RESEARCH PAPER

Acquired Methemoglobinemia – A Sporadic Holi Disaster

Sanjeevani Satish Masavkar, Anupama Mauskar, Gaurav Patwardhan, Vasudeva Bhat and Mamta V Manglani

From Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai, India.

Correspondence to:
Dr Sanjeevani Satish Masavkar, Associate Professor, 242/9458, Kannamwar Nagar 2, Vikhroli E, Mumbai 400 083, India.
nagotkar.leena@gmail.com
Received: July 08, 2016;
Initial review: October 20, 2016;
Accepted: March 03, 2017.

Objective: To study clinical profile and outcome in patients with methemoglobinemia following exposure to toxic colors during Holi festival. **Methods:** This retrospective study included 112 children (5 to 12 years) admitted with methemoglobinemia after playing Holi. Clinical and treatment details were reviewed. **Results**: The common symptoms were giddiness, vomiting and headache. Treatment included thorough skin wash, intravenous fluid and methylene blue in 111 children. Age 7-9 and > 11 years, vomiting, giddiness, cyanosis, PaO2 < 80 mm Hg and oxygen saturation < 95% were associated with higher need for methylene blue. All children had a good outcome. **Conclusion**: Timely diagnosis and management of acquired methemoglobinemia can save lives.

Keywords: *Exposure, Management, Methylene blue, Toxic colors*.

Acquired methemoglobinemia occurs with contaminated colors (aniline dyes) [1]. Holi, a popular Indian festival, is celebrated using powdered or water-based colors in India. It marks the beginning of spring [2]. With the use of modern synthetic colors, which may be contaminated, the risk of methemoglobinemia has aggravated [3]. Toxic methemoglobinemia is also known after exposure to oxidant drugs, local anesthetic agents, high-nitrate food and aniline dyes, coloring compounds or cleaning solutions [4-9]. Though rare, it can be life threatening if not recognized and treated promptly. Though there are anecdotal reports and case series in literature, there are no large studies published so far [1,2,4-10]. We report 112 children with acquired methemoglobinemia during celebration of Holi in March 2012 with the objectives of studying their clinical profile, association of the requirement of methylene blue with clinical parameters as well as methemoglobin level, PaO_2 and oxygen saturation and outcome.

Methods

This is a retrospective analysis of records of all children below 12 years with acquired methemoglobinemia due to contaminated colors. History and clinical findings were reviewed from their charts for analysis with special reference to methemoglobinemia and its central nervous system consequences. Approval from Institutional ethics committee was obtained for publishing these data. Methylene blue was administered intravenously in the dose of 2 mg/kg/dose and repeated after one hour if cyanosis persisted. The number of doses of methylene blue required was noted.

Methemoglobinemia was defined as methemoglobin level >3% [6]. Children were grouped based on methemoglobin level and symptoms into 3 to 15%, 16 to 30%, and >30% for association with methlylene blue requirement [6,11]. Odds ratio and 95% CI were calculated as a measure of association. Statistical analysis was done using Stata 11.

Results

A total of 112 children (87 boys) with a mean (SD) age of 9.6 (1.88) years, who came to our hospital within 3 to 4 hours' time, were included. Seventeen children were aged between 5 to 7 years, 26 in the 7-9 year age group, 50 in 9-11 years, and 19 above 11 years. The common presenting features were giddiness (52, 46.4%), vomiting (50, 44.6%), headache (47, 42%), abdominal pain (16, 14.3%), and altered sensorium (15, 13.4%). Seizures were present in two children and breathlessness in three children.

On examination, 69 (61.6%) children had bluish discolouration of mucous membranes, 15 (13.4 %) were drowsy, and 2 (1.8%) had tachycardia. Glasgow Coma Scale in 15 children with altered sensorium was 5 to 10 in one and >10 in 14. Arterial blood gas analysis revealed acidosis in 47 (42%) children. On co-oxymetry, 70 (62.5%) children had PaO_2 less than 80 mm Hg and 83

WHAT THIS STUDY ADDS?

- Toxic contamination of Holi colors can lead to acquired methemoglobinemia, which should be promptly diagnosed and treated to save lives.

(74.1%) had SaO_2 less than 95%. The level of methemoglobin varied from 3% to 74%, with 3 to 15% in 71 (63.4%), 16 to 30% in 25 (22.3%) and >30% in 16 (14.3%) children.

Of the 80 children who required single dose of methylene blue, 66 had methemoglobin levels between 3 to 15% and 14 had levels 15 to 74%**.** Among the 22 who required two doses of methylene blue, 14 had 15-74% levels of methemoglobin, and all 9 children who required three does had high (>15%) methemoglobin level. It was found that age group of 7 to 9 years and more than 11 years; presence of giddiness, vomiting and cyanosis; level of methemoglobin; oxygen saturation less than 95%; and PO_2 less than 80 mmHg were significant determinants of higher need for methylene blue (***Table* I**).

Sixteen children with higher initial concentration (>30%) of methemoglobin showed gradual (in 24 h) reduction in methemoglobin levels with treatment. None of them required ventilator or inotropes, and were discharged within 36 (109 children) and 48 hours (3 children).

DISCUSSION

Chemical dyes in colors used during Holi festivals can harm humans and the environment [3,6,10]. High levels of methemoglobin following exposure to contaminated colors can lead to cyanosis, dyspnea, headache, giddiness, metabolic acidosis, CNS depression, seizure, coma and death [1-3]. In the present study too, children with methemoglobin between 3 to 15% had giddiness, vomiting, dyspnea, headache, fatigue and abdominal pain, with altered sensorium in those with level >15%; those with level >30% had altered sensorium, cyanosis and seizures in addition. Clinical presentation varied with the level of methemoglobin.

Arterial blood gases (PaO_2 and SaO_2) provide the level of decompensation, while co-oxymetry differentiates various states of hemoglobin, giving the level of methemoglobin [12].

The study has a limitation of being a retrospective analysis, and hence, lacks planned investigations such as a complete blood count and G6PD levels. There was no time to find out the contaminant as it was a mass casualty with 112 children within 3 to 4 hours. However, on follow up, the toxic substance was identified as aniline dye, used in leather industries in the locality. Fortunately, because of this, action was taken and this kind of disaster did not recur in subsequent years during the festival of Holi.

We conclude that colors used by children during Holi festival should be standardized and monitored for quality. Also, physicians should be aware of this rare cause of acquired methemoglobinemia for timely diagnosis and prompt treatment.

TABLE I FACTORS ASSOCIATED WITH HIGHER REQUIREMENT OF METHYLENE BLUE IN CHILDREN

Variables	*OR (95% CI)*	*P value*
Age (y)		
7.1 to 9	10.0 (1.1-87.5)	0.037
9.1 to 11	5.2 (0.6 - 43.3)	0.128
>11	11.6 (1.3-106.7)	0.030
Vomiting	3.9 (1.6-9.4)	0.002
Giddiness	4.1 (1.7-10)	0.002
Cyanosis	2.6 (1-6.6)	0.054
PO_2 <80 mmHg	0.2 (0.1-0.6)	0.005
SaO_2 (%) <95	0.2 (0.1-0.8)	0.021
Level of methemoglobin >15%	31.8 (9.6-105.4)	<0.001

Acknowledgments: We thank our former Dean, Dr. Sandhya Kamath and present Dean, Dr. Suleman Merchant for permission to publish this manuscript.
Contributors: SSM: conceived and designed the study, collected data, analyzed the study, and prepared manuscript; GP, VB: helped in management of patients and collection of the data; AVM: reviewed the manuscript and carried out critical revision; MVM: guided in management of patients, preparing the manuscript and finalization of the manuscript. The final version of manuscript was approved by all authors.
Funding: None; *Competing interests*: None stated.

REFERENCES

1. Mauskar A, Karande S, Kulkarni M. Acquired methemoglobinemia due to contaminated colours: A preventable disaster. J Trop Pediatr. 2009;55:139-40.
2. Zaki SA, Jadhav A, Chandane P. Methaemoglobinaemia during Holi festival. Ann Trop Paediatr. 2009;29:221-3.
3. Microsoft Word - Factsheet 8 Holi.doc - microsoft-word-Factsheet-8-Holi.pdf. Available from: *http://e-oexist.com/products/Holi/microsoft-word-factsheet-8-Holi.pdf*.

Accessed February 26, 2016.
4. Hadjiliadis D, Govert JA. Methemoglobinemia after infusion of ifosfamide chemotherapy: First report of a potentially serious adverse reaction related to ifosfamide. Chest. 2000;118:1208-10.
5. Dahshan A, Donovan GK. Severe methemoglobinemia complicating topical benzocaine use during endoscopy in a toddler: a case report and review of the literature. Pediatrics. 2006;117:e806-9.
6. Ashurst J, Wasson M. Methemoglobinemia: A systematic review of the pathophysiology, detection, and treatment. Delaware Med J. 2011;83:203-8.
7. Singh R, Vinayagam S, Vajifdar H. Methemoglobinemia as a result of accidental lacquer thinner poisoning. Indian J Crit Care Med. 2012;16:44-7.
8. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: A retrospective series of 138 cases at 2 teaching hospitals. Medicine (Baltimore). 2004;83:265-73.
9. Venkateswari R, Ganesh R, Deenadayalan M, Mahender E, Ramachandran B, Janakiraman L. Transient methemoglobinemia in an infant. Indian J Pediatr. 2007;74:1037-8.
10. Velpandian T, Saha K, Ravi AK, Kumari SS, Biswas NR, Ghose S. Ocular hazards of the colours used during the festival-of-colours (Holi) in India— malachite green toxicity. J Hazard Mater. 2007;139;:204-8.
11. Prasad R, Singh R, Mishra OP. Dapsone induced methemoglobinemia: Intermittent vs continuous intravenous methylene blue therapy. Indian J Pediatr. 2008;75:245-7.
12. Mack E. Focus on diagnosis: co-oximetry. Pediatr Rev. 2007;28:73-4.