Other case reports

Severe methaemoglobinaemia treated with adjunctive hyperbaric oxygenation

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Abstract

(Lindenmann J, Fink-Neuboeck N, Schilcher G, Smolle-Juettner FM. Severe methaemoglobinaemia treated with adjunctive hyperbaric oxygenation. *Diving and Hyperbaric Medicine*. 2015June;45(2):132-134.)
Methaemoglobinaemia results from exposure to oxidizing substances such as nitrates or nitrites. Iron within haemoglobin is oxidized from the ferrous to the ferric state, which blocks the transport of oxygen and carbon dioxide, with subsequent inhibition of the respiratory chain. We describe the case of a 23-year-old male suffering from severe methaemoglobinaemia of 68% after consumption of nitrites ('poppers') in association with considerable ethanol consumption. Toluidine-blue was administered as first-line antidotal therapy immediately followed by hyperbaric oxygenation (HBOT). HBOT resulted in enhanced reduction of methaemoglobin, and rapid tissue re-oxygenation by the oxygen dissolved in plasma was provided, independent of the degree of methaemoglobinaemia. The patient recovered uneventfully and was discharged three days later. This case illustrates the potential of supportive HBOT as a time-saving therapeutic tool in this unusual situation, enabling a quick and sustained reduction in methaemoglobinaemia.

Key words
Hyperbaric oxygen therapy; drugs; toxicity; hypoxia; neuroprotection; case reports

Introduction

Acquired methaemoglobinaemia results from exposure to oxidizing substances such as nitrates or nitrites. Iron within the haemoglobin molecule is oxidized from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}). This converts haemoglobin to methaemoglobin which blocks the transport of oxygen and carbon dioxide. Due to the subsequent inhibition of the respiratory chain, cellular hypoxia develops, resulting in generalized mitochondrial respiratory insufficiency. Coma occurs rapidly once methaemoglobin levels of 60% of total haemoglobin are reached; death is usually associated with levels of more than 70%.[1,2]

The efficient management of patients suffering from methaemoglobinaemia remains a therapeutic challenge. The gold standard of treatment comprises 100% oxygen and intravenous administration of antidotes, i.e., methylene blue or toluidine blue. Hyperbaric oxygen treatment (HBOT) for severe methaemoglobinaemia is not standard clinical practice and its use remains controversial.[2] We report the case of a young male suffering from severe methaemoglobinaemia, treated with HBOT.

Case report

A 23-year-old male presented suffering from severe methaemoglobinaemia after oral ingestion of nitrites ('poppers') in combination with excessive alcohol consumption whilst at a party. Before the patient was picked up at the scene by the local emergency physician on duty, syncope had developed, followed by vomiting after he regained consciousness. After a brief stop at the nearest peripheral hospital for medical assessment confirming the suspected diagnosis, the patient was transferred to the university hospital because of the presence of a hyperbaric chamber there.

On admission, the patient was fully conscious (Glasgow coma scale 15) and deeply cyanosed, with a dark grey tinge and pronounced blue lips and fingers (Figure 1). Respiratory, cardiovascular and neurological examination was unremarkable. Continuous oxygen was provided

Figure 1
Clinical appearance of the patient's severely cyanotic hand on admission, compared to a normal person's

by mask as intubation and artificial ventilation were not considered to be indicated clinically. Arterial blood pressure was 110/80 mmHg, heart rate 137 beats per minute and temperature 37.1°C. Electrocardiogram revealed sinus tachycardia with no evidence of myocardial ischaemia; cardiac ultrasound confirmed normal function. Chest radiograph was normal.

Blood samples were drawn immediately on admission, before any diagnostic or therapeutic interventions. These revealed a methaemoglobinaemia level of 68% (normal range 0.4–1.0%), lactate 4.1 mmol·L^{-1} (normal range 0.5–2.2 mmol·L^{-1}), haemoglobin 15.7 g·L^{-1} (normal range 13–17.5 g·L^{-1}), haematocrit 45% and a mild leukocytosis. Blood alcohol level was 2.48% (53.9 mmol·L^{-1}) but further drug screening was negative. Samples were analysed according to international laboratory quality standards using the ABL800 FLEX analyzer to the manufacturer's instructions (Radiometer, Bronshoj, Denmark).

Following initial emergency department evaluation, 100 mg intravenous toluidine blue was administered. Immediately thereafter, HBOT (60 minutes 100% oxygen breathing at 303 kPa pressure and 30 minutes at 223 kPa) was initiated. After the first HBOT, the patient was transferred to the intensive care unit for further continuous oxygen administration combined with haemodynamic and respiratory monitoring. At this time, his cyanosis had reduced considerably, and laboratory values, apart from an increased leukocytosis, were improved (Table 1). After the second HBOT, the patient was transferred to the regular ward. The patient remained in a stable condition, and after a third HBOT, laboratory values had normalised (Table 1). His further course was uneventful, and he was discharged on the third day.

Discussion

A variety of different chemicals are capable of producing elevated levels of methaemoglobin, although nitrites or nitrobenzenes represent the most common causative substances. Inhalation of nitrous oxide or oral intake of nitrites ('poppers') is observed commonly amongst young adult party-goers. The rare but sometimes harmful consequences of these compounds are not well recognised and, therefore, underestimated in many cases.[3] Methaemoglobinaemia results in considerable cellular hypoxia and respiratory insufficiency. The clinical course in the present case, without any neurological sequelae, is noteworthy considering the fact that levels of methaemoglobinaemia exceeding 60–70% of total haemoglobin are usually associated with sudden coma and death.[1,2]

Up to now, intravenous administration of toluidine blue is the first-line antidote in the emergency treatment of patients with methaemoglobinaemia.[4,5] Toluidine blue (or methylene blue) accelerates the enzymatic reduction of methaemoglobin by NADPH-methaemoglobin reductase resulting in increasingly unblocking the respiratory chain. This vital process can be speeded up by adjunctive HBOT because the half-life of methaemoglobin is reduced by the higher oxygen partial pressures under hyperbaric conditions due to its competitive binding to the haemoglobin molecule. An additional rationale for using HBOT is based on the increased oxygen physically dissolved in the plasma while the patient is breathing 100% oxygen under elevated ambient pressure. At 283 kPa, the solubility of oxygen in whole blood is increased by approximately 6 vol%, approximately 300 ml of oxygen in a 5 L blood volume, which is sufficient for human basal metabolism, temporarily obviating the need for haemoglobin-bound oxygen transport under these conditions.[2,4,6,7]

To our best knowledge, this is the first report of HBOT in a case of severe methaemoglobinaemia, where the affected patient remained completely stable without deep unconsciousness throughout his entire course, although he also had excessive alcohol consumption. Notwithstanding that he was conscious and in a stable condition, this was a life-threatening situation. The loss of consciousness before admission, the concomitant ethanol poisoning and a methaemoglobinaemia of 68% represent three unpredictable components which might have resulted in sudden deterioration of the patient´s general condition resulting in possible cardiac arrest. Considering these factors and the clinical outcomes reported in the recent literature, HBOT appears to have served as an important supportive treatment option in this case.[2,4]

Table 1

Methaemoglobin levels, lactate and arterial blood gases before and after treatment

HBOT – hyperbaric oxygen treatment; MetHb – methaemoglobin; O_2Hb – oxyhaemoglobin; COHb – carboxyhaemoglobin; HHb – deoxyhaemoglobin; pO_2 – oxygen partial pressure; pCO_2 – carbon dioxide partial pressure; SO_2 – oxygen saturation; n/a – not applicable

	MetHb (%)	O_2Hb (%)	COHb (%)	HHb (%)	pO_2 (mmHg)	pCO_2 (mmHg)	pH	SO_2 (%)	Lactate (mmol·L^{-1})
On admission	68	30	1.6	2.3	135	34	7.39	99	4.1
After 1st HBOT	26	74	1.2	1.2	270	36	7.44	98	2.6
After 2nd HBOT	0.9	97	2.5	1	98	40	7.43	97	1.3
After 3rd HBOT	0.9	n/a	2.7	n/a	n/a	n/a	n/a	n/a	1.1

HBOT may be used as a sole treatment or combined with systemic administration of methylene blue.[2,4,8–10] When used, HBOT has been found to decrease the methaemoglobin level at a rate of about 8% per hour of exposure.[11] Due to the lack of a standardized treatment algorithm for HBOT in severe methaemoglobinaemia, and regarding the somewhat similar toxic mechanisms to that of carbon monoxide (CO) poisoning, we modified the HBOT protocol used for CO poisoning.[12] HBOT was initiated at a pressure of 303 kPa and daily treatments were given over three days.

In conclusion, the combination of toluidine blue or methylene blue administration and adjunctive HBOT enables a rapid and sustained reduction of methaemoglobinaemia in a severe poisoning. HBOT is a time-saving therapeutic tool that not only accelerates the elimination of methaemoglobin but may also have a protective effect against neurological sequelae from hypoxia by enhancing oxygen delivery to vital organs at a critical time.

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Acknowledgement

We thank the patient for his permission to report his case and use the photo of his hand.

Submitted: 11 July 2014, revised 08 October 2014 and 02 December 2014
Accepted: 11 April 2015

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