jmr Junior Medical Research

Full Text Article Open Access

Case Report

Methemoglobinemia: A rare complication of commonly used topical anaesthetic cream.

Daar Ghaniya [1*], Soni Naharmal [1], Hummler Helmut [1,2], Gupta Samir [1,3], More Kiran [1].

1: Sidra Medicine, Pediatric Department, Neonatology Unit, Doha, Qatar.
2: Weill Cornell Medicine, Doha, Qatar.
3: Durham University, United Kingdom.
* Corresponding Author.
Correspondence to:
ghaniyadaar@gmail.com
Publication Data:
Submitted: December 5, 2024
Accepted: March 12,2025
Online: April 30,2025

This article was subject to full peer-review.

Abstract

Cyanosis is a physical sign stemming from several causes that can develop at any age. However, its occurrence in the newborn period creates the utmost diagnostic and treatment challenges due to a very fragile period of the lifespan. Methemoglobinemia is a condition with life-threatening potential due to diminution of the oxygen-carrying capacity of circulating hemoglobin. Congenital methemoglobinemia is characterized by significantly reduced enzymatic activity to transform methemoglobin into functional hemoglobin. Acquired forms are more commonly seen and usually related to exposure to certain drugs and agents leading to the increased production of methemoglobin.
We herein report a rare case of acquired methemoglobinemia developed secondary to the local anesthesia applied for circumcision.

Keywords

Cyanosis; lidocaine; methemoglobinemia; newborn.

Introduction

Methemoglobinemia is a life-threatening hemoglobinopathy related to the oxidation of divalent ferro-iron of hemoglobin (Hb) to ferri-iron of methemoglobin (MetHb) that affect oxygen transport. Acquired Methemoglobinemia forms are the most common and occur due to the exposure to substances that cause oxidation of the Hb directly or indirectly [1,2].

Observation

A thirteen-day-old male was referred from another facility for circum-oral and peripheral cyanosis. This was noted by parents six hours after circumcision performed under local anesthesia: topical anaesthetic cream applied an hour before the procedure. The patient was born at term, via an uncomplicated vaginal delivery. No familial history of blood diseases or favism was noted. Weight of 3315g, a length of 51cm and a head circumference of 35.5 cm were recorded. Vital signs were normal. The patient was pale and dusky with peripheral cyanosis. Cardiac and peripherals pulses examination was normal. G6PD deficiency and sepsis were ruled out.
Oxygen therapy at 4 L/min was started with mild improvement of the saturation which variated around 85-88%. Chest X-ray and echocardiography did not reveal any cyanotic heart disease. Capillary blood gas analysis revealed a methemoglobin level of 46%, lactate 1.6 mmol/L and normal blood electrolyte levels. The diagnosis of methemoglobinemia was confirmed. Methylene blue of 0.5 mg/kg diluted in Dextrose 5% was given with slow infusion over 10-15 minutes using a filter. The patient recovered totally and rapidly within 2 hours after the treatment with methylene blue. All results of capillary blood gas analyses are shown in Table 1.

	Before the first dose of methylene blue	Before the second dose of methylene blue	One hour after the second dose	Two hours after the second dose
pH	7.42	7.43	7.39	7.48
pCO_2 (mmHg)	38	33	36	31
pO_2 (mmHg)	33	52	55	42
Oxygen saturation (%)	99.6	94.4	95.3	92.2
Lactate (mmol/L)	1.6	2.1	2.4	1.2
Hemoglobin (gm/dL)	164	141	156	134
Glucose (mmol/L)	4.7	4.9	5.5	4.6
İonized calcium (mmol/L)	1.38	1.29	1.35	1.41
HCO_3 (mmol/L)	23.8	23.5	22.6	25.1
Base excess (mmol/L)	0.4	-1.6	-2.7	0.5
Methemoglobin (%)	46.5	2	2.2	1.6

Table 1. Capillary blood gas analyses evolution under treatment.

	Age/ gender	agent	manifestations	Meth-Hb	Treatment
Larson et al. (2013)	4 months/female	EMLA ® application over torso and lower limbs	Seizure	22.8%	Anti-convulsant medication intravenous methylene blue 1.5 mg/kg
Shachor-Meyouhas et al. (2008)	28 days/female	EMLA ® application over lower back	-	32%	IV MB 0.3 mg/kg
Sinisterra et al. (2002)	7 months/female	EMLA ® application over both groins to cover an area of ~8 cm^2	-	16%	Double dose of intravenous methylene blue 2 mg/kg
Couper et al. (2000)	4 days/ male	EMLA ® application over penis	-	16%	-
Elsner et al. (1997)	7 days/-	EMLA ® application over 10 cm^2 on sacrum, right buttocks, upper leg	Sleepiness		-
Kuiper-Prins et al. (2016)	12 days/ male	EMLA ® application over penis	-	16%	Oxygen
Jakobson et al. (1985)	3 months /male	EMLA ® application over back of the hands and in cubital regions	-	28%	Intravenous methylene blue 1 mg/kg
Bohnhorst et al. (2017)	1 day/male	Intravenous lidocaine infusion	Seizure	13.8%	Oxygen
Gala et al. (2017)	26 days/male	Combination of exogenous (application of silver sulfadiazine cream over umbilicus) and endogenous (sepsis, diarrhea and acidosis)	Loose motions, vomiting and drowsiness	31%	Intravenous methylene blue2 mg/kg
Erol et al (2017)	1 day,male	Maternal prilocain administration for pudendal anesthesia	Cyanosis	40%	Double dose of 300 mg/kg of ascorbic acid

Table 2: methemoglobinemia treatment literature review.

Discussion

We herein report thirteen-day-old neonate with the diagnosis of methemoglobinemia developed after the application of lidocaine/prilocaine containing local anesthesia for circumcision. The patient completely recovered following the treatment with intravenous methylene blue. Neonatal methemoglobinemia can be congenital or acquired. Congenital form reveals progressively with increasing central cyanosis just after birth [3-5]. This form is related to genetic enzymes deficiency and is rarely responsive to oxygen therapy. However, acquired methemoglobinemia develops secondary to precipitating agents and may occur at any time in the neonatal period including birth in case of maternal exposure during delivery [6]. The exposure causes acceleration of Hb oxidization from the ferrous to the ferric state. Several drugs were reported in methemoglobinemia cases. The most common drugs are benzocaine and lidocaine [7,8]. Newborn infants are particularly susceptible to the development of methemoglobinemia because the activity of cytochrome b5 reductase (CYB5R) is lower compared to adult. As MetHb does not transport oxygen, symptoms are essentially respiratory cardiovascular. Both intravenous ascorbic acid and methylene blue are effective treatments. Methemoglobinemia should always be considered in the differential diagnosis of cyanosis in newborns and neonates. Prompt diagnosis and treatment are crucial for complete recovery. Local anaesthetic including lidocaine/prilocaine should be used with caution for routine circumcision.

Citation: Daar Gh, Soni N, Hummler H, Gupta S, More K. Methemoglobinemia: A rare complication of commonly used topical anaesthetic cream. Jr. med. res. 2025; 7(1):12-14.

Conflict of Interest: None

References

[1] Iolascon A, Bianchi P, Andolfo I, Russo R, Barcellini W, Fermo E, Toldi G, Ghirardello S, Rees D, Van Wijk R, Kattamis A, Gallagher PG, Roy N, Taher A, Mohty R, Kulozik A, De Franceschi L, Gambale A, De Montalembert M, Forni GL, Harteveld CL, Prchal J ; SWG of red cell and iron of EHA and EuroBloodNet. Recommendations for diagnosis and treatment of methemoglobinemia. Am J Hematol. 2021 Dec 1 ;96(12) :1666-1678.
[2] Batton R, Villard S, Popoff B. Méthémoglobinémie [Methemoglobinemia]. Rev Med Interne. 2024 Aug;45(8):479-487.
[3] McNulty R, Kuchi N, Xu E, Gunja N. Food-induced methemoglobinemia: A systematic review. J Food Sci. 2022 Apr;87(4):1423-1448.
[4] Gao H, Basri R, Tran MH. Acquired methemoglobinemia: A systematic review of reported cases. Transfus Apher Sci. 2022 Apr;61(2):103299.
[5] Ivek I, Knotek T, Ivičić T, Rubinić B, Bajlo P, Hamzić J. Methemoglobinemia: A Case report and literature review. Acta Clin Croat. 2022 Jun;61(Suppl 1):93-98.
[6] Couper RT. Methaemoglobinaemia secondary to topical lignocaine/ prilocaine in a circumcised neonate. J Paediatr Child Health. 2000 Aug;36(4):406-7.
[7] Larson A, Stidham T, Banerji S, Kaufman J. Seizures and methemoglobinemia in an infant after excessive EMLA application. Pediatr Emerg Care. 2013 Mar;29(3):377-9.
[8] Shachor-Meyouhas Y, Galbraith R, Shavit I. Application of topical analgesia in triage: a potential for harm. J Emerg Med. 2008 Jul;35(1):39-41.
[9] Sinisterra S, Miravet E, Alfonso I, Soliz A, Papazian O. Methemoglobinemia in an infant receiving nitric oxide after the use of eutectic mixture of local anesthetic. J. pediatr.2002;141(2):285-86.
[10] Kuiper-Prins, E., Kerkhof, G.F., Reijnen, C.G.M. et al. A 12-Day-Old Boy with Methemoglobinemia After Circumcision with Local Anesthesia (Lidocaine/Prilocaine). Drug Saf - Case Rep 3, 12 (2016)
[11] Jakobson B, Nilsson A. Methemoglobinemia associated with a prilocaine-lidocaine cream and trimetoprim-sulphamethoxazole. A case report. Acta Anaesthesiol Scand. 1985 May;29(4):453-5.
[12] Gala HC, Madave A. An Unusual Case of Neonatal Methemoglobinemia. Indian Pediatr. 2017 Feb 15;54(2):163.
[13] Erol S, Arslan Z, Han Celik I, Yagmur Bas A, Demire N. Transient Methemoglobinemia in three Neonates due to Maternal Pudendal Anesthesia Journal of the College of Physicians and Surgeons Pakistan 2017, Vol. 27 (12): 783-784.
[14] Rzayev T, Arıcı Ş, Memişoğlu A, Özdemir H, Bilgen H, Özek E. Neonatal methemoglobinemia after subcutaneous injection of Lidocaine to the mother at birth. Turk Arch Pediatr. 2022 Sep;57(5):571-572

Citation: Daar Gh, Soni N, Hummler H, Gupta S, More K. Methemoglobinemia: A rare complication of commonly used topical anaesthetic cream. Jr. med. res. 2025; 7(1):12-14.