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Intoxication by Massive Ingestion of Poppers: A Case Report

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Abstract

Background: Poppers are commonly inhaled for their recreative properties. Oral intakes are scarce, and clinical presentation and management of massive ingestions are poorly described in literature. We report a haemodynamic failure due to massive oral intake of poppers, and its evolution.

Case presentation: A 47 years old healthy man drank by mistake about 5 mL of poppers. Respiratory and haemodynamic failures grew quickly; requiring admission in intensive care unit, oxygen therapy, volume expansion and norepinephrine up to 2 mg/h. Methaemoglobinemia reached 32% and required methylene blue infusion, falling to less than 5% after 6 hours. Respiratory failure gradually improved, as well than hypotension allowing norepinephrine withdrawal in the first 24 hours. Patient was then promptly discharged at home without any aftereffect.

Conclusions: This case mainly brings to light the strong hemodynamic effect of a massive oral intake of poppers and its fast kinetics, poorly described in literature. Physiopathological mechanisms involved and pharmacological properties of aryl-nitrites are fully compatible with our clinical observation.

Keywords: Poppers; Ingestion; Hemodynamic failure; Respiratory failure; Metheamoglobinemia

Abbreviations: MetHb: Methaemoglobin; NO: Nitric Oxide; O_2: Dioxygen; SpO_2: Pulse Oximetry; pO_2: Partial Pressure of Oxygen; ICU: Intensive Care Unit

Introduction

Poppers are solutions of volatiles aryl-nitrites used since 60s for their vasodilator properties. They were initially used as medicine to treat angina, after being replaced by other NO-producer like trinitrine. Nowadays, poppers have been withdrawn from French pharmacopeia but their use has grown since the 70's, for their recreational properties [1,2]. Poppers are sold as volatiles liquids, generally packaged in 10 to 30 mL vials. Its volatility has inspired the common name Poppers, due to the noise pop made by the opening of these vials.

In France, poppers have been forbidden since the beginning of the 90s, but they now can be legally sold (mainly in sex-shops) since 2013 [3]. Isobutyl-based poppers are forbidden in European Union since 2017 because of their carcinogenic effects.

Poppers are often consumed in association with other legal or illegal psycho-active substances, like alcohol or drugs. The vasodilatation induced by poppers involve production of nitric oxide, and is responsible of a flush associated with a quick but brief euphoria (<5 min), which can lead to high-risk behaviors (unsafe sex, consumption of other psycho-active substance) [4]. On a pharmacological side, poppers inhalations can be associated with several short-term side-effects like cardiovascular depression, acute hemolysis or methemoglobinaemia. Chronic consumption can lead to hematological disorders or maculopathies. Oral intakes are uncommon, with a clinical presentation usually dominated by a respiratory failure [5]. We report a case of a massive ingestion of poppers.

Case Presentation

A 47 years old patient was admitted in intensive care unit for both hemodynamic and respiratory failure following an oral intake of poppers. This patient did not present significant comorbidities, and had excellent physical condition as he was regularly involved in ultra-trail challenges. He was participating in a festive evening with friends. He had significant alcohol consumption during the party and one of his friends presented him a poppers vial. He took it for an alcohol shot and drank about 5 mL of this vial. The patient rapidly complained for discomfort and respiratory distress. On scene, the patient had a low blood pressure (60/30 mmHg) with tachycardia (100 per min), skin mottling, oxygen desaturation (SpO_2=88% on air) and cyanosis. The patient remained conscious (Glasgow coma scale of 15). First treatment included oxygen therapy, volume expansion with 750 mL of crystalloids and increasing doses of norepinephrine.

Once stabilized, the patient was transferred in our intensive care unit. On arrival, the patient was hemodynamically stabilized with 2 mg per hour of norepinephrine without clinical signs of shock. SpO_2 was 88% despite 15 L/min of oxygen. High flow oxygen therapy (Optiflow) did not improved oxygen status. Blood gas reported pH=7.36, lactate=3 mmol/L, pO_2=18.5 kpa, and methaemoglobinaemia=32%. In addition to standard ICU care, intravenous 1.5 mg/kg of methylene blue was administered. Oxygen flow and norepinephrine infusion were gradually decreased and finally stopped 12 hours after the admission. Six hours after methylene blue infusion, methaemoglobinaemia fell to

4.9% and was <1% after 24 h. The patient remained in intermediate care during one day and was then discharged home.

Discussion

Although poppers distribution in France is no longer restricted since 2013, these compounds are associated with several life-threatening risks as illustrated in this clinical case, reporting an observation of poppers ingestion, which is an uncommon way of consumption. If several authors have already described this kind of intoxication [5], the originality of our reports consists in the degree of hemodynamic failure which has never been described to our knowledge.

Indeed, if inhalation provides several pharmacological results desired by the user, they remain time-limited and small (flush, euphoria). Ingestion is responsible of a greater intake, increasing these effects in time and intensity (discomfort, vasodilatation with potential hemodynamic failure, respiratory distress, haemoglobinaemia), which can lead to potential life-threatening clinical situations. In most severe intoxications, early symptomatic measures are necessary, such as oxygen therapy and, in case of severe hypotension, drug-based hemodynamic support. This hypotension is the consequence of NO release, leading to vasodilation [4]. But if this effect can be powerful and life-threatening in case of massive intakes, it remains time-limited due the short half-life of aryl-nitrites, typically less than one hour. In our case, despite the massive ingestion leading to a significant hypotension needing up to 2 mg/h of norepinephrine, this pharmacological support could be rapidly decreased and stopped 12 hours after ingestion, illustrating the intense metabolism of the drug.

The respiratory failure is typically due to methaemoglobinaemia. Indeed, massive intakes of nitrites are responsible of direct and indirect chemical effects on hemoglobin molecules, leading to their oxidation in methaemoglobin (MetHb) [6]. In physiological conditions, this oxidation is controlled by red blood cells anti-oxidant systems and MetHb remains inferior to 1-2%. Massive oxidant stress represented by the great amount of nitrites can overload these protective mechanisms, allowing oxidation of hemoglobin in MetHb [7]. This MetHb is unable the release oxygen molecules due to the irreversible fixation between O_2 and MetHb $Fe3^+$. Clinically, the result is a cyanosis and a respiratory distress with a bad response to oxygen therapy. Pulse oxymetry measurements can be fault by the different absorption spectrum of MetHb [4]. Clinico-biological signs of hypoxia can then be found. These disorders due to metabolic perturbation last much longer than vascular effects: indeed, the oxidative effect on hemoglobin is almost immediate. MetHb thus formed remains i until reduction in hemoglobin, and is then not affected by the short half-life of oxidant agent. This implies than the respiratory effects can persist much longer than hemodynamic effects, which are directly linked to nitrites pharmacokinetic. Specific treatment of methaemoglobinaemia consists in administration of 1-2 mg per kg of methylene blue, restoring a redactor potential in red blood cell allowing conversion of MetHb in functional hemoglobin. In our case, parenteral infusion of 1.5 mg/kg of methylene blue dramatically decreased the MetHb level from 31.7% to 4.9%. A spectacular respiratory improvement was associated with this biological measurement.

Conclusion

Finally, our case report illustrated an uncommon but brief hemodynamic failure needing norepinephrine after ingestion of aryl-nitrites, associated with a respiratory distress due to methaemoglobinaemia well described in literature.

Competing Interest

The authors declare that they have no competing interests.

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Author's Contribution

AB and MD clinically managed the patient and collect clinic-biological data. PA and CC brought the pharmacological expertise. All authors contributed, read and approved the final manuscript.

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