EXPLORING THE UTILITY OF THE INNOVATIVE NICOTINE DELIVERY SYSTEMS AS NICOTINE REPLACEMENT THERAPY TOOLS

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Nicotine-Replacement Tools: Tobacco Heating Systems & E-Cigarettes
Conclusions

- Heated tobacco products is an old (and initially failed) concept
- New developments and products (some already marketed in many countries, others to follow)
- Resemble tobacco cigarettes in patterns of use
- No visible side-stream smoke, but bad smell (very similar to smoking)
- “Side-stream smell”, implying emissions
- Lower throat hit compared to tobacco cigarettes
- Significantly lower toxic emissions than smoking, but higher than new-generation e-cigarettes
- They seem to represent a harm-reduction option for dual users or smokers who cannot quit with e-cigarettes
  - Not satisfactory (probably disgusting) for established e-cigarette users

- Independent studies needed
There exist 2 problems:
Smoking cessation? Harm reduction?

Cigarette Smoker (CS) → E-cigarette (EC) User

Smoking cessation? → Harm reduction?

An inverse linear relationship between the cigarette price and smoking prevalence (%) in the UK

UK 2005-2017

"... A number of immune-related genes whose expression was significantly decreased was six times greater in e-cigarette users than in cigarette smokers (53 vs. 358)."

Goal and Tasks

Goal: Conducting preclinical trials of the novel nicotine delivery systems to reduce the harmful effects of tobacco smoking in people with bronchopulmonary diseases

A. Who were examined?
- Smoking patients observed at the pulmonological division of one of the city hospitals in Moscow with a diagnosis of COPD, asthma, etc.;
- Healthy volunteers from the hospital personnel;

B. Where, how and what was investigated?
Experimental data were acquired from:
- Vascular pulse oximetry;
- Pulmonary function testing (spirometry) at active & passive smoking & consumption of aerosols from nicotine delivery systems;
- Complete blood count and monitoring the activity of phagocytes by the whole-blood chemiluminescence;
- Urinalysis on the content of the biomarkers of oxidative stress;
- Saliva analysis on peroxidase activity;

Location of the research: smoking room 4x3x3 with the forced ventilation and monitoring the total volatile organic compounds (TVOC) & PM$_{2.5}$;

Fletcher Curve (Adapted from C. Fletcher, R. Peto, Br. Med. J. 1977, 1, 1645-1648.)
Antonov: электронные сигареты не помогают бросить курить

“…Electronic cigarettes do not help to quit smoking…”

“…Confessed that he is himself a smoker, but never used electronic cigarettes…”

“…Electronic cigarettes are no less harmful than conventional ones…”

“…Electronic cigarettes are not marked with nicotine and tar content, etc. …”
Target Group of Patients

- % of the global population affected by COPD; 3

- Smoking rate in the Russian Federation (% of adults); 35

- % COPD patients have a higher risk for depressive symptoms, smoking cessation attempts may be less successful and proportion of relapses may be higher; 70

- % COPD-related patients are current or ex-smokers; 85
The main question in the questionnaire: Would you agree to participate in the experiment, in which you will have to give up smoking switching to e-cigarette (EC) for 1 month?

Conditions: Patients were offered to test for 1 day the e-cigarette of the Pons type without or with the possibility of subsequent investigation and asked to answer the questionnaire. All patients (males only, groups of 10 individuals) diagnosed with COPD were over 60 years old.
OUTCOMES # 1: Disposable Cigalikes

“A cigalike is an electronic cigarette designed to look as much as a tobacco cigarette as possible. They are small, light and mimic analogs almost to perfection”

[http://vaperanks.com/what-is-a-cigalike/]

1. Visual assessment of a cigarette-like e-cigarette without the possibility of testing the product plays a minor role in making a decision by a COPD patient to participate in the experiment.

2. On average, 1 person out of 5 agrees to participate in the experiment after testing the product (e-cigarette type is cigalike), but without additional information.

3. Informing the test participant on e-cigarette design and the presence of deficiencies in it immediately after testing, but before starting the questionnaire, affects adversely the patient's desire to participate in the experiment.
The main question in the questionnaire: Would you agree to participate in the experiment, in which you will have to give up smoking switching to tobacco heating product (THP) for 1 month?

Conditions: Patients tested THP without or with detailed information about the THP design and were offered to answer the question of the questionnaire. All patients (males only, groups of 10 individuals) diagnosed with COPD were over 60 years old.
OUTCOMES # 2: Tobacco Heating Products (THPs)

1. THPs a priori look more attractive for a smoker with experience, if he is previously notified about the presence of tobacco in sticks and tell about the mechanism of aerosol generation. However, this is the only advantage of THP over conventional e-cigarettes. On average, 3 out of 10 individuals agree to participate in the experiment after testing the product and obtaining the detailed information about it.

2. Patients with COPD were indeed very selective and picky about alternative nicotine delivery systems. The greatest preference from them received THPs, which were further used for extensive testing.

3. For the time being, we have not yet recruited enough volunteers among patients with COPD to organize full-fledged clinical trials.

4. It was decided to conduct testing with healthy volunteers from the medical personnel of the hospital under the pertinent approval by the Local Ethics Committee.
FACTORS INFLUENCING THE DECISION MAKING 
(Based on the EC testing and polling the patients)

1. Factors of refusal to participate in the experiment (patients with COPD older than 60 years) - a group of "dissenters":
   A. The discrepancy between the expected and habitual taste, as well as tactile sensations in all cases of nicotine delivery systems, including THP;
   B. Difficulties in the settings and use of devices (THP and EC of the tank type);
   C. High starting costs for the purchase of devices and additions;

2. Consent of participation in the experiment - a group of "consonants":
   A. The similarity of the form and content of devices with their prototypes (especially, the presence of tobacco inside THP);
   B. Relative ease of use (for cigalikes and glo™);
   C. Moderate costs;

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<th>“Dissenters”</th>
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<tr>
<td>A</td>
<td>80%</td>
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<td>B</td>
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Experimental Design for Testing the Nicotine Products

Passive vaping (EC, THP) & smoking

2 men X 1 cig X 10 min

TVOC
PM$_{2.5}$
Air Quality in the Smoking Room

The TVOC gas analyzer measures the total concentration of substances with an ionization potential below 10.6 eV by the photoionization method.

**Outcome:** THP “vaping” results in 6-fold lower concentration of toxic organic compounds in the ambient air compared to cigarette smoking.

Persistent ambient concentrations of PM$_{2.5}$ > 20 mg/m$^3$ are associated with increasing severity of respiratory symptoms related to airway obstruction, chronic bronchitis, and asthma.

**Outcome:** Peak concentration of PM$_{2.5}$ particles in the ambient air upon THP "vaping" is 10-fold lower compared to that upon smoking!
Results: Passive THP “Vaping” vs. Passive Smoking

HS = healthy smoker; NSA = non-smoker with light asthma form;
CC = passive smoking of conventional cigarette;
GLO_5(60) = passive “vaping” of glo™ (5/60 is the time after session, min);
Passive THP “Vaping” vs. Passive Smoking: Healthy Smoker

Conclusion: Both passive smoking and passive THP "vaping" affect the basic parameters of spirometry. BUT! The consequences of passive THP "vaping" disappear quickly, in contrast to passive smoking!
Spirometry upon Active Smoking vs. Vaping: Smoker with Light Asthma Form, Nicotine Inhalation

Conditions:
Smoker with light asthma form, male, 30 y.o., Smoking history: 12 pack*years;
Conventional Cigarette (Conv. Cig.): 0.4 mg of nicotine, 4 mg of tar;
E-cigarette (E-cig): Vaporesso+tank, 8 mg/ml nicotine in propylene glycol (PG), ceramic heater, T = 200 °C;
Vaping session: 5 min, time between sessions was 4 h;

Conclusion: Whereas smoke from conventional cigarette causes a prolonged bronchial obstructive effect, the nicotine from e-cigarette exhibits merely a short-term impact.
Spirometry upon Bacterial Endotoxin (LPS) Inhalation: Non-Smoker

There exist up to 1 µg of endotoxin (lipopolysaccharide, LPS) in one conventional cigarette, up to 10% of which may be transferred into the smoke.
Tobacco Heating Systems: Influence on the Spirometry Parameters of Healthy vs. Astmatic Individuals

Conclusion: THP impose mild effects on the human respiratory system.
**Conclusion 1:** Tobaccos from the THP sticks are less active towards cells of immune system than tobaccos from conventional cigarettes.

**Conclusion 2:** Heated tobacco from glo™ exhibits nominal activity towards phagocytes (compared to the control samples), the properties of tobacco from IQOS upon heating remain unchanged, while tobaccos from conventional cigarettes upon heating suppress (inhibit) the phagocytic activity.
CONCLUSIONS

(1) Patients with COPD due to their age and habits experience severe difficulties with refraining from smoking;
(2) Tobacco heating products (THP), as the alternative nicotine delivery systems closest to their prototype (tobacco cigarettes), partially meet the needs of smokers with COPD;
(3) THP merit attention and further investigations as potential nicotine-replacement therapy tools for patients with COPD, their potential benefit compared to e-cigarettes not to the least extent are associated with their advanced consumer properties;
(4) The latest developments in the field of the THP design are not much inferior to e-cigarettes in terms of reducing the emission of toxic products. Moreover, in THP, the work of the evaporator is adequately stable and controlled, which excludes local overheating and the "dry" inhalation characteristics reported in the literature for some of e-cigarettes and their operation modes;
(5) Compositions and biological properties of aerosols generated by the THPs decisively depend on the quality of the tobacco in THP sticks.
Thank you for your attention!