Comparison of Near-Infrared Spectroscopy and Somatosensory Evoked Potentials for the Detection of Cerebral Ischemia During Carotid Endarterectomy

Ulrich Beese, MD; Harald Langer, MD; Werner Lang, MD; Michael Dinkel, MD

Background and Purpose—We sought to assess the clinical value of regional cerebral saturation (rSO2) obtained by means of the cerebral oximeter INVOS 3100A (Somanetics) in comparison to monitoring of somatosensory evoked potentials (SEP) for the reliable detection of severe cerebral ischemia requiring shunt placement in the individual patient undergoing carotid surgery under general anesthesia.

Methods—In 317 patients undergoing reconstructive surgery on the internal carotid artery, simultaneous recordings of SEP and rSO2 were obtained throughout the operation.

Results—All 287 patients with preserved cortical SEP remained neurologically intact. Shunt placement was performed in 27 patients (9%) after flattening of cortical SEP during cross-clamping of the internal carotid artery. A stable rSO2 value just before cross-clamping and the lowest value after cross-clamping were registered, and the decrease was calculated. A statistically significant (P<0.01) decrease of rSO2 after cross-clamping could be found in patients without (64.9±8.3% to 60.9±9.9%) as well as in patients with consecutive loss of cortical SEP (65.8±9.1% to 56.1±13.4%). The difference of the decrease of rSO2 in both groups was highly significant (6.9±9.0% versus 15.6±14.0%; P<0.001).

However, substantial interindividual variability of rSO2 and derived change of rSO2 did not allow the definition of a threshold value indicating need of shunt placement.

Conclusions—The reliability of SEP for the detection of clamp-related hypoperfusion has been reaffirmed. As long as rSO2 threshold values indicating critical cerebral ischemia are not defined, therapeutic interventions based on monitoring with the cerebral oximeter INVOS 3100A are not justified. (Stroke. 1998;29:2032-2037.)

Key Words: carotid stenosis # cerebral ischemia # evoked potentials, somatosensory # intraoperative monitoring # oximetry # surgery

The efficiency of surgical therapy for prevention of stroke in patients with >70% carotid stenosis has recently been clarified. The inherent risk of surgery is perioperative stroke. A major cause of cerebrovascular accidents is hypoperfusion during cross-clamping of the internal carotid artery (ICA). The prompt and reliable recognition of insufficient collateralization is crucial for a good neurological outcome of patients. General use of an intraluminal shunt bears the risk of embolization and undetected shunt malfunction. Therefore, proper neuromonitoring needs to identify patients who will benefit from shunt placement not only with a high sensitivity but with a high specificity as well.

The use of electroencephalography, somatosensory evoked potentials (SEP), and transcranial Doppler sonography are established forms of neuromonitoring in patients undergoing carotid surgery. However, technical expertise and experience in interpreting the results of these monitors are necessary.

Cerebral oximetry appears to be an attractive alternative because it relies on a continuous, noninvasive measurement principle and is easy to use. Previous studies provided evidence that changes in cerebral oxygenation caused by cross-clamping of the ICA can be monitored by means of near-infrared spectroscopy (NIRS). Since no “gold standard” with which to test the sensitivity and specificity of cerebral oximetry exists, the results of NIRS need to be compared with other validated forms of neuromonitoring. A loss of cortical SEP is a good indicator of cerebral hypoperfusion and is able to identify patients at risk for intraoperative stroke. However, given the relatively low incidence of clamp-related ischemia in carotid surgery, it is obvious that a large number of patients must be studied to obtain sufficient data from patients developing severe cerebral ischemia. This could not be accomplished by previously published studies.

After validating the results of SEP with the individual neurological outcome of the patients, we compared the changes of cortical SEP and regional cerebral saturation (rSO2), obtained by the cerebral oximeter INVOS 3100A,
Subjects and Methods

After approval by the local ethics committee of the medical faculty of the University of Erlangen-Nuremberg and after we obtained informed and written consent, 317 patients (215 men, 102 women) aged 42 to 89 years were included. Preoperative neurological classification and angiographic findings are summarized in Table 1.

Patients with known arterial hypertension or coronary artery disease were instructed to take their usual antihypertensive or antianginal medications until the day of the operation. A standard antihypertensive protocol the mean value in the last 2 minutes before clamping was noted. When the carotid complex was exposed, the lowest value was documented as the calculated change of $rSO_2$ between patients with preserved and those without cortical SEP and SEP loss were performed with the Mann-Whitney U test.

Results

Reconstruction of the ICA was successfully completed in all 317 patients. The most commonly performed procedures were thromboendarterectomy with patch closure (n=208, 65.6%) and eversion endarterectomy (n=79, 24.9%). No deaths occurred during the observation period. The range of fluctuations for mean arterial pressure between the points at which preclamp and postclamp $rSO_2$ was determined was +18% to −14% for the studied population. The mean duration of carotid cross-clamping was 35 ± 11 minutes, with a range of 7 to 106 minutes.

Continuous recording of SEP and $rSO_2$ was possible in all patients.

All patients were extubated in the operation theater. At this point patients were tested for the development of any new neurological deficit. Patients were followed until the time of discharge from the hospital.

Mean ± SD values are expressed. The Wilcoxon test was used to compare $rSO_2$ values before and after cross-clamping of the ICA. Comparisons of $rSO_2$ values before and after cross-clamping as well as the calculated change of $rSO_2$ between patients with preserved cortical SEP and SEP loss were performed with the Mann-Whitney U test. All P values were 2-sided, and significance was assessed at the 0.05 level. A commercially available statistical package, SPSS for Windows, version 6.1 (SPSS Inc) was used for performing the statistical analysis.

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TABLE 3. Comparison of rSO2 Before (rSO2-1) and After Carotid Cross-clamping (rSO2-2) and the Calculated Decrease of rSO2 (ΔrSO2=rSO2-1−rSO2-2) in Patients With and Without SEP Loss During Cross-clamping of the ICA

<table>
<thead>
<tr>
<th></th>
<th>SEP Preserved (n=287)</th>
<th>SEP Loss (n=30)</th>
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<tbody>
<tr>
<td>rSO2-1</td>
<td>64.9±8.3 (39–87)</td>
<td>65.8±9.1 (44–76)</td>
</tr>
<tr>
<td>rSO2-2</td>
<td>60.9±9.9 (30–87)*</td>
<td>56.1±13.4 (12–74)*</td>
</tr>
<tr>
<td>ΔrSO2</td>
<td>4.1±4.8 (−9–34)†</td>
<td>9.8±6.7 (0–32)†</td>
</tr>
</tbody>
</table>

Values are median±SD (range), expressed as percentages. Patients with SEP loss had lower rSO2 values after carotid cross-clamping (*P<0.05, Mann-Whitney U test) and a higher decrease from the preclamp value (†P<0.001, Mann-Whitney U test).

SEP remained neurologically intact after surgery. In 30 patients (9.5%), an SEP loss with unaffected cervical components occurred during the clamping phase. In 27 of these patients shunt placement was performed. Cortical SEP recovered after shunt placement in all patients. Three patients were not shunted despite a loss of SEP. The reasons were hypoplastic vessel (1 case) or SEP loss in the late clamping phase and impairment of arteriotomy closure (2 cases). In 1 of these patients cortical SEP was restored by carotid declamping within 6 minutes; the patient remained neurologically intact. The other 2 patients and 4 patients who received an intraluminal shunt during cross-clamping of the ICA awoke with a new neurological deficit on the side of the endarterectomy. That deficit resolved completely within 12 hours in all patients.

Corresponding preclamp and postclamp rSO2 values, as well as the calculated change of rSO2 (ΔrSO2) for patients with preserved SEP and SEP loss during cross-clamping of the ICA, are summarized in Table 3. On average the initial absolute values of regional cerebral oxygenation in patients with or without later SEP loss were nearly identical; however, considerable variability was noted. In both groups a statistically significant decrease of rSO2 (P<0.01 by nonparametric Wilcoxon test) after cross-clamping was found. Patients with restricted cerebral collateralization and consecutive loss of cortical SEP after cross-clamping had significantly lower rSO2 values than patients with unaffected SEP (P<0.05; nonparametric Mann-Whitney U-test). The difference of the calculated change of rSO2 in both groups of patients was highly significant (P<0.001; nonparametric Mann-Whitney U-test). However, the magnitude of change again showed a high variability (Figure 1).

As the accuracy parameters in Table 4 indicate, no critical threshold value of ΔrSO2 could be defined that could identify patients with SEP loss who would benefit from shunt placement.

Discussion

Reconstructive surgery at the carotid bifurcation is particularly suitable to evaluate NIRS as a new form of neuromonitoring.15 In addition to the fact that cross-clamping of the ICA offers a well-defined period in which cerebral damage due to hypoperfusion is most likely to occur, the results of cerebral oximetry can be compared with other simultaneously em-

TABLE 4. Results of Validating Decrease of rSO2 (ΔrSO2) Against SEP Loss During Carotid Cross-clamping

<table>
<thead>
<tr>
<th>ΔrSO2</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5</td>
<td>76</td>
<td>64</td>
<td>18</td>
<td>96</td>
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<tr>
<td>&gt;10</td>
<td>40</td>
<td>88</td>
<td>27</td>
<td>93</td>
</tr>
<tr>
<td>&gt;15</td>
<td>17</td>
<td>97</td>
<td>36</td>
<td>92</td>
</tr>
<tr>
<td>&gt;20</td>
<td>7</td>
<td>99</td>
<td>50</td>
<td>91</td>
</tr>
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</table>

Different thresholds for ΔrSO2 were used for calculations.
develop. This should answer the question of whether NIRS can replace SEP, which is more technically demanding.

The results of our study confirmed that SEP monitoring reliably identifies patients with impending cerebral damage, since all patients with preserved cortical SEP remained neurologically intact. In 30 patients (9.5%), a loss of cortical evoked potentials was found after cross-clamping of the ICA. Six patients (1.8%) awoke with a new neurological deficit, which was transient in all cases.

Previous studies had demonstrated that absolute numbers of rSO2 are of little value in interpreting results obtained by means of INVOS 3100A.7,9,10,21-30 That is why the definition of "normal values" for rSO2 is highly questionable.

Misra and colleagues28 recently reported wide scattering of rSO2 values obtained by normal subjects. Using the same kind of cerebral oximeter, Samra et al9 found a similar high variability in awake patients undergoing carotid endarterectomy under regional anesthesia. They noted that a wide range of rSO2 values are obviously unrelated to neurological dysfunction. The results of our study confirmed the variability of this parameter. Accordingly, we focused our interest on the individual change of rSO2. For the calculation we used a stable value just before cross-clamping of the ICA and the lowest stable value after cross-clamping. The use of a stable value after cross-clamping should ensure that autoregulatory changes were taken into account, increasing the specificity of the derived threshold value. Two minutes were allowed for stabilization because results by Lam and coworkers31 suggest that autoregulation after cross-clamping usually occurs within 1 minute. Since the blood pressure was kept stable throughout the procedure, the displayed rSO2 values could be expected to reflect the changed oxygen balance of cerebral tissue after application of the cross-clamp.

On average, rSO2 values in patients with SEP loss after carotid cross-clamping were lower than in patients with preserved cortical SEP. In turn, the calculated decrease of rSO2 was significantly higher in patients with SEP loss. However, no calculated value would reliably identify patients with SEP loss who will benefit from shunt placement with high sensitivity and acceptable specificity and predictive power. Given a residual error of the displayed readings of ±10%,28 an arbitrary threshold value of >10% decrease of rSO2, as done by Duffy et al,20 is not appropriate. Therefore, selective use of an intraluminal shunt based exclusively on the results of NIRS cannot be recommended.

Whether a reduction of interindividual variability can be achieved is uncertain for various reasons. As suggested by Kurth and Uher,32 this variability originates in the continuous-wave NIRS technology, since there is no way to measure optical path length and absorption. Therefore, the algorithm for calculation of rSO2 is based on several assumptions, which may lead to an oversimplification of that very complex issue.11,30,31 Anatomic variations leading to differences of extracranial layers of scalp, skull, and cerebrospinal fluid need to be considered as well as changes resulting from biological variations in cerebral hemoglobin concentration.27,20,30 The estimated proportions of blood in the venous, arterial, and capillary compartments are assumed to be stable. However, the fulfillment of this condition in a clinical situation is difficult to verify.24,30 A sudden decrease of cerebral blood flow during cross-clamping of the ICA under general anesthesia is possibly the closest approximation.16 If variability of rSO2 values unrelated to neurological function occurs under these circumstances, the usefulness of this device in more complex clinical situations such as intensive care patients or patients undergoing cardiac surgery must be questioned.53

Since early concerns were raised by Harris and Bailey41 in 1993, the issue of extracranial contamination of the derived signal has been a matter of considerable debate. Based on experimental studies on artificial models, there is evidence that changing emitter-detector separation will cause differential spatial resolution.35 The fixed interoptode spacing of 3 and 4 cm in the INVOS 3100A sensor is supposed to ensure that by subtracting the signals from superficial layers, extracranial contamination can be effectively reduced.10 This assumption has been challenged by various authors.27,36 Obviously, the fixed interoptode spacing of the sensors will lead to differences in the effectiveness of reducing extracranial contamination due to differences in the anatomy of the patient’s skull.30,31 In contrast to other applications, carotid surgery provides the unique opportunity of selectively clamping the external carotid artery, thereby greatly reducing the influence of extracranial tissue. Studies in which sequential clamping of the external carotid artery before the ICA was performed provided contradictory results. Duncan and colleagues2 found a nonsignificant fall of the displayed rSO2 after clamping of the ECA. Using a different type of cerebral oximeter (NIRO-500, Hamamatsu), Lam and coworkers31 showed that the contribution of extracranial vascular circulation to the results of NIRS was significant. In contrast to the study by Duncan, parallel monitoring of superficial blood flow by means of laser-Doppler flowmetry was used. This offers the advantage of controlling extracranial contamination, making collateral flow from the contralateral side detectable. Furthermore, this monitor will track blood pressure fluctuations that predominantly influence in a pressure-passive fashion the extracranial vascular territory and are a significant source of artifact. We believe that in future investigations efforts should be made to adopt this proceeding and not to rely on spatial resolution claimed for the SomaSensor used in the INVOS 3100A. The importance of extracranial contamination was highlighted in a recently published study by Kirckpatrick et al.37 Using the same device as in the study by Lam, the authors were able to identify all patients with severe cerebral ischemia, as indicated by a fall of MCA velocity >60% or sustained fall in cortical electric activity by means of a derived parameter of NIRS. However, this threshold was only apparent when extracranial contamination was reduced by previous clamping of the ECA. In our study we did not try to resolve the extracranial and intracranial vascular territories by sequential clamping of the carotid arteries. Therefore, it is possible that the displayed rSO2 values are heavily influenced by extracranial contamination. However, the results of our study showed that severe cerebral ischemia, as indicated by cortical SEP loss, occurred in some patients with minimal or even no change of the displayed regional cerebral oxygenation. Removal of extracranial con-
tamination will probably increase specificity of derived threshold values, indicating need for intervention. However, most important for the outcome of the patients and the value of the monitoring device is prompt recognition of all patients with impending cerebral ischemia.

The discrepancy between cortical SEP loss and no or minimal change of rSO₂ after carotid cross-clamping might be attributed to the different monitoring areas. Given the low spatial resolution of the measurement system,²⁹,³⁰ placement over the parietal middle cerebral artery territory, as advocated by Williams and coworkers,¹⁰,²² might lead to a better agreement between SEP monitoring and NIRS.¹⁹ However, this approach is hampered by the necessity of shaving an area of the skull without having to shave them first needs to be addressed by the manufacturers. Interestingly, the threshold values indicating severe cerebral ischemia in the study by Kirkpatrick et al²⁷ could be defined with sensors placed over the patient’s forehead, the same area as recommended for the Soma-Sensor INVOS system.²⁸

Further studies are needed to evaluate the importance of probe positioning for the sensitivity and specificity of NIRS. As suggested by previous studies and our own clinical experience, NIRS appears to work extremely well in some cases.⁷,⁹,¹⁹ As shown in Figure 2, a dramatic fall of rSO₂ occurred immediately after cross-clamping of the ICA in a patient in whom an SEP loss was documented. In addition, rSO₂ showed a prompt recovery after shunt insertion and a hyperperfusion phenomenon after definite declamping. The fall of rSO₂ occurred much earlier than the loss of the cortical SEP because reduction of cerebral perfusion leads to predominantly venous desaturation, and concomitant fall of rSO₂ before cerebral dysfunction occurs. However, the clinical relevance of an early detection of impending cerebral ischemia before cerebral dysfunction remains unclear, since no patient in our series developed sustained neurological deficits when shunt placement was performed after the complete loss of cortical SEP. A possible relationship between changes in cerebral oxygenation and more subtle adverse neurological outcome, such as cognitive deterioration, needs to be addressed in further studies.³⁹

The advantage of NIRS is that it is easy to use and that it offers a real-time and noninvasive means for the assessment of cerebral oxygenation. Unfortunately, these advantages cannot outweigh the represented methodological problems in the cerebral oximeter INVOS 3100A. Since our study and previous investigations² were unable to define a threshold value indicating severe cerebral ischemia in individual patients, we would not advise therapeutic interventions based on obtained rSO₂.²⁵-²⁷,³⁰ and would suggest not using this instrument for detection of cerebral ischemia in patients undergoing carotid endarterectomy under general anesthesia.

References


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