DOI: 10.4274/tpa.308

Methemoglobinemia due to prilocaine administration

Mehmet Tayip Arslan[1], Vefik Arıca[2], Murat Tutanç[2], Seçil Günher Arıca[3]

[1]*Mustafa Kemal University Medical Faculty, Department of Pediatrics, Hatay, Turkey*
[2]*Private Defne Hospital, Clinic of Pediatry, Hatay, Turkey*
[3]*Mustafa Kemal University, Department of Family Medicine, Hatay, Turkey*

Summary

Prilocaine is the one of the most utilized agents during dorsal penile block in order to prevent pain during circumcision. It is known that prilocaine may lead to methemoglobinemia in neonates and infants. Here we present a 56 days old male patient with prilocaine induced methemoglobinemia who had been referred to intensive care unit for his frank and instant cyanosis after circumcision. Detailed history taking revealed that he needed 1 mg/kg prilocaine administration twice for adequate anesthesia. Patient had frank cyanosis at administration with no other sign. During admission rate of methemoglobin was 16.2% in the blood of the patient and conservative measures lead to complete resolution of all symptoms. Since infants below six months of age are particularly prone to methemoglobinemia due to their low cytochrome b5 levels and fetal hemoglobine is closer to "ferric" state than adult hemoglobine, it is emphasized in this paper that other alternative anesthetic agents should be utilized instead of prilocaine for regional anesthesia in infants under six months age. *(Turk Arch Ped 2012; 47: 301-302)*

Key words: Methemoglobinemia, prilocain, circumcision

Indroduction

Circumscision is removal of the foreskin covering the end of glans penis by a surgical procedure. It has been reported to be the most common operation performed in the newborn period in USA (1,2). In recent publications, many benefits of circumscision including decrease in the frequency of urinary tract infections, prevention of cancer of the penile skin and prevention of contamination of viruses including human papilloma virus and HIV have been reported (1).

Dorsal penile nerve block (DPNB) is frequently used as a limited anesthesia method to prevent pain during circumscision (2). Prilocaine is being almost constantly used as an anesthetic substance (3). Methemoglobinemia is a complication of local anesthetic agents which may be fatal. Iron in hemoglobin is normally present as reduced ferrous iron (Fe^{+2}). The transformation of this iron to ferric iron (Fe^{+3}) by losing electron is prevented by cytochrome b5 system of the body and normally only 1-2% of hemoglobin is present in ferric state in the body. Since the blood cytochrome b5 level in young children is half of the level in adults, increase in methemoglobin level may lead to significant hypoxia in the tissues and cells in children (4).

In this article, a 56 day-old male infant in whom DPNB was performed for two times during circumscision and who was referred to the intensive care unit after two hours with a complaint of cyanosis was presented.

Case

A 56 day-old male patient was brought to the emergency department with a complaint of cyanosis two hours after administration of DPNB with prilocaine for two times at a dose of 1 mg/kg during circumscision and was internalized in the intensive care unit. On physical examination, the consciousness was open and pulmonary and cardiac sounds were found to be normal. However, the patient had cyanosis. The blood pressure was measured to be 74/42 mmHg. Oxygen at 5 L/min was started. Arterial blood gases were as follows: pH:7.43, PCO_2 36.8 mmHg, PO_2 98 mmHg and oxygen saturation 76%. Complete blood count and biochemical values were found to be

Address for Correspondence: Vefik Arıca MD, Mustafa Kemal University Medical Faculty, Department of Pediatrics, Hatay, Turkey
E-posta: vefikarica@hotmail.com **Received:** 09.07.2010 **Accepted:** 01.20.2011

normal. Lung graphy was found to be normal. The patient was continued to be breasfed. Methemoglobin level was measured to be 16.2% at the time of hospitalization. After one day cyanosis regressed and methemoglobin level decreased to 8.4% after 24 hours. Asymptomatic patients with a methemoglobin level below 20% may be followed up with preventive methods. Thus, methylene blue or ascorbic acid were not administered to our patient, since the methemoglobin level was 16% and no severe symptoms were present. The infant was discharged to come back for follow-up visits. In the follow-up, presence of Hb H was found on Hb electrophoresis.

Discussion

Since fetal hemoglobin is more apt to ferric state compared to adult hemoglobin (Hb A2), newborn infants have a greater tendency to methemoglobinemia. In addition, the fact that the activity of cytochrome b5 reductase enzyme is transiently deficient in the first 3-4 months of life leads to a tendency towards methemoglobinemia in newborns and infants (5). Our patient and a large proportion of the patients reported in the literature are below the age of four.

Delivery of oxygen to tissues markedly decreases in methemoglobinemia which occurs as a result of reduction of ferrous iron to ferric iron and potentially life-threatening hypoxemia occurs.

When methemoglobin level is above 10%, cyanosis appears primarily. Unless methemoglobin level exceeds 30-40% hypoxemia and signs related to decreased oxygen delivery are not observed. In the patient presented, the fact that no sign of hypoxemia except for cyanosis was observed suggested that this was related with a level of methemoglobin below 30-40%. Therefore, methemoglobinemia should be considered in the differential diagnosis of patients who present with cyanosis (3). When methemoglobin level in the blood exceeds 70%, convulsions, coma, cardiovascular collapse and even death may be observed (4,5).

If methemoglobin level is above 30%, 1% methylene blue can be administered intravenously at a dose of 1-2 mg/kg. If cyanosis does not improve in one hour, the same dose may be repeated. However, our patient improved with only breastmilk without a need for an additional treatment. It is not known if the improvement was spontaneous or related to breastmilk. If methemoglobin level is above 70% hyperbaric oxygen and exchange transfusion may be needed additionally. However, methylene blue increases methemoglobinemi in G6PD deficiency; it should not be administered, since it may lead to dyspnea, chest pain, tremor, cyanosis and hemolytic anemia. In this case, ascorbic acid (300 mg/day) may be used in treatment. Ascorbic acid reduces methemoglobin by an in vitro non-enzymatic route. The role of ascorbic acid in treatment of methemoglobinemia is predominantly related to long-term and oral use in hereditary methemoglobinemia (6).

In the literature, 2 mg/kg prilocaine has been used in patients younger than 6 months with prilocaine-related methemoglobinemia. In patients older than 6 months, doses higher than 2.5-5 mg/kg have been used. Prilocaine at a dose of 2 mg/kg has been reported to lead to methemoglobinemia in infants younger than 6 months in the literature (7). Therefore, prilocaine use is not recommended in infants younger than 6 months (7).

References

1. Razmus IS, Dalton ME, Wilson D. Pain management for newborn circumcision. Pediatr Nurs 2004; 30(5): 414-417.
2. Taddio A. Pain management for neonatal circumcision. Paediatr Drugs 2001; 3(2): 101-111.
3. Boran P, Tokuc G, Yegin Z. Methemoglobinemia due to application of prilocaine during circumcision and the effect of ascorbic acid. J Pediatr Urol 2008; 4(6): 475-476.
4. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med 1999; 34(5): 646-656.
5. Sivasli E, Gursoy T, Yurdakok M. Which local anesthesia should be used in neonatal circumcision in newborns? Saudi Med J 2005; 26(4): 690-691.
6. Honig GR. Hemoglobin disorder. In: Behrman RE, Kleigman RM, Jenson HB, (eds). Nelson textbook of pediatrics. Philadelpiha: Saunders, 2004:1478.
7. Guay J. Methemoglobinemia related to local anesthetics: a summary of 242 episodes. Anesth Analg 2009; 108(3): 837-845.