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Anaesthetic Management Of A Patient With Methemoglobinemia: Case Report And Review Of Literature

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Abstract

Methemoglobinemia is a rare but serious haemoglobin disorder when red blood cells contain methaemoglobin at levels higher than 1%. Basically, it results from the oxidation of the ferrous iron in haemoglobin to the ferric iron. Methaemoglobin is incapable of carrying O_2, and high levels can impair O_2 delivery to the tissues. Methemoglobinemia can be congenital or acquired. Acquired methemoglobinemia is more common than the congenital variety.

Several factors must be considered when anesthetizing patients with methemoglobinemia, which include the potential for decreased oxygen delivery, which may be exacerbated by intraoperative blood loss and anaemia, interference with normal intraoperative monitoring devices, and the potential for medications to cause or exacerbate methemoglobinemia.

Here we describe a patient with congenital methemoglobinemia, which was diagnosed during preop evaluation for renal transplant on the basis of a discrepancy between the O_2 saturation noted by pulse oximetry and that obtained from arterial blood gas analysis and found to have NADH cytochrome b5 reductase deficiency. He is now posted for parathyroidectomy and total thyroidectomy. Anaesthetic care of patients with methemoglobinemia is discussed with a brief review on the topic.

Key words: Methemoglobinemia, Thyroidectomy, Oxygen delivery. Oxygen saturation-interpretation.

Introduction

Methemoglobinemia is a condition with a life-threatening potential in which a reduction in the

oxygen-carrying capacity of circulating haemoglobin occurs due to conversion of some or all of the four iron species from the reduced ferrous [Fe^{2+}] state to the oxidized ferric [Fe^{3+}] state. Ferric iron is unable to bind and transport oxygen. So Increased levels of methaemoglobin results in a state of functional anaemia.

Methemoglobinemia may result from congenital or acquired causes. Congenital forms of methemoglobinemia are due to autosomal recessive defects in the enzyme cytochrome b5 reductase (CYB5R) or due to autosomal dominant mutations in the genes that code for globin proteins collectively known as haemoglobins M [1]. Acquired methemoglobinemia, is much more common, is the result of exposure to substances that cause oxidation of the haemoglobin either directly or indirectly. This exposure results in the production of methaemoglobin that exceeds the body's capacity to convert the iron within the haemoglobin back to its ferrous state. Acquired methemoglobinemia may be due to exposure to direct oxidizing agents (e.g., benzocaine and prilocaine), indirect oxidation (e.g., nitrates), or metabolic activation (e.g., aniline and dapsone) [2].

We report a patient with diagnosed congenital methemoglobinemia undergoing parathyroidectomy and total thyroidectomy. The pathophysiology, aetiology, clinical manifestations, anaesthetic considerations, and treatment options of methemoglobinemia are discussed.

Case report

A middle aged male, known case of diabetes, hypertension, coronary artery disease, post renal transplant presented to hospital with swelling infront of neck of one year duration. He was found to have hyperparathyroidism also. Ultrasonography of neck showed TR 1/2/3 nodule of both thyroids and 7.7 x 6 mm lesion right hemi thyroid. Parathyroid hormone (PTH) level was found to be high. MIBI scan showed parathyroid adenoma. So he was planned to undergo parathyroidectomy and total thyroidectomy by endocrine surgeons.

Percutaneous transluminal coronary angioplasty had been done twice a few years back. He developed chronic kidney disease and underwent a successful renal transplant couple of years back. He was diagnosed to have methemoglobinemia due to NADH cytochrome b5 reductase deficiency at the time renal transplant.

He had poor effort tolerance of less than 4 METS. The physical findings were unremarkable, except for mildly cyanotic lips and nails. Vitals were pulse rate of 60 beats/min, regular and blood pressure of 160/90mm Hg in the right arm in sitting position. Patient's initial pulse oximetry reading was 91% on room air. On assessment of the airway, mouth opening was normal with adequate neck movements and Mallampati grade was 2. Neck examination revealed grade 2 goitre without compressive features or retrosternal extension. He had no features of hypo or hyperthyroidism.

His blood investigations were - Hb 17.7gm%, platelet count - 1.65 lakhs/mm^3, total count 6900 cells/mm^3, packed cell volume 57.2%, serum creatinine 1.25 mg/dl, serum sodium 137 meq/L, serum potassium 4.2 meq/L, random glucose 159 mg/dl, total thyroxine/T 4 7.51 ug/dl, TSH 0.823uIU/ml, PTH 251, serum calcium 10.1, phosphorous 3. Methemoglobin work up showed methemoglobin level 9.8% (normal $< 2\%$) and NADH-cytochrome b5 reductase level 15.59 IU/gHb (normal value 30-40). Chest X-ray showed cardiomegaly and electrocardiogram showed T wave inversion in I, aVL, V5, V6 leads. Echo showed concentric left ventricular hypertrophy, regional wall motion abnormality and grade 2 left ventricular diastolic dysfunction.

Cardiology, Nephrology and Haematologist opinions were obtained before taking for surgery. Written informed high-risk consent was taken before surgery in view of CAD, CKD, methemoglobinemia and patient kept fasting for 6-8 hours.

On the day of surgery, In the premedication room, a chocolate-brown coloured blood was noted

while cannulating the vein. He received injection midazolam 1mg, 0.2mg glycopyrrolate, 8 mg dexamethasone, 4mg ondansetron and antibiotic under supervision and monitoring.

In the operation theatre, all standard ASA monitors - 5 lead ECG, non-invasive blood pressure and pulse oximeter were attached. Room air saturation was 90%. Preoxygenation was done with 100% oxygen for 5 minutes. Saturation was increased to 100%. He was given fentanyl 100 mcg, priming done with atracurium and induced with etomidate 16 mg. Induction was performed with care to avoid hypotension and hypoxia. Atracurium 40 mg was given and intubated with 8 mm ID cuffed NIM FLEX endotracheal tube (nerve integrity monitoring Endotracheal tube) with cuff pressure of 25 cm H_2O and fixed it after bilateral air entry was confirmed. Maintenance was done with oxygen, air, sevoflurane and fentanyl 50 mcg/hr ensuring adequate depth of anaesthesia using entropy value of 40-60. Further administration of muscle relaxant was avoided because it will interfere with myographic signal with nerve integrity monitoring. An arterial line was inserted in the left radial artery. Intraoperatively, 1 Gram Paracetamol was given as infusion. We avoided NSAIDs and all drugs which will may precipitate methemoglobinemia like lidocaine, eutectic mixture of local anaesthetics cream, nitrous oxide, metoclopramide, nitroglycerine, sodium nitroprusside [3,4]. Adequate hydration was given with crystalloids ringer lactate and balanced salt solution (Sterofundin). Patient was positioned in a slight head up and neck extended position.

Patient was mechanically ventilated in a PCV-VG mode and the ventilatory settings were adjusted to end tidal carbon dioxide monitoring and care given particularly to avoid hypoxia. The temperature was monitored using a probe and maintained at 35◦C to 36◦C. Intermittent pneumatic compression device for thromboprophylaxis was placed. Intraoperatively patient was hemodynamically stable throughout the procedure. Once the surgery was over, neuromuscular blockade was reversed with 3 mg of neostigmine and 0.6 mg glycopyrrolate intravenously. He was extubated and then shifted to post operative ICU. Patient was kept in a slight propped up position and oxygen were supplemented at 4-6L/min via Hudson facemask.

Discussion

Methaemoglobin forms when haemoglobins Fe ion oxides from ferrous (Fe^{2+}) to ferric (Fe^{3+}). In healthy adults, a small amount of haemoglobin oxides to methaemoglobin and then it is rapidly converted back to haemoglobin such that methaemoglobin levels remain below 1% [5]. Methemoglobinemia is a rare but serious haemoglobin disorder when red blood cells contain methaemoglobin at levels higher than 1% [5].

Symptoms of methemoglobinemia appear depending on methaemoglobin level in blood. Chocolate colour cyanosis presents at levels of 5-15% and appears early in anaemic patients. At 30-40%, weakness, headache, dyspnoea, tachycardia and dizziness occurs. Patient will be lethargic, stuporous, confused and comatose at concentration of 55-60%. At 70%, circulatory collapse occurs [3,4].

Methemoglobinemia may result from congenital or acquired causes. Congenital forms of methemoglobinemia are due to autosomal recessive defects in the enzyme cytochrome b5 reductase (CYB5R) or due to autosomal dominant mutations in the genes that code for globin proteins collectively known as haemoglobin M [1]. Acquired methemoglobinemia is usually due to the exposure of drugs or chemical substances such as amyl nitrite, ethyl nitrite, sodium nitrite, silver nitrate, bismuth subnitrate, nitro-glycerine, quinones, dapsone, sulphonamide, sulphapyridine, sulfathiazole, aniline dye, acetanilid, aminobenzenes, aminophenol, benzocaine, prilocaine, and phenacetin [3,6]. The drugs used in anaesthetic practice that has the potential to cause methemoglobinemia are prilocaine, benzocaine, amyl nitrite, nitroglycerine, phenacetin, and sulphonamide.

Methaemoglobin has the same absorbability as Oxyhaemoglobin and Deoxyhaemoglobin so can affect oxygen saturation measurements by the pulse oximeter [7]. Therefore, the pulse oximeter cannot monitor methaemoglobin levels. Arterial blood gas analysis calculates oxygen saturation based on arterial oxygen tension and the temperature and may not reflect actual oxygen saturation. Methemoglobinemia diagnosis includes cyanosis; low arterial oxygen saturation that cannot be explained by a problem in the respiratory system or cardiovascular system; and when the normal oxygen partial pressure in the arterial blood gas analysis does not align with the oxygen saturation by the pulse oximeter. Oxygen carrying status is most accurately measured by analysis of all haemoglobin types with a co-oximeter [8].

Intraoperative monitoring should ideally include co-oximetry, which detects the presence as well as quantifies methaemoglobin level [9]. Pre-operative treatment with vitamin C helps in non-enzymatic reduction of methaemoglobin. Injection methylene blue is the antidote and the dose is 1-2 mg/kg IV over 3-5 min [10,11]. It acts by increasing the level of NADH methaemoglobin reductase, which helps in conversion of ferric ion to ferrous ion [12]. Exchange transfusion and haemodialysis is indicated in severe cases. In acquired methemoglobinemia offending drug should be withdrawn and care should be taken to avoid further exposure to the offending agent.

Conclusion

In conclusion avoidance of exposure to oxidizing agents is important in patients with congenital methemoglobinemia because of their deficient enzymatic pathways and decreased oxygen-carrying capacity. Preoperative considerations for congenital methemoglobinemia include the supplementation of oxygen of higher concentration, examination of methaemoglobin by co-oximetry to determine whether the oxygenation is adequate, avoidance of the use of oxidizing drugs (such as lidocaine, benzocaine, prilocaine, nitroglycerine), and treatment with methylene blue if methemoglobinemia deteriorates severely. If the patient is not responsive, exchange transfusion should be considered. To deliver safe anaesthesia in patients with congenital methemoglobinemia, it is important to recognize the nature of this rare disease, and to know how to correctly treat the patient who has sustained oxygen desaturation.

References

1. Curry S. Methemoglobinemia. Ann Emerg Med 1982; 11:214-21.

2. Bradberry SM. Occupational methaemoglobinaemia. Mechanisms of production, features, diagnosis and management including the use of methylene blue. Toxicol Rev2003; 22:13-27.

3. Hall DL, Moses MK, Weaver JM, Yanich JP, Voyles JW, Reed DN. Dental anesthesia management of methemoglobinemia-susceptible patients: A case report and review of literature.Anesth Prog. 2004; 51:24-7.

4. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: Etiology, pharmacology, and clinical management. Ann Emerg Med. 1999; 34:646-56.

5. Jaffe ER. Methaemoglobinaemia. Clin Haematol. 1981; 10:99-122.

6. Zosel A, Rychter K, Leikin JB. Dapsone-induced methemoglobinemia: case report and literature review. Am J Ther 2007; 14:585-7.

7. Haymond S, Cariappa R, Eby CS, Scott MG. Laboratory assessment of oxygenation in methemoglobinemia. Clin Chem. 2005; 51:434-444.

8. Alexander CM, Teller LE, Gross JB. Principles of pulse oximetry: theoretical and practical

considerations. Anesth Analg 1989; 68:368-76.

9. Kumar U, Aggarwal P, Handa R, Saxena R, Wali JP. Central cyanosis in a young man. Post grad Med J. 1999; 75:693-6.

10. Ralston AC, Webb RK, Runciman WB. Potential errors in pulse oximetry. III: Effects of interferences, dyes, dyshaemoglobins and other pigments. Anaesthesia. 1991; 46:291-5.

11. Prasad R, Singh R, Mishra OP, Pandey M. Dapsone induced methemoglobinemia: intermittent vs continuous intravenous methylene blue therapy. Indian J Pediatr 2008;75: 245-7.

12. Melarkode K, Prinzhausen H. Hemoglobin M variant and congenital methemoglobinemia: methylene blue will not be effective in the presence of hemoglobin M. Can J Anaesth 2008;55: 129-30.