Bedside Assessment of Cerebral Vasospasms After Subarachnoid Hemorrhage by Near Infrared Time-Resolved Spectroscopy

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Abstract We examined the usefulness of near infrared time-resolved spectroscopy (TRS) for detection of vasospasm in subarachnoid hemorrhage (SAH). We investigated seven aneurysmal SAH patients with poor clinical conditions (WFNS grade V) who underwent endovascular coil embolization. Employing TRS, we measured the oxygen saturation (SO_2) and baseline hemoglobin concentrations in the cortices. Measurements of TRS and transcranial Doppler sonography (TCD) were performed repeatedly for 14 days after SAH. In four of the seven patients, the SO_2 and hemoglobin concentrations measured in the brain tissue of the middle cerebral artery territory remained stable after SAH. However, in three patients, TRS revealed abrupt decreases in SO_2 and total hemoglobin between 5 and 9 days after SAH. Cerebral angiography performed on the same day revealed severe vasospasms in these patients. Although TCD detected the vasospasm in two of three cases, it failed to do so in one case. TRS could detect vasospasms after SAH by evaluating the cortical blood oxygenation.

1 Introduction

Arterial vasospasm is the most common cause of delayed ischemic neurological deficits in patients with aneurysmal subarachnoid hemorrhage (SAH) [1]. Transcranial Doppler sonography (TCD) has been used to detect vasospasms after SAH [2–4], but its sensitivity is not high [3, 5–7]. In addition, TCD does not provide information about the cerebral circulation and oxygenation in the cortex. A simple, non-invasive method for bed-side assessments of cerebral ischemic status is still required. In this pilot study, we examined whether near infrared time-resolved spectroscopy (TRS), which permits quantitative measurement of the Hb concentrations [8], can detect cerebral ischemia caused by

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E. Takahashi, D.F. Bruley (eds.), *Oxygen Transport to Tissue XXXI*,
Advances in Experimental Medicine and Biology 662,
DOI 10.1007/978-1-4419-1241-1_73,

vasospasm in patients with aneurysmal SAH. Initially, we measured normal values for the Hb concentrations and oxygen saturation (SO_2) in various cortical regions of normal adults. We then repeatedly measured the SO_2 and Hb concentrations in patients after SAH, and these data were compared with the results of TCD. In addition, we evaluated whether TRS measurements on day 1 after SAH can be useful for predicting the occurrence of vasospasm and clinical outcome.

2 Methods

We evaluated seven patients with poor clinical condition (e.g. WFNS grade V) who had undergone embolization of their aneurysms within 24 h after SAH using Guglielmi detachable coils. The hemorrhagic pattern on initial CT scan was assigned to Fisher group III in all patients. The systemic blood pressure, systemic oxygen saturation, Hb concentrations, and hematocrit were maintained within normal ranges during the course of the examinations; there were no significant differences in Hb concentration or hematocrit between the patients and controls. This study was approved by the Committee for Clinical Trials and Research on Humans of Nihon University School of Medicine, and the ethical committee of our university hospital approved the protocol. We measured the baseline concentrations of Hb in the subjects with a TRS-10 system (Hamamatsu Photonics K.K. Hamamatsu, Japan), which has been used in several studies on normal adults [9, 10] and newborn infants [11]. The optical probes were attached to mainly the MCA territory of the temporal lobes with an optode distance of 3 cm, since these areas are commonly affected by vasospasm after SAH. Details of this system have been described by us previously (Fig. 1) [9, 12]. To determine the reduced scattering coefficient (μ_s') and absorption coefficient (μ_a) at each wavelength first, we fit a solution of a semi-infinite homogeneous media with zero boundary condition in reflectance model [13] into the observed temporal profiles obtained from TRS using the non-linear least squares method. Based on the assumption that light absorption in the living body in this wavelength region occurs from oxy-Hb, deoxy-Hb and water, and also that there is no other background absorption in the living body [14], the concentrations of oxy-Hb, deoxy-Hb, total Hb (= oxy-Hb + deoxy-Hb; tHb) and SO_2 were calculated using the obtained μ_a each wavelength [9]. The concentrations of Hb were expressed in mM. TRS measurements were performed repeatedly for 14 days after the onset of SAH. The blood flow velocity in the MCA (M1 portion) was measured by TCD (EME Transcranial Doppler System, Nicolet Biomedical Inc., WI, USA); a 2-MHz-pulsed Doppler probe was used via the transtemporal window. TCD measurements were performed repeatedly by the same investigator (S.N.) for 14 days after SAH. Occurrence of vasospasm was considered to take place when the mean flow velocity was greater than 120 cm/s [5].

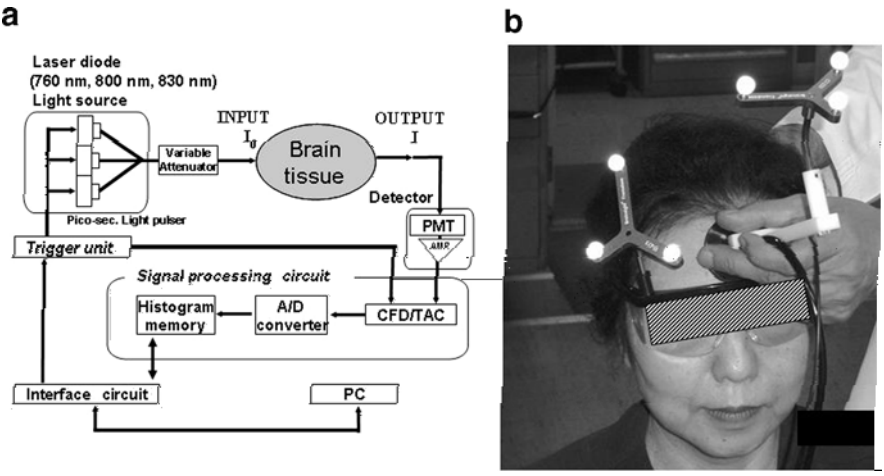

Fig. 1 (a) Block diagram of the TRS-10 system. (b) Placement of optical fibers on the head. A frameless stereotaxic system was used for identification of the TRS measurement sites on the cortex

3 Results

In four of the seven patients, TRS demonstrated only small changes in SO_2 and oxy-Hb, deoxy-Hb and t-Hb concentrations in the MCA territory during the course of the examinations (Fig. 2). Cerebral angiography performed at 7 days after SAH did not reveal vasospasms in these patients. In contrast, the three other patients (patients No.1, 2, and 7) showed abrupt decreases in SO_2 and tHb between 5 and 9 days after SAH. The cerebral angiography performed on the same day demonstrated severe vasospasms of the MCA in these patients. Figure 3 represents an example (patient No. 2) of the chronological changes in SO_2 and t-Hb. TRS showed abrupt decreases of SO_2 and tHb at 5 days after SAH. Intra-arterial injection of fasudil hydrochloride (30 mg) relieved the vasospasm and increased the SO_2 and t-Hb to the previous levels. TCD, however, failed to detect the vasospasm in this patient (flow velocity of the MCA < 100 cm/s); it revealed an acceleration of blood flow velocity indicative of vasospasm in the other two cases.

4 Discussion

The present study represents the first application of TRS to patients with SAH. Prior to this study, we have assessed the reliability of TRS measurements by undertaking simultaneous measurements of TRS and PET in normal adults [9]. We revealed significant correlations between the changes in TRS-measured

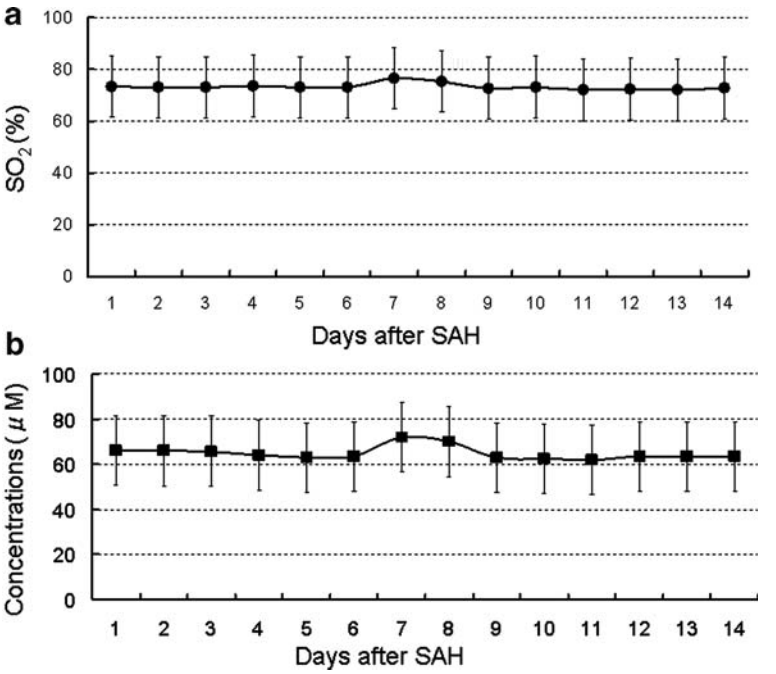

Fig. 2 Typical changes of SO_2 (a) and t-Hb (b) in the MCA territory of SAH patients without vasospasms. The ordinates in a and b indicate the oxygen saturation (%) and Hb concentrations (mM), respectively. The abscissae indicate the number of days after SAH. The error bars are standard deviation

CBV and PET-measured CBV in the corresponding cortical region during acetazolamide administration at optode spaces of 2–5 cm. These findings indicate that the present TRS measurements (3 cm of optode distance) reflected the Hb concentrations in the cortex. By means of TRS, we were able to detect the occurrence of vasospasm in all three patients with angiographical vasospasm, while TCD failed to detect vasospasm in one of them. It should be noted that TRS detects vasospasm by evaluating the ischemic status (i.e., decreases of SO_2 and t-Hb) in the cortex caused by vasospasms, and can therefore detect vasospasms regardless of the affected artery insofar as vasospasm causes cortical ischemia which decreases the SO_2 and t-Hb. In contrast, TCD could fail to detect vasospasms extending to the peripheral MCA because narrowing of the peripheral MCA increases the vascular resistance, which tends to suppress the acceleration of blood flow in the M1 segment [15]. Our results suggest that TRS is more sensitive than TCD for detecting vasospasms after SAH, although further studies are needed to clarify the differences in sensitivity and specificity between TRS and TCD. The limitations of TRS require discussion. Firstly, the Hb concentrations measured by TRS are the average concentrations within the illuminated area including the extracranial and intracranial tissues. At present,

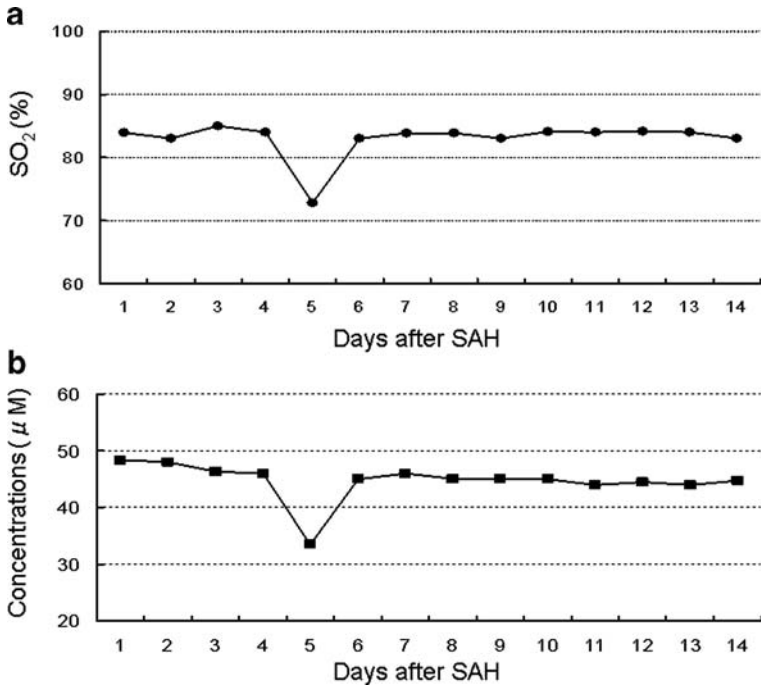

Fig. 3 Changes of SO_2 (a) and t-Hb (b) in the MCA territory of an SAH patient with vasospasm (patient No. 2). The ordinates in a and b indicate the oxygen saturation (%) and Hb concentrations (mM), respectively. The abscissa indicate the number of days after SAH

selective measurement of the Hb concentrations in the brain is difficult because the absorption coefficient (m_a) of each compartment of the head including the brain tissue in living humans is not available. In addition, the contribution ratio of the NIRS signal of the brain tissue remains under discussion, although several studies on NIR light propagation in the human head have been performed [16, 17]. Recently, Liebert et al. have attempted to differentiate between the absorption changes occurring in the intra- and extracerebral compartments of the head by employing TRS and a bolus of indocyanine green (ICG) [18]. Secondly, TRS yields a mixed arterial venous signal in the cortex; however, the contribution ratios of the vascular compartments are not yet clear [8]. In the present study, the mean values of SO_2 in the controls were similar to those of SjO_2 in patients with unruptured aneurysms [19], suggesting that TRS measures the blood oxygenation predominantly in the venous compartment. Thirdly, NIR light propagation in the brain with SAH may differ from that in the normal brain, since the cerebrospinal fluid in the subarachnoid space exerts a significant effect on photon migration within the brain [16]. Finally, TRS may not evaluate the cerebral circulation correctly in patients whose anatomical structures of the head including the brain and skull are not normal. Further

studies such as comparisons of TRS measurements of the skin, the skull and the cortex are needed.

5 Conclusion

Although our preliminary data from a small number of patients cannot provide firm conclusions, we consider that TRS may be a useful tool for evaluating the cerebral circulatory status in SAH patients. TRS can detect vasospasm by evaluating the cortical ischemic status, and may be more sensitive than TCD, which assesses the blood flow velocity in the M1 portion. In addition, TRS performed on day 1 after SAH may be useful for predicting the occurrence of vasospasm and clinical outcome. Finally, TRS may be applicable for evaluation of the ischemic status in acute stroke patients.

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