THE BLUE LADY - A CASE REPORT

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SUMMARY

Methylene blue is a drug commonly used in the operation theatres. Here we report a rare complication encountered following laparoscopic tubal patency test using methylene blue. Prompt recognition and effective management is vital in the management of such rare but potentially fatal complications.

Keywords: Methylene blue toxicity, Cyanosis, Methemoglobinemia.

Methylene blue has been a standard agent in clinical medicine for the past 100 years. Its medical uses are as a treatment for methemoglobinemia and as an antidote for cyanide poisoning. More commonly it is used as a marker for tracing fistulae and other aberrant tracts, and the patency of Fallopian tubes. But it must be remembered that it is a “drug” and like any other drug should be administered with due regards for proper dosage and potential side effects, as this case report will highlight.

Case report

A 23 year old lady, who was diagnosed to have tuberculous endometriosis with bilateral tubo-ovarian masses and who had completed a 4 drug regimen of anti tuberculosis treatment for 9 months came in for laparoscopic patency testing of her Fallopian tubes. The case was accepted under ASA I, and a premedication of oral Ranitidine and Diazepam at night and on the morning of the surgery were administered. The patient was induced with Thiopentone, paralysed with inj.Vecuronium and inj.Pethidine was used for analgesia. The patient was intubated with a 7.5 mm Portex oral cuffed endotracheal tube and the tube was fixed at 19 cms. Anaesthesia was maintained using 60% N₂O, 40% O₂ and Halothane 0.5% using Boyle’s apparatus with manual intermittent positive pressure ventilation using a circle system and a soda lime absorber.

Intraoperatively tubal patency was tested with 30 ml of 1% Methylene blue. Having confirmed the patency, peritoneal wash was given with normal saline. Fifteen minutes after the introduction of methylene blue into the Fallopian tube, the patient turned blue in colour. Both central and peripheral cyanosis was noted. The pulse oximeter saturation dropped from 99% to 85%. Oxygen flow was found to be adequate, endotracheal tube was patent and the chest was clear with good and equal air entry bilaterally. Nitrous oxide was cut off; and 100% oxygen was administered. The pipeline oxygen was changed over to cylinder oxygen with no improvement in cyanosis. As the patient was otherwise stable, the possibility of methylene blue absorption into the blood stream from the peritoneal cavity was considered. The arterial blood gas was found to be normal (pH-7.45, pCO₂-30.1, pO₂-128.5, HCO₃-20.4, Sat-99.0%). Over a period of 45 minutes the pulse oximeter saturation improved to 96%. The patient remained blue, but the cyanosis of the tongue and the nail bed improved. The patient was reversed with inj. Neostigmine and inj. Glycopyrrolate and was extubated. The patient was stable, breathing well, responding to commands and was pain free.

The bluish discoloration of the skin and mucous membranes that the patient developed intraoperatively persisted for the next 2 days following which, it gradually improved. The patient also complained of mild dysuria. Saliva and stools were also stained blue. It gradually decreased by the third day.

Repeated arterial blood gases were performed on the day of the surgery and postoperative day 1 and 2.

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All other investigations were within normal limits. Serum methemoglobin levels were estimated using spectrophotometric analysis at our biochemistry lab, on the day of the surgery, on the first, second and the third
postoperative days. The levels were: Immediate post op: 25% Post op day 1: 15% Post op day 2: 3% Post op day 3: 1%.

A final diagnosis of "Methylene blue induced methemoglobinemia" was made. Since the patient was stable clinically and improved rapidly over two days, no active correction of methemoglobinemia was required other than 1 gram of ascorbic acid PO for 3 days. The patient was discharged on the third postoperative day and had no complaints on follow up.

Discussion

Methylene blue is 3,9- bisdimethyl amino phenazothionium or tetramethylthionine chloride. Its uses are based on its tissue staining properties and its oxidation-reduction functions. In low concentrations, its reduced form appears to increase the speed of the reversal of methemoglobin to haemoglobin.

Paradoxically, in high concentrations, methylene blue oxidizes the ferrous iron of reduced haemoglobin to the ferric state, thus changing haemoglobin to methemoglobin. This apparent paradoxical effect of methylene blue suggests an equilibrium between the ability of methylene blue to oxidize haemoglobin directly to methemoglobin and the ability of methylene blue to reduce methemoglobin to haemoglobin. This equilibrium seems to be established in favour of the reducing properties of methylene blue unless excessively large doses of methylene blue are given or the NADPH-methemoglobin reductase system is abnormal.1

Methemoglobin (ferric haemoglobin) cannot carry oxygen and when present in excess, results in a functional anemia. It also shifts the oxygen dissociation curve to the left, limiting the release of oxygen to tissues. Symptoms are due to hypoxia and anaerobic metabolism.2

Various systems normally operate to keep methemoglobin at physiologic levels (1% of the total haemoglobin concentration). Methods to convert methemoglobin to haemoglobin include NADH-methemoglobin reductase (responsible for 95% of the baseline activity), NADPH-methemoglobin reductase, and the ascorbic and glutathione systems. When supplied with the co-factor methylene blue, the capacity of the NADPH-methemoglobin reductase system is greatly increased. Because this enzyme is dependent on NADPH, individuals with a glucose-6-phosphatase dehydrogenase deficiency have profound impairment in the ability to reduce methemoglobin after oxidant exposure.3

The diagnosis is confirmed by measuring the methemoglobin levels by co-oximetry (photospectrometry). The pulse oximeter values are not reliable, when blood contains methemoglobin or other substances that have absorptive characteristics similar to oxyhaemoglobin or deoxyhaemoglobin such as methylene blue. Methemoglobin interferes with pulse oximeter readings in a complicated manner. Initially the pulse oximeter saturation will drop with increasing methemoglobin levels. This fall in saturation is not exactly proportional to the fraction of methemoglobin, as the pulse oximeter overestimates the level of oxygen saturation. At methemoglobin concentration approaching 30% the pulse oximeter saturation approaches 85% and will show no additional change in saturation, regardless of further increases in methemoglobin concentration. Although the pulse oximeter readings in methemoglobinemia may not be accurate it may be helpful when we compare it with that of the ABG. If there is a difference between the measured oxyhaemoglobin of the pulse oximeter and the calculated oxyhaemoglobin of the ABG, then a "saturation gap" exists and methemoglobin may be the cause.4

The metabolic acidosis that the patient developed in the immediate postoperative period can be explained by the anaerobic metabolism secondary to methemoglobinemia. The alkalosis that the patient developed on postoperative Day 1 could be secondary to her vomiting. Neither the acidosis or alkalosis was severe enough for correction, and the patient improved with symptomatic treatment.

Methylene blue induces methemoglobinemia at doses greater than 7 mg kg\(^{-1}\) of body weight. Methylene blue is contraindicated in patients with glucose-6-phosphatase dehydrogenase deficiency because it can cause haemolysis. If the methemoglobin level is too high or if G6PD deficiency is present, exchange transfusion is indicated.5

Conclusion

We have described and discussed a rare and potentially fatal complication that we faced in our operation theatre. It is best to re-iterate that no material or drug given to a patient intra or post operatively should be considered inconsequential and should be administered with due care regarding its dosage and side effects.

References

1. Ernest Nadler, Henry Green, Rosenbaum. IV injection of methylene blue and its toxic symptoms and effects on ECG American Journal of Medical Sciences 1934; 188: 15-21