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Clinical Study

Initial clinical experience with near-infrared spectroscopy in assessing cerebral tissue oxygen saturation in cerebral vasospasm before and after intra-arterial verapamil injection

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ABSTRACT

Cerebral vasospasm is a devastating complication after subarachnoid hemorrhage. The use of cerebral tissue oxygen saturation ($SctO_2$) to non-invasively assess changes in cerebral tissue perfusion induced by intra-arterial (IA) verapamil treatment has not been described to our knowledge. A total of 21 consecutive post-craniotomy patients scheduled for possible IA verapamil treatment of cerebral vasospasm were recruited. The effect of IA verapamil injection on $SctO_2$ being continuously monitored on both the left and right forehead was investigated. Comparisons between changes in $SctO_2$ monitored on the ipsilateral and contralateral forehead in relationship to the side of internal carotid artery (ICA) injection were performed. A total of 47 IA verapamil injections (15 left ICA, 18 right ICA, and 14 vertebral artery injections) during 18 neurointerventional procedures in 13 patients were analyzed. IA verapamil administration led to both increases and decreases in $SctO_2$. Changes in $SctO_2$ ipsilateral to the ICA injection side were more pronounced ($p = 0.02$ and 0.07 for left and right ICA injections, respectively) and favored compared to contralateral $SctO_2$ changes. We were unable to obtain reliable measurements on the side ipsilateral to the craniotomy during four procedures in three patients, presumably secondary to pneumocephalus. The local cerebral vasodilating effect of IA verapamil injection is suggested by the differential changes in $SctO_2$ ipsilateral and contralateral to the ICA injection side. The inconsistent changes in $SctO_2$ and the limitations of applying cerebral oximetry in this patient population needs to be recognized.

1. Introduction

Cerebral vasospasm secondary to subarachnoid hemorrhage (SAH) is a devastating disease. Avoidance of vasospasm related cerebral ischemia remains challenging [1]. The purpose of intra-arterial (IA) verapamil therapy is to dilate the spastic cerebral artery/arteriole [2–8] and the efficacy of this technique can be evaluated using angiographically measured changes in the diameter of the spastic artery [4–8], in addition to symptomatic improvements [4,5]. However, the efficacy may be difficult to assess as changes in arterial caliber are often delayed in the case of IA verapamil injection without angioplasty, and neurologic examination often cannot be performed intraprocedurally. Furthermore, these assessments provide no objective information regarding therapeutic effects on cerebral tissue perfusion. A tool that can continuously and non-invasively assess changes in cerebral tissue perfusion induced by IA verapamil treatment may facilitate the diagnosis and treatment of cerebral vasospasm.

Cerebral tissue oxygen saturation ($SctO_2$) measured using near-infrared spectroscopy assesses the balance between cerebral tissue oxygen consumption and supply in superficial brain regions continuously and non-invasively [9,10]. It is used as a surrogate of cerebral tissue perfusion [11]. Although cerebral oximetry has been applied in various clinical settings [12], its use in patients undergoing IA verapamil treatment of SAH-induced cerebral vasospasm has not been reported to our knowledge. In this pilot observational study, our objective was to determine the effect of IA verapamil injection on $SctO_2$ in patients with cerebral vasospasm.

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We hypothesized that IA verapamil injection would cause an increase in ipsilateral $SctO_2$ within 15 minutes as a consequence of cerebral vasodilation and increased cerebral blood flow.

2. Methods

The study was approved by the Institutional Review Board at the University of California, San Francisco. Both verbal and written informed consent was obtained from either the competent patients or the patients' surrogates.

2.1. Study population

Patients were recruited from our institutional Neurointensive Care Unit. The inclusion criteria were: (1) SAH due to a ruptured aneurysm or arteriovenous malformation; (2) cerebral vasospasm based on clinical signs and symptoms, with or without transcranial Doppler evidence; (3) a high likelihood of IA verapamil injection as determined by the treating neurointerventional radiologists; and (4) planned general anesthesia with endotracheal intubation for the neurointerventional radiology procedure.

2.2. Anesthesia and procedures

All patients received general endotracheal anesthesia for the procedure. Anesthesia was induced using intravenous lidocaine (1–2 mg/kg), propofol (1–3 mg/kg) and rocuronium (0.5–1 mg/kg), with or without fentanyl (1–2 mcg/kg) and maintained with sevoflurane (0.5–1.5 minimum alveolar concentration) at the discretion of the anesthesia team. The patients were monitored using standard American Society of Anesthesiologists monitoring and blood pressure was monitored via a radial arterial catheter. Blood pressure goals were established based on the agreement between intensivist, neuroradiologist and anesthesiologist by taking the patient's baseline value, bleeding risk and severity of vasospasm into consideration. The blood pressure was typically supported using phenylephrine infusion, with norepinephrine and vasopressin as alternative options. If applicable, the external ventricular drain was transduced and drained to achieve an intracranial pressure goal of less than 20 mmHg.

The neurointerventional radiology procedure was conducted with the patient in the supine position. The left or right groin area was punctured for vascular access, with or without ultrasound guidance. Transdermal nitroglycerin ointment was placed over a 1 square inch area on the left upper chest at the radiologist's request. Following the angiographical confirmation of vasospasm, 5–20 mg verapamil (0.5 mg/ml) was injected over 5–10 minutes into the corresponding artery, depending on the severity and location of vasospasm. Multiple injections were possible, either at the same location or at different locations during the same procedure. The interval between different injections was typically more than 10 minutes. The dose, time and location of verapamil injections were noted and performed at the discretion of the interventional neuroradiologist.

2.3. Monitoring

$SctO_2$ was monitored electronically every 2 seconds using a cerebral oximeter (FORE-SIGHT Elite; CASMED, Branford, CT, USA) with two probes placed on the left and right upper forehead, respectively. Pulse oximetry oxygen saturation (SpO_2), heart rate (HR) and perfusion index (PI) were also recorded every 2 seconds (Radical-7; Masimo Corporation, Irvine, CA, USA). Monitoring data from the anesthesia workstation (Aisys Carestation, GE Healthcare, Madison, WI, USA) were recorded every 2–5 seconds, including mean arterial pressure (MAP), minute ventilation (MV), end-tidal carbon dioxide ($EtCO_2$), end-tidal oxygen (EtO_2) and end-tidal anesthetic agent (EtAA).

2.4. Statistical analysis

The median values of the continuous data within a 30 second period were used for analysis. The pre-treatment (baseline) values were defined as measurements immediately before verapamil injection. Post-treatment values were defined as 15 minutes after the start of the IA verapamil injection. If a subsequent injection was given within 15 minutes of the previous injection, the measurements immediately before the following injection were used instead as the post-treatment values. The differences between post-treatment and pre-treatment values (Δ = post – pre) were used in analysis. To account for repeated measurements, linear mixed effect model was used to evaluate the effect of each variable including ΔMAP, ΔHR, ΔSpO_2, ΔPI, ΔMV, $\Delta EtCO_2$, ΔEtO_2, ΔEtAA and verapamil dose on left and right $\Delta SctO_2$. Age, sex, and body mass index were included as potential covariates. The effect of the location of IA verapamil injection (left internal carotid artery [ICA], right ICA, and vertebral artery [VA] with left and right combined) on $\Delta SctO_2$ ipsilateral and contralateral to the injection side was also investigated using the same analytical model. A p-value of <0.05 was considered significant. All data analysis was performed using the R package (https://www.r-project.org).

3. Results

A total of 21 patients were recruited in this study. Eight patients were excluded from the final analysis because six of them did not have vasospasm angiographically even though it was clinically suspected before the procedure, one patient had intra-procedural posterior cerebral artery rupture, and another patient had no measureable $SctO_2$ signal on both left and right forehead likely due to post-craniotomy pneumocephalus.

Data from 13 patients were included in analysis. The demographic characteristics, diagnosis and craniotomy approach were summarized in Table 1. All these patients had SAH with the bleeding source from a ruptured aneurysm in 12 patients and arteriovenous malformation in one patient. All these patients underwent craniotomy for either aneurysm clipping or arteriovenous malformation resection. In these 13 patients, 18 neurointerventional radiology procedures were performed with a total of 47 IA verapamil injections. These interventions were done on a median of 6.5 days post-craniotomy (range 1 to 13), corresponding to a median of 11 days post-SAH (range 2 to 19). None of these injections involved angioplasty. Fifteen injections were administered into the left ICA, 18 into the right ICA and 14 into the left or right VA combined.

The effect of IA verapamil injection on $SctO_2$ was inconsistent but more pronounced and favored on the side ipsilateral to the injection (Fig. 1). The $SctO_2$ either increased or decreased following verapamil injection; however, the $\Delta SctO_2$ ipsilateral to the side of ICA injection either increased more or decreased less than the contralateral side. If $SctO_2$ increased on one side of the forehead and decreased on the other, the side with the increase was ipsilateral to the side of ICA injection and the side with the decrease was contralateral. There were only two verapamil injections in the left ICA and two in the right ICA that had changes opposite to the above observations. The difference between ipsilateral and contralateral $\Delta SctO_2$ was significant when verapamil was injected into the left ICA ($p = 0.02$), and followed a similar trend when injected into the right ICA ($p = 0.07$) but was not significant when injected in to the VA ($p = 0.7$) (Table 2).