Propofol in Exhaled Alveolar Gas and in Plasma During Clinical Relevant Steady States in Comparison to the BIS

Astrid E. Berggreen, M.D., Dammon Ziaian, M.Sc., Andreas Hengstenberg, Ph.D., Lutz Dümbgen, Ph.D., Stefan Zimmermann, Ph.D., Hartmut Gehring, M.D., Martin Grossherr, M.D.

University of Luebeck, Luebeck, Germany

Background

During anesthesia steady states are established to realize a constant depth of anesthesia and a hemodynamic stability at a similar surgical stimulus. In clinical practice depth of anesthesia monitoring with the bispectral index (BIS), hemodynamic monitoring or a target controlled infusion system (TCI) are being used to realize a constant plasma concentration of propofol. An alternative method is to measure propofol in exhaled alveolar gas with the ion molecule reaction mass-spectrometer (IMR-MS) to estimate the plasma concentration of propofol [1]. Hornuss et al. could demonstrate that the expiratory gas concentration has a close correlation to the propofol effect in the brain measured with the BIS [2].

This study compared the accuracy of steady states for the propofol concentration in plasma and in the exhaled alveolar gas with the steady state measured with the BIS.

Methods

After approval from the regional ethic committee in charge and informed consent we included 18 patients in this investigation. After induction of anesthesia with remifentanil and propofol with a TCI system we intended to maintain a target plasma concentration of propofol of 2 µg/ml and 4 µg/ml preoperatively as well as 2 µg/ml postoperatively. After 10 and 15 minutes of each steady state we took venous blood samples to analyze the plasma concentration of propofol. Besides the standard anesthesia monitoring we recorded continuously BIS and propofol in expiratory gas measured with the IMR-MS. Additionally to the descriptive analysis with mean value and standard deviation we characterize the steady states with the Steady State Phase Accuracy (SSPA), which is an analysis of variance described by Ziaian et al. [2]. It provides a characteristic number for the compliance of steady states in percent, whereby 100% is the maximum.

Results

With all methods the steady states could be observed. The steady states of 2 µg/ml could be distinguished from the one of 4µg/ml with the IMR-MS. The steady states measured with the BIS, the IMR-MS and with the plasma concentration are comparable. The SSPA-value indicates a smaller variance of the steady states measured with the IMR-MS and the Propofol concentration in the plasma compared with the BIS.

Conclusion

For the monitoring of a constant application of propofol during steady states the measurement of propofol in the exhaled alveolar gas is comparable with the propofol concentration in the plasma. With the BIS the steady states could be detected as well, but the variability was higher compared with the other methods.

Literatur


<table>
<thead>
<tr>
<th>TCI Target (µg/ml)</th>
<th>Propofol Plasma (µg/ml)</th>
<th>IMR-MS (ppb)</th>
<th>BIS mean±SD</th>
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</thead>
<tbody>
<tr>
<td>2 ± 0</td>
<td>2.59 ± 0.47</td>
<td>7.09 ± 1.69</td>
<td>38.69 ± 9.77</td>
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<tr>
<td>4 ± 0</td>
<td>5.86 ± 1.14</td>
<td>15.03 ± 3.59</td>
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<td>2 ± 0</td>
<td>2.64 ± 0.61</td>
<td>10.06 ± 3.07</td>
<td>40.35 ± 7.67</td>
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<td>SSPA</td>
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<tr>
<td></td>
<td>98.20 ± 2.08 %</td>
<td>98.26 ± 1.04 %</td>
<td>95.84 ± 4.49 %</td>
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</tbody>
</table>
Propofol in Exhaled Alveolar Gas and in Plasma Compared With the Bispectral Index During Recovery From Anesthesia

Astrid E. Berggreen, M.D., Dammon Ziaian, M.Sc., Andreas Hengstenberg, Ph.D., Sebastian Brandt, M.D., Stefan Zimmermann, Ph.D., Martin Grossherr, M.D., Hartmut Gehring, M.D.

University of Luebeck, Luebeck, Germany

Background

Bispectral index (BIS) as indicator of the depth of anesthesia and the use of the target controlled infusion system (TCI) to realize a constant plasma and effect-site concentration of propofol has been established in clinical routine in Europe during the last years.

Currently a continuous monitoring method for propofol in plasma is not available. The awakening propofol concentration in plasma has only been identified in the context of pharmacokinetic and -dynamic studies by analyzing blood samples. Several studies demonstrated, that there is a major inter- and intraindividual bias for the correlation of these plasma values and the BIS. An alternative method to assess the propofol concentration in plasma is the detection of propofol in the exhaled alveolar gas with the ion molecule reaction mass-spectrometer (IMR-MS). Hornuss et al as well as other authors like Perl et al observed a correlation of this method of measurement with the propofol concentration in plasma and with the BIS [1, 2].

In this investigation we compare different monitoring methods during the awakening phase of an anesthesia with propofol.

Methods

After approval from the regional ethic committee in charge and informed consent we investigated 16 patients pre- and postoperative with a standardized course of anesthesia. The induction and maintenance of anesthesia was achieved with remifentanil and propofol with a TCI System. After the end of the surgery a steady state with a target plasma concentration of 2 µg/ml of propofol was held over 15 minutes before remifentanil and propofol infusion was stopped. At the end of anesthesia the infusion line was changed to prevent an accidental bolus application of propofol. Then the patient was called with his name and was touched slightly at the shoulder every 30 seconds. 15 to 30 seconds after the first time of eye opening the airway device was removed.

Besides the routine monitoring during anesthesia we recorded continuously the BIS and propofol in expiratory gas with the IMR-MS. At the time of stopping the propofol infusion, 2 minutes later and at time of extubation venous blood samples were taken to determine the propofol concentration in plasma.

Results

The patients were comparable in regard to age, gender and weight. The mean time of anesthesia was 173,38 min ± 36,59 min.

At the end of anesthesia the target TCI plasma propofol concentration was 2 µg/ml. Therefore only a small difference of the propofol concentration in plasma between terminating the propofol infusion and the time of extubation could be observed. This result is similar to the measured propofol concentration in expired gas. The bispectral index at time of eye opening is only slightly above the recommended normal range for anesthesia. The propofol plasma and effect site concentration calculated with the TCI are lower as the measured plasma concentration at time of extubation.

Conclusion

In contrast to the effect for the patient especially for his consciousness the transition from anesthesia to eye opening (awakening) measured with different methods is small, if you regard the plasma and the breath concentration of propofol as well as the BIS.

Literatur


Figure 1

<table>
<thead>
<tr>
<th>time of measurement</th>
<th>TCI cp (µg/ml) mean±SD</th>
<th>TCI ce (µg/ml) mean±SD</th>
<th>Plasma (µg/ml) mean±SD</th>
<th>BIS mean±SD</th>
<th>IMR-MS (ppb) mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>end of anesthesia</td>
<td>1,96 ± 0,14</td>
<td>1,97 ± 0,11</td>
<td>2,53 ± 0,49</td>
<td>40,54 ± 0,91</td>
<td>9,94 ± 2,98</td>
</tr>
<tr>
<td>2 min after the end of anesthesia</td>
<td>1,56 ± 0,14</td>
<td>1,66 ± 0,15</td>
<td>2,10 ± 0,41</td>
<td>45,25 ± 8,42</td>
<td>9,71 ± 3,04</td>
</tr>
<tr>
<td>extubation</td>
<td>1,10 ± 0,15</td>
<td>1,13 ± 0,17</td>
<td>1,67 ± 0,43</td>
<td>66,58 ± 6,43</td>
<td>7,76 ± 2,09</td>
</tr>
</tbody>
</table>

Tab 1: SD=standard deviation; TCI cp=plasma concentration of propofol calculated by the TCI; TCI ce =effect-site concentration of propofol calculated by the TCI

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Breath Gas Propofol Concentration Measurement - The Next Generation for Anesthesia Monitoring

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University Medical Center Schleswig-Holstein, Luebeck, Germany

**Introduction:**

Breath gas measurement of propofol concentration has been introduced since 2003 [1]. The clinical implementation during anesthesia with an applicable monitoring on one site as well as the follow-up on a course from induction of anesthesia to recovery of awareness on the other site is focused in this study. Main targets were: 1. the test of a monitoring sensor modul compared to a reference system in breath gas and 2. the implementation in a standardized anesthesia profile.

**Method:**

After ethics committee approval and with patient informed consent we investigated 16 patients with an ASA status 1 and 2 undergoing endourological procedures. Propofol concentration in breath gas were monitored continuously with two methods: 1. with Ion Molecule Reaction - Mass Spectrometry (IMR-MS) as the reference and 2. with an electrochemical sensor device (Propofol Sensor Modul - PSM) [based on 2] as the test system. Target controlled infusion (TCI; Infusion Workstation Orchestra Base Primera" with two Orchestra DPS Visio" infusion pumps; Fresenius Vial, Infusion Technology, Fresenius Kabi) serves as application modul (Marsh model for propofol). With the second infusion pump a target level of 5 ng/ml remifentanil in plasma was established for the measurement periods. After introduction of anesthesia (time points 0, 1, and 2) with a target plasma propofol concentration in the range of 5 to 8 ug/ml we select two steady states of propofol (2 ug/ml and 4 ug/ml plasma levels) preoperatively and a second 2 ug/ml steady state postoperatively - each represented by two time points in table 1. After termination of the propofol and remifentanil infusion we follow-up the effects at two more time points (2 minutes after the end of propofol and remifentanil infusion and when patient is awake). Plasma levels of propofol were measured by high performance liquid chromatography (HPLC) [3].

**Results:**

Results of the implemented 10 time points are presented in Tab. 1. Measurements of breath gas concentrations in parallel (test and reference device) was successful in each patient and within the selected schedule. The bolus effect of the introduction period established in the anesthesia profile is not clearly represented due to introduction of an airway device. PSM tends to overestimate the values of IMR-MS, an effect which is to discussed.

**Conclusion:**

Both methods of propofol breath gas monitoring allow the assessment of propofol plasma levels at the steady states as well as of the time course after termination of propofol application.

**References:**


Generation Change in Hemoximetry and the Impact on Methemoglobin and Carboxyhemoglobin Measurements

Hartmut Gehring, M.D., Ph.D., Alexander Opp, M.Eng., Sebastian Brandt, M.D.
University Medical Center Schleswig-Holstein, Lubeck, Germany

Introduction:
Hemoximetry is the reference behind testing and calibration of pulse oximeters. Currently there is a change from the first hemoximeter generation (OSM 3 and IL 682) with a low number of wavelengths (100) of wavelengths (ABL80 FLEX CO-OX). Further pulse oximeters (PO) are in the market now, which display an equivalent value for methemoglobin (MetHb) and carboxyhemoglobin (COHb). This might have an impact on clinical decisions, because rapid detection of dyshemoglobins (e.g. methemoglobin; MetHb, carboxyhemoglobin; COHb) is essential in anesthesia, emergency medicine and critical care.

While the production of OSM 3 stopped some years ago, since last year there are no services, consumables or spare parts available on the market anymore. In this study we test the precision of next generation CO oximeters compared to the reference system regarding MetHb and COHb.

Method:
With approval of the local ethics commission and written informed consent 10 volunteers were included into the study protocol. The volunteers participated in a rapid desaturation study for the calibration of sensors and pulse oximeters. Measurements were recorded simultaneously on two OSM3, two ABL80 FLEX CO-OX (both Radiometer Medical, Brønshøj, DK) and two IL682 (Instrumentation Laboratory, Bedford, MA, USA) CO-oximeter systems. Bland-Altman analyses were calculated using the mean of the two simultaneous measurements for COHb and MetHb. Linear regression lines were plotted if the slope significantly differed from zero.

Results:
We analyzed in total 250 time points for the OSM3 and the ABL80 FLEX CO-OX and 248 time points for the IL682 device.

Discussion:
The next generation CO oximeter detected COHb and MetHb with similar precision compared to the traditional systems OSM3 and IL 682. However because the physiologic range for both dyshemoglobins is lower than 1 to 2 % the impact of the systematic company-dependent differences on calibration of PO systems should be regarded with respect to accuracy.

1 ISO 80601-2-61 Particular requirements for basic safety and essential performance of pulse oximeter equipment

Table 1:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OSM3 vs. ABL80</th>
<th>OSM3 vs. IL682</th>
<th>IL682 vs. ABL80</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bias 95% LoA</td>
<td>Bias 95% LoA</td>
<td>Bias 95% LoA</td>
</tr>
<tr>
<td>COHb (%)</td>
<td>1.1 0.5 to 1.7</td>
<td>0.7 -0.4 to 1.7</td>
<td>0.4 -0.4 to 1.3</td>
</tr>
<tr>
<td>MetHb (%)</td>
<td>0.5 -0.1 to 1.1</td>
<td>0.5 0.0 to 1.1</td>
<td>-0.1 -0.5 to 0.4</td>
</tr>
</tbody>
</table>

Figure 1

Figure 2
**Propofol in the Exhaled Alveolar Gas As a Setpoint for Closed-loop Controlling**

Astrid E. Berggreen, M.D., Balamurugan Varadarajan, Ph.D., Katharina Beisenherz, Student, Hartmut Gehring, M.D., Martin Grossherr, M.D.
University of Luebeck, Luebeck, Germany

**Background**

Different methods are available to measure propofol concentration in exhaled alveolar gas in real time. This information may help in the assessment of anesthesia quality and underlay the current anesthetic monitoring with indices about plasma levels of propofol (1). Closed-loop techniques enable an automatic controlling of the anesthesia. Until this time in anesthesia data of the bispectral index (BIS) and the expiratory concentration of volatile anesthetics were introduced as setpoints for closed-loop techniques (2). In this study the question should be answered if the propofol concentration measured in the exhaled alveolar gas can serve as a setpoint for a closed loop controlling in anesthesia.

**Methods**

After approval from the regional department in charge we investigated 7 pigs in general anesthesia with propofol. The propofol concentration in the expiratory gas as the setpoint for the closed loop controller was continuously measured with the ion molecule reaction mass-spectrometer (IMR-MS) in ppb. A controller in the control loop regulated the infusion rate of propofol over the infusion pump Fresenius Base A. With this experimental design the question should be cleared if a defined target concentration of propofol in the exhaled alveolar gas as a setpoint in the closed-loop controller could be reached in a set time of 60 minutes. For additional monitoring and detection the propofol concentration in the expiratory gas and in the plasma was measured at 4 times (T1 to T4) discontinuously. T1 was at the beginning of the experiment, T2, T3 and T4 at the end of each interval, in which the targeted concentration of propofol in the expiratory gas as setpoint should be reached (figure 1). As information about the propofol side effect the BIS was also recorded continuously.

**Results**

The infusion rate of the infusion pump could be regulated with the controller, so that within 15min a 50% lower respectively 50% higher targeted concentration of propofol in expiratory gas measured with the IMR-MS could be reached as the setpoint and the steady state could be maintained until the next change of the setpoint (figure 1 and 2). The discontinuous measurements of propofol in the exhaled alveolar gas and in the plasma demonstrated a comparable progress. In parallel the BIS rose respectively declined in an adequate manner.

**Conclusion**

Propofol concentration in the expiratory gas can be used in an experimental setting as a setpoint for a closed loop controller. Anesthesia profile monitoring has a further dimension.

**Literature**


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**Figure 1**

![Figure 1](image1.png)

**Figure 2**

![Figure 2](image2.png)
Next Generation Hemoximeter Accuracy During Rapid Desaturation Procedures

Sebastian Brandt, M.D., Alexander Opp, M.Eng., Hartmut Gehring, M.D., Ph.D.
University Medical Center Schleswig-Holstein Campus Lubeck, Lubeck, Germany

Introduction:

Rapid desaturation procedures in volunteers following a standardized protocol[1] are an essential tool for the calibration of sensors and pulse oximeters. For the calibration process precise hemoximetry should be able to measure rapidly with a high number of blood samples on distinct oxygenation levels. In blood gas analyzer integrated CO-oximeter modules do not have the performance on this demand. So in tradition the first generation of hemoximeters (e.g. OSM3; Radiometer Medical, Brønshøj, DK, IL-682; Instrumentation Laboratory, Bedford, MA, USA) with a low number of wavelengths (100) of wavelengths (ABL-80 FLEX CO-Ox; Radiometer Medical, Brønshøj, DK). Furthermore next generation pulse oximeters provide in addition to the saturation (SpO2) an equivalent value for total hemoglobin (ctHb).

In this study we test the precision of first and next generation hemoximeters regarding SaO2 and ctHb.

Method:

With approval of the local ethics commission and written informed consent 10 volunteers were included into the study protocol. Hemoximetry measurements were recorded simultaneously on two OSM3, two ABL80 FLEX CO-Ox (both Radiometer Medical, Brønshøj, DK) and two IL682 (Instrumentum Laboratory, Bedford, MA, USA) CO-oximeter systems. Bland-Altman analyses were calculated using the mean of the two simultaneous measurements for SaO2 and ctHb. Linear regression lines were plotted if the slope significantly differed from zero.

Results:

We analyzed in total 250 timepoints for the OSM3 and the ABL80 FLEX CO-Ox and 248 timepoints for the IL682 device. The ABL80 FLEX CO-Ox demonstrated a tendency for higher SaO2 measurements with increased variance at lower SaO2 levels compared to OSM3 and IL682. Both new CO-oximeters tend to measure lower ctHb values than the OSM3. Bias and limits of agreement were highest for the IL682.

Discussion:

The systematic manufacturer dependent differences may have consequences for the calibration of sensors and pulse oximeters. So we suggest introducing the mean values of data recorded with doubled hemoximetry devices of different manufacturers for reducing systematic error with respect on this results.

[1] ISO 80601-2-61 Particular requirements for basic safety and essential performance of pulse oximeter equipment

Figure 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OSM3 vs. ABL80 FLEX CO-OX</th>
<th>OSM3 vs. IL682</th>
<th>IL682 vs. ABL80 FLEX CO-OX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bias</td>
<td>95% LoA</td>
<td>Bias</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>1.8</td>
<td>0.4 to 3.2</td>
<td>0.7</td>
</tr>
<tr>
<td>ctHb (g/l)</td>
<td>-1.0</td>
<td>-13 to 10</td>
<td>-4.0</td>
</tr>
</tbody>
</table>

Figure 2
Gas Phase Analysis of Lidocaine and Prilocaine by Solid Phase Micro Extraction (SPME) and Gas Chromatography - Mass Spectrometry (GC-MS): A Feasibility Study

Svetlana Stockmann, M.Eng., Oliver Elsner, M.D., Ellen Spies, Not Applicable, Leif Dibbelt, Ph.D., Hartmut Gehring, M.D., Ph.D.
University of Luebeck, Luebeck, Germany

Introduction:
Lidocaine and prilocaine are extremely low volatile local anesthetics of amide type. The aim of our work was to develop a fast and easy way of detecting lidocaine and prilocaine in plasma concentrations near the toxic ones (5 μg/ml for lidocaine and prilocaine, respectively).

Using SPME (solid phase micro extraction) as the analytical tool we investigated experimental conditions for detection of lidocaine and prilocaine in the gas phase over plasma. The analytes were detected by gas chromatography - mass spectrometry (GC-MS).

Methods:
1. SPME
Experiments were performed by incubating the SPME fibre in the gas phase over 6 ml aqueous solution or over 1 ml plasma in 10 ml glass vials.

We started with aqueous solutions (pH=7.4) containing 1 μg/ml of each drug and tested distinct SPME fibres (100 μm polydimethylsiloxane (PDMS) and 85 μm polycarbonate (PA)).

The plasma containing 1 μg/ml of lidocaine and prilocaine, respectively, was investigated using different extraction times without and with agitation.

Finally, we studied different extraction temperatures. The concentration of lidocaine and prilocaine in plasma samples was 1 μg/ml and 4 μg/ml.

2. GC-MS
The column used was a Factor Four 5 ms capillary column (30m x 0.25 mm I.D.).

The injector temperature was 270°C. The injection mode was splitless. The GC temperature was programmed for an initial hold of 2 min at 100°C, the temperature was increased at 20°C/min to 280°C. The final temperature of 280°C was kept for 3 min. The helium flow was 1.8 ml/min.

MS was performed in selected ion mode (m/z=86 for lidocaine and prilocaine, respectively).

Results:
100 μm PDMS and 85 μm PA fibres were compared. Because PA fibre showed higher peak areas for both lidocaine and prilocaine, we used PA fibre in the following experiments.

Different extraction times were tested with and without agitation (fig. 1 and 2). Both lidocaine and prilocaine showed higher peak areas with agitation. We applied an extraction time of 90 minutes for further experiments.

Figure 1

Figure 2

The effects of incubation temperature (36, 40, 60 and 70°C) were studied (tab. 1). Strong signals were detected using 70°C in all cases.

Table 1

Conclusion:
Using SPME-GC-MS we detected strong signals of lidocaine and prilocaine at incubation times of 30 min and longer and at 70°C incubation temperature, indicating the presence of both local anaesthetics in substantial concentrations in the gas phase over plasma samples at these conditions. At 36°C we found moderate signals for lidocaine, in the case of prilocaine signals were extremely low.

Figure 1
<table>
<thead>
<tr>
<th>Extraction temperature [°C]</th>
<th>Lidocaine Peak area</th>
<th>Prilocaine Peak area</th>
<th>Prilocaine Peak area</th>
<th>Prilocaine Peak area</th>
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<tbody>
<tr>
<td>36</td>
<td>1835</td>
<td>6311</td>
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</table>
Gas Phase Analysis of Bupivacaine and Ropivacaine by Solid Phase Micro Extraction (SPME) and Gas Chromatography - Mass Spectrometry (GS-MS) - A Feasibility Study

Oliver M. Elsner, M.D., Svetlana Stockmann, M.Eng., Ellen Spies, Not Applicable, Leif Dibbelt, Ph.D., Hartmut Gehring, M.D.,Ph. D.
University Medical Center Schleswig-Holstein, Luebeck, Germany

Introduction:
Bupivacaine and ropivacaine are extremely low volatile local anesthetics of amide type.

The aim of our work was to develop a fast and easy way of detecting bupivacaine and ropivacaine in plasma concentrations near the toxic ones (1.5 \( \mu \text{g/ml} \) for bupivacaine and 4 \( \mu \text{g/ml} \) for ropivacaine, respectively).

Using solid phase micro extraction (SPME) as the analytical tool we investigated experimental conditions for detection of bupivacaine and ropivacaine in the gas phase over plasma. The analytes were detected by gas chromatography – mass spectrometry (GC-MS).

Methods:

1. SPME

Experiments were performed by incubating the SPME fibre in the gas phase over 6 ml aqueous solution or over 1 ml plasma in 10 ml glass vials.

We started with aqueous solutions (pH=7.4) containing 1 \( \mu \text{g/ml} \) of each drug and tested distinct SPME fibres (100 \( \mu \text{m} \) polydimethylsiloxane (PDMS) and 85 \( \mu \text{m} \) polyacrylate (PA)).

The plasma containing 1 \( \mu \text{g/ml} \) of bupivacaine and ropivacaine, respectively, was investigated using different extraction times without and with agitation.

Finally, we studied different extraction temperatures. The concentration of bupivacaine and ropivacaine in plasma samples was 1 \( \mu \text{g/ml} \) and 4 \( \mu \text{g/ml} \).

2. GC-MS

The column used was a Factor Four 5 ms capillary column (30m x 0.25 mm I.D.).

The injector temperature was 270°C. The injection mode was splitless. The GC temperature was programmed for an initial hold of 5 min at 100°C, the temperature was increased at 20°C/min to 280°C. The final temperature of 280°C was kept for 5 min. The helium flow was 1.8 ml/min.

MS was performed in selected ion mode (m/z=140 for bupivacaine and m/z=126 for ropivacaine).

Results:

100 \( \mu \text{m} \) PDMS and 85 \( \mu \text{m} \) PA fibres were compared. Because PA fibre showed higher peak areas for both bupivacaine and ropivacaine, we used PA fibre in the following experiments.

Different extraction times were tested with and without agitation (fig. 1 and 2). Both bupivacaine and ropivacaine showed higher peak areas with agitation (bupivacaine: when extraction time was 70 min or longer). We applied an extraction time of 90 minutes for further experiments.

Figure 1

Figure 2

The effects of incubation temperature (36, 40, 60 and 70°C) were studied (tab. 1). Strong signals were detected using 70°C in all cases.

Table 1

Conclusion:

Using SPME-GC-MS we detected strong signals of bupivacaine and ropivacaine at incubation times of 30 min and longer and at 70°C incubation temperature, indicating the presence of both local anaesthetics in substantial concentrations in the gas phase over plasma samples at these conditions. At 36°C, however, signals were extremely low.
**Figure 2**

![Graph showing the relationship between peak area and extraction time for Ropivacaine with and without agitation.](image)

**Figure 3**

<table>
<thead>
<tr>
<th>Extraction temperature [°C]</th>
<th>Bupivacaine</th>
<th>Ropivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 µg/ml</td>
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<tr>
<td></td>
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</table>
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Standardized Finger Perfusion Control for Perfusion Index Assessment of Pulse Oximeter

Hartmut Gehring, M.D., Ph.D., Alexander Opp, M.Eng., Soehnke Boye, M.D.
Anesthesiology, University Medical Center Schleswig Holstein, Luebeck, Germany; Institute of Medical Engineering, University of Luebeck, Luebeck, Germany

Introduction: Pulse oximeter (PO) display a perfusion index (PI) calculated from the ratio of the pulsatile and the uniform components (AC/DC × 100), presented in arbitrary units (AU) [1]. The algorithms behind this calculation are not uniform for different PO manufacturers. In this context we have addressed two questions: 1. Can the perfusion at the finger site be reduced and increased in a standardized manner for testing PI? 2. In what range are the data presented by PO of several manufactures under these conditions?

Methods: With ethics committee approval and written informed consent 14 volunteers were included in the study protocol. Perfusion on both arms, hands and fingers were modified in parallel with application of cold and warm air. The sensors of two identical PO of three manufacturers were randomized and applied to index, middle and ring finger on each hand. The temperature (T in °C) differences [2] measured between finger (4 sensors) and body core (2 sensors) and the flux (AU) measured with a laser Doppler sensor (LD) served as reference. All data were recorded continuously. It was intended to establish steady state conditions approx. 10 minutes on four plateaus (P 1-P 4) by adjusting the finger temperature with cold or warm air to 35, 20, 15, and 35°Celsius.

Results: A standardized alteration of perfusion at the finger site with the establishment of steady state plateaus for both temperature and vasoconstriction was successful with 14 volunteers in this controlled randomized study. The perfusion at the finger site could be reduced to a PI lower than 0.3 (AU) which in some cases caused a loss of the PO signal reading.

Conclusion: Testing of pulse oximeter performance-standardized in [3] for the parameter "SpO2" - with respect to changes of perfusion due to cold induced vasoconstriction at the finger site can be established in a standardized and controlled manner.

References:

From Proceedings of the 2010 Annual Meeting of the American Society Anesthesiologists.

<table>
<thead>
<tr>
<th>Plateaus</th>
<th>P 1</th>
<th>P 2</th>
<th>P 3</th>
<th>P 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>References</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
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<tr>
<td>T core [[start_en]00B0;C]</td>
<td>36.4 ± 0.10</td>
<td>36.7 ± 0.04</td>
<td>36.8 ± 0.02</td>
<td>36.8 ± 0.02</td>
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<td>T finger [[start_en]00B0;C]</td>
<td>34.0 ± 0.65</td>
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<td>Flux LD [AU]</td>
<td>334 ± 43</td>
<td>112 ± 28</td>
<td>116 ± 24</td>
<td>345 ± 38</td>
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<td>PO PI</td>
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<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
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<td>PO-A [AU]</td>
<td>3.56 ± 1.01</td>
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<td>PO-B [AU]</td>
<td>4.12 ± 0.91</td>
<td>0.66 ± 0.12</td>
<td>0.46 ± 0.10</td>
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<td>PO-C [AU]</td>
<td>0.97 ± 0.20</td>
<td>0.29 ± 0.07</td>
<td>0.22 ± 0.05</td>
<td>0.86 ± 0.17</td>
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</table>
The Effect of Cardiac Output Variations on Exhaled Breath Propofol Concentrations

Balamurugan Varadarajan, M.Sc., Martin Grossherr, M.D., Joerg Meyer, Ph.D., Hartmut Gehring, M.D., Ph.D., Andreas Hengstenberg, Ph.D.
Department of Natural Sciences, University of Luebeck, Luebeck, SH, Germany; Research Unit, Draegerwerk AG & Co.KGaA, Luebeck, SH, Germany

Background: The influence of cardiac output (CO) on propofol kinetics and its inverse relation with plasma propofol concentrations (CpP) were described in previous studies [1, 2]. Recent studies have shown that after propofol infusion propofol can be detected in exhaled breath using ion molecule reaction mass spectrometry (IMR-MS)[3, 4]. The effect of CO on breath propofol concentrations (CpB) during propofol infusion has not been examined. The goal of this study was to monitor and track the changes in CpB when CO was increased by means of dobutamine infusion.

Methods: After the regional committee's approval 11 pigs were premedicated, anesthetized and intubated for measurement of propofol in breath. The IMR-MS system (Airmass Mass Spectrometry System, V & F Medical Development, Absam, Austria) was directly connected to the endotracheal tube with a T-piece. During anesthesia with a constant propofol infusion (9.6 mg/kg bodyweight * h) CO was determined by means of the thermodilution method (using a swan ganz catheter - Monitor: Sirecust 1260, Munich, Germany). When CpB reached steady state (maintained for at least 20 minutes after infusion start), dobutamine (50µg/kg/h) was infused for 10 minutes. CO was determined (each value was measured five times and the mean of final three values were recorded) and arterial blood samples were collected at 10 minutes before infusion start, 10 minutes after infusion start and 10 minutes after stop of dobutamine infusion.

Results: CO increased after the start of dobutamine infusion and decreased after the stop of infusion. The inverse effect was noted in CpP and CpB. The figure 1 shows time course of CO, CpP, CpB and the arrows indicate start and stop of infusion. Table 1 shows the changes observed in CO, CpP and CpB during dobutamine infusion.

Table 1

<table>
<thead>
<tr>
<th>Differences observed in CO, CpP and CpB induced by dobutamine infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference in CO L/min (mean ± SD)</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>After start of dobutamine infusion</td>
</tr>
<tr>
<td>After stop of dobutamine infusion</td>
</tr>
</tbody>
</table>

Conclusion: The CO induced changes in CpP (CO increment with 10 minutes dobutamine infusion) are reflected in breath propofol concentrations. Our work demonstrates that even small changes which occur in CpP induced by CO shifts may be followed in breath propofol concentrations.


From Proceedings of the 2010 Annual Meeting of the American Society Anesthesiologists.
Introduction: Liposuction with local tumescent anesthesia (LTA) is broadly established as cosmetic procedure. Lidocaine and prilocaine are the common local anesthetics in LTA technique combined with epinephrine and triamcinolone. One risk is the toxicity of high local anesthetic levels in blood and - especially with prilocaine - the generation of methemoglobin (MetHb). Since pulse oximeter (PO) technology is available for non invasive control of MetHb levels the following questions were focused: 1. How are the incidence and the quantity of MetHb levels higher than 8 % measured by PO? 2. How accurate are the SpMet data of the PO with respect to MetHb values of CO oximetry?

Methods: With ethics committee approval and written informed consent we followed 133 patients with liposuction procedure in a private hospital. The mixture of prilocaine 2 % (10 ml) and lidocaine 2 % (10 ml) combined with epinephrine 1:1.000 (0.7 ml) in NaCl 0.9 % (1029 ml) was infused as LTA into the subcutaneous fat. Patients were monitored with a Masimo Radical 7 pulse oximeter using a reusable fingerclip (SpMet in %) and basic blood samples were drawn via venous access prior to the the procedure. When SpMet values higher than 8 % were displayed a second venous sample was drawn and the patients were further monitored. In these patients the blood MetHb levels were controlled intra- and postoperatively - when a maximum was displayed - and the next morning. Blood probes were analyzed with a GEM 4000 (Instrumentation Laboratory) blood gas analyzer.

Results: In 34 patients (26 %) the PO displayed SpMet values higher than 8 %. The maximum value for MetHb was 18 % with the corresponding value for SpMet of 31 %. The PO overestimated the MetHb levels measured with a reference method (Figure 1) and (Figure 2).

Conclusion: Non invasive monitoring of MetHb in patients with LTA including prilocaine is strongly recommended with respect to unexpected and undetected high levels of MetHb in the intraoperative, postoperative and late postoperative phase.

From Proceedings of the 2010 Annual Meeting of the American Society Anesthesiologists.
Pulse Oximeter Performance during Rapid Desaturation Procedures and with Reduced Perfusion Index

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Anesthesiology, University Medical Center Schleswig Holstein, Luebeck, Germany; Institute of Biomedical Engineering, University of Luebeck, Luebeck, Germany

Introduction: Pulse oximeter (PO) displayed a perfusion index (PI) calculated from the ratio between the pulsatile and the uniform components (AC/DC × 100) and presented in arbitrary units (AU) [1]. The decrease of PI implicates a loss of PO signal quality and presents also information about patient status [2]. We investigated the following questions: 1. In which range are the time delays of the PO data in a controlled decrease and increase of the PI? 2. In which range are the differences with respect to the presented SpO₂ data?

Methods: With ethics committee approval and written informed consent 14 volunteers were included in the study protocol. Perfusion in both arms, hands and fingers were modified in parallel with application of cold and warmed air. The sensors of two identical PO of three manufacturers were randomized and applied to index, middle and ring finger on each hand. Two forehead sensors of two PO manufacturers completed the PO set up and served as control.

The temperature (T in°C) differences measured between finger (4 sensors) and core (2 sensors) and the flux (AU) measured with a laser Doppler sensor (LD) served as reference. All data were recorded continuously. At steady state conditions on four plateaus (P1 to P4) we introduced rapid desaturation procedures with two steps: 1. from 97 % to 85 % and holding a 3 min plateau; 2. from 85 % to 75 % with a plateau - and back to initial level. Delay time was calculated during step down to 85 % and on the way back to the initial value. Differences between forehead and finger sensors were calculated at the initial position, at the plateaus on 85 % and 75 % and after reaching the initial level.

Results: A standardized alteration of perfusion index at the finger site with the establishment of steady state plateaus was successful with 14 volunteers in this controlled randomized study. Signal delay times (Table 1) and SpO₂ differences (Table 2) between forehead and finger sensors increased with respect to P1 to P3. This effect was reversible after rewarming and with normal perfusion index (P4).

<table>
<thead>
<tr>
<th>Plateaus</th>
<th>SpO₂ step direction</th>
<th>Finger</th>
<th>Forehead</th>
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<tbody>
<tr>
<td>P1</td>
<td>down</td>
<td>14 ± 7</td>
<td>6 ± 6</td>
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<td></td>
<td>up</td>
<td>6 ± 4</td>
<td>4 ± 4</td>
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<td>P2</td>
<td>down</td>
<td>51 ± 13</td>
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<td></td>
<td>up</td>
<td>37 ± 11</td>
<td>6 ± 5</td>
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<td>P3</td>
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<td>P4</td>
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<td>10 ± 7</td>
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<tr>
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<td>up</td>
<td>8 ± 4</td>
<td>5 ± 5</td>
</tr>
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</table>

Mean ± SD of all sensors at the finger and at the forehead site, respectively

SpO₂ differences (in %) at different PI plateaus

<table>
<thead>
<tr>
<th>SpO₂ step period</th>
<th>before</th>
<th>at 85 %</th>
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<tr>
<td>Plateaus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P1</td>
<td>0.17 ± 0.99</td>
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<td>-1.39 ± 0.94</td>
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<td>P2</td>
<td>0.81 ± 0.89</td>
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<td>P3</td>
<td>0.88 ± 1.01</td>
<td>0.91 ± 1.37</td>
<td>-2.21 ± 2.56</td>
<td>0.65 ± 0.98</td>
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<tr>
<td>P4</td>
<td>-0.31 ± 0.80</td>
<td>-0.11 ± 0.61</td>
<td>-1.40 ± 0.84</td>
<td>0.06 ± 1.46</td>
</tr>
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</table>

Mean ± SD of all sensors at the finger and at the forehead site, respectively


From Proceedings of the 2010 Annual Meeting of the American Society Anesthesiologists.
Prilocaine-Induced Methemoglobinemia in Regional Anesthesia Using Maximum Recommended Doses

Objective: The local anesthetic agent prilocaine is characterized by a low systemic toxicity, but may induce methemoglobinemia in a highly interindividual variation. Increased values may be hazardous in patients with anemia or cardiopulmonary disease. In this prospective observational study we examined the arterial methemoglobin levels after performing an interscalene plexus blockade or a combined femoral/sciatic nerve blockade, each one with maximum recommended doses.

Material and Method: 20 patients received 300 mg of prilocaine 1% via an interscalene plexus catheter and 20 patients 2 x 300 mg of prilocaine 1% for a combined femoral/sciatic nerve blockade. All blocks were performed using a nerve stimulator. Continuously we monitored non invasively the Pulse CO-Oximetric values with the Masimo Radical7 (Masimo Corp., Irvine, CA), a new Pulse CO-Oximeter designed to measure methemoglobin (SpMet). Before and 15, 30, 60, 120, 180, 240, 300 and 360 minutes after prilocaine injection methemoglobin levels were determined in arterial blood samples with a hemoximeter (Radiometer ABL 625, Copenhagen). These values were compared with the corresponding Pulse CO-Oximeter readings of the Radical7 (mean one-minute-value of SpMet).

Results: The mean maximum level of methemoglobin in the interscalene plexus group was 2.3% (sd +/-0.8 %) (range 0.6 - 4.9 %) reached after 120 minutes. For combined femoral/sciatic nerve block peak blood levels for methemoglobin were reached 4-5 hours after prilocaine injection with a mean value of 4.0% (sd +/- 1.5 %) (range 0.9 – 6.6 %). For evaluation of accuracy and precision of the Masimo Radical7 we analyzed 360 data pairs using statistical techniques recommended by Altman and Bland: The precision of the device was 0.99 % and the bias 0.26 %.

Conclusion: After injection of the maximum recommended doses of prilocaine for interscalene block and for combined femoral/sciatic nerve block we found no methemoglobin levels above 7 %. Peak level were reached after interscalene plexus blockade 2 to 3 hours earlier than after combined femoral/sciatic nerve block. The Pulse CO-Oximeter Masimo Radical7 is able to monitor continuously and accurate methemoglobin levels during regional anesthesia using prilocaine as local anesthetic agent.

Anesthesiology 2008; 109 A558
Changes of Bispectral Index and of Propofol Concentrations in Breath after Stopped Propofol Infusion

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Research Unit, Draegerwerk AG & Co. KGaA, Luebeck, Germany

Introduction:
Monitoring methods that continuously provide information about propofol being infused into a patient can be either based on determining the effect of propofol or on providing information about plasma concentration. EEG-Monitoring such as bispectral index reveals information about the effect of propofol on the brain. Monitoring of propofol concentrations in breathing gas provides information about changing plasma concentrations. We monitored changes of bispectral index and of propofol concentration in breathing gas when the infusion is stopped.

Methods:
After IRB approval and informed consent patients (n=6) undergoing cardiac surgery were monitored for changes during recovery from a standardized propofol anesthesia (3 mg*kg-1* h-1 for more than 120 min) with bispectral index and with an electrochemical sensor system for propofol in breathing gas. Additional blood samples were obtained for the determination of propofol concentration in plasma before stopping an infusion and when patient opened the eyes on command. The intervals from stopping the infusion until detecting changes in bispectral index and in the sensor system for propofol in breathing gas were recorded.

Results:
From stopping infusion until eye opening on command propofol concentrations in plasma decreased 0.45-0.94 µg*ml-1 and in breathing gas 1.7-4.1 ppb. Changes in bispectral index occurred after 199-700 s, while changes in breathing gas were preceding those changes in bispectral monitoring 120-221 s after stop of infusion. [Figure 1]

Conclusions:
Stop of propofol infusion can be detected as a decrease of propofol in breathing gas followed by an increase in bispectral index. The difference in time course of changing signals reflects their origin from different compartments.

Anesthesiology 2008; 109 A199
Non-Invasive and Direct Determination of Hemoglobin in Native Blood Present in Sampling Tubes

Alexander Opp, M.S., Sebastian Look, Leif Dibbelt, M.D., Soehnke Boye, M.D., Hartmut Gehring, M.D., Ph.D. 
Institute of Medical Engineering, University of Luebeck, Luebeck, Germany

Introduction:

The corpuscular concentration of hemoglobin (ctHb) determines the capacity of human blood to distribute oxygen to the body and is thus a critical laboratory marker. Current assays measure ctHb by hemolyzing the erythrocytes of a distinct sample and chemically converting all Hb species in the hemolysate to a unique, strongly absorbing derivative; they therefore are invasive, laborious and time-consuming. A fast, non-invasive, reagent-free photometric method of hemoglobin concentration (ctHb) measurement was developed for utilization on tubes. With respect to the physiological range of ctHb, the procedure should cover the concentration between 70 g/L and 170 g/L ctHb. For this measurement procedure either lasers or light emitting diodes (LEDs) can be used. In the present investigation we introduce an optical sensor based on LEDs which is designed to measure in a tube and can therefore be used in clinical areas, where blood is taken from the body via a drainage system such as during blood donations.

Method:

The measurement utilizes two wavelengths in the infrared range around the isosbestic points of the oxy- and deoxyhemoglobin absorption curves, at 800nm and 1300nm (1).

Once the sensor is attached to the sample tube, two photodiodes located opposite the LEDs, measure the amount of light absorbed by the respective blood.

To eliminate interferences caused by the sample tube, a first measurement is taken with an empty tube to provide a baseline calibration; the second measurement taken from the same tube filled with blood provides information of the actual ctHb.

A number N of commercially available tubes (MacoPharma, France) and a 50 mL perfusor syringe as blood reservoir were used for each of the five different hemoglobin concentrations prepared by appropriately mixing plasma and erythrocyte concentrate. Sensor data were compared to results obtained from calibrated industry-standard analyzers. The reference values shown below is the arithmetic mean of five different samples taken invasively and measured by three hemoglobin analyzers (Hb 201+, Hemocue; Grossostheim, Germany) and two blood gas analyzers (OSM3, Radiometer; Copenhagen, Denmark).

Results:

The ctHb values measured with the optical LED sensor achieved standard deviations comparable to those of the reference values (Table 1). The measuring range of the sensor covers concentrations up to 150 g/L ctHb.

Discussion:

The ctHb values measured with the optical LED sensor achieved standard deviations comparable to those of the reference values (Table 1). The measuring range of the sensor covers concentrations up to 150 g/L ctHb.

References:


Anesthesiology 2008; 109 A1688

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<th>Reference Data:</th>
<th>ctHb [g/L] (Mean)</th>
<th>94.2</th>
<th>114.6</th>
<th>137.8</th>
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<td>Standard Deviation [g/L]</td>
<td>2.95</td>
<td>3.21</td>
<td>4.32</td>
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<th>Measured Data:</th>
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<td>ctHb [g/L] (Mean)</td>
<td>93.4</td>
<td>115.3</td>
<td>139.9</td>
<td>152.0</td>
<td>157.0</td>
<td></td>
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<tr>
<td>Standard Deviation [g/L]</td>
<td>2.76</td>
<td>3.64</td>
<td>3.02</td>
<td>2.35</td>
<td>2.69</td>
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</tbody>
</table>

Table 1: Numerical data of measured ctHb in comparison with reference ctHb
Capnometry Accuracy with Ambient and Body Conditions

Hartmut Gehring, M.D., Ph.D., Susanne Landsmann, Alexander Opp, Ph.D., Soehnke Boye, M.D.
Department of Anesthesiology, University Clinic SH, Campus Luebeck, Luebeck, Germany

Introduction: The measurement of carbon dioxide concentration in expired gas is a sensitive method of ventilation and gas exchange monitoring and it has become a care standard of ventilated patients [1, 2]. Therefore, the accuracy of the carbon dioxide concentration analyzer is an essential condition. The aim of the present study was the evaluation of the accuracy of five commercially available capnometers under standardized in vitro conditions.

Methods: The evaluated devices were two sidestream capnometers (Microcap® Plus, Oridion, Israel; Capnosat, Draeger, Germany) and three mainstream systems (Infinity Delta, Draeger, Germany; C/S 3, Datex Ohmeda, Finland; Argus Pro, Schiller, Switzerland). Measurements were performed under ATPS (Ambient Temperature, Pressure, Saturated) and BTPS (Body Temperature, Pressure, Saturated) conditions using five certificated gas mixtures of defined concentrations (gas A: 2 % CO₂, 2 % O₂, 96 % N₂; gas B: 5 % CO₂, 12 % O₂, 83 % N₂; gas C: 5 % CO₂, 20 % O₂, 75 % N₂; gas D: 10 % CO₂, 0 % O₂, 90 % N₂; gas E: 5 % CO₂, 95 % O₂, 0 % N₂). The BTPS conditions were created by use of the tonometer 237 (Instrumentation Laboratory, Kirchheim, Germany). For the statistical analysis the measured data were compared to the calculated set points including measured humidity, temperature, and barometric pressure.

Results: The calculation of the set points for the ATPS conditions was based on the following measured mean values: 21,72°C temperature, 13,63 % humidity, and 768,33 mmHg barometric pressure. For the BTPS conditions the following mean data were measured: 33,49 °C temperature, 99,9 % humidity, and 771,78 mmHg barometric pressure. The measured values are shown as mean difference ± standard deviation (sd) in table 1 and 2.

Conclusion: The gas composition and the mode (ATPS vs. BTPS) - sometimes chosen automatically by the devices, when CO₂ is detected - may decrease the accuracy.


Anesthesiology 2008; 109 A1479

<table>
<thead>
<tr>
<th>Devices</th>
<th>Gas A</th>
<th>Gas B</th>
<th>Gas C</th>
<th>Gas D</th>
<th>Gas E</th>
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<td>Microcap® Plus</td>
<td>-0,01 ± 0,71</td>
<td>-2,43 ± 1,24</td>
<td>-1,25 ± 0,67</td>
<td>1,06 ± 2,40</td>
<td>-3,96 ± 0,85</td>
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<td>Capnosat</td>
<td>1,59 ± 0,67</td>
<td>-2,53 ± 1,99</td>
<td>-3,05 ± 1,87</td>
<td>-4,39 ± 2,07</td>
<td>-4,96 ± 0,65</td>
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<td>Infinity Delta</td>
<td>0,29 ± 0,0</td>
<td>-0,78 ± 0,0</td>
<td>-0,9 ± 0,3</td>
<td>-1,34 ± 0,87</td>
<td>1,39 ± 0,0</td>
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<td>0,34 ± 0,22</td>
<td>0,22 ± 0,0</td>
<td>0,1 ± 0,3</td>
<td>1,86 ± 0,45</td>
<td>1,29 ± 0,83</td>
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<tr>
<td>Argus Pro</td>
<td>-0,81 ± 0,0</td>
<td>0,38 ± 0,37</td>
<td>-0,2 ± 0,0</td>
<td>1,09 ± 0,30</td>
<td>2,19 ± 0,0</td>
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</table>

Tab. 1: ATPS conditions with gas mixtures A to E (mean diff. ± sd in mmHg)

<table>
<thead>
<tr>
<th>Devices</th>
<th>Gas A</th>
<th>Gas B</th>
<th>Gas C</th>
<th>Gas D</th>
<th>Gas E</th>
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<tbody>
<tr>
<td>Microcap® Plus</td>
<td>0,64 ± 0,0</td>
<td>-1,37 ± 0,0</td>
<td>-1,53 ± 0,36</td>
<td>-0,27 ± 2,34</td>
<td>-4,51 ± 0,3</td>
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<td>Capnosat</td>
<td>0,24 ± 1,16</td>
<td>-1,97 ± 1,2</td>
<td>-3,88 ± 1,16</td>
<td>-4,87 ± 1,63</td>
<td>-6,46 ± 0,8</td>
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<td>Infinity Delta</td>
<td>2,14 ± 1,12</td>
<td>0,23 ± 1,07</td>
<td>-1,33 ± 0,22</td>
<td>-0,82 ± 1,04</td>
<td>0,59 ± 0,0</td>
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<td>Datex Ohmeda</td>
<td>2,09 ± 0,8</td>
<td>1,38 ± 1,44</td>
<td>0,52 ± 1,64</td>
<td>0,13 ± 1,49</td>
<td>-1,96 ± 0,49</td>
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<tr>
<td>Argus Pro</td>
<td>1,06 ± 0,39</td>
<td>3,02 ± 0,82</td>
<td>-0,31 ± 0,46</td>
<td>0,85 ± 0,85</td>
<td>1,27 ± 0,3</td>
</tr>
</tbody>
</table>

Tab. 2: BTPS conditions with gas mixtures A to E (mean diff. ± sd in mmHg)
Accuracy of Capnometry in Critically Ill Adult Patients

Hartmut Gehring, M.D., Ph.D., Susanne Landsmann, Alexander Opp, Ph.D., Beate Sedemund-Adib, M.D., Soehnke Boye, M.D.
Department of Anesthesiology, Medical University SH, Campus Luebeck, Luebeck, Germany

Introduction: Capnometry has become a standard monitoring of ventilation in anesthesia and critical care medicine. Two modes of PCO₂ measurement systems promise a noninvasive handling and allow also the monitoring of spontaneously breathing patients [1,2]. The aim of the present study was the evaluation of a transcutaneous (tc) and an endtidal (et) capnometer compared to blood gas analysis (BGA) under four clinical conditions: (I) endotracheal tube, controlled mechanical ventilation with lying and sedated patient; (II) endotracheal tube, spontaneously breathing with sitting patient; (III) spontaneously breathing with sleeping and (IV) patient after extubation.

Methods: After approval of the local ethics committee and obtaining informed consent, 30 adult intensive care patients of the ASA groups II and III with an indwelling arterial catheter were considered. Randomized in two groups of each 15 patients, the tc-system (TOSCA®, Linde, Switzerland) was either used in standard (sm) or calibration mode (cm). The TOSCA-sensor was applied at the earlobe with a clip. The PetCO₂ values were performed with a sidestream capnometer (Microcap® Plus, Oridion, Israel) using the FilterLine™ for ventilated patients and the Smart CapnoLine™ O₂ for spontaneously breathing patients. In each of the four measurement phases (I-IV) PtcCO₂, PetCO₂ and PaCO₂ values were measured. For statistical comparison the paired t-test and the Bland-Altman analysis were utilized. P<0.05 was considered statistically significant.

Results: Under the defined clinical conditions the transcutaneous system overestimates the PaCO₂ values. Irrespective of the technical mode (sm or cm) differences and standard deviations of the transcutaneous data increase (tab. 1), especially in phases II and III. In contrast to this, the endtidal system underestimates the arterial values. Differences increase in the phases of spontaneous respiration (III and IV). (table) Conclusion: In the critical situation of extubation increase the differences of the tc-system with ear sensor. In spontaneously breathing patients the et-system does not provide a definite assessment of PCO₂. Ventilation/perfusion ratio seems to be responsible for the differences between phase I and II.


Phases | (P_tCO₂ - P_aCO₂) ± sd [mmHg] sm group | (P_tCO₂ - P_aCO₂) ± sd [mmHg] cm group | (P_etoCO₂ - P_aCO₂) ± sd [mmHg]
---|---|---|---
I | 8,31 ± 3,83 | 1,29 ± 1,4 | -3,62 ± 3,08
II | 14,31 ± 12,16 | 3,34 ± 4,17 | -0,76 ± 4,07
III | 11,23 ± 9,25 | 5,66 ± 5,70 | -7,87 ± 7,55
IV | 2,99 ± 4,53 | 0,40 ± 2,88 | -6,51 ± 4,88

Tab. 1: Mean differences and standard deviations of the transcutaneous (standard mode - sm; calibration mode - cm) and endtidal data

Filename: D:/Strands/Content/ASA/asaabstracts/2008/EQUIPMENT, MONITORING, and ENGINEERING TECHNOLOGY/abs_a1172.htm
Propofol Sensing in Breath: Chemical Identification of Volatile Substances in Exhaled Breath

Andreas Hengstenberg, Ph.D., Hartmut Gehring, M.D., Thorsten Meier, M.D., Leif Dibbelt, Ph.D., Martin Grossherr, M.D.
Research Unit, Draegerwerk AG, Luebeck, Germany

Introduction:
Several Studies suggest that non-invasive online monitoring of propofol in breathing gas has the potential to become a useful tool to improve management of anesthesia[1, 2]. In order to introduce this approach to clinical practice suitable sensor technologies for the detection of low concentrations of propofol have to be identified. In preclinical studies electrochemical sensing technology has been used to continuously monitor propofol application during anesthesia [3].

However besides the exhaled drug compound other volatile substances present in breathing gas may possibly interfere with the use of a sensor system. In this study breathing gas samples were screened for their chemical composition during sedation with propofol using gas chromatography mass spectrometry. Volatile substances in breathing gas were identified and classified based on their origin of release.

Methods:
With the approval of the ethics committee and after obtaining written informed consent we collected samples of exhaled breathing gas during sedation in patients (N=12) after aorto coronary bypass grafting. After cardiopulmonary bypass and transfer to the ICU the patients received propofol and piritramide for sedation and samples of 500 ml breathing gas were collected onto sampling tubes filled with Tenax TA over a period of 5 minutes. Chemical analysis of the volatile compounds bound to the adsorption material was carried out with a gas chromatography mass spectrometry (GCMS) system equipped a thermodesorption unit. Chemical identification of compounds in exhaled breath was performed with a comparison of the obtained mass spectra with a computer library containing reference data of 280 000 different compounds. The concentration of the compounds was estimated on the basis of a calibration of the GCMS system with toluene.

Results:
The substances that were identified can be put into three categories: 1) markers of endogenous origin 2) compounds originating from medication and treatment (e.g. propofol) 3) compounds from the ventilation system and materials used. No interference for an electrochemical sensor system has been identified.

Conclusions:
The results indicate that the setting and the devices that are used (e.g. respirator, medication…) have a significant contribution to the composition of breathing gas during artificial ventilation. The substances that have been identified should not interfere with propofol monitoring based on electrochemical sensor technology.


Anesthesiology 2007; 107: A1429
Propofol Concentration in Bronchoalveolar Lavage - Changes during Anesthesia

Martin Grossherr, M.D., D.E.A.A., Leif Dibbelt, Ph.D., Andreas Hengstenberg, Ph.D., Hartmut Gehring, M.D., Ph.D., Torsten Meier, M.D.
Anesthesiology, UK Schleswig-Holstein, Campus Luebeck, Luebeck, Schleswig-Holstein, Germany

Background: There is no established procedure to monitor the concentration of propofol in plasma non-invasively and directly. The measurement of propofol in breathing gas may become an alternative [1,2]. Therefore, the part of the lung in propofol exhalation has to be described more exactly. It is not known whether propofol, a highly volatile phenol, accumulates during propofol infusion in the alveolar space. The following study investigates the effect of a propofol anesthesia on the propofol concentrations in the bronchoalveolar lavage (BAL).

Method: After approval of the local ethic board and after obtaining written informed consent patients were anesthetized for elective ear, nose and throat operations. After premedication anesthesia was induced with propofol (2 mg/kg bodyweight; BW), sufentanil (0.5 microg/kg BW) and rocuronium (0.5 mg/kg BW) for intubation. For maintenance of anesthesia propofol was continuously applied (6 mg/kg BW x h) and further sufentanil (0.2 mcg/kg BW) was given if necessary.

Patients were normocapnic ventilated and the FiO₂ was held between 0.35 and 0.4 to gain a peripheral oxygen saturation between 95 -100 %.

Reducing the effects of the procedure 3 groups were randomly selected for BAL: Group I (n = 22) after induction of anesthesia at the beginning; group P (n =15) at the end of the anesthesia, ventilated with a PEEP of 10 cm H₂O; group E (n = 15) ventilated without a PEEP. Propofol concentrations in the BAL were measured using an established method [1]. Data was presented as median and 25% and 75%. Significant differences between two groups were analyzed with the Mann-Whitney U test. A P-value < 0.05 was considered to indicate statistically significant differences.

Results: In all 52 patients the BAL was successful. Duration of operation was 155.2 minutes for group P and 147.5 minutes for group E. For the groups with the procedure at the end of a propofol anesthesia we found slightly higher propofol concentrations in the BAL, which reached the level of significance for the patients ventilated with a PEEP of 10 cm H₂O (see table 1).

Conclusion: At the end of a propofol anesthesia higher propofol concentrations were measured in the BAL. Though propofol is a highly volatile phenol, this may express some kind of an accumulation in the alveolar space.

Literature

Propofol Concentration in BAL after induction and at the end of anesthesia

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group P</th>
<th>Group E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (mcg/l)</td>
<td>45.5</td>
<td>74.5 *</td>
<td>52.5</td>
</tr>
<tr>
<td>25%/75% Percentile (mcg/l)</td>
<td>33.0 / 60.4</td>
<td>49.7 / 101.5</td>
<td>46.8 / 64.5</td>
</tr>
</tbody>
</table>

Group I: BAL at the beginning of anesthesia; Group P: BAL at the end of anesthesia ventilated with PEEP (10 cmH₂O); Group E: BAL at the end of anesthesia ventilated without PEEP; * P < 0.05 vs group I
Continuous Monitoring of Propofol Concentration in Breathing Gas – New Insights in the Lung’s Role

Martin Grossherr, M.D., D.E.A.A, Andreas Hengstenberg, Ph.D., Leif Dibbelt, Ph.D., Bernd-Wolfgang Igl, Ph.D., Hartmut Gehring, M.D., Ph.D.
Anesthesiology, University Clinic Schleswig-Holstein, Cp Luebeck, Luebeck, Schleswig-Holstein, Germany

Background: Propofol concentration in plasma can not be measured non-invasively and continuously. The continuous measurement of propofol in breathing gas may become an alternative for the assessment of propofol concentration in plasma [1, 2]. To verify this feature the role of the lung in propofol exhalation has to be defined more precisely, therefore [3]. The following investigation compares the courses of propofol concentrations in plasma and breathing gas, continuously and discontinuously measured, under a constant propofol infusion in pigs.

Material and methods: After approval of the local board for animal protection we determined the propofol concentrations in plasma and breathing gas continuously and discontinuously before and during a propofol anaesthesia in 6 pigs. Propofol was constantly infused (9.6 mg/kg bodyweight x h). Samples of plasma and breathing gas were drawn at five points of time (T0-T4) before application of propofol and after 10, 20, 30 and 40 minutes. An electrochemical sensor was used for the continuous monitoring of propofol concentration in breathing gas [2]. To describe the course of propofol concentration in plasma and in breathing gas as a function of time alone the values of each point of time were compared to point of time 4. This was done for each individual and the values were calculated as a ratio.

Results: Propofol concentration ranged between 1.9 to 3.7 microg/ml in plasma and 1.1 to 7.6 ppb for continuous measurement and 1.0 to 4.3 ppb for discontinuous measurement in breathing gas. Data of the calculated ratios are shown in table 1 as mean and standard deviation in percent.

Conclusion: The appearance of propofol in the endtidal breathing gas during a continuously applied propofol dosage is delayed in the first 30 min as compared to plasma levels.

Literature

Course of plasma and breathing gas ratio during a constant propofol infusion at 5 time points (T0-T4)

<table>
<thead>
<tr>
<th>Ratio (T/T4)</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CpPl [%]</td>
<td>0.0 (0)</td>
<td>69.2 (11)</td>
<td>83.8 (3)</td>
<td>94.5 (4)</td>
<td>100 (0)</td>
</tr>
<tr>
<td>cont CpA [%]</td>
<td>-1.1 (9)</td>
<td>24.1 (9)</td>
<td>56.2 (5)</td>
<td>89.2 (9)</td>
<td>100 (0)</td>
</tr>
<tr>
<td>discont CpA [%]</td>
<td>2.6 (3)</td>
<td>46.4 (22)</td>
<td>68.7 (13)</td>
<td>79.0 (15)</td>
<td>100 (0)</td>
</tr>
</tbody>
</table>

Legend: CpPl: Propofol concentration in plasma; CpA: Propofol concentration in alveolar gas; cont: continuously measured by a sensor; discont: discontinuously measured.
Continuous Real-Time Monitoring of Propofol in Breathing Gas during Anesthesia

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Research Unit, Draegerwerk AG, Luebeck, Germany

Introduction: During the administration of i.v. anesthetic drugs, information about their blood concentrations is limited. Studies [1,2] have shown that low concentrations of propofol (2,6-di-isopropylphenole) are found in exhaled breathing gas during anesthesia and relate to plasma concentrations. Due to the low concentrations of propofol in breathing gas, complex analysis equipment such as gas chromatography mass spectrometry (GC/MS) and specialized mass spectrometers have been used. However, a continuous real-time monitoring of propofol in breathing gas in the clinical setting requires suitable detection technologies that are robust, easy to use, and economically feasible. In this study, we present first results on the detection of propofol in breathing gas employing electrochemical gas sensor technology.

Methods: After approval by the regional authority for animal research we collected samples of exhaled breathing gas, arterial, and mixed venous blood during anesthesia in an animal study with pigs (n=9). First anesthesia was maintained using etomidate until blank samples were collected. Then anesthesia medication was changed to propofol and ketamine. An electrochemical gas sensor was used for a continuous side stream measurement of propofol concentrations in breathing gas. Additional reference samples of breathing gas were collected and analyzed with GC/MS. Blood samples were collected simultaneously and analyzed with high performance liquid chromatography (HPLC). Propofol infusion rates were varied over time to induce changes in blood concentrations. The results obtained with the two different gas analysis methods were compared and the correlation of propofol concentrations in breathing gas and blood plasma was studied.

Results: Propofol concentrations in breathing gas were observed in a range from 0 to 32 ppb. Propofol concentrations in blood plasma ranged from 0 to 11 μg/ml. The electrochemical sensor adequately responded to the changes in propofol concentrations in exhaled breathing gas. The comparison of the breathing gas concentrations measured by the electrochemical sensor with the data based on the GC/MS-Method revealed an agreement of both methods. The electrochemical sensor indicated higher results than the GC/MS measurements (Mean difference between both methods: 5.2 ppb). A correlation of propofol concentrations in blood plasma with concentrations in breathing gas was found (Range of r values: 0.53-0.98).

Conclusions: The results of the study indicate that online monitoring of propofol in breathing gas may become feasible using electrochemical gas sensor technology. Further studies will have to address improvements of the gas sensing system in response time as well as sampling and handling issues.

Literature:

Anesthesiology 2006; 105: A577
Monitoring of Propofol Concentrations in Expired Air and Arterial Plasma during Ventilation

Martin Grossherr, M.D., D.E.A.A., Andreas Hengstenberg, Ph.D., Torsten Meier, M.D., Leif Dibbelt, Ph.D., Hartmut Gehring, Ph.D., M.D.
Anesthesiology, University of Luebeck, Luebeck, Germany

Introduction:
The measurement of propofol concentrations in exhaled alveolar gas seemed to be a feasible method for information about the blood concentrations. Studies [1,2] have shown that low concentrations of propofol (2,6-di-isopropylphenole) are found in exhaled breathing gas during anesthesia and that they could be related to plasma concentrations. Due to the low concentrations of propofol in breathing gas, complex analysis equipment such as gas chromatography mass spectrometry (GC/MS) and specialized mass spectrometers have been used [2]. In this study, we present first results regarding the monitoring of propofol in breathing gas and arterial plasma samples during anesthesia in patients.

Methods:
With the approval of the ethics committee and after written informed consent we collected samples of exhaled breathing gas and arterial blood during anesthesia in a patient undergoing aorto coronary bypass grafting. After induction of anesthesia with 40 µg sufentanil and application of 20 mg etomidate patient was relaxed by 8 mg pancuronium and blank samples were collected twice from the respiratory gas and in triplicate from the arterial line. The gas samples were withdrawn about one minute (10 respiratory cycles) from a t-piece at the endotracheal tube using 2 glass syringes of 100 ml volume. Between t-piece and glass syringe there was an adsorption tube inserted filled with Tenax™. Then anesthesia medication was changed to propofol 300 mg/h with discontinuous application of sufentanil. Samples of breathing gas were collected at 10 min steps before starting the cardiopulmonary bypass, followed by two measurements at the ICU, first at the arrival and second when patient opened the eyes. The volatile compounds bound on the adsorption tubes were analyzed with GC/MS. Arterial blood samples were collected simultaneously and analyzed with high performance liquid chromatography (HPLC).

Results:
In the period before cardiopulmonary bypass we were able to collect 5 samples for the expiration gas and the arterial plasma. [Figure 1] Propofol concentrations in breathing gas were observed in a range from 0 to 13 ppb, while the concentrations in blood plasma ranged from 0 to 1.6 µg/ml. The results of the two measurements at the ICU followed in trend the effect side until patient opens the eyes.

Conclusions:
This is the first demonstration of the comparison between propofol concentrations in exhaled breathing gas and arterial blood in a patient. These initial results of an ongoing study indicate that online monitoring of propofol in breathing gas may become feasible technology for monitoring plasma concentrations in patients.

Literature:
Anesthesiology 2006; 105: A580

Figure 1
Blood Gas Partition Coefficient and Pulmonary Extraction Ratio of Propofol in Goats

A1613
October 18, 2006
9:00 AM - 11:00 AM
Room Hall E, Area B

Martin Grossherr, M.D., D.E.A.A., Andreas Hengstenberg, Ph.D., Torsten Meier, M.D., Leif Dibbelt, Ph.D., Gehring Hartmut, Ph.D., M.D.
Anesthesiology, University of Luebeck, Luebeck, Germany

Introduction

As an extrapheatic place of propofol elimination expiration via the lung can be used for monitoring the propofol concentrations in plasma [1]. Further possible pathways of the propofol elimination in the lungs are metabolism and distribution between blood and tissue. The metabolism of propofol in human lungs is controversially discussed [2, 3]. Furthermore, a redistribution of propofol is observed after the first passage of the lung [3].

However, it is not clear whether changes of propofol dosages lead to changes of the pharmacokinetic properties of the lung. In this study we determined the blood gas partition coefficient (BGPC) and the extraction coefficient (EC) of the lung as pharmacokinetic parameters under different propofol dosages.

Animals and methods

After approval by the regional authority for animal research established procedures were used for measuring propofol concentration in alveolar gas (cpA) and in plasma (cpPL) of mixed venous and arterial blood [1] during continuous application of propofol for general anesthesia to 5 goats. Propofol infusion rates for a 10 minute period were varied to modify cpPL.

Calculation of BGPC and EC:

BGPC = arterial cpPL / cpA;

EC = (mixed venous cpPL – arterial cpPL) / mixed venous cpPL.

The median values of BGPC and of EC were presented for each sampling point. The data pool was statistically compared with the non-parametric Friedman test and Wilcoxon test, regarding a p < 0.05 as significant.

Results

The values of cpA were measured between 0 and 10.2 ng/l, while cpPL ranged from 0 to 8 µg/ml. There were significant differences of the BGPC and of the EC for propofol under the varied dosages (table 1). Only the significant data between BGPC and EC of period 1 to other periods were marked.

Conclusion

The changes of BGPC and of EC for propofol under different dosages demonstrate that the lung tissue plays an important role for the distribution of propofol between the plasma and the alveolar space in goats. This has to be considered for methods using the alveolar gas for monitoring propofol concentrations in plasma.

Literature


Anesthesiology 2006; 105: A1613

Blood gas partition coefficient (BGPC) and the extraction coefficient (EC) of the lung under different propofol dosages

<table>
<thead>
<tr>
<th>Period</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage (mg/kg/h)</td>
<td>16</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>BGPC (x1000)</td>
<td>39.5</td>
<td>4.1 §</td>
<td>5.2§</td>
<td>7.5§</td>
<td>6.6</td>
<td>17.1</td>
<td>5.5§</td>
</tr>
<tr>
<td>EC (1)</td>
<td>0.48</td>
<td>0.81§</td>
<td>0.80§</td>
<td>0.82§</td>
<td>0.83</td>
<td>0.62</td>
<td>0.76§</td>
</tr>
</tbody>
</table>

§: p<0.05
**Intelligent Analysis of Capnograms in Spontaneously Breathing Patients**

Hartmut Gehring, M.D., Norman Stein, Farhan Ahmad, Holger Matz, Ph.D., Uli Hofmann, Ph.D.
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**Introduction:** Capnography becomes more and more essential in the monitoring of spontaneously breathing patients with i. v. analgesia and sedation during diagnostic interventions or in the postoperative period at the recovery room [1]. Several systems are now available on the market for sampling exhaled gas during continuous application of oxygen. The gas supply on one side and the breathing pattern on the other may influence the gas sampling visible on the deformation of the capnographic shape. Due to this effect the displayed data of the endtidal CO2 partial pressure (PetCO2) varies in a large range and demonstrates furthermore an increased difference to the arterial PCO2 [1]. "InCAP" (Intelligent Capnography) is a software tool for analysing the raw capnographic data files in order to identify shapes similar to the as "normal" defined capnogram.

**Method:** The capnographic data pool of a recent study [1] was introduced retrospectively to this program for testing the system. The data revealed from an et-system Microcap® Plus (sampling rate 100 msec) employed in a randomized manner with each of 8 patients fitted with the oral/nasal FilterLine® (nasal cannula – NC; Ordon, Luebeck) for measuring PetCO2, and to each of 8 patients with a normal facial mask (FM) and CO2 sampling employing the sidestream procedure. A self organizing cluster algorithm classified the capnograms of a defined period (range of 3 to 8 min.) to several groups, ordered in the range of "perfect shape" to "noise". At each of these groups the capnograms were summarized to one representing capnogram from which algorithms calculate PetCO2 and the angles alpha and beta [2].

**Results:** Each included file consists of the raw data of 8 min. Table 1 represents the distribution according to the different clusters and the benefit of PetCO2 calculation by using "InCAP". The normal range of the angles alpha and beta [2] is 100-110° and 90°, respectively measured under the conditions of intubated and ventilated patients.

**Conclusion:** Intelligent capnographic analysis might be able to distinguish between curves of normal shape and those of abnormal shape or artefacts which helps to identify those curves that represent PetCO2 values within the expected range of PaCO2.

Anesthesiology 2005; 103: A852

<table>
<thead>
<tr>
<th>NC</th>
<th>PetCO2</th>
<th>Alpha</th>
<th>Beta</th>
<th>FM</th>
<th>PetCO2</th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 ± 11</td>
<td>35 ± 6</td>
<td>108 ± 4</td>
<td>104 ± 10</td>
<td>28 ± 15</td>
<td>32 ± 4</td>
<td>106 ± 3</td>
<td>117 ± 7</td>
</tr>
<tr>
<td>17 ± 5</td>
<td>33 ± 8</td>
<td>109 ± 4</td>
<td>108 ± 9</td>
<td>17 ± 7</td>
<td>30 ± 4</td>
<td>106 ± 3</td>
<td>115 ± 6</td>
</tr>
<tr>
<td>19 ± 8</td>
<td>30 ± 10</td>
<td>111 ± 4</td>
<td>116 ± 15</td>
<td>22 ± 6</td>
<td>26 ± 6</td>
<td>108 ± 2</td>
<td>125 ± 14</td>
</tr>
<tr>
<td>21 ± 8</td>
<td>27 ± 11</td>
<td>111 ± 7</td>
<td>114 ± 13</td>
<td>24 ± 10</td>
<td>26 ± 5</td>
<td>117 ± 13</td>
<td>128 ± 17</td>
</tr>
<tr>
<td>13 ± 8</td>
<td>23 ± 12</td>
<td>110 ± 5</td>
<td>117 ± 17</td>
<td>19 ± 10</td>
<td>20 ± 6</td>
<td>111 ± 7</td>
<td>131 ± 11</td>
</tr>
</tbody>
</table>

Each row corresponds for a cluster, including the mean ± SD of the 8 patients. The total of 1586 capnograms were analysed (NC 801, FM 785). N displays the distribution of the number of capnograms on each cluster.
Breath Analysis and Artificial Ventilation: Chemical Identification and Classification of Volatile Substances in Exhaled Breath during I.V. Anesthesia

Andreas Hengstenberg, Ph.D., Martin Grossherr, M.D., Torsten Meier, M.D., Hartmut Gehring, M.D.

Research Unit, Draegerwerk AG, Luebeck, Germany

Introduction: Measurement of volatile substances in the expired alveolar gas has the potential to become a non-invasive method for controlling plasma concentrations of I.V. anesthetic drugs [1] and may be used as a diagnostic tool [2]. Since the chemical gas analysis, especially at very low concentrations (0 to 10 p.p.b.), requires specialized equipment and operating staff, electronic noses have been proposed as an approach to extract information from exhaled breath [2]. Besides the volatile marker substances indicating a disease or plasma level of a drug other volatile compounds may interfere with the chemical analysis. In a recent investigation breathing gas samples were screened for their chemical composition during i.v. anesthesia. Volatile substances were identified and classified based on their origin of release.

Methods: After approval by the animal welfare authority of our local district administration, substances contained in expired alveolar gas were investigated during intravenous anesthesia and artificial ventilation. At preset CO2-concentrations a pump was activated and end tidal gas was removed from the breathing circuit for analysis. Alveolar gas from several breathin cycles was collected into sampling tubes filled with Tenax TA and transferred into a gas chromatography mass spectrometry (GCMS) system with a thermodesorption unit. Chemical identification of compounds in exhaled breath based on a comparison of the obtained mass spectra with a computer library containing reference data of 280 000 mass spectra. The concentration of the compounds was estimated on the basis of a calibration of the GCMS system with Toloul. Samples were collected at different times and medications.

Results: The identified substances (see table 1) can be assigned to three categories: 1) markers of endogenous origin 2) compounds originating from medication and treatment 3) compounds from the ventilation system and materials used (e.g. endotracheal tubes). The concentrations of some of these compounds were not stable during anesthesia and were changing over time.

Conclusions: The results demonstrate that the experimental setting (e.g. respirator, medication...) has substantial contributions to the composition of exhaled breath at trace levels. This has to be considered when breath analysis is used as a diagnostic tool.


Table 1: Chemical identification of substances in breath 15 min after intubation

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration µg/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>volatile halogenated substance</td>
<td>2300</td>
</tr>
<tr>
<td>2-Propanol</td>
<td>1000</td>
</tr>
<tr>
<td>1-Propanol</td>
<td>45</td>
</tr>
<tr>
<td>Silanol</td>
<td>55</td>
</tr>
<tr>
<td>Cyclohexan</td>
<td>90</td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-p-kresol (BHT)</td>
<td>15</td>
</tr>
</tbody>
</table>

Chemical identification of substances in breath 15 min after intubation

Filename: D:/Strands/Content/ASA/asaabstracts/2005/EQUIPMENT, MONITORING, and ENGINEERING TECHNOLOGY/abs_a1397.htm
Assessment of Gas Exchange in Spontaneously Breathing Patients

Hartmut Gehring, M.D., Norman Stein, Holger Matz, Ph.D., Ewald Konecny, Ph.D.
Department of Anesthesiology, Medical University SH, Campus Luebeck, Luebeck, Germany.

Introduction: Capnography and pulse oximetry are essential aspects in the monitoring of mechanically ventilated patients. Recommendations have now been made to employ CO₂ monitoring also in spontaneously breathing patients (1). The goal of this prospective study was to evaluate two procedures undergoing continuing development, i.e. transcutaneous (tc) and endtidal (et) PCO₂ measurement, regarding their applicability and precision compared to blood gas analysis (BGA).

Methods: With the approval of the local ethics committee and after written informed consent was obtained, 30 patients of the ASA groups II and III with arterial access were monitored in the recovery room after extubation. The tc-system (TOSCA, Fa. Linde, Switzerland) was fixed with a combination sensor for CO₂ and SpO₂ at the ear lobes. The et-system Microcap plus was employed in a randomized manner with each of 15 patients fitted with the newly developed oral/nasal FilterLine (Fa. Oridion, Luebeck) for measuring PetCO₂, and to each of 15 patients with a normal facial mask and CO₂ sampling employing the sidestream procedure. In addition to respiratory rates and PetCO₂ values, capnography curves were digitally displayed and analyzed with respect to the guidelines of (2). In the statistical evaluation of both procedures data from 5 measurement points were taken between administration at the recovery room and transferral to regular care wards.

Main results: Both systems could be used for monitoring in the recovery room. Respiration rate indicated by the et-monitor provided more sophisticated information about breathing activity than did PetCO₂ values (given in table 1), which differed significantly. In contrast, using curve analysis and the fitting algorithm, reference curves could be established that represented PetCO₂ values within the range of the PaCO₂. The Tosca system overestimated PaCO₂ significantly but could be calibrated using PaCO₂ and provided a more effective monitoring amongst less cooperative patients.

Summary: Both procedures allow only a rough estimation of PaCO₂. Because of the continuity of the data display, the tc-procedure is better suited as a trend monitor, while the et-method also display respiratory rate and thereby serve as a monitor for apnoea, a none too trivial advantage.


Results of main variables

<table>
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<tr>
<th></th>
<th>PaCO₂</th>
<th>PtcCO₂</th>
<th>p</th>
<th>PetCO₂</th>
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<td>n</td>
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<td>140</td>
<td></td>
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<tr>
<td>mean</td>
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<td>47.7</td>
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<td>7.9</td>
<td></td>
<td>9.6</td>
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<td></td>
<td>SaO₂</td>
<td>SpO₂ (ear)</td>
<td>p</td>
<td>SpO₂ (finger)</td>
<td>p</td>
</tr>
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<td>n</td>
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<td>mean</td>
<td>95.3</td>
<td>96.3</td>
<td>&lt; 0.01</td>
<td>97.5</td>
<td>&lt; 0.01</td>
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<tr>
<td>sd</td>
<td>2.6</td>
<td>2.7</td>
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Filename: D:/Strands/Content/ASA/asaabstracts/2004/RESPIRATION/abs_a1672.htm
Monitoring of Propofol Concentrations in Plasma and Expired Air during Artificial Ventilation: A Feasibility Study

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Introduction: A direct and non-invasive procedure for determining propofol concentration (cProp) in plasma, and as such an easy procedure for monitoring the anesthetic effect of propofol, does not yet exist. The measurement of cProp in respiratory gas (RG) represents one approach to do this (1). It should be considered, however, that measured values in RG might not necessarily reflect cProp in plasma because of metabolism of propofol in the lungs (2). The goal of this study was to establish a procedure for measuring cProp in RG and plasma, and to use this procedure to determine to which extent plasma and RG levels are comparable.

Methods: After approval by the Society for Prevention of Cruelty to Animals of the district administration, substances contained in endtidal RG both before and during continuous application of propofol (1.6 % in combination with ketamin) to a goat (65 kg body weight) were adsorbed on Tenax tubes using a CO2-controlled sampling arrangement with a rapid, reproducible and flow-controlled acquisition of the end-tidal gas samples in the sampling tubes. Volatile compounds bound to Tenax then were thermally desorbed in a stream of inert carrier gas, and transferred to GC/MS analysis. For measuring plasma cProp, 3 ml of arterial blood were sampled in parallel with the RG samples; following centrifugation, plasma proteins were precipitated, and the residual supernatant was fractionated by RP-HPLC with fluorescence detection. cProp means, SDs and coefficients of variation were calculated (CV in %) from triplicate determinations.

Main results: cProp in both expired air and plasma could be measured in 2 animals in all. As shown in figure 1, the measured gas concentration of propofol follows the plasma and the infusion levels within a single animal. CV of cProp in plasma ranges from 0 to 5.22 % and for cProp in gas from 0 to 6.43 %. The correlation coefficient for both variables was r = 0.84. The concentrations in RG tend to follow the propofol dosing, but not with a linear relationship compared to the concentration determined in plasma. Summary: Initial results demonstrate that the laboratory procedures mentioned here offer the opportunity to monitor RG for propofol, and allow a more precise description of the relationship between cProp in RG and plasma.


Anesthesiology 2004; 101: A139

Figure 1
A-561
2002

The Accuracy of a New Generation of Pulse Oximeters

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Introduction: Recent reports have questioned the accuracy of pulse oximeters (PO) in clinical practice using 1 or 2 established PO (1). Standardization for testing PO performance is still a matter of debate (2). Here, a new approach using local bias and precision was compared with established statistical procedures for validating screening accuracy over the range between 70 and 100% SaO2.

Methods: Eleven healthy volunteers participated after written informed consent and local Ethics Committee approval were obtained. Arterial blood sampled within 5 min plateaus at 5% saturation steps between 70 and 100% served as references checked using 3 CO-oximeters (OSM 3, ABL 725, Radiometer, Copenhagen; CC 270, Bayer Diagnostics). The PO battery consisted of: a D-0 3900 P, a Philips CMS B.0, a Nellcor N-395, a Masimo Radical V. 3, a Siemens MicrO2+, a Criticare 504 DX, a Weinmann/MCC Oxicount Mini, a Nonin 8600, and a Novametrix MarSpO2, M. 2001. Raw data for x and y were replaced by 100-x and 100-y to display 100% as the “natural” point. Decreasing the small but systematic error introduced by the PO delay time, the 964 data pairs were reduced by averaging at each of the 5% saturation steps. The data pairs approaching 100% were discarded to eliminate truncation effects.

Consistent with the equation “y = A + Bx + error”, statistical analysis included an estimator for A and B, the sd for A and B, a p–value for (A,B) = (0,1) with the F-test, a p-value for linear vs. non-linear regression (T-test), an sd (sigma) for random error and the root mean square error (RMSE). Bland & Altman’s bias and precision focused on 3 ranges (< 75%, 76-85%, 86-95%) between 70 and 95% SaO2 served as a basis for providing accuracy.

Results: Results were presented anonymously, as recommended by the International Standard Organisation (ISO). Table 1 shows RMSE and the local bias and precision of different SaO2 ranges.

Anesthesiology 2002; 96: A561

<table>
<thead>
<tr>
<th>Pulse Oximeter</th>
<th>RMSE</th>
<th>bias (&lt; 75)</th>
<th>sd (&lt; 75)</th>
<th>bias (76-85)</th>
<th>sd (76-85)</th>
<th>bias (86-95)</th>
<th>sd (86-95)</th>
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<tr>
<td>PO 1</td>
<td>2.18</td>
<td>-0.78</td>
<td>2.58</td>
<td>-1.49</td>
<td>1.66</td>
<td>-1.64</td>
<td>1.57</td>
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<tr>
<td>PO 2</td>
<td>2.69</td>
<td>-3.03</td>
<td>2.39</td>
<td>-2.51</td>
<td>1.60</td>
<td>-1.79</td>
<td>1.50</td>
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<td>PO 3</td>
<td>2.06</td>
<td>0.10</td>
<td>2.43</td>
<td>1.41</td>
<td>1.73</td>
<td>0.58</td>
<td>1.82</td>
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<td>PO 4</td>
<td>2.01</td>
<td>0.31</td>
<td>2.05</td>
<td>-0.83</td>
<td>1.93</td>
<td>-1.40</td>
<td>1.49</td>
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<tr>
<td>PO 5</td>
<td>2.49</td>
<td>-2.03</td>
<td>2.64</td>
<td>-1.22</td>
<td>2.33</td>
<td>0.17</td>
<td>2.46</td>
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<td>PO 6</td>
<td>3.2</td>
<td>1.81</td>
<td>3.51</td>
<td>0.68</td>
<td>3.41</td>
<td>-0.88</td>
<td>2.25</td>
</tr>
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<td>PO 7</td>
<td>1.91</td>
<td>0.83</td>
<td>2.69</td>
<td>0.28</td>
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<td>PO 8</td>
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<td>1.81</td>
<td>2.54</td>
<td>1.70</td>
<td>0.65</td>
<td>1.76</td>
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<td>PO 9</td>
<td>1.86</td>
<td>-0.54</td>
<td>2.07</td>
<td>1.20</td>
<td>1.39</td>
<td>0.98</td>
<td>1.69</td>
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</table>
Artifact Resistance of Newest Generation of Pulse Oximeters in Volunteers Undergoing Hypoxemia

Hartmut Gehring, MD; Christoph Hornberger, PhD; Holger Matz, ME; Ewald Konecny, PhD; Peter Schmucker, MD
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Background: When it is necessary to abandon pulse oximeter monitoring, temporarily or permanently, the most common reasons are restricted peripheral perfusion and movement artifacts. The objective of this study therefore was to test the effects of motion artifact and/or low perfusion on the performance of a new generation of pulse oximeters in healthy adult volunteers undergoing hypoxemia. Special attention was directed to \( \text{SpO}_2 \) and pulse rate accuracy, and to the handling of warning messages. Methods: During episodes of induced hypoxemia in ten healthy volunteers a continuous recording was made of \( \text{SpO}_2 \) and pulse rate and of signal-quality warnings. Five different pulse oximeters from four different manufacturers were tested: Datex-Ohmeda 3900, Agilent Technologies (formerly Hewlett-Packard) CMS monitor software Rev. B.0, Nellcor/Mallinckrodt N-3000 and N-395, and a Schiller OX-1 (the European version of the US Masimo/Ivy 2000) with Masimo SET ™ technology. Volunteer test subjects participated after written informed consent and approval by the Ethics Committee. Motion artifacts were generated using exogenous motion generated by a standardized and repeatable motion machine as well as by having the test subject perform voluntary tapping and scratching motions. Perfusion to the finger was reduced by use of an inflatable balloon impinging on the brachial artery. The pulse oximeters' readings were compared to control pulse oximeters (Nellcor N-3000) on an unperturbed reference hand. Pulse rates from the test oximeters were compared to an ECG-derived heart rate. Warnings that alerted the user to possible untrustworthiness of the displayed value were analyzed.

Results: Performance of the different instruments was compared over a wide range of artifact influence. The percentage of time when the \( \text{SpO}_2 \) deviation was within ±3% \( \text{SpO}_2 \) of reference reading was >95% for all instruments without artifact simulation.

For the most difficult situation for pulse oximeters, which was the combination of motion and reduced perfusion, the percentage of errors exceeding given limits are listed in table 1. The first two rows give the percentage of \( \text{SpO}_2 \) error larger than ±3 % and ±6 % respectively. In the third row the percentage of \( \text{SpO}_2 \) error > 10% is given in situations when the pulse oximeter gave no warning message. In the last row the pulse rate errors exceeding 25 bpm are listed.

Table 1: Percentage of \( \text{SpO}_2 \) and pulse rate errors during the period of motion and reduced perfusion

<table>
<thead>
<tr>
<th></th>
<th>Agilent</th>
<th>Datex-Ohmeda</th>
<th>Masimo/Ivy</th>
<th>N-3000</th>
<th>N-395</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{SpO}_2 )-error &gt;3%</td>
<td>50%</td>
<td>41%</td>
<td>43%</td>
<td>52%</td>
<td>38%</td>
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<tr>
<td>( \text{SpO}_2 )-error &gt;6%</td>
<td>26%</td>
<td>21%</td>
<td>27%</td>
<td>26%</td>
<td>13%</td>
</tr>
<tr>
<td>( \text{SpO}_2 )-error &gt;10% and no warning</td>
<td>6.5%</td>
<td>8.6%</td>
<td>14%</td>
<td>5.1%</td>
<td>2.1%</td>
</tr>
<tr>
<td>pulse error &gt;25 bpm</td>
<td>8.5%</td>
<td>53%</td>
<td>1.1%</td>
<td>37%</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

Conclusion: Combining performance with respect to \( \text{SpO}_2 \) accuracy, pulse rate accuracy and alarm handling, the Nellcor N-395 was best, followed by the Agilent and the Masimo/Ivy2000. The performance of the Datec-Ohmeda is lowered by poor pulse rate accuracy. The Nellcor N-3000, one of the best instruments of the previous generation, placed last in the evaluation.
Near-Patient Determination of Mannitol for the Monitoring of Irrigating Fluid Absorption

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Introduction: Mannitol is an osmotically active component of irrigation fluid used for endoscopic interventions involving electrocoagulation, such as transurethral resection of the prostate (TURP) or hysteroscopy with endometrial ablation. Near-patient determinations of mannitol concentrations would allow not just a reliable detection of irrigation fluid absorption, but also an estimation of the volume absorbed (1), and represents a clear alternative to the established ethanol monitoring (2). The aim of the present study was to develop a new simple near-patient photometric assay for determining mannitol concentration in human blood and to compare this method with the ethanol monitoring procedure (1,2) in patients with TURP.

Method: The photometric assay is based on the enzymatic oxidation of mannitol catalyzed by a commercially available mannitol dehydrogenase (mannitol:NAD oxidoreductase EC 1.1.1.67) preparation isolated from Leuconostoc mesenteroides. For this assay, serum or blood is deproteinized with ice-cold trichloroacetic acid and the supernatant is mixed with NAD and the enzyme before it is incubated at pH 8.0 and 37 °C for between 30 and 60 minutes. At the end of incubation, the solution is diluted as appropriate and the concentration of NADH formed by mannitol oxidation is determined photometrically at 340 nm. In the clinical investigation patients undergoing TURP with general anesthesia were investigated after acquiring their written informed consent and with approval by the Ethical Committee. The irrigation fluid used during surgery (0.5 % mannitol, 2.7 % sorbitol) contained 0.75 % (w/v) ethanol.

Results: The lower limit of detection of serum mannitol was 0.1 mmol/l and the linear range of measurement extended to about 4 mmol/l. At mannitol concentrations of 0.48, 1.30, and 3.41 mmol/l, interassay coefficients of variation of 8.8, 6.5, and 4.7 % were obtained. Of 23 different monosaccharides and polyalcohols tested, none exhibited a measurable substrate activity and only D-fructose significantly inhibited the oxidation of mannitol at concentrations of 5 (<5 %) and 25 mmol/l (23 %). Measurement of mannitol and ethanol concentration in serum from patients undergoing TURP revealed a linear correlation (R² = 0.79, see fig. 1).

Conclusions: The patient-near determination of mannitol in human blood using the photometric assay described seems to be suitable as a new tool for detecting irrigation fluid absorption during and after endoscopic surgery.


Figure 1