Case Report

Acute methaemoglobinaemia initially treated as organophosphate poisoning leading to atropine toxicity

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Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.100836

Quick response code

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ABSTRACT

A case of unknown compound poisoning is presented. It was initially treated as organophosphate poisoning with lack of response. A timely diagnosis of acute methaemoglobinaemia and iatrogenic atropine toxicity was made based on clinical evaluation. Treatment of methaemoglobinaemia using oral methylene blue and of atropine toxicity with supportive measures could save the patient.

Key words: Acute methaemoglobineamia, atropine toxicity, methylene blue

INTRODUCTION

Suicide is a major cause of premature mortality globally, for which a variety of chemicals are used. The treatment of poisoning due to an unknown compound becomes a challenge. It becomes more difficult when laboratory support to detect a certain specific poison is unavailable. Inj. Atropine and inj. PAM (pralidoxime) are used as the universal antidotes by some physicians for all pesticides poisoning. The consequences of misusing these drugs are rarely reported in the literature. Hence, timely diagnosis and treatment of acute methemoglobinaemia and iatrogenic atropine toxicity based on clinical evaluation is reported.

CASE REPORT

A 40-year-old female was referred from a peripheral hospital as a case of organophosphate (OP) poisoning. She had consumed poison the previous night and was admitted in the afternoon of the next day, after a lapse of 12 h, to our hospital. She had vomited once, and had loss of consciousness for some time. She had received stomach wash, inj. Atropine and inj. PAM as treatment for presumed OP poisoning.

At the time of admission to our hospital, she was drowsy and cyanosis of nails and lips were present. The tongue was bitten and the patient was afebrile. Pulse rate was 84/min and blood pressure (BP) was 130/80 mmHg, respiratory rate (RR) was 10/min and the pupils were normal sized and reacting to light. $SpO2_2$ was 82–84% on room air. Oxygen (O_2) supplementation was given with face mask. Inj. Atropine 3 mg IV stat was given and again 6 mg was repeated after 5 min, and then 1.8 mg hourly was continued. Inj. PAM 1 g IV and antibiotic were given. The serum cholinesterase level was 7850 U/L and the chest X-ray was normal.

After 2 h, the patient became irritable and tachypnoeic. SpO_2 was 82% with 8 L O_2 by mask. Pulse rate was 120/min and blood pressure was 130/80 mmHg, respiratory rate was 30/min and cardiovascular and respiratory systems were normal. Arterial blood gas (ABG) analysis showed pH of 7.39, $PaCO_2$ of 36.2 mmHg, PaO_2 of 68 mmHg and base excess of -2.4.

How to cite this article: Kakhandki S, Yahya M, Praveen M. Acute methaemoglobinaemia initially treated as organophosphate poisoning leading to atropine toxicity. Indian J Anaesth 2012;56:397-400.

Based on clinical condition and ABG analysis, the patient was sedated and intubated and put on ventilatory support. The patient's condition remained the same over the next 24 h. Later, on Day 2, the patient became agitated and was febrile. The pupils were dilated and reacting to light and cyanosis was present. The pulse rate was 140/min and blood pressure was 140/92 mmHg. Cardiovascular and respiratory systems were normal. Abdomen was distended. SpO_2 was 84% with FiO_2 0.8 on SIMV mode. ABG was repeated and showed pH of 7.44, $PaCO_2$ of 37 mmHg, PaO_2 of 269 mmHg and base excess of -1.7.

The presence of clinical cyanosis with normal PaO_2 and low SPO_2 was highly suggestive of methemoglobinaemia, which was further corroborated by the bed side test, which showed the presence of dark brown colour in patient's blood that failed to turn bright red on shaking and later not turning to chocolate red on drying.[1]

A total of 50 mL of 1% methylene blue solution was given in two divided doses at an interval of half an hour through the Ryles tube as an IV preparation was not available. After 1.5 h, the SpO_2 increased to 94%. The patient's consciousness level improved and ventilatory support was continued.

The next day, on Day 3, the patient was conscious, alert and haemodynamically stable. Ventilatory support weaned off and the trachea was extubated and put on face mask. After about 6 h of extubation, the patient became restless, irritable and tachypnoeic and the pulse rate was 120/min, blood pressure was 130/100 mmHg and SpO_2 came down to 84%. ABG was done and showed pH 7.4, $PaCO_2$ 36.8 mmHg, PaO_2 79 mmHg and base excess of -1.8.

The patient was reintubated and put on SIMV mode. This hypoxic state was suspected to be due to either atropine toxicity or due to methaemoglobinaemia as a result of release of poison from tissue stores.[1] Hence, atropine was stopped and a repeat dose of 50 mL of 1% methylene blue was given through the Ryle's tube. Ventilator support was continued overnight.

On the morning of Day 4, the patient was conscious, oriented and haemodynamically stable. SpO_2 was 98% with FIO_2 0.4. The patient was put on "T" piece for 2 h. ABG was done, which showed pH 7.42, PCO_2 37.6 mmHg, PaO_2 299 mmHg and base excess of -2.4. The patient was extubated and put on face mask. The patient was monitored for 48 h and then discharged from the Intensive Care Unit. Further recovery was uneventful.

DISCUSSION

Hospitals in rural areas bear the brunt of problems of poisoning, with case fatalities of 15–30%. These hospitals are not adequately staffed or equipped to deal with very sick patients. Intensive care beds and ventilators are in short supply and even unconscious patients are managed in open wards, with antidotes being poorly used or unavailable. Atropine and PAM are used as universal antidotes by some physicians for all pesticides poisoning. The consequences of misusing these drugs are rarely discussed in the literature.[2]

Atropine is the drug of choice for the treatment of OP nerve agent and insecticide intoxication. Adverse reactions to atropine may occur, and are of two types: toxic and allergic.[3,4] Toxic reactions are the most common, which result from anti-muscarinic effects of the drug. For treatment, Inj. physostigmine IV is preferred, along with monitoring of respiratory functions, level of consciousness and ECG. In few case reports, toxicity was reversed without the use of antidotes, with respiratory and haemodynamic support.[5] In our case, which was a case of methaemoglobinaemia, inappropriate atropine therapy resulted in iatrogenic atropine toxicity, which was timely recognized, and the patient improved with stoppage of atropine, along with respiratory and haemodynamic support.

Methaemoglobin is a derivative of normal haemoglobin in which iron of the haem complex has been oxidized from ferrous to ferric form. It does not combine with O_2 and thus will not take part in O_2 transport. Concentration of methemoglobin in the blood is less than 1% normally. This reduction of methemoglobin is accomplished by two mechanisms. One is the hexose-monophosphate shunt pathway within the RBC and the second uses two enzyme systems: Diaphorase–I, which requires NADH and Diapharease-II, which requires NADPH enzyme. The term methaemoglobinemia is used to describe excess accumulation of methaemoglobin in RBC.[6]

Causes of methaemoglobinemia include ingestion of phenacetine, sulphonamide, primaquine, dapsone,

nitrates, nitrites, nitrobenzene compounds, aniline dyes, deficiency of NADH/NADPH–haemoglobin reductase enzyme, abnormal haemoglobin with tendency to oxidize, etc.[6] [Table 1].

Diagnosis is based on definite cyanosis in the absence of cardiorespiratory disease, which persist on O_2 therapy and low SpO_2 with normal PaO_2 on ABG (calculated SaO_2).[8] The blood has a chocolate-brown colour, which does not disappear on O_2 therapy. It can also be identified spectrophotometrically by its absorption band part of the spectrum at 630 nm.[6] Pulse oximetry behaves differently in methaemoglobinemia. Methaemoglobin causes optical interference to the pulse oximeter by falsely absorbing light, which leads to a plateau in the oxygen saturation at 85%. In methaemoglobinemia, the severity of the cyanosis or the percentage of methaemoglobin in the blood does not correspond to the pulse oximetry reading. The diagnosis can be confirmed by measurement of methaemoglobin by a multiple wavelength co-oximeter.

Treatment mainly involves gastric lavage, stopping further exposure through skin and respiratory tract and ventilator support may be required. Methylene blue is the antidote of choice for methaemoglobinaemia. It accelerates the NADPH-dependent methaemoglobin reductase system by acting as a co-factor. The initial dose is 1–2 mg/kg IV over 5 min. Response will occur within 1 h.[7] It can also be given orally.[7,8] High absolute bioavailability of aqueous oral formulation makes it equally effective when administered orally.[9] Methylene blue is absorbed from the gastrointestinal tract. It is believed to be reduced in the tissues to leucomethylene blue. It is slowly excreted, mainly in the urine, together with some unchanged drug. In large doses, methylene blue can itself produce methaemoglobinemia. It should be used with caution in a renal impairment patient and in patients with G6PD deficiency and in pregnancy.[9]

A rapid disappearance of cyanosis in response to methylene blue would be expected within 1 hour, but may not occur if a patient has erythrocyte G6PD or NADPH-diaphorase deficiency or if methaemoglobin is due to ingestion of large amounts. A second dose may be required in these patients.[9]

Table 1: Signs and symptoms that are correlated with methemoglobin percentage[7]

Methaemoglobine %	Signs and symptoms
10–30	Only cyanosis
30–50	Tachycardia, dyspnoea, dizziness, fatigue
>50	Acute panic, vomiting, lethargy, stupor
>70	Death

In this case, the initial suspicion of OP poisoning made by the referral hospital and absence of clear signs due to the treatment initiated by them made us continue the same treatment as there was no facility to detect specific poisoning. Lack of response to treatment and clinical suspicion of methaemoglobinemia made us treat the patient with methylene blue. There was dramatic improvement in the patient's condition following this intervention, which was followed by deterioration. This deterioration was initially suspected to be due to atropine toxicity. Stopping of atropine and repeat dose of methylene blue improved the patient's condition.

CONCLUSION

Cases of methaemoglobinaemia due to agricultural (nitrobenzene) compounds' poisoning can be mistakenly treated as OP compound poisoning using inj. Atropine and inj. PAM as universal antidote in the periphery, resulting in fatal outcome. Timely diagnosis of methaemoglobinaemia based on clinical findings and treatment with oral methylene blue and also recognizing atropine toxicity due to its inappropriate use can prevent complications.

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Source of Support: Nil, **Conflict of Interest:** None declared

Conference Calendar Details

Name of the conference: 60th Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2012
Date: 26th to 29th December 2012
Venue: Labh-Ganga Convention Centre, MR 10-Bypass Junction, Indore, M. P., India
Organizing Secretary: Dr. Kishore Arora, Associate Professor of Anaesthesiology, M. G. M. Medical College & M. Y. Hospital, Indore 452 001, Madhya Pradesh, India
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Email: secretaryisacon2012@gmail.com, kkarora25@gmail.com
Website: www.isacon2012.com

Name of the conference: International Congress on Pediatric Airway
Dates: 8th & 9th September, 2012
Venue: Hotel Green Park, Chennai
Organising Secretary: Dr. S Ramesh, Kanchi Kamakoti CHILD's Trust Hospital, 12 A, Nageswara Road, Chennai – 34, Tamil Nadu, India
E-mail: info@icpa2012.com, paedsramesh@yahoo.com
Website: www.drsramesh.com

Name of the conference: XXV – BJSAC – 2012, 25th Annual State Conference of Bihar & Jharkand Chapter
Dates: 22nd & 23rd September, 2012
Venue: RIMS, Ranchi
Organising Secretary: Dr. PK Tiwari, Department of Anaesthesiology & Critical Care, Rajendra Institute of Medical Sciences, Ranchi – 834009, Jharkhand, India
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E-mail: drpkt80@gamil.com
Website: www.bjsac2012.com

Name of the conference: KISACON – 2012, 26th Karnataka State Conference of Indian Society of Anaesthesiologists
Date: 5th to 7nd October, 2012
Venue: T V Ramana Pai Convention Centre, Mangalore
Organising Secretary: Dr. AV Mallikarjun, Surgical Day Care Centre, "Sanjeevini" Falnir Road, Mangalore – 575 002, Karnataka, India
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Name of the conference: MASCON 2012
Date: 5th to 7nd October, 2012
Venue: The Convention Centre of the Residence, Powai
Organising Secretary: Dr. Vijjay Shetty, Tower 1, A-1402 Vikar Paradise, L. B. S. Road, Mulund (W), Mumbai – 400 080, India
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Name of the conference: 5th SAARC Critical Care Congress (SCCC) and 2nd International Conference on Recent Advances in Anesthesiology (INCRAA)
Date: 5th to 7nd October, 2012
Venue: New Delhi, India
Organising Chairperson: Dr. Chandralekha, Mobile: 9810413332/9868397800
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Name of the conference: ISACON Kerala - 2012, 36th Annual State Conference of ISA Kerala State Chapter
Date: 13th & 14th October, 2012
Venue: Kasaragod
Organising Secretary: Dr. Santosh Kamath, "Ashwathi", Opp. Ayyappa Temple, Nullippady, Kasaragod, Kerala 671 121, India
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Name of the conference: WISACON 2012, 9th West Zone and 45th Gujarat State Chapter of ISA, 2012
Date: 13th & 14th October, 2012
Venue: Institute of Management, Nirma University Campus, S G Highway, Ahmedabad, Gujarat, India
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Name of the conference: 3rd National Difficult Airway Conference (NDACON 2012)
Date: 26th & 28th October, 2012
Venue: Belgaum, Karnataka, India
Organising Chairperson: Dr. CS Sanikop
Organising Secretary: Dr. Rajesh S Mane, J. N. Medical College, KLE University Campus, and KLES Dr. Prabhakar Kore Hospital & MRC, Nehru Nagar, Belgaum - 590010, Karnataka, India
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Name of the conference: RSACPCON – 2012, 22nd National Conference of Research Society of Anaesthesiology and Research Pharmacology
Date: 26th to 28th October, 2012
Venue: B.M. Birla Science and Technology Research Center, Statue Center, Jaipur
Organising Secretary: Dr. SP Sharma, B – 77, Sethi Colony, Jaipur – 302 004, Rajasthan, India
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Name of the conference: 5th Annual Conference of Indian Association of Pediatric Anesthesia IAPA CON 2013
Workshop: Pediatric Regional Anesthesia and Difficult Airway - 8th February 2013
Date: 9th and 10th February, 2013
Venue: Hotel Taj gateway , Vadodara, Gujarat
Organising Secretary: Dr. Falguni Naregal, Neel Surgical Hospital for Children, Near Atithi Gruh, Akota, Vadodara - 390020, Gujarat, India
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Website: www.iapacon2013.org

Name of the conference: 10th Congress SAARC Association of Anaesthesiologists
Date: 22nd to 24th February, 2013
Venue: Bangabandhu International Conference Centre, Agargaon, Sher-E-Bangla Nagar, Dhaka-1207, Bangladesh
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