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Case Report

Anaesthesia Section

Challenges Encountered during Anaesthetic Management of a Patient with Congenital Methaemoglobinemia Posted for Laparoscopic Inguinal Hernia Repair: A Case Report

VINITA JAIN[1], NIDHI SULTANIA[2]

ABSTRACT

Methaemoglobinemia is a rarely encountered haematological condition that can be congenital or acquired. Methaemoglobin is an abnormal type of haemoglobin that is oxidised and incapable of delivering oxygen to tissues. This can lead to cyanosis, hypoxia, acidosis, arrhythmias, and more, depending on the methaemoglobin concentration, and can be fatal. A thorough understanding of the disease process is essential to develop a suitable anaesthesia plan and prevent complications. Ensuring adequate tissue oxygenation, assessing oxygenation using appropriate monitoring tools, and avoiding trigger agents are the cornerstones of anaesthetic management. A co-oximeter is the gold standard for monitoring, as it detects and quantifies methaemoglobin levels. Methylene blue acts as an antidote, functioning as an oxidising agent that converts itself to leukomethylene blue, which reduces methaemoglobin back to haemoglobin. In the present case of a 60-year-old male, the authors present the anaesthetic management and challenges in a diagnosed case of congenital methaemoglobinemia undergoing laparoscopic inguinal hernia repair surgery. Methylene blue was administered prophylactically preoperatively. An arterial line was established before anaesthesia induction for close haemodynamic monitoring and quick blood gas and oxyhaemoglobin sampling, as a co-oximeter was not available. Adequate oxygenation during induction and emergence was ensured to prevent hypoxia, given the lower amount of normal haemoglobin in these patients. All potential trigger agents, such as nitrous oxide, local anaesthetics, nitrates, and metoclopramide, were avoided. The patient had an uneventful intraoperative and postoperative course and was discharged after one day.

Keywords: Co-oximeter, Methylene blue, Oxyhaemoglobin

CASE REPORT

A 60-year-old male was scheduled for laparoscopic inguinal hernia repair. The patient had a history of congenital methaemoglobinemia diagnosed 10 years ago and was being treated with a daily 100 mg tablet of ascorbic acid and intermittent injections of 1% methylene blue at a dose of 1 mg/kg, usually given once a month or when experiencing symptoms such as headache, fatigue, or bluish discolouration of the skin. The patient had no other co-morbidities, drug allergies, unremarkable physical examination findings including no cyanosis, and good exercise tolerance. In the family history, the patient's son was also diagnosed with methaemoglobinemia but did not require treatment. Preoperative routine investigations were within normal limits, and the patient's methaemoglobin level was 5%. Preoperative arterial blood gas analysis showed normal values with an oxyhaemoglobin saturation of 95%.

The patient was taken for surgery after providing informed consent and fasting for six hours. A preoperative dose of methylene blue at 1 mg/kg was administered 30 minutes before the surgery as prophylaxis over a five-minute period. All routine monitoring was established, and an invasive arterial catheter was placed for arterial blood gas analysis, oxyhaemoglobin level measurement, and haemodynamic monitoring. The patient's SpO_2 was 98%.

Preoxygenation with 100% oxygen was performed for three minutes, followed by premedication with intravenous Glycopyrrolate 0.2 mg and Midazolam 1 mg before inducing anaesthesia with propofol at 2 mg/kg intravenously. Tracheal intubation was facilitated with atracurium at 0.5 mg/kg intravenously. Anaesthesia was maintained with a mixture of 50% oxygen and 50% air, along with Sevoflurane at 1-2%. Arterial blood gas analysis was conducted 30 minutes after the start of the surgery, showing pH 7.4, pCO_2 38 mm Hg, pO_2 260 mm Hg, and oxyhaemoglobin at 97%. The patient's vital signs remained stable throughout the procedure, with an SpO_2 of 96%. The surgery lasted for one hour, and the patient was successfully extubated after adequate neuromuscular recovery.

Postoperatively, the patient remained stable and received oxygen at a rate of 6 L/min via a Hudson's mask for one hour. Subsequent Arterial Blood Gas (ABG) analysis showed no signs of acidosis, with an oxyhaemoglobin level of 95%. The methaemoglobin level was also measured and remained at 5%. After one day of observation, the patient was discharged and during a follow-up visit with the surgeon after seven days, the patient remained haemodynamically stable and did not require intravenous methylene blue postsurgery.

DISCUSSION

Haemoglobin contains two alpha and two beta globin chains. Each chain binds to iron (Fe^{2+}) containing heme. When the iron atom gets oxidised (Fe^{2+} to Fe^{3+}), methaemoglobin is formed, which does not bind to oxygen and shifts the oxyhaemoglobin dissociation curve to the left by allosterically increasing the affinity of the rest of the heme to oxygen [1]. Normally, the methaemoglobin level is 0.4-1.5%. It is maintained with the help of the enzyme Nicotinamide Adenine Dinucleotide Hydrogen (NADH) cytochrome b5 reductase (95%) and Nicotinamide Adenine Dinucleotide Phosphate Hydrogen (NADPH) methaemoglobin reductase (5%), which reduce methaemoglobin back to deoxyhaemoglobin [2]. Methaemoglobinemia can be congenital or acquired. Congenital methaemoglobinemia can occur due to haemoglobin M, which has a mutation in the alpha/beta globin chain (autosomal dominant). In haemoglobin M, iron is stabilised in the ferric state. It can also be due to NADH methaemoglobin reductase 1 deficiency (autosomal recessive). It has three types. In type 1, enzyme deficiency is in erythroid cells. In type 2, it is in non erythroid cells and the Central Nervous System (CNS). In type

3, it is in non erythroid cells but the CNS is spared [3]. Acquired methaemoglobinemia is caused when oxidative stress overwhelms the normal enzymatic reductive pathway [4]. In the present case, as per the family history of the patient, an autosomal recessive variant is expected as the parents and siblings do not have this condition.

Methaemoglobinemia has a wide range of clinical presentations depending on methaemoglobin levels, its rate of accumulation, the level of enzyme activity to reduce it back, the patient's general condition, and oxidative stress. At >10%, mild cyanosis occurs peripherally, at >35%, weakness, headache, tachycardia, tachypnea, nausea, vomiting, dizziness, and palpitations occur, at >55%, syncope, seizures, coma, arrhythmia, lethargy, delirium and acidosis happen, and at >70%, it is fatal [5].

There are certain considerations to keep in mind while anaesthetising patients with methaemoglobinemia. There is interference with monitoring oxygen saturation. A standard pulse oximeter uses differential absorption at 660 nm (oxyhaemoglobin) and 940 nm (deoxyhaemoglobin) to determine oxygen saturation. Pulse oximetry is inaccurate in measuring oxygen saturation in patients with methaemoglobinemia as methaemoglobin shows equal absorption at 660 nm and 940 nm, resulting in a pulse oximetry reading around 85% [6]. A co-oximeter, which uses multiple wavelengths, can measure it accurately [7]. PaO_2 on arterial gas analysis represents dissolved oxygen in the blood, not saturated haemoglobin or the content of arterial oxygen, and is therefore misleading [8]. In a set-up where a co-oximeter is not available, the oxyhaemoglobin level should be measured on ABG analysis intraoperatively. Patients should be monitored for signs of hypoxia throughout surgery.

Preoperatively, all metabolic abnormalities should be corrected. An arterial catheter should be inserted to allow close haemodynamic monitoring, frequent blood gas analysis, and measurement of oxyhaemoglobin levels. In patients with methaemoglobinemia during induction and emergence from anaesthesia, a modest amount of respiratory depression causes a significant decrease in arterial oxygen due to the lower amount of normal haemoglobin [9]. Therefore, adequate oxygenation is recommended. Intraoperative blood loss should be well calculated and compensated for the prevention of hypoxia. The chocolate colour of arterial blood is indicative of methaemoglobinemia. Therefore, the colour of arterial blood should also be noted. Certain drugs frequently used by anaesthesiologists can trigger methaemoglobinemia. Substances at high-risk are prilocaine, benzocaine, nitroglycerin, nitrates/nitrites. The authors used air instead of nitrous oxide and avoided the use of local anaesthetics as they can trigger methaemoglobinemia. Lignocaine, nitrous oxide, bupivacaine, acetaminophen, aspirin, and fentanyl are at moderate risk. Propofol, thiopentone, inhalational agents, benzodiazepines, and succinylcholine are considered safe [9].

Methylene blue was administered prophylactically to the patient in the present case before the induction of anaesthesia. Methylene blue 1-2 mg/kg i.v. over five minutes is the first-line treatment for acute methaemoglobinemia. It works quickly, and methaemoglobin levels decrease within one hour. It can be repeated every 30-60 minutes until a total dose of 7 mg/kg is reached [3]. It works as a cofactor for NADPH reductase. It is ineffective in patients with G6PD deficiency as this pathway requires Glucose-6-phosphate Dehydrogenase (G6PD) as a cofactor and should be avoided during pregnancy [10]. One of the most common adverse effects of methylene blue is the bluish-green discolouration of urine. Another common adverse effect is limb pain following i.v. administration. Methylene blue may contribute to serotonin syndrome if combined with other serotonergic drugs such as Selective Serotonin Reuptake Inhibitors (SSRIs) Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) Tricyclic Antidepressants (TCAs) Monoamine Oxidase Inhibitors (MAOIs) due to the MAOI activity of methylene blue. Methylene blue can induce symptoms associated with the central nervous system in adults, including headaches, dizziness, and disorientation. Ascorbic acid 100-300 mg/day can be considered as an alternative drug. Hyperbaric oxygen, homologous transfusion, and exchange transfusion can be used in resistant cases [3]. Methylene blue and blood should be available before taking the patient for surgery. Supportive treatment by providing 100% oxygen and correction of metabolic acidosis should be done.

In the postoperative period, the patient should be provided with oxygen supplementation, monitored for signs of hypoxia, and undergo arterial blood gas analysis.

CONCLUSION(S)

Congenital methaemoglobinemia is a rare and complex pathological entity. Understanding it thoroughly will help the anaesthesiologist to draft a suitable anaesthesia plan and prevent complications. Anaesthetising patients with methaemoglobinemia is challenging due to the risk of hypoxia, potential triggers by drugs, and interference with monitoring. Avoiding potential trigger agents, using co-oximetry or intraoperative oxyhaemoglobin measurement serially, and having methylene blue available are paramount in the successful management of such cases.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Consultant, Department of Anaesthesia, Mangalam Plus Medicity Hospital, Jaipur, Rajasthan, India.
2. Senior Resident, Department of Anaesthesia, PGIMS, Rohtak, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Nidhi Sultania,
House No. 197, Sector 14, Rohtak-124001, Haryana, India.
E-mail: nidhi_sultania0110@rediff.com

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