Teaching Point
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Unexpected cyanosis in a haemodialysis patient—did someone add hydrogen peroxide to the dialysis water?

Nicholas Newbigging, Willis Peel, Ewan Bell and Christopher Isles

Renal Unit, Anaesthetics and Department of Biochemistry, Dumfries and Galloway Royal Infirmary, Dumfries DG1 4AP, UK

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Introduction

Haemodialysis patients are at risk of poisoning by contaminants in dialysis fluid [1]; they are exposed to large volumes of water every time they dialyse, dialysis membranes offer a less effective barrier than the gastrointestinal tract and their renal failure renders them less able to eliminate toxins. Aluminium remains the classic example of such toxicity. Renal patients are also at risk of exposure to chemicals used to disinfect their dialysis water [2]. We wish to report the cases of four patients who became unwell during dialysis and were found to have methaemoglobinaemia following inadvertent exposure to hydrogen peroxide that had been used to decontaminate the hospital’s main water tank. We believe that this is only the second such report of its kind and that patients dialyzing in renal units that still rely on mains water for dialysis remain at risk.

Case reports

A 60-year-old man developed multi-organ failure after surgery for perforated duodenal ulcer, for which he required ventilation, dialysis and inotropic support. His condition improved slowly with treatment until the fourth post-operative day when pulse oximetry showed an unexpected fall in SpO₂ from 98 to 90% while on 38% oxygen. Following an increase in inspired oxygen to 100% his SpO₂ was 87% with SaO₂ 100%, PaO₂ 57.1 kPa (429 mmHg), PaCO₂ 5.5 kPa (41 mmHg) and H⁺ 33.9 (pH 7.47). Methaemoglobinaemia was suspected and confirmed at 9% (normal <1%). Dialysis was stopped, 100% oxygen was continued but no other specific treatment was prescribed. Methaemoglobin levels returned to normal over the course of the next 48 h. Haemoglobin fell from 87 to 63 g/l as a result of haemolysis requiring transfusion. The patient went on to make a full recovery.

The demonstration of methaemoglobin in this patient prompted the immediate review of all 16 patients dialyzing in Dumfries Infirmary that day. Abnormally high methaemoglobin levels of 27.2, 4.9 and 2.2% were detected in three others, all of whom were dialyzing in the hospital’s main renal unit. The most severely affected of these patients was being treated for acute renal failure and became cyanosed with SpO₂ 56%, SaO₂ 97% and PaO₂ 54.1 kPa (407 mmHg) despite increasing to high-flow oxygen (Table 1), and went on to develop significant anaemia with fall in haemoglobin from 79 to 57 g/l over the next 48 h. Treatment with high-flow oxygen led to a full recovery. Meanwhile in biochemistry, the analysers had produced unusual results for glucose, uric acid, cholesterol and triglyceride. The assays for these tests all use peroxidase enzyme as an intermediate step in the analytic process. An alternative water supply was required temporarily.

The cause of the methaemoglobinaemia in these patients, and of the disruption to biochemistry, was subsequently shown to have been hydrogen peroxide that had been used, unbeknown to us, to decontaminate the hospital’s mains water following isolation of Legionella bacteria in the main supply tank (Figure 1). Hydrogen peroxide in dialysis water from this tank was detectable at a concentration of 30 mg/l. All four affected patients had been exposed to dialysis water from this source. None of the 12 patients who were dialyzing with water from the renal unit’s water treatment plant were noted to be cyanosed. Water supply to the renal unit’s water treatment plant was held in a separate tank that had not been treated with hydrogen peroxide. Measurements of SpO₂, methaemoglobin and haemoglobin before and after the incident in one of these 12 patients were all normal. Hydrogen peroxide in dialysis water from the water treatment plant was undetectable (Table 1).

Discussion

We report four cases of methaemoglobinaemia in dialysis patients that occurred when hydrogen peroxide was added
The clue to the diagnosis of methaemoglobinaemia in our cases was the difference between oxygen saturation as measured by pulse oximetry and oxygen saturation calculated from arterial blood gas analysis, the so-called saturation gap \([4,5]\). Pulse oximetry is a simple spectrophotometric method that measures the contribution of oxyhaemoglobin and deoxyhaemoglobin to oxygen saturation. Hence, if a patient has significant methaemoglobin, which is unable to bind and carry oxygen, the SpO\(_2\) will be low. In contrast, arterial blood gas analysis uses an oxygen electrode to measure the partial pressure of oxygen dissolved in whole blood (PaO\(_2\)) and to estimate arterial oxygen saturation (SaO\(_2\)). SaO\(_2\) is a derived value, calculated by blood gas analysers from PaO\(_2\), pH and haemoglobin. Oxygen dissolved in whole blood (PaO\(_2\)) is normally in equilibrium with oxygen carried by haemoglobin in red cells except when dyshaemoglobins such as methaemoglobin are present. Thus, in the presence of methaemoglobin, both PaO\(_2\) and SaO\(_2\) are usually normal \([6]\).

Hydrogen peroxide is a powerful oxidizing agent that is generally considered both safe and effective. It has a wide number of applications that include the treatment of contaminated group waters, destruction of organic material in industrial effluent and the purification and disinfection of drinking water \([7]\). In our case, it was used successfully to remove Legionella from the hospital’s main water tank. It is not recommended as a disinfectant for dialysis water and only contaminated our supply because the renal unit was not informed that disinfection was taking place. Had we known then we would have flushed the system after disinfection until all traces of hydrogen peroxide had disappeared. The fact that hydrogen peroxide was not added to the water supply in the water treatment plant meant that the majority of our patients were unaffected and that only those exposed to water from the main water tank developed methaemoglobinaemia.

We subsequently reviewed the literature but found only one other report of methaemoglobinaemia due to hydrogen peroxide in dialysis patients. Nine children developed methaemoglobinaemia with levels 3.1–11% when a new dialysis unit opened in Israel. Hydrogen peroxide had been used to disinfect the water tank immediately before the first dialysis, but had not been flushed out before the first dialysis, and only contaminated our supply because the renal unit was not informed that disinfection was taking place. Had we known then we would have flushed the system after disinfection until all traces of hydrogen peroxide had disappeared. The fact that hydrogen peroxide was not added to the water supply in the water treatment plant meant that the majority of our patients were unaffected and that only those exposed to water from the main water tank developed methaemoglobinaemia.

 unexpectedly cyanotic in a haemodialysis patient

Table 1. Methaemoglobinaemia, measures of oxygenation and haemoglobin in selected ITU and renal unit patients according to water supply

|                      | Hospital main water tank | Water treatment plant |
|----------------------|--------------------------|-----------------------|
|                      | ITU                      | Renal unit            |
| MetHb (%)            | 9.0                      | 27.2                  |
| SpO\(_2\) (%)        | 87.0                     | 56.0                  |
| SaO\(_2\) (%)        | 100                      | 97                    |
| PaO\(_2\) (kPa)      | 57.1                     | 54.1                  |
| Hb before incident g/l| 89                       | 79                    |
| Hb after incident g/l | 74                       | 57                    |
| H\(_2\)O\(_2\) in dialysis water mg/l | ~30 | ~30 | Undetectable |

To convert PaO\(_2\) in kPa to mmHg: divide by 0.133.

Table 2. Causes of methaemoglobinaemia

| Congenital (less common than acquired) |
|---------------------------------------|
| Hereditary methaemoglobinaemia (Haemoglobin M)\(^a\) chemicals |
| Methaemoglobin reductase deficiency\(^b\) |
| Aniline, naphthalene, paraquat, potassium perchlorate, hydrogen peroxide |

Oxidant drugs

| Local anaesthetics esp lignocaine, benzocaine and prilocaine |
| Antibiotics esp dapsone, trimethoprim, sulphonamides |
| Nitrites including nitroglycerin, isosorbide dinitrate, isosorbide mononitrate, amyl nitrate |
| Antimalarials, primaquine and chloroquine |

\(^a\) A form of Hb that cannot carry oxygen.

\(^b\) A defect in body’s ability to reduce MetHb to Hb.

to their water supply following detection of Legionella bacteria in our hospital’s main water tank. Methaemoglobinaemia occurs when the iron in haemoglobin is oxidized from the ferrous to ferric state. Causes may be congenital or acquired and include a number of oxidizing drugs and chemicals (Table 2) \([3]\). Symptoms, which arise because ferric iron cannot carry oxygen, are related to the degree of methaemoglobinaemia. Normal methaemoglobin is \(<1\%\) of total haemoglobin. In a healthy individual, methaemoglobin levels of up to 20% will only cause cyanosis. Headache, weakness, tachycardia and breathlessness develop progressively when levels exceed 20%. Concentrations \(>70\%\) may be fatal \([3]\).
in whom SpO2 is low, but PaO2 and SaO2 are normal. The
differential diagnosis in such patients will include other dis-
orders in which a reduced amount of ferrous iron is present
such as carboxyhaemoglobinemia and sulphhaemoglobin-
aemia [6]. Notwithstanding, the sudden and unexpected
occurrence of central cyanosis, low SpO2, but normal ar-
terial gas analysis in a dialysis patient should lead the clin-
ician to suspect that an oxidizing agent such as hydrogen
peroxide has been added to the water supply.

**Teaching points**

1. Methaemoglobinaemia should be considered in any pa-
tient who presents with central cyanosis in whom SpO2
is low but PaO2 is normal.

2. The key to the diagnosis is the difference between
oxygen saturation as measured by pulse oximetry and
oxygen saturation calculated from arterial blood gas
analysis, the so-called saturation gap.

3. The differential diagnosis includes other disorders in
which a reduced amount of ferrous iron is present such
as carboxyhaemoglobinemia and sulphhaemoglobina-
emia.

4. The sudden occurrence of central cyanosis with low
SpO2 but normal arterial gas analysis in a dialysis
patient suggests that an oxidizing agent such as hy-
drogen peroxide has been added to the water supply.

5. Dialysis units that continue to receive at least some of
their water from their hospital’s main water tank remain
at risk.

**Conflict of interest statement.** None declared.

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