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Case Report / Olgu Sunumu

Severe methemoglobinemia following intravenous lidocaine administration during coronary artery bypass surgery: The use of methylene blue and extracorporeal membrane oxygenator

Koroner arter baypas ameliyatı sırasında intravenöz lidokain uygulamasını takiben şiddetli methemoglobinemi: Metilen mavisi ve ekstrakorporeal membran oksijenatör kullanımı

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ABSTRACT

A 63-year-old male patient underwent coronary artery bypass surgery under cardiopulmonary bypass. Preoperative test results were all normal. During surgery, sudden methemoglobinemia developed after the intravenous administration of lidocaine which was used to prevent arrhythmias. In the intensive care unit, methylene blue was given to the patient and an extracorporeal membrane oxygenator was used to correct deep hypotension and worsening hemodynamic parameters. However, the patient died from multiorgan failure secondary to hypoxia. In conclusion, many factors may play a role in the etiology of methemoglobinemia. Treatment options are limited. Methylene blue is used as an effective method in the treatment. Lidocaine is one of the most common drugs used in the practice of cardiology and cardiovascular surgery. Therefore, the possibility of developing methemoglobinemia should be always kept in mind.

Keywords: Extracorporeal membrane oxygenator, lidocaine, methemoglobinemia, methylene blue.

ÖZ

Altmış üç yaşındaki erkek hastaya kardiyopulmoner baypas ile koroner arter baypas cerrahisi yapıldı. Ameliyat öncesi test sonuçlar normaldi. Cerrahi sırasında aritmileri önlemek amacıyla kullanılan intravenöz lidokain uygulamasının ardından ani methemoglobinemi gelişti. Yoğun bakım ünitesinde, hastaya metilen mavisi verildi ve derin hipotansiyonu ve kötüleşen hemodinamik parametreleri düzeltmek için ekstrakorporeal membran oksijenatörü kullanıldı. Ancak hasta hipoksiye sekonder çoklu organ yetmezliğine bağlı kaybedildi. Sonuç olarak, methemoglobinemi etyolojisinde çok sayıda faktör rol oynar. Tedavi seçenekleri sınırlıdır. Tedavide metilen mavisi etkili bir yöntemdir. Lidokain, kardiyoloji ve kardiyovasküler cerrahi uygulamasında en sık kullanılan ilaçlardan biridir. Bu nedenle, methemoglobinemi gelişme olasılığı her zaman akılda tutulmalıdır.

Anahtar sözcükler: Eksrakorporeal membrane oksijenatör, lidokain, methemoglobinemi, metilen mavisi.

Hemoglobin is an iron-containing protein and transports oxygen from lungs to the tissues in the body. A disorder of its structure or its abnormal levels can result in serious consequences. The iron in hemoglobin must be in ferrous form (Fe+2) to bind oxygen. If the iron in hemoglobin structure becomes oxidized to the ferric state (Fe+3), this hemoglobin is, then, named "methemoglobin" and cannot bind oxygen. In normal circulating blood, only a small percentage of hemoglobin (1 to 2%) is oxidized to methemoglobin. If methemoglobin level increases, methemoglobinemia occurs, leading to hypoxia, weakness, headache, metabolic acidosis, cardiac arrhythmias, coma, and death.[1] Methemoglobinemia can be congenital or acquired.[2] Patients with congenital methemoglobinemia are more tolerable to higher levels of methemoglobin than those with acquired methemoglobinemia.[1] Acquired methemoglobinemia

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may occur due to the ingestion or inhalation of nitrates, sulfonamides, aniline content materials, dapsone, and local anesthetics such as lidocaine and benzocaine.[3,4]

In the literature, although there are some reports of acquired methemoglobinemia due to the use of local anesthetics, dapsone and nitrates, there is no report of intravenous administration of lidocaine. Herein, we describe a severe methemoglobinemia case acquired after intravenous lidocaine administration during cardiopulmonary bypass (CPB), present our experience during its treatment and the results of using an extracorporeal membrane oxygenator.

CASE REPORT

A 63-year-old male patient weighing 80 kg with a body mass index of 26.4 kg/m^2 was admitted to our cardiology department due to acute chest pain during exercise. He was a smoker for 20 years. His medical history revealed no previous surgery or diabetes. He was using 50 mg/day oral metoprolol for two years for hypertension. He had a history of tooth extraction five years ago using local anesthetics with no complication. His electrocardiogram showed only a minimal ST-segment elevation in V1 and V2 leads. After a rapid initial evaluation, ischemic heart disease was suspected and coronary angiography was performed. A diagnosis of multivessel coronary artery disease was made and it was decided to perform coronary artery bypass grafting (CABG). The patient was informed about the disease and possible risks and benefits of surgical treatment. A written informed consent was obtained.

As a preparation for surgery, preoperative routine tests including complete blood count, blood biochemical test, determination of blood group, blood coagulation tests including activated partial thromboplastin clotting time, prothrombin time and international normalized ratio test, chest X-ray, pulmonary function tests, cardiac echocardiography, and carotid Doppler ultrasound were performed. All test results were normal. His left ventricular ejection fraction was 50% and he had no valvular disease. After anesthesia induction, an arterial blood gas (ABG) test was obtained which revealed normal results. The patient underwent four-vessel CABG under CPB. The ABG samples were taken at routine intervals during the operation.

The cross-clamping time and CPB time were 36 min and 55 min, respectively. During weaning period for CPB, 1 mg/kg of lidocaine was administered due to ventricular arrhythmias. This moment was the most critical time for the course of the operation. A few minutes later after the administration of lidocaine, the arterial blood color turned into venous color, indicating a major problem with the oxygenator, and we initiated mechanical ventilation with 100% oxygen and discontinued the CPB. We checked CPB circuit and oxygenator for possible blood clot; however, there was no problem with the CPB circuit or oxygenator. During mechanical ventilation, we obtained ABG samples which made us alert. At first, we attempted to solve oxygenation problem by hyperventilation, but this maneuver did not work. The patient's oxygen saturation was low, and the blood was in dark chocolate color. We checked the ABG repeatedly and found out that the patient's methemoglobin level was excessively high (35 mmoL/dL). The patient was diagnosed with methemoglobinemia. Immediately, 1 mg/kg of methylene blue was given intravenously over 5 min. The patient was transferred to the intensive care unit with inotropic support of dopamine and norepinephrine. The ABG tests showed that methemoglobin level decreased (25 mmoL/dL), but it was still not within normal levels. The same dose of methylene blue was administered once again. Hemodynamic parameters were deteriorated gradually and high methemoglobin levels persisted. The patient became worse, and an intra-aortic balloon pump was inserted to improve hemodynamic parameters; however, this attempt failed. Extracorporeal membrane oxygenator was started immediately via the femoral artery and femoral vein to save time to provide methemoglobinemia treatment by preserving the hemodynamic parameters. However, hypoxia and high methemoglobin level continued in the ABG tests. The day after extracorporeal membrane oxygenator was initiated, the patient died from multiorgan failure secondary to hypoxia.

DISCUSSION

Methemoglobinemia is an unusual medical problem, and its occurrence and treatment have not been fully understood, yet. There are case reports and case series reporting methemoglobinemia after the use of different drugs and even some foods.[5-7] Some drugs even at therapeutic doses can cause enhanced oxidation of heme iron to form methemoglobin. If methemoglobin levels exceed 10%, cyanosis emerges.[8] Methemoglobin seriously impairs tissue oxygenation, as the ferrous heme cannot bind oxygen. If methemoglobin levels exceed 30%, cardiovascular and cerebral symptoms appear.

In healthy individuals, the methemoglobin levels are kept below 1% by methemoglobin reductase enzyme.[9] This enzyme plays a key role in reducing

methemoglobin, which is in the ferric structure, back to ferrous form, and hereditary deficiencies of its activity results in chronic methemoglobinemia, called hereditary methemoglobinemia.[10]

There are two different ways in the development of acquired methemoglobinemia: direct oxidation or indirect oxidation of hemoglobin. In the direct oxidation mechanism, rarely Fe+2 in hemoglobin can be directly oxidized to Fe+3 to form methemoglobin. Nitrates (e.g., nitroprusside), nitrites (amyl nitrite), and antimalarial quinones (pentaquine, chloroquine) can cause direct oxidation of hemoglobin.[11] Aromatic hydrocarbons (naphthalene, nitrobenzene), sulfonamides (trimethoprim/sulfamethoxazole, dapsone) and local anesthetics (benzocaine, prilocaine) are effective in indirect oxidation of hemoglobin.[11]

One way or another, methemoglobinemia above 30% is a life-threatening problem. In cases leading to severe oxidation, nicotinamide adenine dinucleotide phosphate (NADPH) methemoglobin reductase enzyme activity would be impaired, resulting in severe methemoglobinemia. In our case, the major concern was the development of sudden and severe methemoglobinemia, despite lidocaine administration at a therapeutic dose (1 mg/kg). In the treatment of methemoglobinemia, there are limited treatment options such as acidosis correction, removal of the substance that causes oxidation, and methylene blue administration. In our case, we added extracorporeal membrane oxygenator for three purposes to this treatment to control the patient's hemodynamic parameters (low blood pressure, tachycardia, hypoxia) and to save time to keep the patient alive, while the methylene blue infusion. Unfortunately, extracorporeal membrane oxygenator application did not provide any of these benefits. Of note, we were aware of the fact that extracorporeal membrane oxygenator would not contribute to oxygenation, as the main problem was not in the access of oxygen to the blood as in pulmonary embolism, but in the blood, itself.

In conclusion, many factors may play a role in the etiology of methemoglobinemia. Treatment options are limited. Methylene blue is used as an effective treatment method for methemoglobinemia. Extracorporeal membrane oxygenator application does not seem to be beneficial in the treatment, except it saves time for the patient. The use of plasmapheresis or hemodiafiltration may be effective; however, further studies are needed to draw a firm conclusion on this subject. Lidocaine is one of the most common drugs used in the practice of cardiology and cardiovascular surgery. Therefore, the possibility of developing methemoglobinemia should be always kept in mind.

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