

The Effect of Intravenous Indigo Carmine on Near-Infrared Cerebral Oximetry

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The effects of IV-administered dyes on pulse oximetry have been well described. However, the effects on near-infrared cerebral oximetry have not been well documented. We report a series of four patients undergoing radical prostatectomy who were monitored with cerebral oximetry during surgery. After the administration of indigo carmine, intraoperative desaturations were observed for an extended period. Because clinical use of near-infrared cerebral oximetry is increasing, anesthesiologists should be aware of this issue.

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We describe the effects of IV-administered indigo carmine on cerebral oximetry readings (regional cerebral saturation, rSO_2) in four patients undergoing radical retropubic prostatectomy. These four patients were part of a study investigating intraoperative cerebral desaturations, as measured by the INVOS® near-infrared cerebral oximeter (Somanetics Corp., Troy, MI), and were the only ones who received indigo carmine (as part of their routine surgical care). INVOS self-adhesive sensors were applied to the forehead (left and right) preoperatively. All patients received a standard anesthetic consisting of propofol induction, isoflurane/fentanyl maintenance anesthesia, and vecuronium neuromuscular blockade. At the surgeon's request, patients were given indigo carmine (5 mL, 40 mg IV) intraoperatively to identify the ureteral orifices.

CASE REPORTS

Case 1

The patient was a 58-year-old man with noninsulin-dependent diabetes mellitus (NIDDM), hypertension (HTN), and depression. His rSO_2 declined after indigo carmine administration, reaching a nadir in 7 min. The left side declined 8 percentage points from preindigo carmine levels (38%→30%), whereas the right side decreased 9 percentage points (47%→38%). The pulse oximetry (SpO_2) readings declined as well but rebounded within 1 min to 100%. The cerebral saturations did not rebound within that

time frame. Inspired oxygen (FIO_2) was increased to 1.0 with no change in rSO_2 ($ETCO_2$ 30–35 mm Hg, mean arterial blood pressure 80–90 mm Hg, heart rate 60–70 bpm, esophageal temperature 35.8°C, and hematocrit 21%). One unit of packed red blood cells was administered. His rSO_2 returned to preindigo carmine levels 25 min after administration of the dye.

Anemia was not an issue in the next three cases. In all four patients, Patient State Analyzer (Hospira, Lake Forest, IL) readings of processed cerebral electroencephalographic activity did not change after administration of indigo carmine and no hemodynamic changes were observed.

Case 2

The patient was a 59-year-old paraparetic man with NIDDM, HTN, and gastroesophageal reflux. Immediately after administration of indigo carmine a decrease in rSO_2 occurred, with the nadir 5 min after injection. His rSO_2 decreased by 12 percentage points from preindigo carmine levels (49%→37%) on the left, and 8% points (44%→36%) on the right. Again, FIO_2 was increased to 1.0 with no effect on rSO_2 . rSO_2 rebounded to preindigo carmine levels after approximately 30 min (Fig. 1).

Case 3

The patient was a 61-year-old man with NIDDM, HTN, and depression. Five min after administration of indigo carmine his rSO_2 decreased, reaching a nadir in 9 min. His rSO_2 decreased 10 percentage points from preindigo carmine levels on the left (53%→43%), and 9 percentage points (48%→39%) on the right. FIO_2 was increased to 1.0 with no effect on rSO_2 . His rSO_2 returned to preindigo carmine levels approximately 20 min later.

Case 4

The patient was a 66-year-old man with NIDDM, HTN, and myasthenia gravis. His rSO_2 rapidly declined after administration of indigo carmine, reaching a nadir in 7 min. The left side decreased 8 percentage points from preindigo carmine levels (43%→35%), whereas the right side decreased 6 percentage points (38%→32%). No intervention was performed. His rSO_2 returned to preindigo carmine levels in approximately 35 min.

DISCUSSION

Administration of IV dyes (methylene blue, indocyanine green, and indigo carmine) has been shown to produce transient decreases in SpO_2 (1). This is because the wavelength of light emitted by the pulse

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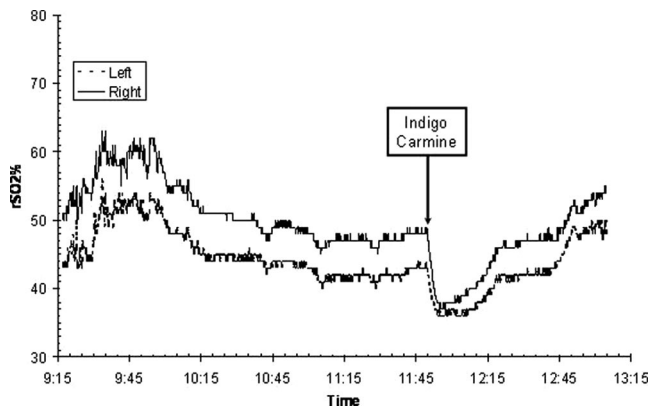


Figure 1. Decline in near-infrared cerebral oximetry after indigo carmine.

oximeter, around 660 nm, is within the absorbance spectrum of the dyes (1). The depth and duration of these declines vary according to the dye being used, but the SpO_2 returns to baseline within minutes (1).

Cerebral oximetry is a technology similar to pulse oximetry but measures a pooled arterial, capillary, and venous hemoglobin saturation (2). Near-infrared light (approximately 700–1000 nm) penetrates tissue effectively and can be used to measure cerebral oxygen saturation through an intact skull (2,3). Each INVOS cerebral oximeter (left and right) emits two wavelengths of light (730 and 810 nm) from small light-emitting diodes, which are received at two sensors a few centimeters away (3). The two sensors at different distances from the emitter detect light traversing different tissue depths below the device (4). Light detected by the sensor nearest to the emitter is largely from the most superficial tissue (scalp) and the more distant from the brain (4). Brain oxygenation is derived from a ratio of deoxygenated to total hemoglobin (oxygenated plus deoxygenated) determined by the differential light absorption, with subsequent computer suppression of the input from superficial tissues (2–4). The reading is updated every 5 sec (5). The right and left measurements may not be identical but should be similar and parallel to each other in the absence of unilateral cerebral deoxygenation (6).

A multitude of dyes with absorption spectra in the infrared range are available. Only indocyanine green is approved for human use, and has been used to measure cerebral blood flow in combination with near-infrared cerebral oximetry (7). Methylene blue absorbs light maximally at a wavelength of 660 nm, with a dramatic decline around 700 nm (1,8). There is some absorption above 700 nm and it might be expected to alter cerebral oximetry readings. However, in the only report of simultaneous clinical use of methylene blue and cerebral oximetry that we could identify, no desaturation was observed (9). Bilirubin interferes with near-infrared cerebral oximetry in icteric patients (10).

Indigo carmine is a water-soluble dye with a 4–5 min half-life after IV injection (11). Its peak light

absorption is at 620 nm, with a similar decline at 700 nm as methylene blue (1,12). Its interference with near-infrared spectrophotometry suggests that there is still significant absorption of light beyond 700 nm.

We believe that the observed cerebral desaturations are artifactual, and not truly indicative of brain hypoxia. This supposition is based on the quick return of SpO_2 to normal levels, the normal Pao_2 measured in one patient during the cerebral desaturation, stable hemodynamic profiles, stable cerebral Patient State Analyzer values, and absence of adverse neurologic sequelae.

The persistence (20–40 min) of the cerebral desaturations in our patients was unexpected, because the SpO_2 recovers within a few minutes (1). One possible explanation for the slow gradual rebound in rSO_2 is pooling of the dye in cerebral and scalp venous beds and/or scalp interstitium (presumably it would not cross the blood–brain barrier) resulting in sustained factitious desaturations (13). Perhaps most likely, the effects of the dye on rSO_2 may persist until the dye is completely eliminated from the circulation (5 half-lives would be approximately 20–30 min), making rSO_2 much more sensitive to indigo carmine than is SpO_2 .

Indigo carmine has structural similarity to 5-hydroxytryptophan and has well-described systemic hemodynamic effects which are thought to be adrenoreceptor mediated (hyper- or hypotension) (14). We cannot exclude a vasoactive effect on the cerebral vasculature, although this seems unlikely given the stable systemic hemodynamics. Furthermore, the cerebral vasculature is largely devoid of adrenergic receptors (15).

This is the first clinical report of a transient decline in rSO_2 after IV administration of indigo carmine. The time course of the decline (20–40 min) lasted considerably longer than the concurrently observed decrease in the SpO_2 (1–3 min). Given this experience, the INVOS Operations Manual is being revised by Somanetics Corporation to caution users about this effect (16). Anesthesiologists and intensivists should be aware of this phenomenon when concomitantly using cerebral oximetry and IV-administered indigo carmine.

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