Methaemoglobinaemia Due to Prilocaine Usage After Hair Transplantation: Case Report

Saç Ekimi Esnasında Prilokain Kullanımına Bağlı Methemoglobinemi

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ABSTRACT Hair transplantation under local anesthesia in the treatment of baldness has become a widely used popular method in recent years. Methaemoglobinaemia cases due to prilocaine use in local anesthesia has been reported in the literature. In this report methaemoglobinaemia that appeared in a 53 year old and 93 kg/180 cm male patient after subcutaneous administration of 600 mg prilocaine for follicular unit transplantation and its treatment with ascorbic acid is presented. Methylene blue is the first treatment choice in methaemoglobinaemia, but in emergency cases where methylene blue is absent, intravenous ascorbic acid may also be used. To the best of our knowledge, this is the first presented methaemoglobinaemia case that appeared after follicular unit transplantation. The aim of this presentation is to inform clinicians about the symptoms of methaemoglobinaemia and the treatment options in emergency situations.

Key Words: Ascorbic acid; prilocaine; methemoglobinemia

ÖZET Lokal anestezi altında saç ekimi son yıllarda kellik cerrahi tedavisinde sıklıkla uygulanan popüler bir yöntemdir. Lokal anestezi için kullanılan prilokaine bağlı methemoglobinemi vakaları daha önce literatürde rapor edilmiştir. Bu yazıda, 53 yaşında 93 kg/180 cm ölçülerinde erkek hastada saç ekimi esnasında kullanılan 600 mg prilokaine bağlı gelişen methemoglobinemi ve ascorbik asit ile yapılan tedavisi sunulmuştur. Methemoglobinemi tedavisindeki ilk seçenek metilen mavisidir fakat metilen mavisinin olmadığı acil durumlarda damar içi askorbik asit tedavisi de kullanılabilmektedir. Bildiğimiz kadarıyla bu vaka saç ekimi sonrasında karşılaşılan ilk methemoglobinemi sunumudur. Bu sunumun amacı, doktorların methemoglobinemi belirtileri ve acil durumlarda tedavi seçenekleri hakkında bilgilendirilmeleridir.

Anahtar Kelimeler: Askorbik asid; prilokain; methemoglobinemi

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Hair loss is an important cosmetic and psychosocial problem. The most common type of hair loss is androgenic alopecia that affects approximately 60% of men and its prevalence increases with age.[1] Hair transplantation is a surgical method for the treatment of baldness and has become popular in recent years.[2] Prilocaine can be used for local anesthesia throughout hair transplantation.[3] It has been reported that prilocaine can cause methaemoglobinaemia during epidural anesthesia, peripheral nerve blocks or local infiltration anesthesia.[4] In this report we presented a methaemoglobinaemia case after subcutaneous administration of 600 mg prilocaine for follicular unit transplantation (FUT) and its treatment with ascorbic acid.

CASE REPORT

Patient attended to our clinic with the complaint of baldness. His baldness was stage V alopecia according to the Hamilton-Norwood scale.[5] Physical examination revealed no pathologic findings. The patient received amlodipine 10 mg daily for the treatment of hypertension for last 2 years. Routine laboratory investigations including blood count, and biochemical tests were within normal limits. His ECG and PA chest x-ray were normal. In the operating room intravenous infusion with Ringer's lactate solution was started (180 ml/h). Heart rate (HR), noninvasive blood pressure (NIBP), peripheral oxygen saturation (SpO_2) and ECG were monitored. Intramuscular Diazepam 10 mg was administered half hour before the operation. Supplemental oxygen (4 L/min) was administered by nasally. Six hundred mg 1% prilocaine with 1:200,000 epinephrine was used for the anesthesia as local multiple injections of intermittent doses subcutaneously.

Total surgery time was six hours. The operative procedure was uneventful. During the surgery HR continued between 68-96 beats per minute and NIBP continued between 120/90-150/95 mm Hg. Towards the end of the operation there was a mild drop on SpO_2 (from 98% to 92%). Fifteen minutes after surgery he developed somnolence, cyanosis, hypotension, and transient respiratory arrest. Ambu ventilation with supplemental oxygen was performed. At this time blood pressure was 70/40 mm Hg, HR 130 beats/min, SpO_2 79% and capillary glucose value 98 mg/dl. Rapid infusion of 500 ml Hydroxyethyl starch 6%/130/0.4 (voluven) was started. Consciousness, breathing and blood pressure were restored 3 minutes later but cyanosis was not improved. Spontaneous respiratory effort was sufficient. There was no reason that can cause obstruction of the airways and breathing sounds were normal and equal bilaterally. Despite 100% oxygen treatment by mask, cyanosis persisted. We suspected a methaemoglobinaemia related to prilocaine. The diagnosis was confirmed with arterial blood gas analysis and values were as follows: pH: 7.41, PaO_2: 104 mm Hg, $PaCO_2$: 40 mm Hg, SaO_2: 77%, HCO_3: 25 mmol/l, methaemoglobin 21%.

Infusion of 50 ml/h 5% dextrose in water was provided in addition to Ringer's lactate via another venous route. Because of the methylene blue was unavailable in our hospital, ascorbic acid 500 mg was injected intravenously and three repeated doses were given. After administration of ascorbic acid, methaemoglobin level decreased gradually from 21% to 2% at the 10th hour (Table 1).

DISCUSSION

Methaemoglobinaemia is caused by the transformation of ferrous iron (Fe^{+2}) to ferric iron (Fe^{+3}) which hasn't got the ability to transport oxygen.[6] Cytochrome 5 reductase deficiency and congenital hemoglobin structural defects may have role in the etiology of methaemoglobinaemia.[7]

Further some oxidant reactors such as local anesthetics may cause acquired methaemoglobinaemia frequently. Prilocaine neurological and cardiologic toxicity rate is fewer than the other local anesthetics. In liver, o-toluidine occurs as a metabolite of prilocaine and may cause methaemoglobinaemia.[8]

Guay et al. have reported 68 methaemoglobinaemia cases caused by prilocaine in 37 children in England literature review between years 1949-2007. From all methaemoglobinaemia cases which were caused by local anesthetics, the rate of methaemoglobinaemia due to prilocaine was 28% (68/242).[4] To the best of our knowledge this is the first presented methaemoglobinaemia case caused by prilocaine during follicular unit transplantation.

TABLE 1: The progress of oxygen saturation and methaemoglobin levels per hour.

Time (hour)	SpO_2%	Methaemoglobin %
0	77	21
1/2	82.5	15.6
1	86.7	12.1
3	90.3	7.4
5	94.3	4.2
10	96.4	2

The safety dose range for Prilocaine is accepted as 8 mg/kg to 600 mg. Methaemoglobinaemia formation with local anesthetic dose was reported as at least 7.4 mg/kg[4]. In this present case total prilocaine dose was 6.5 mg/kg.

A recent study reported methemoglobin levels as 2.7% (0.9-15.4%) three hours later after general anesthesia and 300-400 mg prilocaine infusion.[9] Soeding et al. reported 4.1% (2.0-6.6) and 2.3% (1.1-4.9) methaemoglobin levels in patients whom peripheral neural blockage had been performed with 600 mg and 300 mg prilocaine.[10]

High rates of methaemoglobin levels in general anesthesia might have resulted from thiopental's hepatic enzyme induction. With this induction o-toluidine metabolite rates might increase and cause methaemoglobinaemia rapidly. Case reports of methaemoglobinaemia caused with co-medication of barbiturate and local anesthetic also support this theory.[11]

Similarly in the presented case, diazepam infusion might have a role in facilitation of methaemoglobin formation. Physiological level of methaemoglobinaemia in blood is lower than 2%. Clinical findings are closely related with tissue hypoxia with the decreasing of oxygen transporting ability. Fifteen percent of cases are asymptomatic and have a normal skin color. However 15% of cases have persistent cyanosis despite oxygen treatment. Neurological, respiratory and cardiologic problems occur when methaemoglobinaemia level is higher than 30% and these cases are fatal with a rate of 70%.[12] Methaemoglobinaemia may occur easily in patients with anemia and heart associated disease. We faced central cyanosis with syncope, hypotension and respiratory arrest in this case. Central cyanosis which could not be treated with supplemental oxygen therapy has dragged us to think of methaemoglobinaemia in this patient. High methaemoglobinaemia levels in arterial blood confirmed the diagnosis. If biochemical analysis could not be performed, central cyanosis (low SaO_2 levels) and brown chocolate colored blood despite normal PaO_2 may confirm the diagnosis too.

First treatment option of methaemoglobinaemia is methylene blue infusion. This treatment is performed when patient is asymptomatic and metHb level is higher than 30% or 20% MetHb levels with symptoms of disease. Additionally dextrose infusion should be applied to supply glycolysis, hexose monophosphate shunt and the efficacy of methylene blue. In cases of Glucose 6-phosphate deficiency methylene blue treatment is ineffective.[13]

Ascorbic acid infusion is the other treatment option in situation of absence of methylene blue. Doses of ascorbic acid may differ with a range 3.1–253.2 mg/kg. Recovery time for the decrease of MetHb lower than 2% may differ from 0.33 h to 36.2 h.[14]

In vitro studies had showed that ascorbic acid reduces the level of methaemoglobin in animal and human erythrocytes so ascorbic infusion had been thought to be used in methaemoglobinaemia treatment.[15,16] The main usage of ascorbic acid is treatment of prolonged oral therapy in congenital methaemoglobinaemia. The first treatment option in methaemoglobinaemia is methylene blue, but ascorbic acid may also be used too despite its low clinic experience.[17,18] Intravenous ascorbic acid treatment is more effective in patients when I.V methylene blue treatment is not available, in patients who have G6PD deficiency and in patients whose methaemoglobin level is higher than 40%.

In this present case methaemoglobinaemia was treated with the infusion of ascorbic acid. To our knowledge this is the first methaemoglobinaemia case appeared during follicular unit transplantation. Prolonged surgery time and doses of local anesthetics have role in formation of methaemoglobinaemia. Clinicians have to be alert for the symptoms and know the treatment options in emergency situations.

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