CASE REPORT

Pulmonary oedema caused by "liquid ecstasy" ingestion

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In this case report we describe the first recorded case of alveolar gas exchange impairment caused by "liquid ecstasy" ingestion, and perhaps inhalation, by a 4 year old child. The pulmonary gas diffusion disturbance was sufficiently prolonged to raise the suspicion of a direct toxic effect on the alveolar–capillary membrane.

Gamma butyrolactone (GBL), gamma hydroxybutyrate (GHB), and 1,4-butanediol are known as "liquid ecstasy", a family of synthetic compounds with a substantial potential of abuse for their purported effects as euphoriants, natural psychedelics, muscle builders, fat metabolisers, sexual performance enhancers, and chemical submission drugs. In the past decade, they have been largely marketed as dietary supplements.[1–3] GBL is also used as a chemical intermediate, a solvent for polymers, in paint or glue removers, and in drilling oils. After rapid absorption, GBL is converted to GHB and then to GABA (gamma aminobutyric acid) in situ,[4] which exhibits a narcotic effect on the central nervous system (CNS). CNS clinical effects also include euphoria, headache, dizziness, ataxia, confusion, amnesia, hypotonia, hallucinations, loss of peripheral vision, somnolence, unconsciousness, or coma. Gastrointestinal effects can include excessive salivation and vomiting. Metabolic acidosis is often reported, as is hypothermia (35°C or less). Reported cardiovascular effects include bradycardia, hypotension, right bundle branch block, and ST segment elevation. Of interest, described respiratory effects are limited to ventilatory depression or Cheyne–Stokes respiration.[1 5] Respiratory acidosis and apnoeic episodes may also occur.

CASE REPORT

A 4 year old healthy child became unresponsive a few minutes after drinking a chemical compound containing GBL (Destak, marketed as paint remover solvent). On parental examination, he did not respond to vocal and deep painful stimulation. A progressive shortness of breath developed, causing cyanosis and eventually respiratory failure. In the emergency department, his heart rate was 100 beats/min, arterial blood pressure was 100/50 mm Hg, peripheral pulses were palpable, and temperature was 36°C. Respiratory rate was 32 breaths/min, but oxygen saturation on room air fell to 79%; he was intubated and transferred to the paediatric intensive care unit (PICU). Admitting laboratory findings were unremarkable except for a moderate hyperglycaemia (glucose 175 mg/dl) and lactate dehydrogenase elevation (531 UI); urine glucose was 0.5 g/dl. Complete blood count showed haemoglobin 119 g/l, haematocrit 37.9%, red blood cell count 4.930.000/µl, white blood cell count 11220/µl (neutrophils 77.3, eosinophils 1.9, basophils 0.6, lymphocytes 17.8, monocytes 2.3), platelets 268.000/µl. Coagulation status was as follows: prothrombin time 14.9 seconds (70.2%), INR (international normalised ratio) 1.27, activated partial thromboplastin time 26.5 seconds, fibrinogen 200 mg/dl. Electrocardiogram tracing showed a normal sinus rhythm, with no signs of myocardial ischaemia or ectopic activity. Neurological examination showed: profound lethargy, hypotonia, no response to pain, and absence of tendon reflexes; Babinski sign was positive, pupil constriction with absent pupillary light reflexes was recorded, whereas corneal reflexes were still present. Glasgow Coma Score was 3–4. A computed tomography scan of the head was normal.

On arrival at the PICU, in addition to a deep coma state, respiratory compromise was also evident: the child, despite effective pulmonary ventilation via the endotracheal tube (tidal volume 9–10 ml/kg) showed a persisting oxygen desaturation and needed an inspired oxygen fraction (F_{IO_2}) of 0.70 to obtain Sa_{O_2} >90%. On chest examination, diffuse fine rales were found. Chest *x* ray examination (fig 1) showed diffuse bilateral interstitial oedema and the absence of cardiac enlargement. There were no air leaks or pleural effusions. Echocardiographic findings confirmed the absence of structural cardiac defects and a good contractility; pulmonary arterial blood pressure was normal. Cardiac chambers were not enlarged and no pericardial effusion was detectable. Ultrasound examination of the abdomen showed normal structure of liver, spleen, and kidneys. A positive end expiratory pressure value of 5–8 cm H_2O was gradually introduced, resulting in a progressive decrease of F_{IO_2} over the next few hours. Low dose furosemide was added. Four hours after admission the child became aroused, showing agitation and combativeness; his trachea was extubated after six hours of PICU stay. He remained on 0.40 oxygen supplementation for 24 hours because of the persistence of mild hypoxaemia (Pa_{O_2} 42.7 mm Hg, Sa_{O_2} 84% on room air, Pa_{CO_2} 40.8 mm Hg, pH 7.367). After PICU discharge, no neurological/respiratory sequelae persisted on subsequent clinical examinations.

DISCUSSION

The child presented in this case report was admitted to the PICU soon after falling into a sudden coma and respiratory failure, with a known history of "liquid ecstasy" ingestion. It is of great concern that in developed countries, potential drugs of abuse such as GHB and its prodrugs (such as GBL) are widely available in various forms, posing a serious risk to children who may ingest them accidentally. In the past decade, thousands of reported cases of overdoses of "ecstasy like" substances (mostly in adolescents) provoked the recalling of dietary supplements containing GHB and GBL and an increased surveillance against GHB related abuse drugs. Moreover, the presence of GBL in a chemical compound not related to drugs of abuse or dietary supplements (known sources of so called "ecstasy") is extremely worrying.

In a recent review by Shannon and Quang,[1] also describing a case report of GHB precursor intoxication, the attention was focused mostly on neurological and cardiovascular effects of this family of compounds. In fact, the "ecstasy" victims

Abbreviations: CNS, central nervous system; GBL, gamma butyrolactone; GHB, gamma hydroxybutyrate; PICU, paediatric intensive care unit

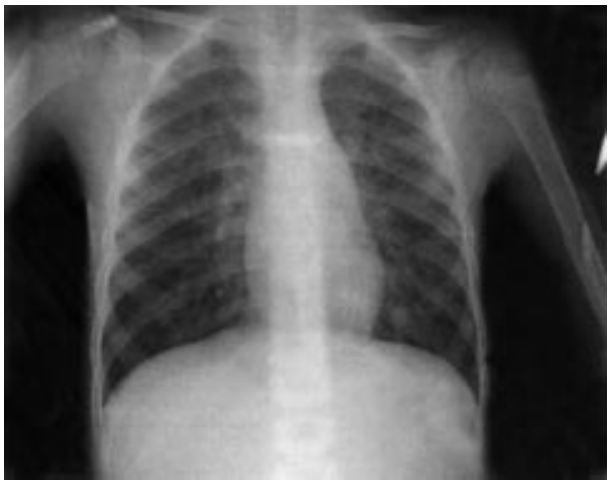

Figure 1 Chest *x* ray examination of the 4 year old boy, showing a diffuse bilateral interstitial oedema and the absence of cardiac enlargement.

described until now suffered from respiratory depression and apnoeic episodes rather than true alveolar gas exchange impairment.[1 5] In this case, however, after GBL ingestion and probably inhalation, a toxic effect acting directly on the alveolar–capillary membrane was evidenced, causing a non-cardiogenic pulmonary oedema, lasting several hours.

In the literature, several cases of poisoning have been reported in children after ingestion of even small amounts (less than 8 ml) of GBL, but no cases of true respiratory gas exchange impairment rather than ventilatory depression were reported. Unfortunately, limited inhalation data from acute exposure are available.[6–8] In rats, inhalation of a saturated atmosphere indicated a low acute toxic effect of GBL; moreover, GBL appears to produce skin irritation when applied dermally to some experimental animals.[9]

In conclusion, emergency or intensive care physicians should keep in mind the possibility of alveolar gas exchange impairment induced by GHB/GBL containing substances; particularly when tracheal intubation and assisted ventilation are not able to overcome the respiratory failure of "liquid ecstasy" victims, in the absence of any heart failure sign.

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