

Can Laparoscopic Chromopertubation with Methylene Blue Dye cause Anaphylactic Reactions like Pulmonary Edema?

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ABSTRACT

Diagnostic laparoscopy has been performed ever since interests in infertility and fertility have developed. Methylene blue is administered to check tubal patency during the procedure. Extravasation of methylene blue is a recognized complication of diagnostic laparoscopy and chromopertubation. Anaphylaxis and anaphylactic reactions in the perioperative period are a significant concern for surgeons and anesthesiologists. The incidence is as high as 1 in 3,500 with a mortality rate of 3 to 6%.¹⁶ There are no relevant literature or research article that provides sufficient data or guidelines for determining the nature of these reactions, mode of treatment algorithm, or the certain specifications we should consider before performing the procedure. This is a review literature for performing a safe practice evaluation and management.

Keywords: Allergy hypersensitivity, Anaphylaxis, Chromopertubation, Methylene blue, Perioperative, Pulmonary edema.

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INTRODUCTION

Anaphylaxis and anaphylactic reactions in the perioperative period are a significant concern for surgeons and anesthesiologists.

The incidence is as high as 1 in 3,500 with a mortality rate of 3 to 6%.¹

Methylene blue is a new tool to evaluate *in vivo* tubal damage, and is a simple method of estimating salpingeal function.² Methylene blue is a common dye used in diagnostic procedures for checking the patency of the fallopian tubes.³ This compound has a unique property

of oxidation–reduction function and tissue staining. It has an opposite effect on hemoglobin depending upon its concentration. In higher levels, methylene blue converts the ferrous iron of reduced hemoglobin to the ferric form and produces methemoglobin. Lower levels help in converting methemoglobin to hemoglobin in drug-induced methemoglobinemia. Evaluation of tubal factor infertility is moving from mere anatomical assessment to morphological and functional enquiry of the patency of the tubes.⁴ These days laparoscopy is being increasingly used in the evaluation of infertility, especially laparoscopic chromopertubation with methylene blue, which has become the gold standard for the functional assessment of the tubes.

Life-threatening anaphylactic or anaphylactoid reactions to methylene blue have been reported in the literature;^{5,6} recently, methylene blue has been used for various conditions like sentinel node biopsy, but due to the rare reporting of its reactions, it was considered safest among dyes.

AIMS AND OBJECTIVE

The aim of the study is to make the surgeons know the complications of methylene blue toxicity during the most common procedure of laparoscopic chromopertubation, which most of us are unaware, and how to be careful and vigilant during the entire procedure.

MATERIALS AND METHODS

Literature review is performed using search terms that included methylene blue, chromopertubation pulmonary edema, anaphylaxis perioperative, and hypersensitivity.

Results were taken from recent case reports, basic science literature, and clinical studies.

Searches in the literature on methylene blue toxicity during laparoscopy chromopertubation were conducted via pubmed, google scholar, medline and chochrene library database. No language restriction was applied to searches.

RESULTS

Although there have been slight variations in the incidences, management, evaluation, and their reporting, the authors do believe in the great saying “prevention is better than cure.”

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Preoperative patient analyses are ruling out glucose-6-phosphate dehydrogenase (G6PD) deficiency, history of allergy to drugs and dyes, and history of chronic pelvic infection. Drug analysis like the right amount of dilution; the right amount to be installed; identification of signs and symptoms on table or during perioperative period; the immediate treatment management protocol like epinephrine, steroids, histamine 1 and 2 blocking agents, and oxygen administration; postoperative cutaneous test; and systematic allergiological investigation of all the drugs and substances given during the perioperative period is important.

DISCUSSION

Normally, methemoglobin levels are <1% when measured by co-oximetry test.⁷ Cyanosis is the classic symptom of methemoglobinemia; this occurs when methemoglobin >1%. Other signs and symptoms include mental status changes, shortness of breath, headache, fatigue, dizziness, and loss of consciousness. Severe methemoglobinemia is when methemoglobin >50% where patients have dysrhythmias, seizures, coma, and death.³ In patients with conditions like anemia, heart and lung disease, G6PD deficiency, and sepsis, methylene blue can induce methemoglobinemia even at normal levels.⁸

Veerendrakumar et al⁹ had injected 20 to 30 mL of 1% methylene blue, and 5 hours later, the patient developed tachypnea, hypotension, bilateral basal crepitations, and bluish-colored urine; patient was transferred to the intensive care unit and treated with oxygen, inotropes, and furosemide. According to the studies, one should always keep in mind the dangerous effect of methylene blue, alternatively diluted povidone iodine can be used. This patient had developed methemoglobinemia 26.4% (according to spectrometric analysis). In Trikha et al's³ case, the patient weighed 53 kg; 20 mL of 1% methylene blue was injected. After 2 minutes, the oxygen saturation declined, and after 5 minutes patient developed crepitations and cyanosis; at 200 mL of fluid patient developed very rare features. The safe limit of the dye is 7 mg/kg. Anaphylactoid reaction occurred due to the dye causing intrapulmonary vascular vasospasm; a generalized vasoconstriction and some amount of anemic hypoxia could have caused this. According to Nolan¹⁰ when the patient was injected with methylene blue dye intracervically, she developed inflammatory peritonitis after approximately 24 hours, where she complained of abdominal distention and pain; exploratory laparotomy was done revealing peritoneal ascites and sterile inflammatory exudates. This pt was treated with corticosteroids. According to Mhaskar and Mhaskar,¹¹ methylene blue is a treatment for methemoglobinemia, but his patient had tuberculosis, i.e., chronic pelvic inflammatory disease, which could be the cause of extravasation of

dye causing methemoglobinemia. Bilgin et al⁸ also presented a case of methemoglobinemia after methylene blue instillation, but his patient had G6PD deficiency. Herath et al¹² stated that bluish discoloration can occur without methemoglobinemia as their patient developed bluish discoloration and cyanosis immediately after injection of 20 mL of the dye intracervically for diagnostic laparoscopy; this could be an anaphylactic reaction to the dye or they might have used a concentrated version instead of 1%.

Ash-Bernal et al⁷ did a retrospective study on 138 cases where they discussed about the acquired cause of methemoglobinemia. The most common drug causing it is dapsone.

Robert and Barbieri¹³ recommend using 10 mg of methylene blue in 150 mL of NS to reduce the symptoms of anaphylaxis.

Dewachter et al¹⁴ observed severe immunoglobulin E-mediated hypersensitivity reaction to 1% methylene blue; cutaneous test and biological assessment positivity confirmed anaphylactic reaction to methylene blue, so investigation is necessary. In Millo et al's¹⁵ case after diagnostic laparoscopy for infertility, patient was shifted to the recovery room; about 15 minutes later, she developed restlessness, cyanosis, and was not maintaining oxygen saturation. Despite efforts of resuscitation, she died. On postmortem findings, the lungs were edematous, congested, blue stained, with features of pulmonary edema. Dhanpal and Joseph¹⁶ injected 30 mL of 1% of methylene blue intracervically; 15 minutes later, patient turned blue with central and peripheral cyanosis. Oxygen saturation dropped spontaneously, and spectrophotometric analysis showed methemoglobinemia. Rzymiski et al⁵ discussed a case of anaphylactic reaction to methylene blue after chromopertubation.

CONCLUSION

It is important to publish clinical research article on the dangerous adverse outcome from techniques commonly used in clinical practice. All these cases highlighted the fact that methylene is highly potential in causing complications that are life-threatening even when not administered nonsystematically. This research article confirms that we need continuous and vigilant monitoring in the preoperative, intraoperative, and postoperative period; none of the complaints should be taken for granted even if it is as simple as a cough. Anesthetists and surgeons should know the immediate treatment protocol and should not be careless in using methylene blue dye in any amount or in any concentration.

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