

## **NOVEL PHARMACOKINETIC STUDY OF NICOTINE AFTER VAPING: RESULTS ARE VERY ENCOURAGING**

### **VAPING IS AN EFFECTIVE TOOL TO QUIT SMOKING**

**The CRIVAPE (Research and Innovation Center for the Vape) and the Strasbourg University Hospital (HUS), created an unprecedented public-private partnership to analyze the uptake of nicotine after vaping using pharmacokinetic tools. Here, the clinical study conducted jointly by several specialists<sup>1</sup> from the Strasbourg University Hospitals and Sébastien Roux, director of CRIVAPE, shows that nicotine from vaping induces a peak in blood concentration 2 minutes after the start of the vaping session, this duration is very close to that observed with a cigarette.**

### **FIRST PROMISING RESULTS**

Many studies have shown the interest of preoperative smoking cessation, even if it is initiated shortly before surgery<sup>2</sup>. Several substitution methods exist and the electronic cigarette is more and more used<sup>3</sup>. However, little is known about the pharmacokinetics of nicotine and its main metabolite, cotinine, after vaping<sup>4</sup>. Here, we have developed a model allowing the pharmacokinetic study of a pulmonary aerosol administration derived from an electronic cigarette. The study focused on the pharmacokinetics of nicotine after vaping, that is to say its absorption, its diffusion, its metabolism and its elimination by the body.

<sup>1</sup>Maryse Hengen, M.D., Sébastien Roux, Ph.D., Yohann Ballu, M.D., Eric Noll, Ph.D., Sophie Diemunsch, M.D., Véronique Kemmel, Ph.D., Pierre A. Diemunsch, Ph.D. Pharmacokinetics of Nicotine Administered by Vaping : An Animal Study. A4104 Congrès ASA, October 13-17, 2018  
Pharmacocinétique de la nicotine après vapotage : étude animale. Hengen M, MD, Roux S, PhD, Ballu Y, MD, Diemunsch S, MD, Noll E, MD, PhD, Kemmel V, MD, PhD, Poster R475, Congrès SFAR, 27-29 Septembre 2018.

<sup>2</sup>Turan A, Koyuncu O, Egan C, You J, Ruetzler K, Sessler DI, et al. Effect of various durations of smoking cessation on postoperative outcomes: A retrospective cohort analysis. *European journal of anaesthesiology* 2018; 35: 256-65.

<sup>3</sup>Baromètre santé 2017 de Santé publique France : En 2017, il y a eu 1 million de fumeurs en moins en France. La cigarette électronique est le premier outil de sevrage tabagique : 26,9% des personnes qui ont fait une tentative d'arrêt du tabac ont eu recours à la cigarette électronique et 18,3% des personnes ont utilisé des substituts nicotiques et 10,4% ont eu recours à des professionnels de santé.

<sup>4</sup>St Helen G, Havel C, Dempsey DA, Jacob P, 3rd, Benowitz NL. Nicotine delivery, retention and pharmacokinetics from various electronic cigarettes. *Addiction* 2016; 111: 535-44.

This novel study was previewed at the SFAR symposium (Société Française d'Anesthésie et de Réanimation), September 28, 2018, then resumed October 16, 2018 at the prestigious Congress of ASA (American Society of Anesthesiology).

**In summary, results show that vaping is the most appropriate tool to quit smoking: the pharmacokinetics of nicotine after vaping is very close to that observed after using a cigarette.**

Nicotine doses range from 0.409 mg to 9.056 mg ( $3.13 \pm 3.99$  mg, n = 4). **The Pulmonary absorption peak of nicotine is fast: 2 minutes.** Peak concentrations are highly variable from 5.5 to 50.6 ng / mL. These concentrations are not proportional to the administered dose. The assays performed on arterial blood show the same pharmacokinetic profile as those performed in venous: a peak at 2 min, then a plate, after which a decrease is observed at 60 to 80 minutes following the vaping session. As expected, measured concentrations are 1.5 to 3 times higher in arterial blood compared to venous blood. Areas under the curve (AUC) of nicotine in venous blood over 120 min are not proportional to the dose administered and varied from 254 to 1556 min.ng/mL. Nicotine clearance varies greatly between each subject from 1152 mL/min to 13281 mL/min.

By way of comparison, conventional nicotine replacement agents (gums and nicotine patches) have much slower pharmacokinetics (the peak occurs about 30 minutes after use), which does not satisfy the nicotine need of smokers. Vaping thus allows a very fast delivery of nicotine to the central nervous system (equivalent to that of cigarette), which gives a feeling of "satiety" to the ex-smoker. This study deconstructs a received idea, widely relayed by the tobacco industry, that e-cigarettes could not deliver nicotine as fast as tobacco would.

## **METHODOLOGY**

This is Phase 1 of a wide scientific project devoted to understand vaping.

This preliminary study dedicated to the assimilation of nicotine was carried **out from September 2017 to July 2018.**

General anesthesia (premedication: Azaperone - Tiletamine, Zolazepam) was induced with Propofol (3 mg/kg) and intubation was carried out with a 6.0 endotracheal tube.

Anesthesia with Isoflurane (0.8 to 1.2% vol - air) is maintained in spontaneous ventilation, after fitting an arterial route and a venous route. The administration of the aerosol was carried out on a duration of 2 minutes of continuous vaping.

The electronic cigarette consisted of an iStick mini <sup>TM</sup> battery (set at 8.5 W) and a GS Air M type atomizer (Both from Eleaf, China) with a resistance of 1.5 Ohm. The e-liquid used was an Original Alfaliquid flavor FR-M (Gaïatrend, France), dosed at 6 mg/mL of nicotine.

The composition of the e-liquid and the aerosol produced is perfectly characterized. Aerosol dose administered is accurately measured by the weighing difference of the device before and after vaping.

Venous and arterial samples were taken just before vaping and then 2, 5, 10, 20, 40, 80 and 120 minutes after the start of the vaping. The contents of nicotine and cotinine were performed by liquid chromatography coupled to a mass spectrometer. The limit of quantification of the method was 2 ng/mL for both molecules.

"This pharmacokinetic study of nicotine after vaping is an interesting and encouraging first step, that was possible thanks to the joint work of the researchers of the University Hospital of Strasbourg. Indeed, vaping proves particularly effective, by meeting both characteristics of successful smoking cessation: a fast and healthy delivery of active molecules of nicotine. These first results are a very positive encouraging for the future: the electronic cigarette wishes to be recognized as a nicotine substitute and significantly reduce the number of smoking-related deaths in the long run" says Sébastien Roux, director of CRIVAPE.

"This common project with CRIVAPE is among our most promising projects and results in promoting the interest of nicotine substitutes, such as electronic cigarettes in the interest of preoperative smoking cessation, and general anesthesia," says Véronique KEMMEL, doctor at the University Lecturer - Hospital Practitioner (MCU-PH) -Strasbourg

## **ABOUT CRIVAPE**

Created in 2016 at the initiative of the Gaïatrend group, the Research and Innovation Center for the vape (CRIVAPE) is an independent organization that contributes to the provision of scientific knowledge for the vape, at the service of smoking cessation and potential applications in the field of health. Consisting of a research team of 20 multidisciplinary scientists (technicians, engineers, doctors).

## **ABOUT THE UNIVERSITY HOSPITALS OF STRASBOURG (HUS)**

### **REQUIREMENT AND INNOVATION AT THE SERVICE OF THE PATIENT**

As the largest employer in Alsace, the HUS consists of six institutions. They ensure a mission of care but also research and teaching. Their specificity of Regional Hospital Center University (CHRU) allows them to provide routine care to the population of Strasbourg and its surroundings, to take care of patients with complex or rare diseases, who come from more distant geographical areas.

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