

# Cow's Milk -An Unusual Cause Of Methemoglobinemia In An Infant

Dr. Venkatesh.H.A

Consultant neonatologist Manipal hospital Bangalore, India

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**Abstract:** Methaemoglobinemia is a haematological disorder in which the iron within the haemoglobin molecule is oxidised from the ferrous to ferric state impairing the transport of oxygen causing cyanosis in children. The normal methemoglobin level in blood is approximately 1%.<sup>1</sup>Methaemoglobinemia can occur due to inherited problems or due to acquired causes (ingestion of certain drugs and chemicals, cow's milk allergy). The inherited form is usually due to deficient activity of NADH cytochrome b5 reductase.<sup>2,3</sup>Neither of these causes occurs frequently but the treating physician must be aware of them. The nitrate induced Methaemoglobinemia is encountered frequently in infants less than 6 months. Diagnosis is made by spectroscopic analysis of blood revealing characteristic absorption spectrum methemoglobin and electrophoresis can be used to confirm the presence of abnormal haemoglobin. Methylene blue is used in the treatment. We report a case in which one month old infant presented with Methaemoglobinemia following cow's milk ingestion.

**Keywords:** Cyanosis, cow's milk, diarrhoea, methemoglobinemia, methyleneblue.

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## I. CASE REPORT

A month old infant was brought to emergency room with history of loose motion since 4 days, bluish discoloration of body and difficulty in breathing since one day. The infant was born at term, by normal vaginal delivery weighing 3 kilograms (between 25<sup>th</sup> and 50<sup>th</sup> percentile). The post natal period was uneventful. Breast feed was introduced from day one of life. A week after birth, cow's milk was introduced in view of inadequacy of mother's milk.

At the time of presentation to emergency room, baby was dehydrated with bluish discoloration of lip, tongue, hands and feet. Baby was tachypnoeic but had a normal heart rate. Chest radiograph was normal. The laboratory investigation revealed the following results: Hb-18gm/dl, PCV-50%, WBC-10,000, N60%, L38%, platelet count-3.5 lakhs/mm, normal CRP and later, a sterile blood culture. Arterial blood gas analysis showed pH-7.36, PO<sub>2</sub>-120mm of Hg, PCO<sub>2</sub>-20mm of Hg and the simultaneous oxygen saturation was 78%. The high PO<sub>2</sub> with 100% inspired oxygen ruled out cyanotic cardiac lesion as a cause of cyanosis and was strongly in favour of abnormal haemoglobin. The colour of blood was chocolate brown. Hence clinical diagnosis of Methemoglobinemia was made. Blood methemoglobin level done at that time was 28% of total haemoglobin. The G6PD level was normal. Cytochrome B5 reductase was not done as the test was not available. Methylene blue, 2mg/kg/dose was administered intravenously. Gradually, the baby improved and cyanosis disappeared. The repeat methemoglobin level done in the next 24 hours was 2%. Mother was counselled and advised to stop cow's milk and encouraged to give breast milk only.

## II. DISCUSSION

Methemoglobinemia is a condition which has impaired ability to transport oxygen and carbon dioxide. NADH methemoglobin reductase protects against oxidative stress and help to reduce methemoglobin. Common causes of methemoglobinemia are due to ingestion of antibiotics (chloroquines and sulphonamides), drugs (Dapsone and phenytoin), industrial compounds, local anaesthetics, nitrates and nitrites and endogenous toxins (related to diarrhoea, infection or systemic acidosis) and rare genetic conditions like NADH methemoglobin reductase deficiency.<sup>3</sup>

Intestinal flora converts the nitrates into nitrites that act as oxidising agents. Small infants may be predisposed to methemoglobinemia as the level of cytochrome B5 reductase at birth is approximately half the level in adulthood (reaches adult level only after 4 months).<sup>4</sup> In addition, fetal haemoglobin is more easily oxidised, compared with the adult haemoglobin.<sup>5</sup> Relatively high gastric pH in infants enhances the bacterial growth in the intestinal tract, and these bacteria convert nitrates to nitrites.<sup>6</sup> Methemoglobinemia occurring in association with diarrhoea may be related to either systemic acidosis, or formation of nitrites from nitrates in gram negative infection or as a result of an idiopathic hypersensitivity reaction occurring in response to the particular protein contained within the milk as it was in our case.<sup>7</sup> Affected infants are most often ill out of proportion of their history of illness. Two other important clues in the diagnosis include cyanosis that does not resolve with administration of supplemental oxygen and blood that appears darker than normal. In patients with methemoglobinemia, arterial blood is frequently mistaken for being venous, and venous blood has chocolate brown colour. Cyanosis may occur when as little as 10% of the haemoglobin is in the methemoglobin form. At higher levels, patients will have marked respiratory distress as seen in our infant with the level of 28%. Haemolysis is more likely to occur in patients exposed to oxidising drugs or in those with G6PD deficiency. Methemoglobinemia may be suspected on history and physical examination. The diagnosis can only be confirmed with serum methemoglobin level measured by co-oxymetry. Pulse oxymetry shows low SaO<sub>2</sub> but normal PaO<sub>2</sub>.

Treatment is based on reducing the oxidised iron within the haemoglobin to its ferrous state. The treatment of choice is methylene blue 1-2 mg/kg given intravenously over 3-5 minutes.<sup>8</sup> Usually symptoms improve within one hour of administration. Methylene blue is recommended for symptomatic patients with methemoglobin levels greater than 20% or for asymptomatic patients with levels greater than 30%. Our index case received methylene blue as the infant was symptomatic and had methemoglobin level >20%. If no improvement occurs after 30 minutes, a dose of 1 mg/kg may be repeated. Though the drug is well tolerated, by itself the drug is an oxidising agent and may cause haemolytic anaemia when given in high doses or to patients with G6PD deficiency.<sup>9,10</sup> Our infant showed improvement with one dose and recovered within 24 hours. The management includes not just diagnosing and treating methemoglobinemia but needs evaluation of underlying cause and treatment. In our case, methemoglobinemia was acquired due to production of nitrites following cow's milk administration. The cause of diarrhoea could be due to hypersensitivity to animal protein. There was no family history of methemoglobinemia and methemoglobin levels done in parents were normal. Haemoglobin electrophoresis was normal.

**Methemoglobinemia should be considered in the differential diagnosis of sick child on cow's milk presenting with cyanosis, shock and respiratory distress.**

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