GAVIN PUBLISHERS

Journal of Pharmacovigilance and Pharmacotherapeutics

Saxena S, et al. J Pharmacovigil Pharm Ther 2017: 106: JPPT-108.

DOI: 10.29011/JPPT-108. 100108

Case Report

Artemether Induced Methemoglobinemia: A Case Report

Nitika Agrawal*, RupaliShirke, Shruti Saxena

Department of Pediatrics, Swami Rama Himalayan University, Dehradun, India

***Corresponding author:** Nitika Agrawal, Department of Pediatrics, Swami Rama Himalayan University, Dehradun, India. Tel: +9826257878; E-Mail: drnitika80@rediffmail.com

Citation: Saxena S, Agrawal N, Shirke R (2017) Artemether Induced Methemoglobinemia: A Case Report. J Pharmacovigil Pharm Ther 2017: 106: JPPT-108. DOI: 10.29011/JPPT-108. 100108

Received Date: 12, May, 2017; **Accepted Date:** 15, May, 2017; **Published Date:** 20, May, 2017

Abstract

Artemisinin derivatives are drug of choice in complicated malaria. Here we describe a case of parenteral. Artemether induced methemoglobinemia with acute kidney injury in a child which we have treated with intravenous ascorbic acid and conservative management this case emphasizes for need of awareness this potential adverse effect i.e., Artemether induced Methemoglobinemia, its prompt recognition and management.

Case Summary

An eleven years old boy presented to pediatric emergency services with bluish discoloration of lips and nails for four days. He also had hematuria for two days. There were no complaints of cough, breathing trouble or palpitation, urinary frequency, urgency or burning sensation. Past history was unremarkable except a recent episode of febrile illness one week back for which he received intramuscular Artemether and oral paracetamol. His clinical examination revealed perioral and nail bed cyanosis with no other systemic abnormalities. His vitals were stable with respiratory rate of 32/min and heart rate of 96/min on admission. Pulse oximeter detected SpO2 of 65% at room air which persisted despite oxygen supplementation [10L/min]. He was shifted to pediatric intensive care unit and evaluated further. Complete hemogram showed microcytic anemia with neutrophilic leucocytosis. Liver and kidney function showed mild derangement. His arterial blood gas analysis showed hyperoxia despite low SpO2 on pulse oximeter. (Table 1)

Parameters	Report
Hemoglobin [g/dl]	6.49
Mean Corpuscular volume [FL]	75.55
Total Leucocytes count [thousands/cmm]	25.07
Differential Leucocytes counts[P/L/M][%]	80/10/10
Platelets [thousands/cmm]	143.6
LDH [U/L]	1683
Potassium/Sodium [mmol/L	2.84
Serum Bilirubin [Total/Direct] [mg/dl]	0.5
Aspartate Aminotransferase [IU/L]	133
Alanine Aminotransferase [IU/L]	26
pH/pCO_2 (mmHg)/pO_2 (mmHg)/base excess (mmol/L)	7.39/29/281/-6.50
Malarial Antigen/ Dengue NS1	Negative

Table 1: Baseline Laboratory Parameters

On the basis of above findings, he was suspected to have methemoglobinemia along with acute kidney. Anemia was probably due to hemolysis as supported by anisopoikilocytosis on peripheral smear and high LDH. He was started on intravenous vitamin C infusion empirically for methemoglobinemia after drawing blood sample for same. A dose of 500mg ascorbic acid was given intravenously over 6 hours. He received total 1500mg of intravenous ascorbic acid over 36 hour. His SpO_2 started improving at 24 hours and normalized at 36 hours from onset of infusion and subsequent doses were not required. On day 2 of admission child developed hypertension [140/100mm of Hg], nausea, abdominal pain along with raising serum creatinine for which symptomatic treatment was provided. However, he remained non-oliguric throughout admission. His hematuria resolved over next 5 days. Maximum serum creatinine noted was 4.4mg/dl and dialysis was not required. Serum methemoglobin level came out 27.5% confirming the diagnosis. He was discharged on day 9 of admission and further follow up of was done on outpatient basis, hypertension resolved in 2 weeks and tab Enalapril was stopped and serum creatinine normalized in 4 weeks (Figure 1).

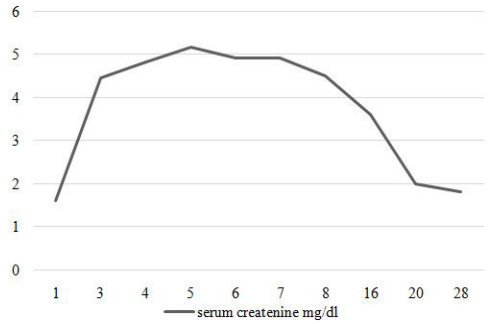

Figure 1: Serum Creatinine Variation against Day of Admission

Discussion

Hemoglobin auto-oxidation causes continuous production of methemoglobin, a variant with ferric iron [Fe3+] moiety in place of ferrous [Fe2+], incapable of binding as well as releasing oxygen. However physiologically its level is maintained below 1% by methemoglobin reductase enzyme system [1] an excess of methemoglobin can cause cellular hypoxia and has varied presentation from shortness of breath, mild dizziness to coma and even death. Any preexisting cardiac, respiratory or blood disorder can tilt the balance towards more toxicity [2,3]. The causation of such oxidative insult is variable. Non-improvement in oxygenation with high flow oxygen without apparent causes and saturation gap of >5% between ABG and pulse oximetry are considered diagnostic clues [4]. Congenital form usually presents in early infantile period and is due to deficiency of NADH-cytochrome b5 reductase mainly [5]. Acquired methemoglobinemia has been associated with various oxidative insults like antibiotics (sulfonamides, trimethoprim, and dapsone), local anesthetics (prilocaine, benzocaine), resburicase, chlorates, metochlopramide, primaquine and many other [6]. A prompt recognition of this and treatment is required as delay might be fatal.

Index case was asymptomatic prior to this episode of ailment. Development of methemoglobinemia in index case was temporally correlated with the administration of Artemether, an antimalarial. This association is not common and there is no usual warning or watch for this side effect in population. Treatment of methemoglobinemia is a watchful expectancy in mild case as resolution after cessation of offending agent has been noted in 36 hours. However, in cases with significant clinical features, distress or dizziness, a prompt treatment with reducing agents has been warranted. Methylene blue got reduced to Leukomethylene blue by NADPH-methemoglobin reductase. Leukomethylene blue acts as an artificial electron donor thus enhancing methemoglobin reduction inside erythrocytes [7]. However, its availability and risk of hemolysis in G6PD deficient person is a concern. Vitamin C or Ascorbic acid has been found to be equally efficacious for this reduction reaction to occur in vivo [8]. Index case received ascorbic acid infusion and showed good recovery. Methemoglobin is toxic to nephrons as well. Reports of acute renal toxicity and occasional requirement of prolonged dialysis are present [9,10]. Even an infusion of ascorbic acid infusion can cause nephrotoxicity [11-13]. Index case had transient non-oliguric acute kidney injury, probably due to methemoglobinemia. A close monitoring of renal function was done during ascorbic acid infusion and later on which showed gradual improvement and normalization in next 4 weeks. This case report highlights the rare occurrence of significant methemoglobinemia with the use of Artemether. An early suspicion and treatment will lead to complete recovery in such cases.

References

1. Wright RO, Lewander WJ, Woolf AD (1999) Methemoglobinemia: etiology, pharmacology and clinical management. Annal of Emerg Med 34: 646-656.

2. Price D (2002) Methemoglobinemia. In: 7. Goldfrank's toxicological emergencies. Mc GrawHill New York: 1438-1439.

3. Tran AN, Koo JY (2014) Risk of systemic toxicity with topical lidocaine/prilocaine a review. J Dermatol 13: 1118-1122.

4. Khanal R, Karmacharya P, Pathak R, Poudel DR, Ghimire S, et al. (2015) Do all patient with acquired methemoglobinemia need treatment- lesion learnt. J Community hospital internal medicine perspective 5: 29079.

5. Baraka AS, Ayoub CM, Kaddoum RN, Maalouli JM, Chehab IR, et al. (2001) Severe oxyhemoglobin desaturation during induction of anesthesia in a patient with congenital methemoglobinemia. Anesthesiology 95: 1296-1297.

6. do Nascimento TS, Pereira RO, de Mello HL, Costa J (2008) Methemoglobinemia: from diagnosis to treatment. Rev Bras Anestesiol 58: 651-664.

7. Khan NA, Kruse JA (1999) Methemglobinemia induced by topical anesthesia: a case report and review. Am J Med Sci 318: 415-418.

8. Topal H, Topal V (2013) Toxic methemoglobinemia treated with ascorbic acid: case report. Iran Red Crescent Med J 15: e12718.

9. Qureshi AH, Soberon DJ, Asif A, Vachharajani T, NayerA (2013) Methemoglobinemia induced acute kidney injury. The Open Urology & Nephrology Journal 6:36-41.

10. Kudale S, Sethi SK, Dhaiwal M, Kher V (2014) Methemoglobinemia due to Quinine Causing Severe AKI in child. Indian J Nephrol 24:394-396.

11. Lamarche J, Nair R, Peguero A, Courville C (2011) Vit CInduced Oxalate Nephropathy. Int J Nephrology 146927: 1-4.

12. Mashour S, Turner JF (2000) Acute Renal Failure, Oxalosis and Vit C Supplementation a case report and review of literature. Chest 118: 561-563.

13. Sunkara V, Pelkowski TD, Dreyfus D, Satoskar A (2015) Acute Kidney Disease Due to Excessive Vit CIngestion and Remote Roux-en-Y Gastric Bypass Surgery Superimposed on CKD. American J Kidney Disease 66: 721-724.