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Case conference

Blue dyes, blue people: the systemic effects of blue dyes when administered via different routes

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Abstract We report 4 patients who had facial color changes to a blue-green-gray color and decreased oxygen saturation as measured by pulse oximetry. Patient 1 received an intravenous (IV) methylene blue solution during a urologic procedure, and the remaining three patients were administered subcutaneous indigo carmine (patient 2) or Patent Blue (Patients 3 and 4) for axillary lymph node mapping. All patients had above normal methemoglobin levels. Two (Patients 2 and 3) had hypotension, and one (Patient 3) required IV ephedrine to restore hemodynamic stability. Patient 4 had a hypersensitivity reaction characterized by systemic urticaria and blue-colored subintegumentary edema due to the subcutaneous administration.

1. Introduction

Vital dyes such as methylene blue, Patent Blue[1], and indigo carmine[2] have been used for many years in a variety of clinical situations. These dyes are known to alter the light absorbance characteristics of plasma and may, therefore, create oximetry artifacts [1]. When the dye is delivered intravenously (IV), anaphylactic reactions with hemodynamic instability may occur [2]. The appearance of methemoglobin in blood also has been described [3]. However, the systemic reactions (desaturation, methemoglobinemia, and hypotension) of all three blue dyes with subcutaneous administration have not been described. We report 4 cases, three of whom received these materials subcutaneously, in which oximetry artifacts and changes in blood pressure (BP)

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[1] Bleu Patente V Sodique 2.5%, Guerbet, Roissy, France. Each 2 mL contains 50 mg of solution for injection via the subcutaneous and intramuscular routes.

[2] Indigotindisulfonate sodium injection, USP. Each 5 mL contains 20mg of indigotindisulfonate sodium, in water for injection, qs, pH-adjusted, when necessary, with citric acid and/or sodium citrate. Sterile, nonpyrogenic.

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increased methemoglobin levels, or allergic reactions occurred. In addition, in all 4 patients, the face changed to a blue, green, or deep gray color. For indigo carmine, this is the first report to note that it can cause methemoglobinemia.

2. Case reports

2.1. Case 1

A 77-year-old, 70 kg, 176-cm man with New York Heart Association functional class II, history of myocardial infarction and coronary bypass graft surgery 10 years before admission, and peptic ulcer disease, was brought to the operating room (OR) for suprapubic prostatectomy for prostate cancer.

Preoperatively, he was given midazolam one mg IV, and 500 mL Ringer's lactate. Monitoring included 5-lead electrocardiography (ECG), pulse oximetry, and noninvasive arterial BP. Oxygen was delivered via face mask. The patient underwent spinal anesthesia with hyperbaric 0.5% bupivacaine 12.5 mg and 25 μg fentanyl.

During the procedure, the patient remained hemodynamically stable, with BPs in the range of 110-120/50-65 mmHg. Intraoperative blood loss was approximately 400 mL, and an additional 700 mL of Ringer's lactate was infused intraoperatively. Pulse oximetry remained normal throughout the procedure.

At the end of the procedure, evaluation for anastomotic leakage was performed by administering an IV injection of 4 mL 12.5% methylene blue solution. Two minutes after injection, oxygen saturation (Spo_2) decreased from 98% to 82%, and BP decreased from 110/60 to 100/50 mmHg. The patient's face and neck turned to a blue to a purple-gray color after administration of the dye, but the patient did not have any discomfort. The patient received 100% oxygen via a non-rebreathing mask, but Spo_2 increased to only 92% during the next 20 minutes.

The patient was transferred to the postanesthesia recovery unit (PACU). Arterial blood gas (ABG) analysis of arterial blood showed 5.3% of methemoglobin (normal laboratory level, 0.6%-1.4%). The patient's face color and Spo_2 returned to normal about one hour after the procedure, and he was discharged to the urology floor thereafter.

2.2. Case 2

A 67-year-old, 67-kg, 170-cm woman with a history of asthmatic bronchitis, pseudomembranous colitis, essential hypertension, and a cerebral vascular accident and a hysterectomy 10 and 8 years, respectively, earlier, was scheduled for "lumpectomy" and sentinel lymph node biopsy.

Monitoring included a 5-lead ECG, pulse oximetry, and noninvasive arterial BP. Anesthesia was induced with midazolam 2 mg, propofol 130 mg, vecuronium 8 mg, and fentanyl 150 μg IV and was maintained with isoflurane after uneventful tracheal intubation. The patient was ventilated with 40% oxygen and 60% nitrous oxide gas mixture. During the surgical procedure, hemodynamic stability was maintained with BP in the range of 120-150/65-70 mmHg, and Spo_2 was about 98%.

For sentinel lymph node mapping, 20 mg indigo carmine was injected below the areolae. Ten minutes later, Spo_2 decreased to 93%, and BP decreased from 150/75 to 105/50 mmHg; the patient's face color was noted to be a light blue to green-gray color.

The patient was administered a bolus of 500 mL Ringer's lactate and was ventilated with 100% oxygen. Her BP returned to normal during the next 5 minutes, and Spo_2 increased only to 95% during the remainder of surgery and when she was in the PACU. The patient's trachea was extubated in the OR, and at that time, she was conscious and comfortable. On transfer to the PACU, she received 50% oxygen via face mask. Arterial blood gas analysis showed a Pao_2 of 240 mmHg, oxygen hemoblogin (Hb) of 100%, and methemoglobin of 2.3%. The patient's face color and Spo_2 returned to normal during the next two hours, and she was discharged to the floor.

2.3. Case 3

A 58-year-old, 64-kg, 161-cm woman with a history of hypothyroidism and right mastectomy for breast carcinoma that was treated postoperatively with chemotherapy and radiotherapy 15 years before admission, was scheduled for lumpectomy and a sentinel lymph node biopsy.

Monitoring included 5-lead ECG, Spo_2, and noninvasive arterial BP. Anesthesia was induced with midazolam two mg, propofol 110 mg, rocuronium 50 mg, and fentanyl 200 μg IV, and maintained with isoflurane. The patient was ventilated with a gas mixture of 45% oxygen and 55% nitrous oxide. She was hemodynamically stable, with BPs in the range of 150-160/65-80 mmHg; Spo_2 was about 99%.

Before surgery, two mL of 2.5% Patent Blue V sodique (Bleu Patente V Sodique, Guerbet, Roissy, France) was injected below the areolae for sentinel lymph node mapping. Five minutes later, Spo_2 decreased to 95%, and BP decreased from 150/70 to 105/65 mmHg; the patient's face color changed to a deep blue-gray. A rapid infusion of 500 mL Ringer's lactate was started, but 5 minutes later, BP decreased to 70/45 mmHg without a change in heart rate (HR). The patient received two boluses of IV ephedrine 5 mg each, and her BP increased to 100-105/60 mmHg. She received an additional 1000 mL Ringer's lactate, and her BP stabilized at about 110/50 mmHg. With this therapy, her Spo_2 increased as well, reaching 96% and remaining at this level until the end of the two-hour surgical case.

The patient's trachea was extubated at the end of surgery. It was then noted that her collected urine was tinted green-blue. At that time, she was conscious and comfortable. The patient was transferred to the PACU where she received