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Acute Effects of Propylene Glycol/Glycerol Intake on Cardiorespiratory Blood Parameters

Introduction

The electronic cigarette is a device generating an aerosol from the "heating" of a liquid (e-liquid), which is inhaled (vaping). Propylene glycol (PG) and glycerol (GLY) are the two components for the vaporization of flavors and eventually nicotine [1]. Its use is booming, in a context where the acute effects of inhalation of propylene glycol and glycerol, major components of e-liquid, are poorly known at the respiratory, metabolic and hemodynamic levels.

We emit the hypothesis that GLY and PG which have the same physicochemical properties[2], are deposited in the pulmonary alveoli and could alter lung gas exchange [3,4]. Considering the hydrophilic properties of PG/GLY and their small sizes, we believe that there may be a passage of the GLY and the PG from the bronchial mucosa to the blood circulation [5]. Once in the circulation, the PG/GLY are metabolized. GLY notably enters into pathways leading to formation of glucose and glycogen. It may also enter in the lipogenesis pathway [6]. PG is metabolized by the liver to lactic and pyruvic acid [7].

We will test the following hypothesis: after inhalation of pure PG/GLY mix (50:50), arterial oxygen partial pressure decreases due to the deep-lung deposition of PG/GLY, which alter lung gas exchanges. We will also test the transcutaneous oxygen tension with the aim to highlight tissue hypoxia after acute nicotine free vaping. We will also assess the presence of metabolic disorders after inhalation of PG/GLY, by measuring the changes in pH, lactate, blood glucose, 2,3-bisphosphoglycerate and anion gap.

Material and Method:

This is a randomized controlled trial, single blinded, at Saint-Pierre hospital (Université Libre de Bruxelles). Thirty patients will be prospectively recruited. The patient will be current tobacco smokers between 35 to 80 years old, who will undergo an elective coronarography. At the end of the coronarography procedure, if no significant incident has occurred, the arterial catheter will be left in place, and the patient will be taken to an adjacent room to the catheterization room for the study. The patient will be randomly assigned to the vaping group (inhalation of a liquid composed of 50% PG and 50% GLY (pharmaceutical grade), without flavors or nicotine) or placebo group (vaping with device turn off). In the vaping group, the patient will vape 1 gram of PG/GLY liquid, while in the placebo group, the participant will mimic vaping (15 puffs) (We initially intented to perform 35 puffs for the placebo vaping group but before initiating the study we decided to match the number of puff performed in the active group and in the placebo group).

The following interventions will be carried out:

- Arterial blood gas test, according to the following chronology: 1 before the start of the vaping, 2 after (at 5 and 20 minutes post-vaping). The samples will be taken thanks to the radial arterial catheter in a pre-heparinized syringe. The volume of the sample will be of 1 cc. The sample will

then be analyzed by an automaton (ABL90 FLEX - Radiometer). The parameters studied will be: arterial partial pressure in oxygen and carbon dioxide, pH, glucose and lactate. The other parameters calculated by the automaton will be: bicarbonate, ions and hemoglobin in its various forms (oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin and methemoglobin).

- Arterial blood sampling: according to the following chronology: 1 samples before the vaping and 2 after (at 20 minutes post-vaping). Arterial sampling will be realized thanks to the radial arterial catheter on an EDTA and SST tube, at the same time as the arterial blood gas. Four ml will be taken for each sample. At the end of the experimental session, the samples will be centrifuged at 3500g for 10 minutes, then they will be immediately aliquoted. The aliquots will be immediately stored in a refrigerator at -80 ° C for storage for future measurement of the 2,3-bisphosphoglycerate, CC16, SP-D and metabolomics analysis.
- Cardiac monitoring (IntelliVue MP40 - Philips), will consist of heart rate measurement as well as continuous electrocardiogram. The monitoring will be started before the first blood sample and before vaping to allow baseline measurements. It will be removed 20 minutes after vaping.
- Pulse oximeter (IntelliVue MP40 - Philipps) will be used to measure the peripheral oxygen saturation. The pulse oximeter will be started before the first blood sample, before vaping. It will be removed at 20 minutes after vaping.
- The blood pressure will be assessed with an automatic sphygmomanometer (IntelliVue MP40 - Philipps). The pressure will be assessed 3 times at 2-minute intervals, before vaping to allow baseline measurements. It will be measured again 3 times at 2 minutes intervals after vaping, as recommended by guidelines.
- A PeriFlux system 5000 (Perimed©, Järfälla, Sweden) will be used to explore the transcutaneous oxygen and carbon dioxide tensions by means of a PF 5040 unit and a dual transcutaneous O2 and CO2 tensions E5280 electrode. The micro-vascular perfusion in skin will also be assessed by a PF 5010 LDPM unit which measures the microvascular flow by means of a Laser Doppler. The device will be started before the first blood sample, at the same time as the pulse oximeter, and be removed 20 minutes after vaping.

The following outcomes will be studied:

- Arterial Gas partial pressure and saturation of oxyhemoglobin (PO)
- Anion gap, lactate, glycemia, pH, to complete the study of the saturation curve of the oxyhemoglobin (SO)
- Arterial 2,3-biphosphoglycerate (SO)
- Arterial metabolomics analysis
- Blood Club cell 16 protein and Surfactant protein-D
- Skin microcirculatory blood flow study

Statistical plan

The objective of this study is to determine whether e-cigarette vaping decreases oxygen arterial blood concentration. Based on our previous researches, we assume that baseline mean arterial oxygen partial pressure will be 100 mm Hg with a standard deviation of 13 mmHg. To demonstrate that e-cigarette vaping significantly decreases arterial oxygen partial pressure, we assume a reduction in arterial oxygen partial pressure of more than 14 mm Hg. We will need 14 patients in each group, with

80% power to detect a group difference of 14 mm Hg in the change of arterial oxygen partial pressure at a two-sided alpha-level of 0.05.

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