

## ORIGINAL ARTICLE

# Intraparenchymal Methylene Blue Injection for Sentinel Lymph Node Biopsy in Breast Cancer Patients does not Interfere with the Pulse Oximetry Readings

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**Purpose:** Alteration in oxygen saturation is a side effect of the dye used in sentinel lymph node biopsy. The object of this study was to determine the possible effects of methylene blue on the oxygen saturation in patients undergoing sentinel lymph node biopsy. **Methods:** The complete peroperative records of 148 patients who underwent sentinel lymph node biopsy with intraparenchymal injection of methylene blue were reviewed. The data reviewed included the preinjection pulse oximeter saturation readings and the postinjection values until the readings returned to the preoperative levels

in the postanesthesia care unit. **Results:** The pulse oximetry values were recorded preoperatively, after intubation and, at 15, 30, 45, and 60 minutes of the operation. The results showed that methylene blue did not cause any significant changes in oxygen saturation levels. **Conclusion:** We suggest that methylene blue might be preferable for the patients with concomitant disease, and for whom close monitoring of their oxygen saturation is required.

Key Words: *Methylene blue, Pulse oximetry, Sentinel node biopsy*

## INTRODUCTION

Sentinel lymph node biopsy (SLNB) has become an accepted alternative to axillary dissection for early-stage breast cancer patients who have a clinically negative axilla. (1,2) This technique provides accurate staging with fewer complications and a lower hospitalization cost than axillary dissection does, and has gained widespread use. (3,4) The technique involves lymphatic mapping by using a combination of preoperative isotope injection and/or intraoperative dye injection. Several vital dyes have been used in this technique, most notably isosulfan blue, patent blue, methylene blue, indigocarmine and indocyanin green. (5) Isosulfan blue has traditionally been the dye to identify the sentinel lymph node. (3) Alternatively meth-

ylene blue is now used by several groups to identify the sentinel lymph node in breast cancer patients. (6-8) Pulse oximetry is the standard method for noninvasive monitoring the peripheral tissue oxygen saturation. (9) It functions via determining of the concentration of oxyhemoglobin and reduced hemoglobin species by measuring the absorbance of light at two wavelengths. (10) The pulse oximeter functions by emitting light at 660 nm (red light) and 940 nm (infrared) respectively. (11) Certain vital dyes are known to alter the light absorbency of blood, which can mimic pulse oximeter desaturations. (10,12,13) Isosulfan blue and patent blue have been reported to interfere with the noninvasive pulse oximeter readings. (14-19) Various physiological and environmental factors can interfere with the accuracy of the oximeter readings, including diminished perfusion, the administration of vasopressors, hypothermia, dyshemoglobinemias, peripheral vascular disease and placement of a sphygmomanometer cuff on the same extremity which is used for pulse oximetry. (9-11) The objective of this study was to determine the possible effects of methylene blue on the oxygen saturation

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of patients undergoing sentinel lymph node biopsies.

### METHODS

This study was approved by the institutional review board for human investigation in our hospital. We reviewed the peroperative data of the patients who underwent surgery for breast cancer at our cancer center from April 2002 to August 2007 by using a computer data base system. A thorough evaluation of the records of 148 patients who underwent sentinel lymph node biopsy with intraparenchymal injection of methylene blue was performed. One hundred forty eight consecutive patients underwent sentinel lymph node biopsy with either methylene blue (Neopharma GmbH & Co, KG, Aschau, Germany) or methylene blue and <sup>99</sup>TcTechnetium tin colloid injection to assess the axillary lymph node status in patients with stage I or stage II breast cancer. The patients with either significant cardiac, respiratory, hepatic, renal or hematological disorders were excluded from the study. All patients were informed about the technique and a written consent was obtained from each patient. All procedures were performed under general anesthesia. The pulse oximeter (Nellcor, Hayward, USA) readings (at wave lengths of 660 and 990 nm) were obtained from the index finger of the contralateral extremity to the side on which the operation was performed. The anesthesia records were started at the time of entry of the patient into the operating room prior to induction of anesthesia. After induction of general anesthesia, 3–5 mL of methylene blue was injected into the breast tissue around the tumor or into the breast biopsy cavity. The breast was massaged for 5 min and then sentinel lymphadenectomy was performed. All sentinel lymph node or nodes were excised

**Table 1.** Demographic data of the patients (number or mean ± standard deviation)

Number of patient	148
Sex (f/m)	148/0
Age (yr)	68.65 ± 18
Height (cm)	161 ± 13
Weight (kg)	68 ± 24
ASA I / II / III	57/84/7

ASA=American Society of Anesthesiologists.

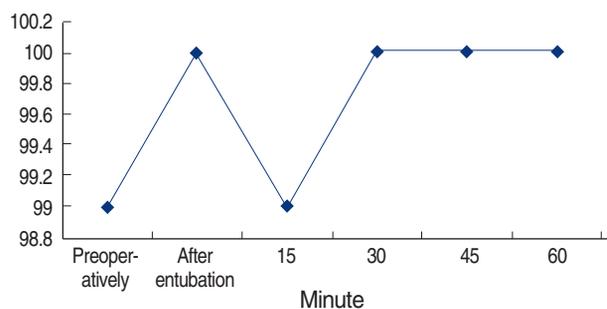
and sent for pathological examination. Frozen-section was performed on the sentinel node or nodes, and in the case of malignancy, a complete axillary lymph node dissection was immediately performed. The data was obtained from the surgical anesthesia records in which the pulse oximeter readings had been recorded at 15 min intervals. Analysis of Variance (ANOVA) test was used for the statistical analysis of the collected data. All the statistical tests were two-sided, and values of  $p < 0.05$  were considered to be significant. The results were given as mean ± standard deviation. The statistical evaluations were performed using standardized software (Statview, SAS Institute Inc, Cary, USA).

### RESULTS

A total of 148 patients ranging from 26 to 84 yr of age (mean 68 yr) underwent a SLNB with intraparenchymal injection of methylene blue. Seventy patients underwent breast-conserving surgery and the remaining 78 patients had mastectomy. The patients' demographic data is presented in Table 1. The pulse oximetry values were recorded preoperatively, after intubation and at 15, 30, 45, and 60 min (Figure 1). The oxygen saturation values were  $99 \pm 1$ ,  $100 \pm 1$ ,  $99 \pm 1$ ,  $100 \pm 1$ ,  $100 \pm 1$ , and  $100 \pm 1$  respectively. These results also showed that methylene blue caused no significant change oxygen saturation.

### DISCUSSION

Pulse oximetry is the standard method for non-inva-



**Figure 1.** The measured oxygen saturation (SpO<sub>2</sub>) values and the time.

sive monitoring of the oxygen saturation in the peripheral tissues. (9) Intravenous dyes are known to have potentially profound effects on pulse oximetry readings, resulting in falsely low measured oxygen saturations. (9,10,15,17) When given intravenously, like other blue dyes, methylene blue also interferes with the pulse oximetry readings. (9) We preferred intraparenchymal injection because of reported cases having skin necrosis with intradermal injection of methylene blue. (3) We believe that with intraparenchymal injection, methylene blue is washed out in a controlled fashion primarily via lymphatics and this results in a controlled systemic distribution. Therefore, it does not result in abrupt changes in spectrophotometric properties of proteins and cellular elements of the blood.

The peak absorption of isosulfan blue is 635 nm, which is close to the standard 660 nm wavelength used by the pulse oximeter. (10,14,16) Because of this, the oximeter interprets the dye's absorption as the presence of reduced hemoglobin and it calculates an artificial decrease in oxygen saturation. (10,14) Although low pulse oximetry readings does not necessarily mean a low SpO<sub>2</sub>, an agent which does not further interfere with the interpretation of pulse oximetry readings is preferred. Methylene blue acts as a cofactor for methemoglobin reductase which is normally inactive and leads to formation of hemoglobin. But this should not be a major factor in the pulse oximetry readings. Because methemoglobin level does not increase significantly with the use of newer anesthetics.

Heinle et al. (10) studied the changes in oxygen saturation after isosulfan blue injection. They compared the change in oxygen saturation as assessed by pulse oximetry and arterial catheterization in 22 breast cancer patients. They found a mean drop of 5.6%, ranging from 2% to 9% in SpO<sub>2</sub>, with no change in the SaO<sub>2</sub>. They concluded that the oximeter interprets the dye's absorption as the presence of reduced hemoglobin and it calculates an artificial decrease in oxygen saturation.

In a retrospective study, El-Tamer et al. (16) reported on the effect of intraparenchymal injection of isosulfan blue on the oxygen saturation readings by using a pulse oximeter in a retrospective study. They found that the mean and the maximal decrease in oxygen saturation

were 5% and 11% respectively. Isosulfan blue has been the preferred dye for SLNB in all over the world but many centers now prefer methylene blue since it is cheaper, more readily available, has fewer reported side-effects and the SLN localization rates are similar to that of isosulfan blue. (6,7,20,21)

Methylene blue dye has a peak absorbance at 660 nm. On the contrary to isosulfan blue, this dye does not have sulfonic acid groups in its structure, and does not bind to endogenous lymph proteins. It circulates in a dissolved form, and diffuses directly into the lymphatics and blood capillaries. Methylene blue theoretically is retained less and cleared more from the blood stream through the kidneys than isosulfan blue. (9,14,22) Scheller et al. (9) reported that the peripheral pulse oximetry was transiently lowered among healthy volunteers who were injected intravenously with 5 mL of 1% methylene blue. This study was reported to be performed on only five patients. So we believe that there is a need for further investigation on this subject. Since there have been no study revealing deleterious effects of methylene blue on pulse oximetry findings unless given with intravenous route, we think that methylene blue is a safe dye of choice to be used in sentinel lymph node biopsy.

There is only one study about the effect of intraparenchymal injection of methylene blue on oxygen saturation. Piñero et al. (14) compared the effects of methylene blue and isosulfan blue on oxygen saturation in a randomized, prospective study. Both dyes interfered with the peripheral saturation reading, but only isosulfan blue showed significant differences. The blood-gas analysis did not show any difference between the groups. Additionally, plasma methylene blue levels were lower than that of isosulfan blue in all measurements. The lesser extent of change in oxygen saturation with methylene blue injection was explained with the lesser amount of dye remaining in the bloodstream.

This study did not reveal a significant change in oxygen saturations with intraparenchymal injection of methylene blue for sentinel lymph node biopsy in 148 breast cancer patients. Our findings were comparable to Piñero's study, (14) which revealed no significant changes in oxy-

gen saturation of patients receiving methylene blue injection. Arterial blood gas analysis is recommended by Heinle et al, (10) to distinguish between the real and false oxygen desaturation. Close monitoring of the blood gases is necessary when performing pulse oxymetry, and especially in patients with pulmonary disease.

In our series, we did not observe a statistically significant difference between breast-conserving surgery group (70 patients) and the mastectomy group (78 patients). In our opinion, this reflects the amount of methylene blue passing to and remaining in the systemic circulation does not change with the type of surgery.

## CONCLUSION

We believe that intraparenchymal methylene blue injection is a preferable technique for SLNB in breast cancer patients with concomitant pulmonary disease and for whom oxygen saturation should be closely monitored. Thus, intraparenchymal methylene blue injection for SLNB may avoid unnecessary invasive arterial monitoring.

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