


Effects of indigo carmine intravenous injection on oxygen reserve index (ORiTM) measurement

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Abstract To retrospectively investigate the effects of indigo carmine intravenous injection on oxygen reserve index (ORiTM) in 20 patients who underwent elective gynecologic surgery under general anesthesia. The study subjects were patients who underwent elective gynecologic surgery under general anesthesia between April 2016 and January 2017, and were administered a 5-ml intravenous injection of 0.4% indigo carmine for clinical purposes during surgery with ORi monitoring. Changes in ORi within 20 min after indigo carmine injection were observed. A relevant decrease in ORi was defined as $\geq 10\%$ reduction in ORi from pre-injection level. ORi rapidly decreased after indigo carmine intravenous injection in all patients. In 10 of 19 patients, ORi decreased to 0 after indigo carmine injection. The median lowest value of ORi was 0 (range 0–0.16) and the median time to reach the lowest value of ORi was 2 min (range 1–4 min) after injection. ORi values returned to pre-injection levels within 20 min in 13 of 19 patients, and the median time to return to pre-injection levels was 10 min (range 6–16 min) after injection. During ORi monitoring it is necessary to consider the rapid reduction in ORi after intravenous injection of indigo carmine.

Keywords ORiTM · Revision L · CO-oximetry · Indigo carmine

To the Editor,

The oxygen reserve index (ORiTM) [1–3] reflects the real-time status of oxygenation under a hyperoxic situation. It is a new oxygenation-related parameter measured by RootTM with Radical-7TM (Masimo Corp., Irvine, CA, USA). With the sensor attached to the finger, percutaneous oxygen saturation (SpO₂), percutaneous total hemoglobin level (SpHb), and ORi can be measured. ORi is expressed as a value between 0.00 and 1.00, lacking a unit; it varies according to the oxygen status of the patient. Since it is a new parameter, there are few relevant reports in the literature.

Indigo carmine is an agent that is rapidly excreted in the urine after intravenous injection and is often used for confirming the presence/absence of ureteral lesions during surgery. The influence of indigo carmine on SpO₂ has been previously reported [4–7], and we have reported that SpHb measured by Radical-7 may also be affected by indigo carmine according to the type of the sensor used [8, 9]. However, to the best of our knowledge, there are no reports on the effects of indigo carmine intravenous injection on ORi. Therefore, we conducted a retrospective study to determine the effects of indigo carmine intravenous injection on ORi.

The present study was retrospective in nature and conducted using medical records. The present study was approved by the Ethics Committee at Fukushima Medical University (No. 2997). The requirement for informed consent was waived by the Ethics Committee. In place of obtaining informed consent from the patients, the study details have been disclosed on the website of Fukushima Medical University.

The study subjects were patients who underwent elective gynecologic surgery under general anesthesia between April 2016 and January 2017, and were administered a 5-ml intravenous injection of 0.4% indigo carmine for clinical purposes

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during surgery with ORi monitoring. The Rainbow™ sensor (R2–25, Revision L, Masimo Corp.) was shielded with a cover to protect it from light exposure, and attached to any of the second to fourth fingers on the contralateral side of the inflatable cuff for noninvasive blood pressure monitoring. The timing of indigo carmine intravenous injection was decided at the discretion of the operator. Data on the time of indigo carmine injection and ORi values of 1-min intervals before and after indigo carmine injection were extracted from the recordings of the automated anesthesia record-keeper ORSYS™ (Philips Electronics Japan, Tokyo). General anesthesia was induced by propofol-remifentanyl and rocuronium, and maintained by propofol-remifentanyl, sevoflurane-remifentanyl, or desflurane-remifentanyl. The anesthetic drug administered varied among patients due to the retrospective nature of the study. The items of investigation were age, height, weight, ORi and SpO₂ values before and after indigo carmine injection. ORi and SpO₂ changes within 20 min after indigo carmine injection were observed. A relevant decrease in ORi was defined as $\geq 10\%$ reduction in ORi from the pre-injection level, similar to SpHb [9].

During the 20 min of the post-injection observation period, no changes in F_iO₂ were made nor were there any events that may otherwise impact the ORi. In most cases, indigo carmine was intravenously injected just before abdominal closure, once hemostasis in the surgical field and a smooth blood circulation was confirmed. Therefore, no patient required fluid resuscitation. Out of the 20 patients included in the study, one patient had an ORi of < 0.1 before indigo carmine injection and was therefore excluded from the analysis. The evaluable 19 patients had a mean age of

53 ± 14 years, mean height of 157.5 ± 6.0 cm, mean weight of 57.2 ± 11.0 kg, a median F_iO₂ of 0.36 (range 0.29–0.53) and a median ORi of 0.36 (range 0.14–0.59) before indigo carmine injection. In all patients, ORi decreased rapidly after intravenous injection of indigo carmine (Fig. 1, Table 1). The ORi was reduced to 0 in 10 of the 19 patients. The median lowest value of ORi was 0 (range 0–0.16), and the median time to reach the lowest value of ORi was 2 min (range 1–4 min) after indigo carmine injection. ORi values returned to pre-injection level within 20 min in 13 of the 19 patients, and the median time to return to the pre-injection level was 10 min (range 6–16 min). In contrast, there were no major changes in SpO₂ after indigo carmine injection (Table 2).

Changes in ORi after indigo carmine injection were analyzed in this study. Now consider what ORi is in the first place. ORi is a new parameter that indicates the real-time oxygenation status in hyperoxia (partial pressure of oxygen of about 100–200 mmHg). ORi can be measured non-invasively by wearing a sensor on a finger. ORi is an “index” parameter with a unit-less scale between 0.00 and 1.00 and changes according to the oxygenation status of patients [1–3, 10].

However, it appears that ORi almost never reaches 1. There is only a short history of ORi measurements in the literature, and its usefulness has only recently started to be discussed. Since a decrease in ORi precedes SpO₂, it has potential use as a predictor of decreased oxygenation in rapid sequence induction, and enables the monitoring of excessive oxygenation. Szmuk et al. studied variations in ORi at the time of induction of anesthesia [2]. They investigated the usefulness of ORi during induction of anesthesia in children and reported that ORi rapidly decreased 31.5 s before SpO₂

Fig. 1 Each patients individual ORi values. All patient shows a decrease of 10% or more from the pre-injection ORi level after the intravenous injection of indigo carmine

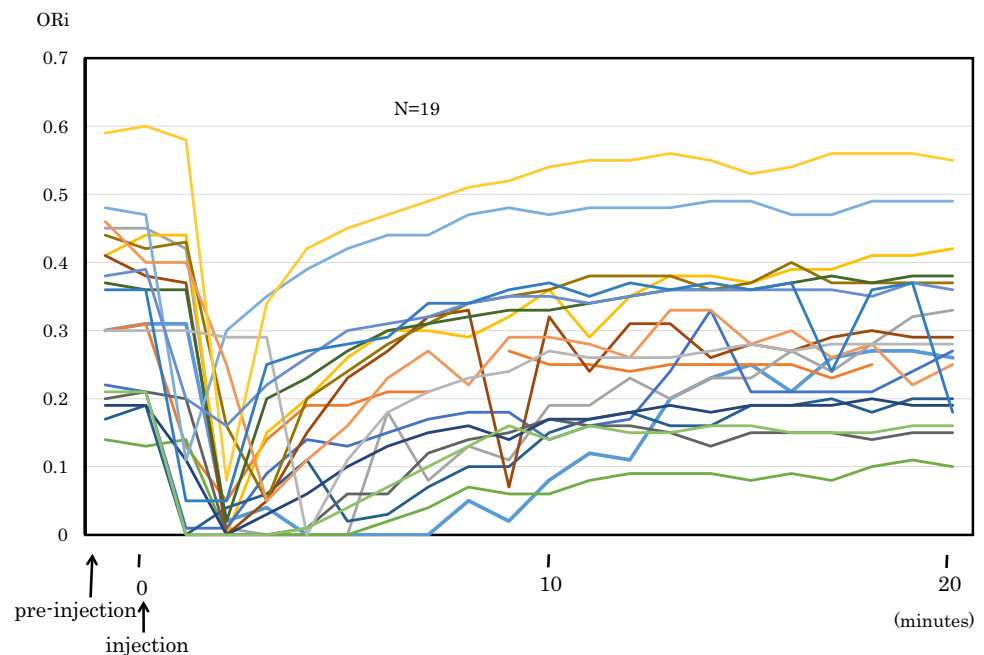


Table 1 Each patients individual ORi values during early phase

Patient	Pre-injection	Injection	1 min	2 min	3 min	4 min	5 min	6 min	7 min
1	0.3	0.31	0.31	0.02	0.04	0	0	0	0
2	0.3	0.31	0.13	0.05	0.14	0.19	0.19	0.21	0.21
3	0.45	0.45	0.42	0.01	0	0	0	0.18	0.08
4	0.41	0.44	0.44	0	0.15	0.2	0.26	0.3	0.3
5	0.22	0.21	0.01	0.01	0.09	0.14	0.13	0.15	0.17
6	0.14	0.13	0.14	0	0	0	0	0.02	0.04
7	0.17	0.19	0	0.04	0.06	0.11	0.02	0.03	0.07
8	0.41	0.38	0.37	0	0.05	0.15	0.23	0.27	0.32
9	0.2	0.21	0.2	0	0	0.01	0.06	0.06	0.12
10	0.44	0.42	0.43	0.16	0.05	0.2	0.24	0.28	0.31
11	0.19	0.19	0.11	0	0.03	0.06	0.1	0.13	0.15
12	0.37	0.36	0.36	0.02	0.2	0.23	0.27	0.3	0.31
13	0.48	0.47	0.11	0.3	0.35	0.39	0.42	0.44	0.44
14	0.46	0.4	0.4	0.25	0.05	0.11	0.16	0.23	0.27
15	0.3	0.3	0.3	0.29	0.29	0	0.11	0.18	0.21
16	0.59	0.6	0.58	0.08	0.34	0.42	0.45	0.47	0.49
17	0.38	0.39	0.2	0.16	0.22	0.26	0.3	0.31	0.32
18	0.21	0.21	0	0	0	0.01	0.04	0.07	0.1
19	0.36	0.36	0.05	0.05	0.25	0.27	0.28	0.29	0.34

All patient shows a decrease of 10% or more from the pre-injection ORi level after the intravenous injection of indigo carmine within four minutes

decreased to 98%. However, reports on this index in the present literature are limited.

All SpO₂, SpHb, and ORi parameters in the present study were measured by Root with Radical-7. We have previously published three studies on SpHb [8, 9, 11], two of these [8, 9] comprised studies of the effects of indigo carmine injection on SpHb. A rapid decrease in ORi after indigo carmine injection was observed in these studies, which led to the conception of the present study.

The relationships between dyes, and SpO₂, SpHb, and ORi, measured by Root with Radical-7, are described below. In regard to the relationship between SpO₂ and dyes, it has previously been reported that intravenous injection of dyes such as indigo carmine, methylene blue, and indocyanine green influences SpO₂ [4–7]. Scheller et al. [4] studied this issue using the Nellcor™ pulse oximeter. They examined changes in SpO₂ using three dyes; methylene blue, indocyanine green, and indigo carmine, and found that these dyes influence SpO₂ to varying degrees. Indigo carmine caused variations in SpO₂ in the fewest patients, with the smallest extent of variations, while SpO₂ varied to the greatest extent following injection of methylene blue. Concerning the reason for these changes, the authors concluded that SpO₂ varied to the greatest extent because the Nellcor pulse oximeter applies light with wavelengths of 660 and 925 nm for measurements, and the absorbance of methylene blue is the highest at around 660 nm. In our study, there were no major changes in SpO₂ after indigo carmine injection. The lack

of influence of indigo carmine on SpO₂ seems to be mostly attributable to improvements in either the device itself or the sensor.

The relationship between SpHb and dyes has been addressed in our previous two studies [8, 9]. With the Revision K sensor [8], prior to the advent of Revision L, SpHb decreased by 1.8 g/dl after intravenous injection of indigo carmine, and it took 4 min for SpHb to reach the lowest level and 15 min to return to the pre-injection level after indigo carmine injection. In addition, depending on the patient, it either took up to 29 min for a return to the pre-injection level or a measured value was not displayed after intravenous injection of indigo carmine. However, with Revision L [9], we did not record an effect of indigo carmine intravenous injection on SpHb. We have also reported that, unlike the Revision K sensor, the Revision L sensor does not influence the measurement of SpHb after indigo carmine intravenous injection.

The present study examined variations in ORi after indigo carmine injection and found a rapid decrease in ORi after injection in all patients. The median time to reach the lowest value of ORi was 2 min (range 1–4 min) after injection. The reduced ORi did not return to the pre-injection level even at 20 min after injection in six patients. This finding should be considered when monitoring ORi. The fact that the wavelength of the ORi measurement is close to the absorbance of indigo carmine may explain the rapid decrease in ORi, as well as SpO₂. However, because methods of measurement

Table 2 Each patients individual SpO₂ values (%)

Patient	Pre-injection	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	11 min	12 min	13 min	14 min	15 min	16 min	17 min	18 min	19 min	20 min	
1	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
2	99	99	97	99	98	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99
3	100	100	100	99	99	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
4	100	100	100	99	99	99	99	99	99	99	100	100	100	100	100	100	100	100	100	100	100	100
5	100	100	100	99	99	99	99	99	99	99	99	99	99	100	100	100	99	99	99	99	99	99
6	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99
7	100	100	99	99	99	99	99	100	100	100	100	99	100	99	100	100	100	100	100	100	100	100
8	99	99	99	98	99	99	100	99	100	99	99	99	99	99	99	99	99	99	99	99	99	99
9	98	98	98	98	98	99	99	99	99	99	99	99	99	98	98	98	98	98	98	98	98	98
10	100	100	99	99	99	100	100	100	100	100	100	100	100	100	99	100	100	100	99	99	99	99
11	98	99	98	98	98	98	98	98	98	98	98	98	98	98	98	98	99	99	99	99	99	99
12	99	99	99	98	99	99	99	99	99	99	99	99	99	100	100	100	99	100	100	100	100	100
13	100	100	98	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
14	100	100	99	100	100	100	100	99	100	100	100	100	100	99	100	99	99	99	99	99	99	99
15	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99
16	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
17	98	97	98	98	98	98	98	98	99	99	99	98	98	98	99	98	99	98	98	98	99	99
18	99	100	98	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99
19	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99

There were no major changes in SpO₂ after indigo carmine injection

have not been fully disclosed, further discussion is not feasible.

The usefulness of ORi in various settings may be reported in the future; however, in the meantime, it should be considered that intravenous injection of the dye indigo carmine causes a rapid decrease in ORi. Another dye, methylene blue, also appears to cause a rapid reduction in ORi, although the accumulation of clinical cases is presently insufficient. We intend to examine the effects of other dyes in further accumulated clinical cases.

ORi decreased rapidly in all patients after intravenous injection of indigo carmine. The median lowest value of ORi was 0, the time to reach the lowest value was 2 min, and the median time to return the pre-injection level was 10 min after intravenous injection of indigo carmine. The rapid reduction in ORi after indigo carmine injection should be considered in ORi monitoring.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study protocol has been approved by the Ethics Committee at Fukushima Medical University.

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