

## Case Reports

# Orthodeoxia and platypnoea after acute organophosphorus poisoning reversed by CPAP: a newly described cause and review of the literature

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The case of a 60-year-old male patient, who survived severe organophosphorus poisoning, and subsequently developed platypnoea and orthodeoxia is described. The patient was mechanically ventilated for a long period of time in the intensive care unit. During the weaning trial, he developed platypnoea and orthodeoxia ( $PaO_2$  85 mmHg in recumbency, and 40 mmHg in upright position). Interestingly, the patient's orthodeoxia was alleviated on continuous positive airway pressure (CPAP) treatment. This is a newly described cause of the platypnoea–orthodeoxia syndrome. The possible pathophysiological mechanisms are discussed and a review of the reported abnormal states associated with this condition is presented.

## Introduction

Dyspnoea in the upright position that is relieved by resuming the supine posture was first described by Burchell *et al.* (1) in 1949, and later Altman and Robin (2) coined the term 'platypnoea' (from the Greek words *platys*=recumbent and *pnoe*=breath). This is a rare form of dyspnoea and is usually accompanied by arterial desaturation in the upright position that is improved during recumbency, a condition that is called orthodeoxia (from the Greek words *orthos*=upright and *deoxia*=desaturation). Both platypnoea and orthodeoxia have been described in patients with different underlying conditions (2–28) (Table 1).

To our knowledge, the platypnoea–orthodeoxia couple has not been previously described in a patient with severe organophosphorus (OP) poisoning.

## Case Report

A 60-year-old farmer was admitted to the intensive care unit after attempting suicide by ingesting an unknown quantity of the OP insecticide dimethoate 2 h previously. On admission the patient was in deep coma, Glasgow coma scale (GCS) 4, had pinpoint-sized pupils and reduced muscle tone and tendon

reflexes. He was haemodynamically unstable with sinus bradycardia, (heart rate 45–55 beats  $\text{min}^{-1}$ ), multiple ( $>5 \text{ min}^{-1}$ ) unifocal ventricular extrasystoles and hypotension (mean arterial pressure  $<60 \text{ mmHg}$ ). He also had severe cyanosis, gasping respirations and diffuse rales on chest auscultation. Chest radiography was normal and  $PaO_2$ /fraction of

Table 1 Abnormal states associated with platypnoea–orthodeoxia

State	References
COPD	2–3
Shunts – intracardiac	4–14
– peripheral	15
Atrial septal aneurysm	16
Postpneumonectomy and postlobectomy	4, 14–19
ARDS	20
Diffuse parenchymal lung disease	21
Autonomic dysfunction	22
Ileus	23
Amiodarone lung toxicity	24
Eosinophilic endomyocardial disease	25
Cirrhosis	26–27
Pulmonary embolii	4
Constrictive pericarditis	28
Organophosphorus poisoning	Present case

Received 14 January 1995 and accepted 20 January 1995.

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COPD, chronic obstructive pulmonary disease; ARDS, adult respiratory distress syndrome.

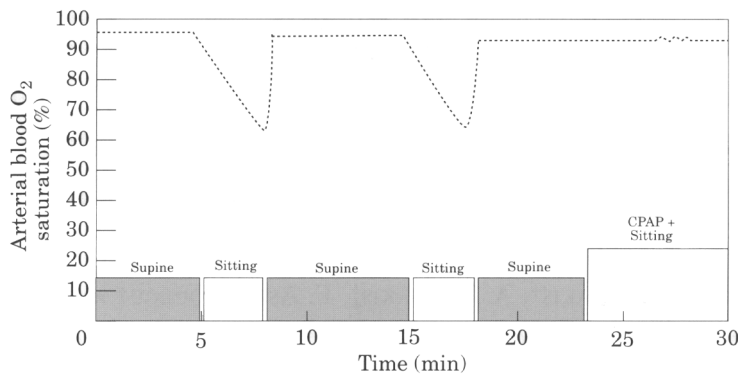


Fig. 1 Arterial blood saturation in sitting and supine positions, before and after CPAP. The desaturation in the sitting position was reversed by CPAP application. CPAP, continuous positive airways pressure.

inspired oxygen taken after 1 h mechanical ventilation was 320. The abdominal wall was soft, there were increased bowel sounds and sialorrhoea. Bouts of diarrhoea started 4 h after admission and lasted for 3 days. The patient was intubated and resuscitated, and mechanical ventilation started. Atropine was given as boluses of 2 mg every 10 min up to 6 mg and subsequently continued as infusion of 0.016 to 0.05 mg kg<sup>-1</sup> h<sup>-1</sup> for 23 days (cumulative dose 649 mg). Pralidoxime (2-PAM) was given as boluses of 1 g 4 and 6 h after admission, and then as 500 mg q.i.d. for 12 days (cumulative dose 24 g). The dose of atropine was adjusted in order to: (i) minimize bronchial secretions; (ii) maintain pupil size as greater than 3 mm; and (iii) keep the heart rate greater than 100 beats min<sup>-1</sup>. The dose of pralidoxime was also adjusted aiming to: (i) normalize acetylcholinesterase (Ache) serum levels, i.e. greater than 3.5 U l<sup>-1</sup>; and (ii) normalize the neuromuscular response, checked clinically and by a relaxograph (Datex, type 100-23-01, Finland).

The remaining therapy included gastric lavage with activated charcoal and manitol every 3 h for the first 24 h, until gastric lavage was free of poison.

Laboratory results on admission were: haematocrit 44%; Hb 14 g dl<sup>-1</sup>; serum urea 6 mmol l<sup>-1</sup> (reference values 2.2–9 mmol l<sup>-1</sup>); serum creatinine 133 mmol l<sup>-1</sup> (range 65–141 mmol l<sup>-1</sup>); K<sup>+</sup> 2.92 meq l<sup>-1</sup> (range 3.5–5.5 meq l<sup>-1</sup>); Na<sup>+</sup> 152 meq l<sup>-1</sup> (range 135–145 meq l<sup>-1</sup>); Ca<sup>2+</sup> 2 mmol l<sup>-1</sup> (range 2.2–2.58 mmol l<sup>-1</sup>); aspartate aminotransferase (SGOT) 70 U l<sup>-1</sup> (range 15–35 U l<sup>-1</sup>); alanine aminotransferase (SGPT) 67 U l<sup>-1</sup> (range 9–39 U l<sup>-1</sup>); lactate dehydrogenase 500 U l<sup>-1</sup> (range 70–280 U l<sup>-1</sup>); and creatine kinase 280 U l<sup>-1</sup> (range 25–185 U l<sup>-1</sup>).

The patient was evaluated twice daily by the same doctor for the severity of his condition (APACHE II

score), central nervous system function (GCS score), respiratory function (Murray's Acute Lung Injury score) (29), and the skeletal muscle function (clinical examination, relaxogram).

The toxicological analysis for dimethoate quantitation by gas chromatography (30) in biological samples gave the following results: serum levels 9.3 µg ml<sup>-1</sup>, gastric fluid 18 mg ml<sup>-1</sup> and urine 43 µg ml<sup>-1</sup>. Serum levels of dimethoate returned to non-toxic levels (<0.05 µg ml<sup>-1</sup>) 15 days later. Ache serum levels on admission and during the following days determined spectrophotometrically (Boehringer Mannheim kit) are shown in Fig. 1. Plasma Ache activity on admission was 480 U l<sup>-1</sup> (reference values 3.5–8.5 U l<sup>-1</sup>), and reached the lower normal range on the twelfth hospital day.

The course of the disease was prolonged, requiring mechanical ventilation for 30 days, atropine therapy for the first 23 days and pralidoxime administration for 12 days (Fig. 2).

Clinical examination showed that the first skeletal muscle to recover was the diaphragm, followed by the muscles of the extremities. The intercostal muscles did not show any clinical activity and the patient had a diaphragmatic type of breathing. The weaning trial of the patient from the mechanical ventilation started 20 days after admission, initially on intermittent mandatory ventilation (IMV) mode, and 6 days later on continuous positive airways pressure (CPAP) (7.5–12.5 cm H<sub>2</sub>O) for 4 days. On the thirtieth day, after the patient had been stable for 3 days breathing 40% O<sub>2</sub> through a tracheostomy and a T-piece, he was put into the sitting position. Minutes later, he developed acute respiratory distress (tachypnoea, tachycardia, cold perspirations, upper chest inspiratory infold and severe cyanosis). Arterial PaO<sub>2</sub> dropped from 85 to 40 mmHg (SaO<sub>2</sub> from 95

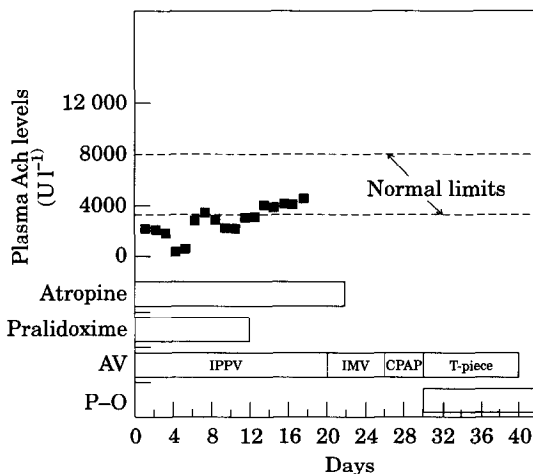


Fig. 2 A summary of the patient's intrahospital course. Plasma acetyl cholinesterase levels, modes of treatment and their duration as well as the duration of the platypnoea-orthodeoxia are depicted. IPPV, intermittent positive pressure ventilation; IMV, intermittent mandatory ventilation; CPAP, continuous positive airways pressure; AV, assisted ventilation; P-O, platypnoea-orthodeoxia.

to 70%). The systemic arterial pressure didn't change significantly and the patient recovered by resuming the supine position. The same episode was induced and repeated whenever the patient was put in the sitting position (orthodeoxia) and was relieved in the supine position (platypnoea). Interestingly, the syndrome was totally alleviated by simple substitution of a T-piece to CPAP (7.5 cm H<sub>2</sub>O) (Fig. 1). No change in PaO<sub>2</sub> was noted in left or right decubitus positions. This condition lasted to a progressively lesser degree for the following 2 weeks. Echocardiography revealed normal left ventricular systolic function. A tilt-table two-dimensional contrast echocardiography did not demonstrate a shunt. A proposed cardiac catheterization and pulmonary angiography was denied by the patient. The patient's hospital course is summarized in Fig. 2.

The patient was discharged 45 days after admission, much improved, without symptoms of platypnoea or orthodeoxia, and with no need for supplemental oxygen. After 4 months, he was able to return to work.

## Discussion

This report documents a 60-year-old man who developed platypnoea and orthodeoxia after mechanical ventilation for severe OP poisoning. To our knowledge, this is the first case of platypnoea and orthodeoxia described in relation to this condition.

All the previously described causes and related abnormal states (Table 1) had been excluded in our patient.

The proposed aetiologic mechanisms for the development of platypnoea-orthodeoxia include intracardiac (4,14,25), pulmonary vascular shunts [congenital (15) or acquired (26,27)] and severe ventilation-perfusion mismatch (2,3,22-24).

Dimethoate (phosphorodithioic acid, 0,0-dimethyl ester), a systemic and contract organophosphorus insecticide is produced and marketed in Greece by various chemical companies under the trade names Dimephos, Dimethoate, Dimethol, Rogor, Roxion, all of them 40% solutions of the active compound. The reported LD<sub>50</sub> value (orally in rats) is 250 mg kg<sup>-1</sup>. Three main types of neurotoxicity have been associated with OP agent poisoning (31): (1) The acute cholinergic crisis, which presents minutes to 24 h after exposure, characterized by a combination of muscarinic, nicotinic and central nervous system signs and attributed to inhibition of carboxylic esterases. (2) The delayed neurotoxicity, a predominantly motor polyneuropathy arising 2-3 weeks after the exposure and attributed to the inhibition of a separate esterase, termed the neuropathy target esterase. (3) The intermediate syndrome, appearing 2-5 days after the acute crisis, characterized by acute respiratory distress and skeletal muscles weakness, which coincides with prolonged cholinesterase inhibition resistant to atropine and oximes treatment.

Although it is obvious that the patient developed a severe and protracted intermediate syndrome after an acute cholinergic crisis both due to OP poisoning, the reason for platypnoea-orthodeoxia is not clear. One possible explanation is the earlier resuming of activity of the diaphragm in relation to intercostal muscles. However, this is based only on the observation of the diaphragmatic type of breathing of the patient. It has been shown that selective contraction of different respiratory muscles may result in changes in the vertical gradient of pleural surface pressure and lung volume, although in normal subjects it appears to be more prominent in the horizontal positions (32-33). In support of this as a cause of platypnoea-orthodeoxia is the improvement of oxygen saturation on the patient's placement on face CPAP, an observation that has not been reported previously. Indeed, small airways closure or microatelectasis has been suggested as the cause of the observed ventilation-perfusion mismatch in platypnoea-orthodeoxia (22), which may have reversed by applying CPAP.

Another explanation could be the automatic nervous system dysfunction as a result of OP poisoning. In this case, when the patient is erect the underlying

autonomic failure followed by a decrease in blood pressure, inadequate perfusion of the upper lung and increased zone I, result in ventilation-perfusion mismatch, hypoxaemia and dyspnoea (22,24,28). This seems impossible in our case because the blood pressure was stable even after the CPAP application. An intracardiac shunt as a possible cause of platypnoea-orthodeoxia was excluded by contrast echocardiography done in both the recumbent and sitting positions.

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