HEATED TOBACCO PRODUCTS: WE STILL NEED TO KNOW A BIT MORE

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REVIEW ARTICLE

HEATED TOBACCO PRODUCTS: WE STILL NEED TO KNOW A BIT MORE

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ABSTRACT

The aim: This research aims to analyze the challenges we came across due to the rapid spread among the population (including young people) of tobacco heating devices.
Materials and methods: Analysis of 20 literature sources containing information about tobacco heating systems was performed. The search for literary sources was carried out in two main scientific databases: Scopus and PubMed. The review included original articles, research, and official recommendations from medical associations.
Conclusions: Tobacco heaters reduce harmful substances in the inhaled air compared to conventional tobacco cigarettes, but these new devices provide effective nicotine absorption, which prolongs a person's nicotine dependence and prevents smoking cessation. The main problem we face due to the rapid spreading of these devices - potentially tobacco heating systems can pose health risks and further research on such risks, especially long - term, are needed. Tobacco heating devices, regardless of their manufacturer and design, should be subject to restrictions similar to traditional cigarettes.

KEY WORDS: Heated tobacco products, health risks, electronic nicotine delivery systems

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INTODUCTION

All forms of tobacco consumption, including smoking cigarettes, cigars, pipes, chewing or sniffing tobacco, as well as the impact of its combustion products on non-smokers (passive or forced smoking), significantly increase morbidity and premature mortality caused by more than twenty different diseases.

Most studies have shown that the risk of disease depends on both the number of cigarettes burned and the duration of smoking. World Health Organization (WHO) experts estimate that 4 million people worldwide die from smoking-related diseases each year. If the smoking situation does not change, in 2025 the annual loss will be 10 million people. In Ukraine, smoking is the indirect cause of one in five deaths of people over the age of 35.

Under the Framework Convention on Tobacco Control (FCTC), the WHO has launched a comprehensive tobacco control strategy [1]. The WHO Framework Convention on Tobacco Control (WHO FCTC) is the first treaty negotiated under the auspices of the World Health Organization. The WHO FCTC is an evidence-based treaty that reaffirms the right of all people to the highest standard of health. The WHO FCTC represents a paradigm shift in developing a regulatory strategy to address addictive substances; in contrast to previous drug control treaties, the WHO FCTC asserts the importance of demand reduction strategies as well as supply issues. Articles 9 and 10 of the FCTC include specific policies to curb tobacco use by regulating ingredients and emissions of tobacco products. The overall goal is to reduce toxicity, dependence and consumer attractiveness. The parties to this convention have committed themselves to limiting the supply and demand of tobacco products through a wide range of policies and measures. Although the FCTC has been successfully applied to traditional tobacco products, questions remain about how to cover new products.

THE AIM

This research aims to analyze the challenges we came across due to the rapid spread among the population (including young people) of tobacco heating devices.

MATERIALS AND METHODS

Analysis of 20 literature sources containing information about tobacco heating systems was performed. The search for literary sources was carried out in two main scientific databases: Scopus and PubMed. The review included original articles, research, and official recommendations from medical associations.

REVIEW AND DISCUSSION

To help countries implement the FCTC, WHO has introduced the MPOWER technical package [2]. MPOWER

are a set of six cost-effective and high impact measures that help countries reduce demand for tobacco. These measures include:

- Monitoring tobacco use and prevention policies.
- Protecting people from tobacco smoke.
- Offering help to quit tobacco use.
- Warning about the dangers of tobacco.
- Enforcing bans on tobacco advertising, promotion and sponsorship.
- Raising taxes on tobacco.

Some 5.3 billion people are now covered by at least one of these measures - more than four times the 1 billion who were covered in 2007 [3]. Some 5.3 billion people are now covered by at least one of these measures - more than four times the 1 billion who were covered in 2007.

More than half of all countries and half the world's population are now covered by at least two MPOWER measures at the highest level of achievement. This reflects an increase of 14 countries and almost one billion more people since the last report in 2019.

More than half of the world's population are exposed to tobacco products with graphic health warnings. However, progress has not been even across all MPOWER measures. Some measures like raising tobacco taxes have been slow to move and 49 countries remain without any MPOWER measures adopted.

However, new nicotine, nicotine - free and tobacco products operated by electronic systems have also been sold aggressively in many countries around the world. These include:

1) *Electronic nicotine delivery systems* (ENDS) and electronic non-nicotine delivery systems (ENNDS), commonly referred to as electronic cigarettes, are devices that heat a liquid to create an aerosol that is inhaled by the user. Aerosols for e-cigarettes typically contain nicotine and toxic substances that are harmful to both users and non-consumers exposed to passive aerosols [4 - 7]. People who use these products in combination with smoking of regular cigarettes, which is the most common form of e-cigarette use, are exposed to toxic chemicals from two or more products [8].

A few years ago, we investigated ENDS and, as a conclusion, noted that they has proven to be effective in removing of tobacco-related complaints, but so far, the ENDS cannot be available as safe and effective method to completely abandon smoking [9]. Existing production regulations do not standardize either the ENDS itself or the liquid for them, because of which the composition (including the content of harmful to health substances) is not actually regulated. In addition, there are no data about the long-term effects of ENDS usage, which is a priority area for further research.

In recent years, there is growing evidence that the use of ENDS is associated with lung injury, with some evidence of acute lung injury, lipoid pneumonia, eosinophilic pneumonia, liquid pneumonia and obliterative bronchiolitis [10]. In addition, additional data suggest that ENDS may have an impact on other aspects of lung health [11]. E-cigarettes can also pose a serious threat to lung health, especially in unregulated conditions. For example, in the second half of 2019, the United States investigated an outbreak of lung injuries related to the use of e-cigarettes or vaporizing products, which has claimed about 70 lives to date. These injuries, known as EVALI (lung injuries associated with the use of e-cigarettes or vaporized products), have since been reported to have a strong link, and research is underway into whether there are other chemicals of concern that could have contributed to these injuries [12].

Lung damage associated with an e-cigarette or evaporation product is determined by the presence of pulmonary infiltrates in the imaging; use of electronic nicotine delivery systems during the previous 90 days; and the absence of other possible causes, such as infection, heart, tumor or rheumatic causes. A significant proportion of patients hospitalized for lung injury associated with e-cigarettes or vapor products required hospitalization in the intensive care unit, and up to a third of patients required mechanical ventilation.

2) *Heated tobacco products* (HTP) are tobacco products that produce aerosols containing nicotine and toxic chemicals when heating tobacco or activating a device containing tobacco. These aerosols are inhaled by users during the process of sucking or smoking with the device. They contain the highly addictive nicotine, as well as tobacco-free additives and often have a flavoring. Tobacco can be in the form of specially designed cigarettes (for example, "thermopiles" and "neo sticks"), pods or corks.

In October 2018, the Conference of the Parties (COP) 8 directly proposed to extend the scope of relevant legislation to HTP. Previous WHO minimization strategies focused exclusively on traditional cigarettes, not on new technical advances, often referred to as modified or reduced exposure / risk. From a toxicology perspective, on the one hand, it makes sense to combine minimization approaches with new technologies. On the other hand, there are concerns that tobacco heaters may create the deceptive impression of almost harmless tobacco consumption and, in addition to residual pollutant emissions, will also have a high potential for addiction.

In Ukraine, the first model came on the market in 2016, which in the literature is called the THS 2.2 (tobacco heating system 2.2). The manufacturer has conducted large-scale studies to reduce harmful and potentially harmful substances in emissions. Subsequent studies have shown that lower exposure also reduces health risks if you completely switch from a regular tobacco cigarette to a tobacco heater. The company then applied to the Food and Drug Administration for the use of modified-risk tobacco products for the sale of its own tobacco heating device with risk reduction claims in 2016, but it was rejected. In 2020, U.S. Food and Drug Administration authorized the marketing of THS 2.2 [13]. This marks the first tobacco products to receive "exposure modification" orders, which permits the marketing of a product as containing a reduced level of or presenting a reduced exposure to a substance or as being free of a substance when the issuance of the order is

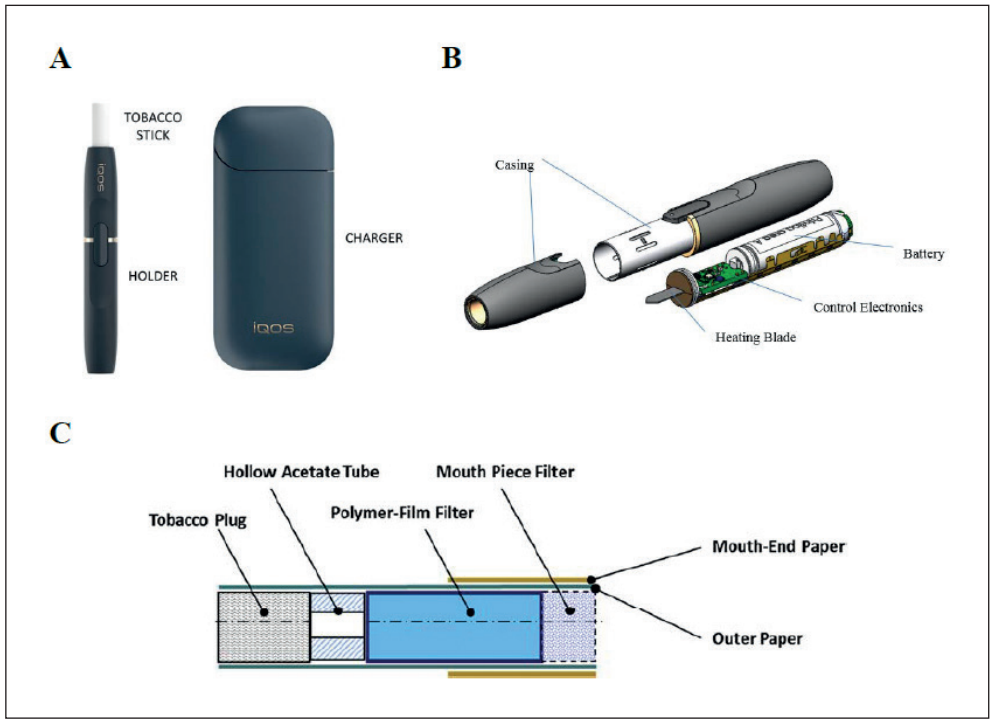

Fig. 1. THS 2.2 components (A), a schematic exploded view drawing of the Holder (B), and a schematic cross-sectional view of the Tobacco Stick (C) (adopted from fda.gov)

expected to benefit the health of the population. Importantly, the authorization for these products requires the company to conduct postmarket surveillance and studies to determine whether the MRTP orders continues to be appropriate, including assessing the potential for increased use among youth. However, this device is now sold in more than fifty countries.

The tobacco heater, available in Ukraine, consists of 3 components with different functions (Fig. 1). This includes a tobacco stick with treated tobacco, a heater (holder) similar to a handle into which a tobacco stick is inserted, which is then heated by an electric heating rod, and a charger (charger) that recharges the heater after use. The tobacco heater automatically stops the heating process after 6 minutes or 14 puffs, so that the products of pyrolysis and the release of contaminants are limited both in time and in the maximum number of puffs per stick. The tobacco stick contains a compressed tobacco stick and several filter elements. The tobacco stick consists of a dried tobacco suspension, which becomes thin for paper with brown tobacco foil. This is about 70% tobacco, as well as humidifiers, binders and flavors. Water and glycerin are used as humectants to prevent drying and support the formation of aerosols when heated. The filter elements consist of 2 independent systems: a polymer film filter that cools the aerosol, and then a mouthpiece filter made of soft cellulose acetate, which mimics the sensory aspects of a regular cigarette.

Conventional tobacco cigarettes are very well researched and standardized products. Cigarette smoke is an aerosol consisting of approximately 4,800 compounds, 89 of which were classified as hazardous to health [14]. With each puff in the glow zone, a temperature of about 900 °C is reached, which causes the tobacco to burn. In the absence of oxygen in the adjacent tobacco rod, endothermic reactions occur, which thermally decompose organic and inorganic material. The gaseous reaction products reach the distillation zone, where the temperature drops to 600–200 °C, depending on the distance from the glow zone. Most of the substances harmful to health are produced here. The aerosol is formed by evaporation of volatile components and distillation. Low-boiling substances enter directly into the smoke. Behind the distillation zone is the condensation zone, where part of the smoke condenses again. Therefore, the inhaled main smoke consists of solid particles and a gaseous phase.

The nicotine value of a tobacco heater is comparable to that of regular cigarettes. The value of the total mass of the particles is sometimes higher. However, the total particle weight of the tobacco heater has a different composition, as the proportion of water and humidifiers is much higher. If we compare the content of carbonyl compounds of formaldehyde, acetaldehyde, acrolein and crotonaldehyde, the emissions of tobacco heater are 80-96% compared to conventional tobacco cigarettes. The content of volatile and semi-volatile compounds in emissions is 97–99% lower in a tobacco heater compared to conventional cigarettes.

Thus, C. Haziza et al. showed that a few days after switching to a tobacco heater, a significant decrease in 16 biomarkers associated with smoking was observed in the blood or urine [15]. Measurement of biomarkers for 1,3-butadiene (monohydroxybutenylmercapturic acid, MHBMA), acrolein (3-hydroxypropylmercaptonic acid, 3-HPMA), benzene (S.-phenylmercapturic acid, S -PMA) and acrylonitrile, respectively, 92 %, 59 %, 94 % and 87 % according to a study conducted in Poland. Compared to the reduced emissions, the impact on the relevant biomarkers was less clear. The other two studies were three-month and

were conducted in Japan and the United States [16, 17]. They also began with a 5-day inpatient phase, followed by 90 days of outpatient care. However, quantitative information on the compliance of study participants is missing in outpatient studies. In a study conducted in Japan, compliance is described as "particularly high." A study in the United States reported a "good" fit for the tobacco heating group, but a "poor" fit for the tobacco withdrawal group, which increased variability and thus made it impossible to interpret the results. In addition, former employees of the manufacturer pointed to violations in the conduct of clinical trials. This emphasizes the need for independent evaluation of the source data.

The study by Schlage et al. (2018) showed that heated tobacco products can reduce the risk of lung cancer [18]. Prolonged exposure to total solids from IQOS had less biological effect on human bronchial epithelial cell line compared to total solids from cigarette smoke. The aerosol ejected from IQOS has been shown to damage human bronchial epithelial cells; however, the cytotoxicity of IQOS was lower than that of flammable cigarettes, but showed higher toxicity than the e-cigarette, which was consistent with data from the tobacco industry. Evidence suggests that the use of IQOS products may increase the risk of respiratory disorders, and this risk is likely to be greater than the risk associated with e-cigarettes [19].

In a study by Walczak et al. (2020) investigated the morphology and dynamics of the mitochondrial network in human bronchial epithelial cells (BEAS-2B) exposed to total solids (TPMs) formed by an aerosol from a tobacco heating system (THS 2.2) [20]. Comparison of the effects of TPM with 3R4F and THS 2.2 showed that a similar range of changes in mitochondrial dynamics and biogenesis was observed at 7.5 μg / ml 3R4F TPM and 150 μg / ml THS 2.2 TPM. The seven-day exposure to the test components of cigarette smoke causes mitochondrial stress, while the 12-week exposure showed signs of cellular adaptation to the stressor.

Quitting smoking significantly reduces the risk of developing serious chronic diseases. Tobacco sponsors now suggest and support that nicotine addicts should switch from regular smoking to alternative products that will at least reduce the overall harm from smoking, although there are not enough longitudinal studies to support this idea. However, there are less invasive and highly effective treatments (drugs or behavioral interventions). On the other hand, heated tobacco products are another alternative that has appeared on the market alongside e-cigarettes.

CONCLUSIONS

Tobacco heaters reduce harmful substances in the inhaled air compared to conventional tobacco cigarettes, but these new devices provide effective nicotine absorption, which prolongs a person's nicotine dependence and prevents smoking cessation. The main problem we face due to the rapid spreading of these devices - potentially tobacco heating systems can pose health risks and further research on such risks, especially long - term, are needed. Tobacco heating devices, regardless of their manufacturer and design, should be subject to restrictions similar to traditional cigarettes.

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The Authors declare no conflict of interest.

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