

ABSTRACT BOOK

4th Scientific Summit

Tobacco Harm Reduction:
Novel products, Research & Policy

by **SOHRE**

Virtual

29 & 30 SEPTEMBER 2021

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4th Scientific Summit

Tobacco Harm Reduction:
Novel products, Research & Policy

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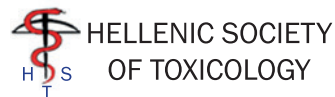
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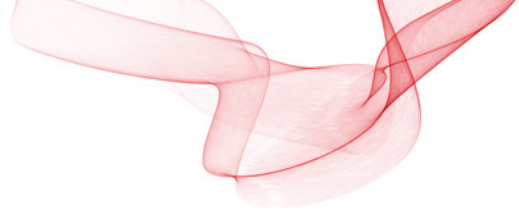
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CONTENTS

5	ABSTRACTS
6	■ BASIC SCIENCE
6	TOXICOLOGY AND AEROSOL CHEMISTRY
	Chemical composition of the aerosol, droplet size and distribution, temperature and toxicants, indoor air quality [01-04]
11	BIOMARKERS' EVALUATION IN ANIMAL OR HUMAN STUDIES [05]
12	PRECLINICAL EVALUATION [06-07]
15	■ EPIDEMIOLOGY & SOCIAL ISSUES [08-10]
18	■ REGULATORY ISSUES [11-12]
21	■ SMOKING CESSATION [13-15]
24	■ CLINICAL ASSESSMENT OF THR & NOVEL PRODUCTS [16-25]
38	AUTHORS' INDEX



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ABSTRACTS

ABSTRACT BOOK

TOXICOLOGY AND AEROSOL CHEMISTRY

AEROSOL FROM A HEATED TOBACCO PRODUCT HAS LESS EFFECT ON LIVER DETOXIFYING ENZYMES THAN CIGARETTE SMOKE

David Bovard, Kasper Renggli, Diego Marescotti, Antonin Sandoz, Majeed Shoab, Claudius Pac, Sandra Ferreira, Anaïs Barbier, Karsta Luettich, Stefan Frentzel, Julia Hoeng, Manuel C. Peitsch

01

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Introduction: The main mechanism behind drug interactions with cigarette smoke (CS) involves activation of hepatic cytochrome P450 (CYP) isoenzymes by the polycyclic aromatic hydrocarbons (PACs) present in CS. Activation of these enzymes can alter the metabolism of drugs, potentially affecting their pharmacologic response. The Tobacco Heating System (THS) emits significantly lower levels of PACs than cigarettes. It is therefore important to understand if THS affects hepatic CYP activation differently than cigarettes, as this could potentially affect drug metabolism in smokers who switch to THS.

Methods: We took advantage of our multi-organ-on-a-chip system to assess the impact of CS and THS aerosol exposure on liver xenobiotic metabolism. Within the same chip circuit, this system connects liver spheroids with 3D human bronchial epithelial tissues that can be exposed directly and physiologically to aerosols. As a case study, we compared the effects of exposure to CS and THS aerosol on these tissues. Bronchial tissues were first exposed twice within 24 h to a subtoxic dose of THS aerosol (up to 56 puffs) or CS (up to 16 puffs) and then placed in our chip and connected to liver spheroids. After 48 h of coculture in the same chip, the activity of various CYP enzymes was measured in the hepatic tissues.

Results: Among the 8 CYPs analyzed in the liver spheroids, only CYP1A2 was strongly induced (250% of the activity observed in the air-exposed condition) 48 h after exposure to 16 puffs of CS. Under the same CS exposure condition, hepatic CYP1A1/1B1 and CYP3A4 activities moderately increased by ~20% relative to the air-exposed control. In contrast, only CYP3A4 activity changed (~30% decrease relative to the air-exposed control) 48 h after exposure to 56 puffs of THS aerosol. We also measured the CYP activity in the bronchial tissues cocultured with the liver spheroids. We found that, after exposure to CS, CYP1A1/1B1 activity increased by 300% relative to the air-exposed control. Under the same exposure condition, CYP1A2 activity was increased by 400%,

ABSTRACT BOOK

while CYP2B6 and CYP3A4 activities were reduced by 30% relative to the air-exposed control. When exposed up to THS aerosol, the bronchial tissues showed no change in CYP activity relative to air-exposed tissues.

Conclusions: We present the results obtained with a new method for detecting potential interactions between aerosols and liver-detoxifying enzymes by using a combination of 3D lung and liver tissues, a multi-organ-on-a-chip system, and a direct aerosol exposure system. We show that CS strongly increased the hepatic activity of CYP1A2 and the bronchial activity of CYP1A1/1B1 and CYP1A2. In comparison, THS aerosol exposure resulted only in a moderate decrease in hepatic CYP3A4 activity; apart from this, THS aerosol had no effect on the activity of other CYP enzymes. Taken together, our results show that THS aerosol exposure causes lower hepatotoxicity and smaller changes in liver xenobiotic metabolism than CS; this reduced effect may potentially result in less drug interactions in THS users than in smokers.

ABSTRACT BOOK

IN VITRO COMPARISON OF CONVENTIONAL CIGARETTE AND NOVEL REDUCED HARM PRODUCTS ON THE DEVELOPMENT OF AGE-RELATED MACULAR DEGENERATION

Georgios Karanasios, Konstantinos Mesiakaris, Marilena Kaperoni

02

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Age-related Macular Degeneration (AMD) is the third leading cause of legal blindness in the world. It is expected by 2040 that more than 300 million people worldwide will be faced with the disease. Apart from natural aging, a series of other factors have been identified as possible inducers of AMD, including smoking and fat-rich diet. Between them, smoking has been proved to be the most important, as smokers tend to have almost 4 times more chances to develop AMD and first symptoms in smokers tend to be considerably earlier, almost by a decade. The aim of this study is to investigate whether reduced risk tobacco products (RRTPs) and electronic cigarettes could have potential effects in the development of AMD. The retinal pigmented epithelium cell line ARPE-19 was used as a model and ARPE-19 cells were exposed to smoke or vapor enriched media. The enriched media were created with use of Borwaldt LM4e and LM1 machines, using the Health Canada Intense regime. Briefly, this regime prescribes puff volume of 55ml, duration of 2 seconds, 1 puff every 30 seconds frequency, with a bell-shaped profile. 3 cigarettes were smoke into 20ml of serum-free DMEM-Ham's F12 media for the tobacco enriched media and their nicotine equivalent of heated tobacco sticks, HTS, (4 sticks) and laboratory made e-cigarette liquid (48 puffs of 18mg/ml nicotine). First, the nicotine concentration of all 3 enriched media was determined with UPLC-MS. + After viability assay on a range of doses from 100% enriched media to 0.5%, the dose of 5% enriched media was used in all cases. In this concentration, cigarette proved to be the most harmful, managing to increase the caspase-3 and bax proteins, increasing apoptosis. HTS and e-cigarette vapor showed, also, an increase of the previous mentioned markers, but considerably smaller. The same results followed the effect of all three products on the senescence markers p16 and p21. Lastly, the antioxidant capacity of SOD and reduced glutathione has measured, showing increased oxidative stress in all 3 products, with cigarette being the more adverse on the oxidative balance.

ABSTRACT BOOK

ABSENCE OF SOLID PARTICLES GENERATED FROM THERMAL PROCESSES IN THE AEROSOL FROM AN ELECTRICALLY HEATED TOBACCO PRODUCT

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03

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Heated Tobacco Products (HTP) were developed as better alternatives to cigarettes to avoid the release of thousands of chemicals formed when the tobacco is being burnt. One such HTP is the Electrically Heated Tobacco System (EHTS) (from Philip Morris International), in which the tobacco material in the Electrically Heated Tobacco Product (EHTP) is heated instead of being burnt. The significant reduction in emissions from EHTPs compared to combusted cigarettes have been extensively substantiated by independent research groups. The absence of solid particle emissions from the EHTP has also been confirmed in published research. As EHTPs have filter elements between the tobacco portion and the mouth-end, their role associated to the conclusion that no solid particles are formed during use has never been investigated to our knowledge. In this work, aerosol collected from the EHTP with and without filter elements during heating as well as without heating was studied to investigate whether solid particles were formed in any part of the product during use. Two different analytical methods were used and the results from both methods showed that no solid particles originating from thermal processes were present in the EHTP aerosol.

ABSTRACT BOOK

COMBUSTED CIGARETTES VERSUS HEATED TOBACCO PRODUCTS: COMPARISON FROM THE POINT OF VIEW OF PARTICULATE MATTER EMISSION AND SOLUBLE MATTER

Ana Amorós-Pérez, Laura Cano-Casanova, María del Carmen Román-Martínez, **María Ángeles Lillo-Ródenas**

04

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Cigarette smoke has shown to be the cause of health problems, and this has led to promote measures for smoking cessation. Besides, several tobacco and nicotine-containing products, such as heated tobacco products (HTPs), have been developed as a less toxic alternative to regular cigarettes. Independent studies must support if HTPs have lower harmful character than combusted cigarettes and, with this aim, the present study focuses on investigating the interaction of cigarette smoke or HTPs aerosol with water, resembling the interaction with water-rich media such as biological (human) tissues is intriguing. For this purpose, an experimental setup has been designed and optimized to collect in a water bed particulate matter or water soluble compounds suspended in cigarettes smoke or the aerosol generated during the use of Heets [HTPs developed by Philip Morris Products (PMP)]. The system allows performing puffing experiments in conditions similar to those of the Health Canada Intense puffing regime and cigarettes and Heets (in IQOS heater), both from PMP, have been used. Complementary studies have been carried out using isopropanol as a trapping liquid media. Laser diffraction and transmission electron microscopy have been used to characterize any particulate matter while the solution has been analysed by the determination of total organic carbon and by UV-vis spectrophotometry. The obtained results have shown that cigarette smoke contains solid particles generated during combustion and, in contrast, the presence of particular matter in the Heets aerosol is non-related to combustion and negligible. Also the cigarettes smoke leaves a much higher amount of compound dissolved in water and in isopropanol. These facts allow us to conclude that HTPs are less harmful than combusted cigarettes.

ABSTRACT BOOK

BIOMARKERS' EVALUATION IN ANIMAL OR HUMAN STUDIES

IN VITRO EVALUATION OF JUUL DIFFERENT FLAVOR PRODUCTS ON HUMAN ALVEOLAR CELL LINES

Konstantinos Mesiakaris, Marilena Kaperoni, Georgios Karanasios, Konstantinos Poulas

05

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This study evaluates the effects of JUUL on human alveolar cell lines on oxidative stress. Human alveolar epithelium are primary cells that take part in the normal function of lungs and are affected after smoking. The observation of changes on alveolar cell lines can answer crucial questions on smoking and vape on human lungs. Adenocarcinomic human alveolar basal epithelial A549 cells and NCI-H292 (HuT-292) human lung mucoepidermoid carcinoma cells were exposed to 5 different JUUL flavor pods. 5 condensates prepared using borgwaldt LM4E smoking machine by bubbling 100 puffs of each pod in impinger trap, using CRM_81, CORESTA RECOMMENDED METHOD No 81 protocol. Several dilutions of condensates were used to determine cell viability and oxidative stress markets. Cell viability, superoxide dismutase (SOD), GSH/GSSG ratio and malondialdehyde (MDA) were determined and are presented.

ABSTRACT BOOK

PRECLINICAL EVALUATION

ELECTRONIC NICOTINE DELIVERY SYSTEMS EXHIBIT LOWER TOXICITY COMPARED TO CIGARETTES. THE “REPLICA STUDY GROUP” EXPERIENCE

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06

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⁹Department of Clinical and Experimental Medicine, University of Catania, Italy

Background: Electronic nicotine delivery systems (ENDS) can reduce the health risks associated with chronic smoke exposure, and their potential benefits are the subject of intense scientific debate. The international “Replica Study Group” replicated independently three relevant studies from the tobacco industry on the cytotoxic and inflammatory effects of cigarette smoke and ENDS aerosol. Our primary goal was to establish the reliability of the results and the robustness of the conclusions.

Methods: In order to assess cytotoxicity of smoke and aerosol, we exposed human bronchial epithelial cell (H292) to cigarette smoke and to ENDS aerosol at air-liquid interface (ALI). Moreover, we aimed to assess different inflammatory and remodeling mediators release (IL-6, IL-8 and MMP-1) from cells exposed to whole smoke (WS) and to smoke deprived of total particulate matter (vapor phase; VP).

Results: We were able to replicate the results obtained in the original studies on cytotoxicity confirming that almost 80% of the cytotoxic effect of smoke is due to the vapor phase of smoke. Moreover, our results substantiated the significantly reduced cytotoxic effects of ENDS aerosol in respect to cigarette smoke. However, our data were notably different in terms of inflammatory and remodeling activity triggered by smoke.

Discussion: Taken all together, the data obtained independently in different laboratories clearly confirm the reduced toxicity of ENDS products (both e-cigs and THPs) compared to smoke, thus providing a valuable tool to the harm reduction strategies in smokers. Otherwise, we were not able to replicate and confirm the results on inflammatory and remodeling mediators released from H292 cells exposed to smoke (WS and VP). This could be due to the lack of normalization of the quantity of cytokines released, with the number of viable cells, in the original paper, since the production of cytokines itself requires the metabolic capability of cells.

ABSTRACT BOOK

TOXICOLOGICAL ASSESSMENT OF THE AEROSOL GENERATED BY A NOVEL PIN-BASED HEATING SYSTEM IN HUMAN BRONCHIAL EPITHELIAL CELLS AND ORGANOTYPIC SMALL AIRWAY EPITHELIAL CULTURES

Pedro Ruiz, Diego Marescotti, Athanasios Kondylis, Yang Xiang, Alain Sewer, Liliana-Ramona Demenescu, Jaquet Vincent, Emmanuel Guedj, Celine Merg, Fabio Maranzano, **Majeed Shoab**, Matthias Guenin, Sophie Scheuner, Keyur Trivedi, Laura Ortega-Torres, Stefano Acali, Sandra Ferreira, Dimitrios Kamperis, Laurent Neau, Florian Calvino, Karsta Luettich, Anita Iskandar, Julia Hoeng, Manuel C. Peitsch

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Introduction: The Pin-based Heating System (PHS; marketed under the brand name of Lil Solid 1.0®) is an electrically heated tobacco system comprised of a device and a tobacco stick, which, heats the tobacco to provide pulmonary delivery of a nicotine-containing aerosol. Philip Morris Products S.A. ("PMPSA") has entered into an agreement with KT&G Corporation by which PMPSA becomes KT&G's worldwide distributor (except for Korea) of KT&G smoke-free products [PHS]. In this study, we comparatively assessed the biological impact of exposure to the aerosols generated by PHS and Tobacco Heating System (THS; marketed under the brand name IQOS®). The biological impact of these aerosols was also compared with that of cigarette smoke (CS) from the 1R6F reference cigarette.

Methods: The PHS 1.0 and THS aerosol fractions, as well as CS were analyzed through impedance-based cytotoxicity and high-content screening assays for various phenotypic endpoints in human normal bronchial epithelial (NHBE) cells. These investigations were complemented by a systems toxicology analysis of the biological impact of these aerosols and CS on human 3D organotypic small airway epithelial (SAEP) cultures.

Results: In NHBE cells, CS exposure caused cytotoxicity, a decrease in mitochondrial health, and an increase in oxidative stress, DNA damage, apoptosis, and cell permeability. In comparison, the PHS and THS aerosols had a reduced impact on these endpoints. Histological analysis of SAEP cultures exposed to PHS or THS aerosol revealed a morphology similar to that in cultures exposed to air; in contrast, cultures exposed to CS presented tissue damage. The transepithelial electrical resistance and ciliary beating frequency following exposure to PHS or THS aerosol were comparable to those in cultures exposed to air and markedly higher than those in CS-exposed cultures. While CS exposure altered the expression of multiple immunoregulatory factors, PHS and THS aerosols had no effect on them. The impact on gene expression

ABSTRACT BOOK

07

associated with PHS and THS aerosols was also lower than the impact linked to CS exposure.

Conclusions: The biological impact of exposure to PHS and THS aerosols is comparable, and this impact is markedly lower than the impact of exposure to CS.

ABSTRACT BOOK

EPIDEMIOLOGY & SOCIAL ISSUES

INTERNET-BASED SURVEILLANCE SYSTEMS ON SMOKING AND ALTERNATIVE TOBACCO PRODUCT USE: EXPLORING THE POTENTIAL OF TWITTER

Konstantinos Kesanopoulos, **Christos Markou**, Ioanna Karefyllaki, Nefeli Giannopoulou-Marini, Georgia Merkouriadi, Dimitra Papadaki, Vasiliki-Athina Tyrologou, Anastasia Barbouni

08

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Internet Based Surveillance (IBS) systems are a promising and complementary extension to the traditional surveillance systems, offering an extensive approach on monitoring issues of public health interest, such as tobacco and alternative tobacco product use, perceptions and sentiments. IBS implements Infodemiology, the “study of the determinants and distribution of health information and misinformation” (Eysenbach).

We developed and evaluated a methodology collecting data to specify, present and interpret the perceptions and sentiments of the population through specific hashtags regarding e-cigarettes in Twitter, used by Greek speakers, native or not, globally. The terms related to e-cigarette were selected based on their search significance evaluated through Google Trends and cross-referenced with Twitter. We used Twitter’s Application Programming Interface (API) and twarc2 to retrieve historical public data and tweets answering a specific query. After sorting and processing them using Python, all tweets were stored in SQL Databases. Using a plugin provided by Wordpress, the application calls for the necessary data and demonstrates them in histograms via a user-friendly web interface.

Through our IBS system, the user can gain immediate visualization to the fluctuations on searches of specific terms, trends and emerging topics related to e-cigarettes during a specified time period.

After testing the system, we concluded to a sample of terms with significant searching performance (f.i. ατμισμα, ecig, vape). During our research, we detected that differently spelled terms displayed uneven popularity. To name a few, “ecig” depicted greater interest in contrast with “Ecig” or “E-cig” and “ατμισμα” greater than “άτμισμα” or “Ατμισμα”.

Infodemiology could be in great use when trying to observe, describe and present the people’s perceptions and sentiments on smoking. It could be a pathway or a motivating power to inform, empower and act on smoking cessation while IBS has the potential to provide input on the epidemiology, perception risk and attractiveness of e-cigarette and other tobacco product use of Greek speakers.

ABSTRACT BOOK

CURRENT TOBACCO CONTROL POLICIES AND OBSERVATION OF E-CIGARETTE USE AND SMOKING CESSATION AMONG RESIDENTS AT A SUBSTANCE ADDICTION REHABILITATION FACILITY IN MALAYSIA

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09

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Background: Cigarette smoking prevalence among Malaysians is 21.3% (2019), a slight (6.6%) reduction compared to 22.8% prevalence in 2015. Despite continuous efforts by the Government towards a Smoke Free status by 2045, current reduction rate will fall short of the target of 15% smoking prevalence by 2025. The disease and socioeconomical burden of cigarette smoking greatly affects many populations, especially those struggling with substance addiction. Technological advancement driving the evolution and access to alternative nicotine delivery systems (ANDS), e.g. e-cigarette, presents an opportunity to rethink tobacco control strategies in the country.

Methods: Regulatory approaches in tobacco control, and ANDS control in Malaysia was summarized. In addition, observation among residents recovering from substance addiction at a rehabilitation facility in Malaysia was conducted.

Results: Malaysian regulators are mainly guided by the WHO's six MPOWER recommendations in tobacco control. Its Ministry of Health (MOH) and external partners provide mQUIT program for smoking cessation using mainly pharmacological and behavioral therapies. While non-nicotine containing e-cigarette liquid has been regulated since 2021, nicotine-containing e-cigarette liquid can only be registered under the Poisons Act 1952 for smoking cessation, to be supplied by licensed pharmacists or medical practitioners. However, unregulated nicotine-containing e-cigarette liquids are widely available, leading to calls by various representative groups (industry, consumer, medical) for regulating nicotine-containing e-cigarette liquid beyond a poison item. Case studies at a rehabilitation center suggest that e-cigarette use leads to smoking cessation among its residents who are recovering from substance use disorder (SUD).

Conclusions: Tobacco harm reduction (THR) can be incorporated into current tobacco control strategies in Malaysia. These observations highlight a need to collect clinical and real-world evidence among SUD patients for enhanced understanding of the benefits and risks of e-cigarettes as a tobacco harm reduction tool. These data can inform both clinicians and regulators.

ABSTRACT BOOK

A JAPANESE PHARMACY STUDY IN CESSATION PATIENTS TO EXPLORE THE COLLECTION OF TOBACCO USE DATA TO SUPPLEMENT REAL WORLD EVIDENCE

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10

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Background: Real-world evidence (RWE) is of key importance to answer questions related to the long-term effects of smoke-free tobacco products. To leverage RWE to answer questions related to the risks of these products, we will need to supplement the data with actively collected smoking history data. This research was conducted at a Japanese pharmacy to evaluate if we could, by means of a questionnaire, collect tobacco product use patterns and other subject characteristics in those prescribed smoking cessation medications in Japan.

Methods: This was an exploratory, observational study of people attending a pharmacy to fill their prescription for smoking cessation medications. The analyses were descriptive in nature, to understand if and how we could collect tobacco product use patterns.

Results: The questionnaire was completed by 748 (73% men) people who were prescribed smoking cessation treatment. The majority (67%) of the participants were between 30 and 59 years old, with the age distribution being similar between sexes. Over 62% of participants had already attempted to quit at least once, and most participants had decided to quit within a month of the consultation.

On average, participants had a smoking history of over 28 years (95% CI, 2.1-55.25), which was lower in those who used heated tobacco products (HTP) (21 years; 95% CI, 3.55-57.42) than in smokers (30 years; 95% CI, 3.55-57.42) and dual users (27 years; 95% CI, 1.81-52.44). Additionally, 51% of participants were receiving treatment for a disease diagnosis.

Conclusions: In this study, most participants filling prescriptions for smoking cessation were 30- to 59-year-old men with a concomitant disease and a smoking history of over 28 years. By conducting this exploratory RWE study, we learned that questionnaire administration in a pharmacy is a viable way to capture tobacco use patterns and history for certain patient populations.

TOWARDS A SMOKE-FREE FUTURE

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11

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The benefits of tobacco control strategies and education efforts to date are undoubted and have significantly decreased the prevalence of smoking in the UK and worldwide. However, there still remains a significant number of continuing smokers and this number disproportionately falls on the underprivileged.

How are we to help this group? It would seem unlikely that the policies which have failed with this group today will work tomorrow. In addition to the existing fiscal and educational policies, we need to endorse new approaches such as harm reduction based on science and innovation, accepting that for a proportion of the population the message 'quit or die' (take the consequences of your actions) is clearly not working. There is ample evidence that the adoption of certain harm reduction approaches can reduce the burden of bad behaviours and poor lifestyle choices. The UK approach to address the AIDS epidemic in the 1980's by a compassionate policy that accepted the use of illegal, recreational drugs but minimised the harm of their use is such an example, resulting in a large drop of the death rate in adult intravenous drug users in the UK in a rather short period of time.

Tobacco Harm Reduction: Opportunities and challenges. There is growing evidence that new innovative smoke-free products (such as snus, vaping devices, heated tobacco products, and nicotine pouches) are less harmful than cigarettes because they expose users to much lower levels of harmful chemicals. This opens up a new avenue to apply harm reduction to continuing smokers. However, to stand a chance in achieving a smoke-free future, we need to take a pragmatic approach. Specifically, such an approach must address the needs of continuing smokers to help as many of them as possible to stop smoking cigarettes, while protecting youth. Ideally, a spectrum of products needs to be available with a regulation in place that is proportional to their risk. Products need to be subjected to defined standards before entering the market and manufacturers should be

ABSTRACT BOOK

obliged to monitor the use and safety of their products. Finally, the sales and advertising of these products has to be restricted to legal age users, while at the same time allowing accurate and truthful product claims and warnings relative to cigarettes that consumers understand.

Conclusions: A smoke-free future is possible if we unleash the full potential new innovative and scientifically substantiated products can bring. To do so, these products need to be regulated properly and responsibly.

ABSTRACT BOOK

SARS-COV-2, SMOKING, AND NICOTINE CONSUMPTION: INVESTIGATING THE INTENDED AND UNINTENDED CONSEQUENCES OF RESPONSES TO COVID-19 AROUND THE WORLD

Samuel Hampsher-Monk

12

BOTEC Analysis

This report was funded with a grant from the Foundation for a Smoke-Free World, a U.S. nonprofit 501(c)(3) private foundation with a mission to end smoking in this generation. The Foundation accepts charitable gifts from PMI Global Services Inc. (PMI); under the Foundation's Bylaws and Pledge Agreement with PMI, the Foundation is independent from PMI and the tobacco industry. The contents, selection, and presentation of facts, as well as any opinions expressed herein are the sole responsibility of the authors and under no circumstances shall be regarded as reflecting the positions of the Foundation for a Smoke-Free World, Inc.

The COVID-19 pandemic brought isolation, social distancing, and economic downturn. The pandemic, and government's response, also appears to have affected the use of tobacco and nicotine products. Stress and anxiety, both well understood drivers of nicotine use, coupled with a reduction in time spent in areas where smoking is banned, may have driven increased consumption. But the pandemic also disrupted social interactions that may promote smoking; reduction in environmental triggers and disposable income coupled with heightened focus on pulmonary health may have promoted cessation. Additionally, two further features of the pandemic require investigation: Misinformation surrounding the unfounded theory that smoking might have a protective effect COVID-19 (resulting from an incomplete scientific understanding of the viral pathology) could have changed perceptions of risk. Regulatory responses to the crisis also likely affected the availability and accessibility of products. The pressure on governments to respond to the pandemic left little time for regulators to consider possible unintended consequences of unprecedented interventions. Tobacco bans in South Africa and Botswana may have inadvertently increased illicit trade in tobacco products (ITTP). And in other locations, the differential lockdown policies for vape-shops and tobacco retailers may have nudged consumers of safer nicotine products towards combustible tobacco. This paper explores how tobacco and nicotine users altered their consumption in response to the pandemic, and investigates which features of the pandemic, and the world's response, drove those changes. A systematic review of English-language, peer-reviewed and pre-print research articles published in the PubMed database, is supplemented with a brief analysis of industry data for combustible tobacco and SNPs to explore how the pandemic affected demand for tobacco and nicotine.

ABSTRACT BOOK

SMOKING CESSATION

HABITA PROJECT, TO STUDY THE SMOKING HABIT AMONG PATIENTS AND FACE THEIR WITHDRAWAL

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13

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Introduction and Objectives: According to the survey EDADES 2019/2020, in Spain the percentage of smokers who do not consider quitting is 37-40% and is increasing. Quitting smoking and staying without doing so is frequently unsuccessful, and among certain groups of patients, it is especially difficult. The Spanish Patient Forum promotes the HABITA project, with the Aragonese Association for Mental Health, the Association of Coronary Patients and the National Federation of Associations of Respiratory Diseases, to study in these groups, the consumption, degree of addiction, their history of withdrawal and motivations, as well as making proposals.

Material and Methods: From March to May 2021, patients answered an anonymous questionnaire, endorsed by the Spanish Society for Healthcare Quality and approved by the Research Ethics Committee of Camilo José Cela University.

Results: There were 111 assessable smokers or ex-smokers (37 from each group under study). The mean age was 61.71 years (SD 11.84), 49.09% currently smoked daily, an average of 17.28 cigarettes per day (SD 11.33) for one mean of 28.46 years (SD 14.76). IPA 24.59. The mean Fagerström value was 4.26.

The main motivation to quit smoking was awareness of the damage to their health, however 39% didn't want to quit smoking. Only 19.35% will try in the coming weeks. 91% tried to stop smoking at some time, but 69% have relapsed, mainly due to stress and anxiety (74%) and for the satisfaction of smoking (13%).

60% tried it without help and only 23% turn to a professional, evaluating the effectiveness of the available supports as low.

Conclusions: Undoubtedly, the population should be discouraged from smoking, but for those who are already smokers, it seems an unattainable goal for many to quit and becomes reasonable to try to reduce the harm of traditional cigarettes, exploring alternatives and substitute devices.

ABSTRACT BOOK

E-CIGARETTES AND SMOKING: CORRELATION, CAUSATION, AND SELECTION BIAS

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14

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Introduction: This study investigates the correlation between electronic nicotine delivery systems (ENDS) and smoking cessation, examines whether there is selection bias in cross-sectional studies of ENDS and cessation, and estimates the causal effect of ENDS on cessation. Whether ENDS encourage cessation from cigarettes or merely complement the smoking habit is a matter of much current study and debate. Individuals choose whether to use ENDS, and that choice is likely to be correlated with unobserved factors related to smoking behavior. Ignoring this issue of selection-into-treatment leads to bias in estimates of the causal effect of ENDS use on smoking.

Data and Methods: The data are from the Korea National Health and Nutrition Examination Survey (KNHANES), 2014 to 2018. Correlation between ENDS use and smoking is assessed with logit regression. Causal effects are investigated with parametric and moment-based models for endogenous treatment effects with binary outcome variables.

Empirical Results: Characteristics of the subpopulation of ENDS users (such as income, education, and binge drinking) changed greatly after a negative government report on ENDS, which provides indirect evidence for selection bias. Such changes suggest that ENDS use shifted towards those for whom cessation is most difficult. Furthermore, logit regression for smoking shows that the apparent positive association between ENDS use and smoking increased during this time, which is consistent with selection bias. Finally, the causal effect leading from ENDS use to a higher probability of cessation is estimated to be positive: ENDS use is associated with a higher probability of cessation.

Policy Implications: Some public health officials, including those in Korea, discourage smokers from using ENDS because ENDS use is positively correlated with smoking. Such officials deduce from this correlation that ENDS causally discourage cessation from tobacco. Our results suggest, instead, ENDS may aid cessation and should be investigated further with studies designed to identify causal effects (e.g. clinical trials) to verify whether they can indeed play a role in reducing smoking.

ABSTRACT BOOK

A MULTI-DISCIPLINARY INVESTIGATION INTO THE DRIVERS OF SMOKING CESSATION IN FIVE COUNTRIES WITH ANDS MARKETS

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15

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Alternative Nicotine Delivery Systems (ANDS) have proliferated in several nations with impressive histories of smoking cessation. However, different nations have taken radically different policy approaches to ANDS, ranging from outright bans to actively encouraging use by current smokers. The relationship between nations' policies and ANDS-related outcomes is not well-understood. Applying the 'lessons learned' in one locale to drive cessation elsewhere requires that we account for these contextual specifics. We synthesize the findings from case studies of Australia, Canada, Japan, South Korea, and the UK. Each employs an interdisciplinary framework combining sociological, policy analytic, and econometric disciplinary approaches into a schema for studying the drivers of smoking cessation at the individual, micro, meso and macro levels. Data on ANDS use, smoking, and cessation from four decades is used to investigate the relationship between tobacco control policies, ANDS use and smoking cessation, as well as other salient aspects of the national tobacco control landscape. Taxation and Stop Smoking Services (SSS) and smoke-free laws were among the most effective cessation drivers. Policies such as plain pack legislation, health warnings and smoke-free laws were less associated with short term reductions in smoking prevalence. Tobacco use continues to be concentrated in socially and economically disadvantaged groups. Where regulations allowed, ANDS (e-cigarettes and heated tobacco in particular) were associated with smoking cessation. Moreover, evidence suggests that e-cigarettes do not re-normalize tobacco use. The results demonstrate how policy decisions affect ANDS use and the latter's value as a cessation mechanism. Regulators should continue to increase tobacco taxes carefully and study how to integrate ANDS with well-funded SSS. Policies should differentiate among nicotine products with respect to their harms profiles. Future cessation programs should target socially and economically disadvantaged groups where tobacco harms continue to be concentrated.

ABSTRACT BOOK

CLINICAL ASSESSMENT OF THR & NOVEL PRODUCTS

FAVOURABLE CHANGES IN BIOMARKERS OF POTENTIAL HARM WHEN SWITCHING FROM CIGARETTE SMOKING TO USING A TOBACCO HEATING PRODUCT FOR 6 MONTHS

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16

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Compared to conventional cigarette smoke, tobacco heating products (THPs) generate lower machine yields of toxicants. In two 5-day, confined clinical studies and a 6-month, ambulatory clinical study, the glo THP has been shown to expose users to lower levels of particulate matter and harmful and potentially harmful compounds compared with smoking cigarettes. However, it is not known whether such exposure reductions lead to changes in biomarkers of potential harm (BoPH).

This randomised, controlled study is investigating whether BoPH are modified when smokers switch from smoking cigarettes to using the glo THP in a naturalistic, ambulatory setting. Control groups include never smokers and smokers who, after enrolment, abstain from cigarette smoking. Levels of the haemoglobin adduct N-(2-cyanoethyl)valine (CEVal) were used to determine compliance with smoking restrictions. Various BoPH related to oxidative stress, cancer, cardiovascular and respiratory diseases were assessed at a baseline study visit and here we report findings for these BoPH after 6 months.

By 6 months, statistically significant favourable changes in the BoPH 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, 8-epi-Prostaglandin F2 α type III, white blood cell count and fractional concentration of exhaled nitric oxide were observed in smokers switching to using glo when compared with those who continued smoking. Levels of 11-dehydrothromboxane B2 were also reduced compared with continued smoking and, whilst not statistically assessed, favourable trends directionally consistent with beneficial changes in health effects were observed in soluble intercellular adhesion molecule-1, high-density lipoprotein and forced expiratory volume, with unfavourable trends seen in continuing smokers. For 6 of these 8 BoPH, the changes were comparable to those experienced by smokers who abstained from cigarette smoking for the same period.

These data add support to the body of evidence suggesting that the negative health impacts of cigarette smoking may be reduced in smokers who completely switch to using glo.

ABSTRACT BOOK

EVALUATING RESPIRATORY SYMPTOMS IN SMOKERS WHO SWITCHED TO ENDS

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17

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Background: Improvement in respiratory symptoms may be a meaningful and motivating driver for adult cigarette smokers to switch completely to electronic nicotine delivery systems (ENDS). However, very little is known about how smokers' respiratory symptoms are affected by complete switching from cigarettes to ENDS. The current study aimed to explore self-reported respiratory symptoms in (1) current smokers ('Smokers'), (2) smokers who switched completely to ENDS ('Switchers'), and (3) former smokers not currently using any tobacco products ('Abstainers').

Method: Respiratory symptoms were assessed with the Respiratory Symptom Questionnaire (RSQ), a reliable and valid 5-item questionnaire appropriate for evaluating respiratory symptoms in adult smokers without respiratory disease. Smokers (n=202; currently smoke; smoked 10+ years), Switchers (n=208; currently use ENDS but no smoking in 6+ months; smoked 10+ years), and Abstainers (n=200; no tobacco product use in 6+ months; smoked 10+ years) completed the RSQ online as part of a study evaluating the psychometric properties of the RSQ. This study reflects secondary analyses conducted on these data.

Results: Mean RSQ scores [range 1 = "Never (0 days out of the last 30 days)" to 5 = "Every day (all 30 days out of the last 30 days)"] were 2.09 for Smokers (SD=0.91), 1.72 for Switchers (SD=0.69), and 1.75 for Abstainers (SD=0.85). Switchers' and Abstainers' RSQ scores were significantly lower than Smokers' (p-values <0.001, d=0.39-0.46); Switchers' and Abstainers' scores did not significantly differ.

Conclusions: Smokers who switched to ENDS reported respiratory symptoms that were significantly lower than Smokers and did not differ from Abstainers. This research provides support for the harm reduction potential of ENDS. Reduction in respiratory symptoms may be a useful harm-reduction metric that is motivating and meaningful for smokers. Future longitudinal research should evaluate intra-individual change in smokers' respiratory symptoms following complete switching to ENDS.

ABSTRACT BOOK

RESPIRATORY AND CARDIOVASCULAR HEALTH EFFECTS OF E-CIGARETTE SUBSTITUTION FOR CIGARETTE SMOKING: A LIVING SYSTEMATIC REVIEW

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18

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Background: To convince clinicians to recommend e-cigarettes hard data is paramount. What clinical data is available? Systematic reviews have combined animal, in vitro, and survey data with clinical trials, obscuring the clinical effects of substitution for tobacco harm reduction. Almost no systematic reviews conducted an assessment of study quality and biases.

Objective: Our two living systematic reviews critically assessed and synthesized human clinical studies on the respiratory and cardiovascular health effects of ENDS substitution for people who smoke.

Methods: Database searching, and secondary searches assured the retrieval of all available data. The reviews conform to PRISMA 2020 standards and AMSTAR 2 criteria. The reviews are current to June 2020 and will be updated semi-annually. JBI quality tools were utilized for quality assessment and were examined with the Oxford Catalogue of Bias. Due to the heterogeneity of the studies, a narrative data synthesis was performed.

Results: The reviews contain 21 respiratory and 25 cardiovascular studies. The cardiovascular tests synthesized were heart rate, blood pressure, ECG, and flow mediated dilatation. The respiratory tests were primarily spirometry tests. The test results indicated no significant differences in acute effects or showed reduced negative effects for ENDS compared to smoking. Longer-term studies also demonstrated either no effect or some modest improvements. Some benefit was found for patients with hypertension, COPD, or asthma. Almost all studies were rated at high risk of bias and contained reporting biases.

Conclusions: At the end of the day, the available evidence shows that ENDS use does not result in more harm than smoking or possibly reduced harm, and some patients may experience benefits over time. Larger N and longer duration studies are required to validate any potential benefits of ENDS substitution.

ABSTRACT BOOK

USE OF INTERRUPTED TIME SERIES ANALYSIS FOR EVALUATING HOSPITALIZATION RATES BEFORE AND AFTER THE INTRODUCTION OF HEATED TOBACCO PRODUCTS IN THE JAPANESE MARKET

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19

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Introduction: Interrupted time series (ITS) analyses using real-world data (RWD) have been used to assess the population-level impact of interventions such as smoking bans on smoking-related disease endpoints. A recent RWD-based study showed that the introduction of HTPs was associated with a reduction in cigarette sales in Japan.

Objective: This study aims to assess the hospitalization rates for chronic obstructive pulmonary disease (COPD) and acute ischemic heart disease (IHD) before and after the introduction of HTPs in Japan, using two different sources of RWD that include different populations.

Methods: The hospitalization rates associated with ICD-10 codes for COPD and IHD from 2013 to 2019 were retrieved from two databases: 1) Medical Data Vision (MDV) and 2) Japanese Medical Data Center (JMDC). The data were analyzed using ITS models, adjusting for age, sex, and tobacco sales data, to describe the hospitalizations due to COPD (all codes), COPD exacerbation, and IHD-related hospitalization before and after the introduction of HTPs.

Results: Results from the MDV data adjusted for age and sex showed a statistically significant decrease in the rate of hospitalizations due to COPD exacerbation ($p < 0.01$) after the introduction of HTPs. The results from the JMDC data, also adjusted for sex and age, showed a statistically significant decrease in the rate of hospitalizations for COPD (any code) ($p < 0.0001$) when using all available data and for IHD hospitalization ($p < 0.00001$) when using only disease-procedure combination (DPC) data. Further adjustments did not alter the results.

Conclusions: Time-trend analyses of hospital admission rates is a viable way to investigate the potential effects of HTPs on smoking-related diseases, with all the well-known caveats (e.g., a causal relationship cannot be established). The results of our recent analyses demonstrate the feasibility of this approach as a first step in evaluating the impact of HTPs on the health of the population.

ABSTRACT BOOK

SMOKING BEHAVIOR OF TOBACCO CIGARETTE SMOKERS AFTER SWITCHING TO ELECTRONIC CIGARETTE OR HEATED TOBACCO PRODUCTS DURING 3 YEARS OF FOLLOW-UP

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20

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Introduction: The use of electronic cigarette (e-cig) and heated tobacco products (HTP) has been recently increased. We interrogated the smoking status of tobacco smokers (TC) who attended a smoking cessation program lasting a month during a 3-year follow-up after completion of smoking cessation program.

Methods: We studied 84 TC. 45 switched to e-cig and 39 to HTP one month after recruitment. All attended the smoking cessation clinic. Among 77 participants who completed the 3-year follow-up, 23.8% of the smokers had made two efforts to cease tobacco smoking with the aid of nicotine replacement therapy or approved medication. We assessed: 1) the status and quantification of use of smoking products (tobacco cigarette, e-cig or HTP), 2) smoking cessation attempts, 3) performing of physical activity at baseline and follow-up.

Results: Out of 84 subjects, 77 completed the 3-year follow-up survey (40 subjects initially using e-cig and 37 using HTP).

During follow-up, 13.3% of e-cig users and 13.5% of HTP users ceased smoking of any smoking product ($p=0.9$). Furthermore, 40% of e-cig users and 24.32% of HTP relapsed to traditional tobacco smoking ($p=0.03$). Interestingly, 24.4% of e-cig users had switched to HTP but no one of the HTP users switched to e-cig use during follow-up.

The HTP users consuming <10 heats per day at baseline were 17.2%, while at 3-year follow-up they were 43.4% ($p=0.024$).

At inclusion 45.9 % of HTP group and 60% of the e-cig group performed physical exercise while at the end of the follow-up period 56.7 % and 67.5% performed physical exercise respectively (10.8% vs 7.5% increase respectively, $p=0.04$).

Conclusions: This observational study showed that tobacco smokers who switched to use of e-cigarettes or HTP achieved a similarly low percent of complete cessation of tobacco smoking and approximately one fourth of e-cig users switched to HTP during a 3-year follow-up.

ABSTRACT BOOK

FEATURES OF THE EFFECTIVENESS OF COMBINED ANTIHYPERTENSIVE THERAPY IN MEN, DEPENDING ON THE TYPE OF TOBACCO PRODUCTS USED

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21

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Introduction: An important role in improving the prognosis of arterial hypertension (AH) is played by the achievement of the target level of blood pressure (BP), especially in male smokers. At the same time, there is the problem that some patients don't want to quit smoking at once. In those cases it is possible to consider the use of harm reduction concept and recommend patient to switch on alternative sources of nicotine delivery. The purpose of the study was to compare the efficacy of antihypertensive therapy in men who smoke regular cigarettes and in men who switched to an electric tobacco heating system (THS).

Material and Methods: We examined 67 male smokers with uncontrolled hypertension of 1-2 degrees, which were divided into 2 groups: group 1 (n=32) who used THS and group 2 (n=35) who smoked regular cigarettes. All patients received as therapy a fixed combination of perindopril and indapamide (Noliprel A Forte / Noliprel A Be Forte, Servier, France) at doses of 5-10 / 1.25-2.5 mg / day. Before and after 8 weeks of therapy, blood pressure was assessed in accordance with modern recommendations and daily monitoring of blood pressure (DMBP) was performed with an assessment of the dynamics of mean daily, daily mean and mean nighttime values of systolic (SBP) and diastolic (DBP) pressure. The measurement of BP was carried out under conditions of free motor activity at intervals of 25 minutes (day), and 50 minutes (night).

Results: The target BP level was achieved in 28 out of 32 (87.5%) patients in the first group versus 25 out of 35 (71.4%) in the second. There was a large decrease ($p < 0.05$) in the daily average and average nighttime values of BP in patients who used THS (SBP by 20.3%, 21.4% and 17.9% and DBP by 21.6%, 22.2% and 19.8%) in comparison with those who smoked regular cigarettes (SBP by 14.5%, 15.6% and 9.9% and DBP by 14.5%, 14.8% and 10.2%).

Thus, the efficacy of combined antihypertensive therapy with

ABSTRACT BOOK

21

perindopril and indapamide was higher in people who used THS compared to those who smoked regular cigarettes.

Conclusions: Smoking cessation plays an important role in the management of hypertension in men. In case of impossibility of complete refusal, the patient can be offered a step-by-step scheme with a temporary transition to THS, which can contribute to the effectiveness of antihypertensive therapy.

ABSTRACT BOOK

NICOTINE PHARMACOKINETICS OF MODERN ORAL NICOTINE POUCHES

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22

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In recent years a new type of oral smokeless, tobacco-free, nicotine product has become available to tobacco consumers, known as nicotine pouches (NP). These NP are regarded as potentially reduced risk products as users are exposed to less harmful and potentially harmful tobacco constituents than combustible cigarettes. Due to their novelty, very little data are available on the nicotine pharmacokinetics (PK) of NP use.

To gain more information on these products a nicotine PK study was conducted comparing commercially available NPs (five different brands: 6-10 mg nicotine/pouch) with a combustible cigarette.

For this study 35 healthy adults who were current dual users of combustible cigarettes and snus were screened and recruited to attend an 8-day confinement period in clinic. On each day of the study after overnight abstinence from nicotine use, participants used one study product for a defined period and blood samples were taken at specified timepoints before and for 6 hours after product use.

All NPs had a longer T_{\max} (60-65 minutes) than the cigarette (7 minutes) as well as a higher AUC_{0-6h} . Results also showed that three of the NPs had a higher C_{\max} than the cigarette and that nicotine plasma concentration was not associated with the nicotine content of the NPs.

Product liking and intent to use product again scores were also measured using single item questionnaires. Scores were lowest for the NP with the lowest nicotine content, while the cigarette had higher scores than any of the NPs.

This study demonstrates that nicotine uptake from NPs can be similar to that of smoking combustible cigarettes following a switch from conventional cigarettes to these potentially less harmful NP products. It also provides an important understanding of nicotine PK and subjective effects during NP use.

ABSTRACT BOOK

B-CARBOLINES AS REVERSIBLE MONOAMINE OXIDASE INHIBITORS

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23

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Monoamine oxidase (MAO) enzymes are an important part of the central nervous system and are responsible for the oxidative deamination of monoaminergic neurotransmitters like serotonin, dopamine, epinephrine, etc. The rate-limiting step of the reaction they catalyze is hydride transfer from the monoaminergic neurotransmitter to the flavin adenine nucleotide cofactor in the active site of the MAO enzyme. While their catalytic activity is key for maintaining normal levels of these neurotransmitters in the organism, the side-effect of MAO catalysis -or rather of regeneration of the flavin cofactor with molecular oxygen- is also production of reactive oxygen species (most notably of hydrogen peroxide), which can cause neurodegenerative diseases, like Parkinson's or Alzheimer's disease. Therefore, controlling or inhibiting the activity of these enzymes also proves to be important for neurodegenerative disease prevention or delay.

One group of reversible MAO inhibitors are β -carbolines -naturally occurring compounds, that can also be found in tobacco leaves, cigarettes, and cigarette smoke. These compounds have a wide variety of effects, achieved through their action on benzodiazepine, serotonin, opioid or imidazoline receptors, with MAO inhibition being one of their most important modes of action. In the study presented here, we used computational molecular modelling methods in order to analyze the conformational, as well as the energy characteristics of β -carbolines binding into the MAO A active site. Using static molecular docking as well as the dynamic pharmacophore approach (based on extended molecular dynamics simulations of β -carbolines bound in the active site) we identified and analyzed the most important interactions between various β -carbolines and the MAO A active site residues. Additionally, we used the Liner Interaction Energy approach to evaluate the energy aspects of β -carboline binding in MAO A.

The results presented here provide important information about both the geometric and the energy aspects of β -carboline binding in MAO A and could serve as a promising jumping-off point towards applications in treatment of neurodegenerative diseases.

ABSTRACT BOOK

RESPIRATORY FUNCTION, PHYSICAL CAPACITY, AND METABOLIC SYNDROME COMPONENTS IN COMBUSTIBLE CIGARETTES AND HEATED TOBACCO PRODUCTS USERS: A TWO-YEAR FOLLOW-UP COHORT STUDY

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24

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Background: Cigarette smoking is the most common risk factor for chronic obstructive pulmonary disease (COPD), which is the fourth leading cause of death in Kazakhstan. Prior literature suggests that HTP (heated tobacco products) might be a better option for people who cannot quit smoking. The aim of this paper was to analyze the long-term effects of shifting to HTP use compared to continued CC (combustible cigarettes) use in long-term smokers.

Methods: A cohort of 1200 participants (400 HTP and 800 CC) aged 40-59 years with a minimum of 10 pack-year smoking history were recruited. The health outcomes compared between HTP and CC users included: (1) COPD Assessment Test (CAT); (2) post-bronchodilator lung function; (3) 6-minute walking distance (6MWD) test; and (4) metabolic syndrome components. Multivariable linear mixed models were used to test associations between health outcomes and smoking type (HTP vs. CC) over time.

Results: After 24 months 188 (117 CC users and 71 HTP users) participants were lost to follow-up, while 107 (9%) participants quit smoking. The loss to follow-up was similar in both groups with 15% for CC users and 18% for HTP users. Linear mixed models showed HTP use was associated with better health outcomes over time compared to CC users. Lung function decrease was significantly less in HTP users, while improvements in CAT scores, waist circumference, and systolic blood pressure were significantly better compared to CC users.

Conclusions: This study has shown significantly better health outcomes in participants who shifted to HTP use, who experienced significantly lesser decrease in lung function and better improvements in CAT score and physical characteristics compared to CC users. The results of this study suggest that HTP might be a safer alternative compared to CC use in people with long history of CC use and who cannot quit smoking.

ABSTRACT BOOK

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ABSTRACT BOOK

THE MIDTERM DIFFERENTIAL EFFECTS OF HEAT-NOT-BURN AND CONVENTIONAL CIGARETTES ON CORONARY FLOW, VASCULAR FUNCTION AND OXIDATIVE STRESS ARE INDEPENDENT OF NICOTINE LEVELS

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25

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Introduction: Heat-not-burn cigarette (HNBC) constitutes a non-combustible smoke product linked to reduced exposure to carbon monoxide (CO).

Methods: We compared the effects of HNBC to those of tobacco cigarette (TCig) on endothelial and coronary function as well as on nicotine levels, oxidative stress and platelet activation after 1 month of switching to HNBC.

We examined 75 smokers. Of those, 50 were switched to HNBC and 25 continued Tcig for 1 month.

At baseline and at 1 month, we assessed a) coronary flow reserve (CFR) by echocardiography, b) flow-mediated dilation (FMD), c) cotinine blood levels, a stable metabolite of nicotine, d) malondialdehyde (MDA), a marker of oxidative stress, and thromboxane B2 (TXB2), a marker of platelet activation, e) the exhaled CO and the number of cigarettes and/or heat sticks of HNBC used. Fagerström score, a marker of dependence from smoking habit was also calculated.

Results: Compared to Tcig smoking, switching to HNBC for 1-month improved CO (difference in CO between groups: 10.42 ppm; 95% CI: 3.07 to 17.76, $p=0.007$), FMD (difference in FMD = 4.3%; 95% CI: 1.23 to 7.51, $p=0.009$), and CFR (difference in CFR = 0.98; 95% CI: 0.23 to 1.80, $p=0.02$). MDA and TXB2 concentration significantly decreased in subjects switching to HNBC compared to tobacco smokers (difference MDA = 0.38 nmol/L; 95% CI: 0.10 to 0.66, $p=0.009$, 45pg/mL; 95% CI: 5.28 to 86.31, $p=0.03$). None of the aforementioned parameters changed in the control group at 1 month compared to baseline ($p>0.05$).

Cotinine blood levels were similar between the Tcig and HNBC group both at baseline and after one month of use ($p>0.05$). However, cotinine blood levels at baseline and 1 month correlated with the number of cigarettes used at baseline ($r=0.45$, $p=0.04$) or the number of heat sticks used at one month ($r=0.50$, $p=0.03$) respectively. Baseline Fagerström

ABSTRACT BOOK

25

score was also associated with number of heat sticks used at 1 month ($r=0.48$, $p=0.04$) and cotinine levels at baseline and at 1 month ($r=0.50$, $p=0.03$ and $r=0.57$, $p=0.01$ respectively).

Conclusions: HNBCs exert a less detrimental effect on vascular function platelet activation and oxidative stress than tobacco smoking that is independent of nicotine levels and is linked with the parallel reduction of the exhaled CO.



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AUTHORS' INDEX

AUTHORS' INDEX

A		D		HANNON MICHAEL J.	17
<hr/>		<hr/>		HARDIE GEORGE	16, 22
ACALI STEFANO	07	DEMENESCU LILIANA-		HARPER PETER	11
AL TOBI MOHAMMED	06	RAMONA	07	HEREMANS ANNIE	10, 19
ALBALUSHI NAJWA	06	DISTEFANO ALFIO	06	HOENG JULIA	01, 07
AMORÓS-PÉREZ ANA	04				
ANDREADOU IOANNA	25	E		I	
ARSENIJEVIC ALEKSANDAR	06	<hr/>		<hr/>	
AZZOPARDI DAVID	22	EBINGER JEAN-		IKONOMIDIS IGNATIOS	20, 25
		CHRISTOPHE	03	ILIC ALEKSANDAR	06
B		EMMA ROSALIA	06	ISKANDAR ANITA	07
<hr/>					
BAQUERO-ÚBEDA JOSE-		F		J	
LUIS	13	<hr/>		<hr/>	
BARBIER ANAÏS	01	FERRANTE MARGHERITA	06	JALANTI TAUNO	03
BARBOUNI ANASTASIA	08	FERREIRA SANDRA	01, 07		
BAROZZI NADIA	10, 19	FRENTZEL STEFAN	01	K	
BARRIOS VIVENCIO	13	FUKUHARA HITOMI	10	<hr/>	
BERTINO GAETANO	18			KAMPERIS DIMITRIOS	07
BLACK RYAN	17	G		KAPERONI MARILENA	02, 05
BOBES-GARCÍA JULIO-		<hr/>		KARANASIOS GEORGIOS	02,
BELARMINO	13	GALE NATHAN	16, 22	05, 06	
BOFFO SILVIA	06	GAVRANIĆ TANJA	23	KAREFYLLAKI IOANNA	08
BOVARD DAVID	01	GIANNOPOULOU-MARINI		KÄRKELÄ TEEMU	03
		NEFELI	08	KATOGIANNIS	
C		GIORDANO ANTONIO	06	KONSTANTINOS	20, 25
<hr/>		GOLDENSON NICHOLAS	17	KESANOPOULOS	
CALVINO FLORIAN	07	GOODALL SHARON	16, 22	KONSTANTINOS	08
CAMACHO OSCAR M.	16, 22	GUEDJ EMMANUEL	07	KHAYAT DAVID	11
CANCIELLO ANGELO	06	GUENIN MATTHIAS	07	KONDYLIS ATHANASIOS	07
CANO-CASANOVA LAURA	04			KOSTELLI GAVRIELLA	20, 25
CAROTA GIUSEPPE	06	H		KOUREA KALLIRROY	20, 25
CARUSO MASSIMO	06	<hr/>		KOVALENKO FEDOR	21
CARUSO TANCREDI	06	HAMPSHER SAMUEL	12, 15		
CHOI ANNA	14	HANKINS MATTHEW	10, 19		

AUTHORS' INDEX

L		P	
<hr/>		<hr/>	
LA ROSA GIUSY RITA MARIA	18	PAC CLAUDIUS	01
LI VOLTI GIOVANNI	06	PAPADAKI DIMITRA	08
LILLO-RÓDENAS MARÍA		PEITSCH MANUEL C.	01, 07
ÁNGELES	04	PERDIH ANDREJ	23
LUETTICH KARSTA	01, 07	POLOSA RICCARDO	06, 18
		POULAS KONSTANTINOS	05, 06
M		PRAH ALJA	23
<hr/>		PRIEGER JAMES	14, 15
MARANZANO FABIO	07	PULVIRENTI ROBERTA	06
MARESCOTTI DIEGO	01, 07		
MARINO MARGARITA	20, 25	Q	
MARKOU CHRISTOS	08	<hr/>	
MARTÍNEZ-GONZÁLEZ		QURESHI MARIA-AHMED	18
DANIEL	13		
MAVRI JANEZ	23	R	
MCCAFFREY STACEY	17	<hr/>	
MCEWAN MICHAEL	16, 22	REDONDO-DELGADO	
MERG CELINE	07	MARTA	13
MERKOURIADI GEORGIA	08	RENGGLI KASPER	01
MESIAKARIS		ROBYR OLIVIER	03
KONSTANTINOS	02,	ROMÁN-MARTÍNEZ MARÍA DEL	
05, 06		CARMEN	04
		RUIZ PEDRO	07
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NEAU LAURENT	07	S	
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O		SANDOZ ANTONIN	01
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O'LEARY RENÉE	18	SEWER ALAIN	07
ODIMEGWU DAMIAN-		SHANMUGAM PREM-KUMAR	09
CHUKWU	18	SHARMAN ALMAZ	24
ORTEGA-TORRES LAURA	07	SHIFFMAN SAUL	17
		SHOAIB MAJEED	01, 07
		SOLLNER-DOLENC MARIJA	23
		SPAMPINATO MARIA-RITA	06
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		TAPPER UNTO	03
		TRIVEDI KEYUR	07
		TSOUMANI MARIA	25
		TYROLOGOU VASILIKI-	
		ATHINA	08
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		VAN DER PLAS ANGELA	10, 19
		VERNOOIJ ROBIN W.M.	18
		VINCENT JAQUET	07
		VLASTOS DIMITRIOS	25
		VOLAREVIC VLADISLAV	06
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		XIANG YANG	07
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		ZADJALI FAHAD	06
		ZUCCARELLO PIETRO	06

