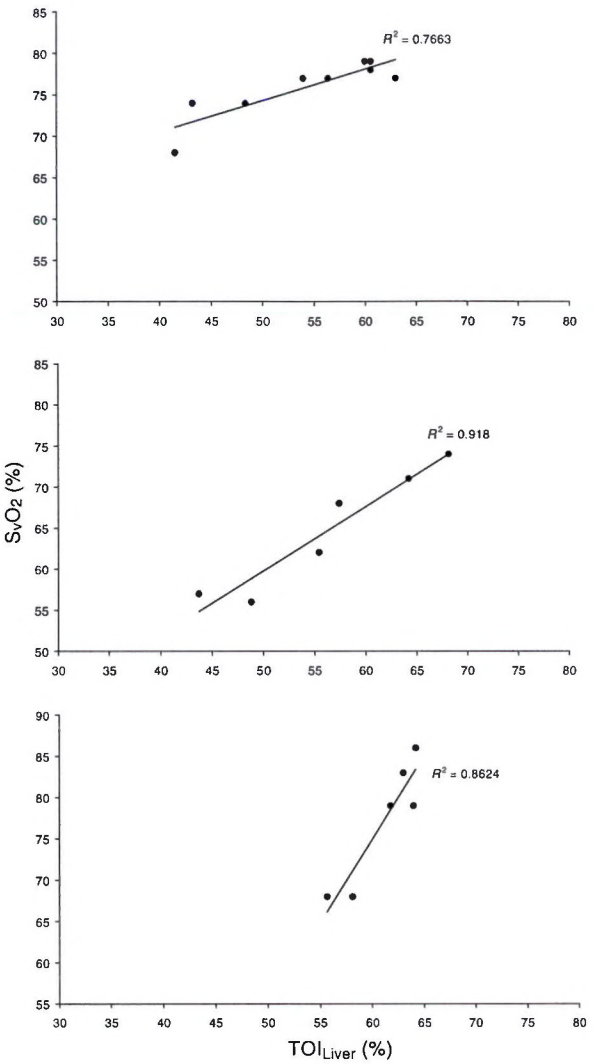


Figure 2
Individual linear regression plots for the comparison of NIRS liver tissue oxygenation index (TOI_{Liver}) with central venous oxygen saturation SvO_2 obtained from three different patients.

parameters between measurements which demonstrated only a moderately improved correlation between $\Delta\%TOI_{Liver}$ and $\Delta\%SvO_2$ values (Table 2). This disappointing finding can be explained by considerable interindividual differences in the steepness of the linear relationship between TOI_{Liver} and SvO_2 (Figure 2). However, the high intra-individual correlation coefficients between TOI_{Liver} and SvO_2 implicate that TOI_{Liver} values provides rather an intra-individual trend monitor than an absolute measure for SvO_2 or $\Delta\%SvO_2$.

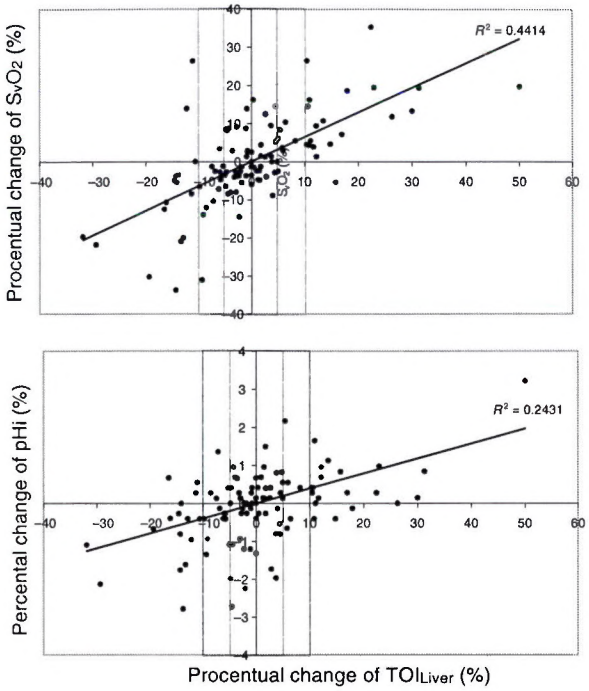


Figure 3
Comparison of proportional changes in NIRS liver tissue oxygenation (TOI_{Liver}) with proportional changes in central venous oxygen saturation (SvO_2) and gastric intramucosal pH (gastric pHi) (n = 20 patients, 108 Δ% values). Level of proportional changes of 5 and 10%) for TOI_{Liver} are indicated by vertical dotted lines.

Table 3
Sensitivity and specificity of NIRS liver tissue oxygenation (Δ% TOI_{Liver}) to indicate deterioration of central venous oxygen saturation (SvO_2) and gastric pHi (pHi) at different levels of proportional changes of Δ% TOI_{Liver} (n = number of intervals)

Level of proportional change of Δ% TOI_{Liver}	*Sensitivity (%)*		*Specificity (%)*	
	SvO_2	*pHi*	*SvO_2*	*pHi*
>0% (n = 108)	76.4	67.3	73.6	62.7
≥5% (n = 77)	89.2	78.6	75.0	72.4
≥10% (n = 48)	95.0	81.3	85.7	81.0

Based on our findings, TOI_{Liver} represented a better trend monitor of global tissue oxygenation as measured by SvO_2 than a trend monitor of splanchnic oxygenation as measured by gastric tonometry. Although splanchnic perfusion falls and rises with changes in cardiac output, this is likely to be caused by the fact that gastric pHi represents a metabolic monitor with delayed answer to intestinal hypoperfusion. Similarly, recovery of pHi is delayed compared with recovery of SvO_2. In contrast, SvO_2 represents on-line values of the balance of global oxygen delivery and oxygen consumption. As NIRS measures oxygenation state in the underlying tissue and reflects a mixture of intravascular oxygenated/deoxygenated hemoglobin of venous, arterial and capillary origin in a proportion of approximately 75 : 20 : 5 (17, 18), it is not surprising that variance of TOI_{Liver} and Δ%TOI_{Liver} was explained by 59.4 and 66.4% respectively by central venous oxygen saturation.

Variance of TOI_{Liver}–SvO_2 differences between patients (Figures 1 and 2) can be explained by interindividual differences in penetration depth and absorption properties of the near-infrared light. The falsely positive and falsely negative trends of TOI_{Liver} to indicate a true fall in SvO_2 (Figure 3), implies that intra-individual TOI_{Liver}–SvO_2 differences also occur during the measuring period. These are suggested to be the result of the following factors: (a) lack of autoregulation of hepatic perfusion leading to pressure-dependent contribution of hepatic arterial blood and portal venous blood influx into the liver, this is supported by an association of MAP and CVP with TOI_{Liver}; (b) alteration of liver oxygen consumption because of temperature changes, anesthetic medications, and metabolic factors; (c) changing absorption properties because of shift of fluid, colloids and blood products into the underlying tissue; (d) distension of the gut by the use of nitrous oxide leading to reduced NIR light penetration depth and probe displacements at the skin. The fact that correlation between TOI_{Liver} and SvO_2 was better prior to surgery and blood loss, implicates that hemodynamic changes, infusion of blood products and fluid shift have important impact on TOI_{Liver} measurements, either because of alteration of venous blood proportion or because of changes in near-infrared light penetration and absorption. Finally, small changes in probe positioning on the skin surface can lead to significant different TOI reading as recently reported for cerebral oxygenation measurements (3, 19).

Based on our study results, transcutaneous measurement of NIRS liver tissue oxygenation in children can reflect changes in global tissue oxygenation, as measured by SvO_2, in an noninvasive simple manner. This may be potentially useful for monitoring improvement or deterioration of tissue oxygenation during circulatory therapy or early detection of

hemodynamic deterioration. However, the sensitivity and specificity of TOI_{Liver} to indicate deterioration of SvO_2 implies that only larger disturbances can be detected and thus transcutaneous liver NIRS cannot be used for precise SvO_2 monitoring in surgical or critically ill children for clinical purposes. It provides useful trend information rather than absolute values and in a clinical situation such as this, it might be helpful to guide therapy (20).

Further work is needed to correlate changes in $_{Liver}TOI$ with other variables, including continuous direct measurement of cardiac output, fiberoptic intravasal SvO_2 and splanchnic/hepatic blood flow under standardized conditions. As there are several local factors affecting transcutaneous NIRS measurement of liver tissue oxygenation as mentioned above, other sites of NIRS measurement should be also included for the correlation of TOI vs SvO_2, such as the brain or muscle. These sites may be less affected by blood pressure and changing absorption characteristics (21).

In conclusion, TOI_{Liver} provided a better trend monitor of central venous oxygenation than gastric intramucosal pH. Because of its limited sensitivity and specificity to indicate deterioration of SvO_2, liver tissue oxygenation measured by transcutaneous NIRS does not provide additional practical information for clinical management. Further research is needed to explore and define the role of NIRS as a noninvasive monitor of hemodynamic function.

Acknowledgements

The study was supported by a Research Grant of the Swiss National Foundation Grant No. 32-56713.99 and by a Research Grant of the Hartmann–Mueller Foundation, Zurich, Switzerland.

References

1 Owen-Reece H, Smith M, Elwell CE *et al.* Near infrared spectroscopy. *Br J Anaesth* 1999; **82:** 418–426.
2 Wahr JA, Tremper KK, Samra S *et al.* Near-infrared spectroscopy: theory and applications. *J Cardiothoracic Vasc Anesth* 1996; **10:** 406–418.
3 Matcher SJ, Kirkpatrick P, Nahid K *et al.* Absolute quantification methods in tissue near infrared spectroscopy. *Proc SPIE* 1995; **2389:** 486–495.
4 Suzuki S, Takasaki S, Ozaki T *et al.* A tissue oxygenation monitor using NIR spatially resolved spectroscopy. *Proc SPIE* 1999; **3597:** 582–592.
5 Roberts KW, Crnkowic AP, Linneman LJ. Near infrared spectroscopy detects critical cerebral hypoxia during carotid endarterectomy in awake patients. *Anesthesiology* 1998; **89:** A934.
6 Higami T, Kozawa S, Asada T *et al.* Retrograde cerebral perfusion versus selective cerebral perfusion as evaluated by cerebral oxygen saturation during aortic arch reconstruction. *Ann Thor Surg* 1999; **67:** 1091–1096.
7 Schulz G, Weiss M, Bauersfeld U *et al.* Liver tissue oxygenation as measured by near-infrared spectroscopy in the critically ill child in correlation with central venous oxygen saturation. *Intensive Care Med* 2002; **28:** 184–189.
8 Bruining H, Ince C, Hendriks J *et al.* Tonometry to assess the adequacy of splanchnic oxygenation in the critically ill patient. *Intensive Care Med* 1994; **20:** 452–456.
9 Kolkmann JJ, Otte JA, Groeneveld AB. Gastrointestinal luminal pCO_2 tonometry: an update on physiology, methodology and clinical applications. *Br J Anaesth* 2000; **84:** 74–86.
10 Dullenkopf A, Frey B, Baenziger O *et al.* Measurement of cerebral oxygenation state in anaesthetized children using the INVOS 5100 cerebral oximeter. *Paed Anaesth* 2003; **13:** 384–391.
11 Bennett-Guerrero E, Panah MH, Bodian CA *et al.* Automated detection of gastric luminal partial pressure of carbon dioxide during cardiovascular surgery using the Tonocap. *Anesthesiology* 2000; **9:** 38–45.
12 Fiddian-Green RG, Pittenger G, Whitehouse WM. Back-diffusion of CO_2 and its influence on the intramural pH in gastric mucosa. *J Surg Res* 1982; **33:** 39–48.
13 Beilman GJ, Groehler KE, Lazaron V *et al.* Near-infrared spectroscopy measurement of regional tissue oxyhemoglobin saturation during hemorrhagic shock. *Shock* 1999; **12:** 196–200.
14 Rhee P, Langdale L, Mock C *et al.* Near-infrared spectroscopy: continuous measurement of cytochrome oxidation during hemorrhagic shock. *Crit Care Med* 1997; **25:** 166–170.
15 Yang W, Hafez T, Thompson CS *et al.* Direct measurement of hepatic tissue hypoxia by using a novel $tcpO_2/pCO_2$ monitoring system in comparison with near-infrared spectroscopy. *Liver Int* 2003; **23:** 163–170.
16 El-Desoky AEH, Jiao LR, Lavlik R *et al.* Measurement of hepatic tissue hypoxia using near infrared spectroscopy: comparison with hepatic vein oxygen partial pressure. *Eur Surg Res* 2000; **32:** 207–214.
17 El-Desoky AEH, Seifalian AM, Davidson BR. Effect of graded hypoxia on hepatic tissue oxygenation measured by near infrared spectroscopy. *J Hepatol* 1999; **31:** 71–76.
18 Teller J, Schwendener K, Wolf M *et al.* Continuous monitoring of liver oxygenation with near infrared spectroscopy during naso-gastric tube feeding in neonates. *Schweiz Med Wochenschr* 2000; **130:** 652–656.
19 Boushel R, Langberg H, Olesen J *et al.* Monitoring tissue oxygen availability with near infrared spectroscopy (NIRS) in health and disease. *Scand J Med Sci Sports* 2001; **11:** 213–222.
20 Franceschini MA, Boas DA, Zourabian A *et al.* Near-infrared spiroximetry: noninvasive measurements of venous saturation in piglets and human subjects. *J Appl Physiol* 2002; **92:** 372–384.
21 Kishi K, Kawaguchi M, Yoshitani K *et al.* Influence of patient variables and sensor location on regional cerebral oxygen saturation measured by INVOS 4100 near-infrared spectrophotometer. *J Neurosurg Anesthesiol* 2003; **4:** 302–306.

Accepted 6 February 2004