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E-cigarettes or heat-not-burn tobacco products: advantages or disadvantages for the lungs of smokers

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Abstract

This is a narrative review considering the use of e-cigarettes and heat-not-burn tobacco products. Advantages and disadvantages of both devices, including biological and clinical consequences, were described. The role of these products in limiting tobacco dependence was also discussed. Possible implications for clinical practice were addressed as well.

Key words: e-cigarettes, heat-not-burn tobacco products, HNB

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Introduction

Many smokers want to quit, but a long-term success achieve only few. All tobacco products are addictive. Health consequences of nicotine dependency are serious. Apart from nicotine, a variable exposure to many toxins and carcinogens is associated with the use of primary addictive products. Manufacturers try to modify tobacco articles using products with filtres, „low tar" and „light". However, all these attempts have not resulted in less harm. Newer proposals of nicotine use may be divided into two types: e-cigarettes and heat-not-burn products (HNB). It is being considered, if these items are able to end or at least markedly limit a liking for smoking .

Heat-not-burn (HNB) tobacco products

HNB are devices that deliver an aerosol from heated not combusted cigarettes. Three companies produce different systems based on tobacco heating (IQOS-Philip Morris, Glo-British American Tobacco) or non-tobacco substrate (IFuse Japan Tobacco) [1]. All systems contain a charger, an electronically controlled heating element and a holder (Fig. 1).

Reports from Europe and Asia point that a number of HNB users is rapidly increasing, exceeding in 2017 in Japan 50% of the adult population [2, 3].

Troublesome data collections

Epidemiological data about results of classical tobacco smoking are well known. Difficulties arise with regard to studies on e-cigarettes and HNB. Variable populations and various motivations to use, different law limitations in particular countries, many demographic discrepancies and relatively short time of the presence of products on markets create difficulties in comparing the results of epidemiological data collections. In a case of e-cigarettes, many complications are caused by a lack of standardized and controlled production systems. The number of liquids used by e-cigarettes manufacturers exceeds 8 thousand, and the number of devices amounts to about 1,000 [4]. Liquid products from the same producer contain not replicable percent of

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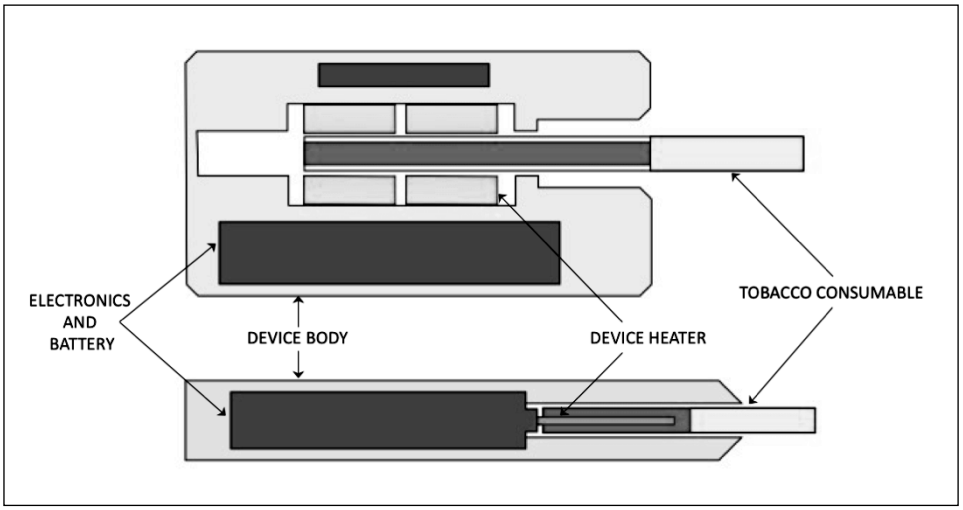

Figure 1. The construction of HNB devices

agents. Thus, some liquids differ signifficantly from the others [5].

A relatively small number of independent studies on HNB exists. To the beginning of 2018 one could have found only eleven independent studies based on EBM methodology, mostly performed in laboratories [1]. Only 4 of them have been epidemiological and their results are undoubtedly insufficient to conclude about the usefulness of HNB for conventional cigarette smoking limitation.

Biomarkers

Good biomarkers are characterized by undoubted dose-response relationship with exposure to chemical agent, quantitative and qualitative identification over low and high concentrations, detection in biospecimens of blood, urine or saliva, stability in specimens during storage for future analyses [6].

Hundreds or even thousands of chemicals with potential harm to human health have been identified in both e-cigarettes and HNB. However, we cannot be satisfied with monitoring of health effects and their expected positive influence on tobacco dependence. The lack of validated biomarkers seems to be one of the most important public health problems. Commonly used tests for nicotine exposure as TSNA (tobacco-specific nitrosoamine metabolites) point only exposure to e-cigarettes, HNB or nicotine replacement therapy, but biomarkers of real health effects in humans that could be used in practice are not available. Only few research groups have performed not expensive, sufficiently specific and sensitive assays to differentiate tobacco use from other nicotine-containing products.

Biomarkers of harmful or potentially harmful compounds in people exposed to HNB remain at much lower level than in smokers [6].

Category of emissions

Usually, emissions from tobacco, HNB or e-cigarettes are categorized according to a place of stream as mainstream, sidestream or secondhand [7]. Mainstream is commonly used as the most important category. It takes a central part of smoke that a man draws on. Mainstream is often described in many laboratory studies by the use of standardized machines, because it replicates human smoking. Sidestream measurements are studied in standardized laboratories to measure environmental exposure. Secondhand smoke combines both exhaled mainstream and sidestream exposure.

Mainstream emission

The standards of studied emissions produced by machines distinguish between methods recommended by IOS (International Organisation for Standardization) and Health Canada Intense (HCI). However, many problems arise, when the results of studies in real life and standardized exposure are compared. Reference cigarettes differed between researches performed in different regions. Some methodological problems of measurements of aerosol constituents are stated, but undoubtedly, HNB produces less harmful emission [8]. Another problem is a difference between cigarettes manufactured as a reference for studies and commercially available products.

It is reasonable to accept that a level of mainstream decides on an influence on dependence on the product. Nicotine emission in mainstream ranges between 1.1 and 1.41 mg in IQOS and is about 50% lower in GLO [8]. In comparison with conventional cigarettes, a mainstream in IQOS contains 57 to 83% of nicotine according to independent study [9]. There is no independent investigation on a level of nicotine in GLO or iFuse.

Many papers have compared the levels of HPHC (Harmful and Potentially Harmful Constituents) like polycyclic aromatic carbons, tar, carbon oxide, nitrosoamines, and nicotine- derived agents. When machine regimens have been used, it seems that mainstream contained lower levels of carbon oxide (reduction almost by 99%), tar, and other HPHC than cigarettes [8, 10]. Suprisingly, one independent study has reported more nitrosoamines and other nicotine-derived amines [11].

Sidestream and secondhand emission

One research funded by a tobacco company that does not manufacture HNB products, has suggested that HNB produces a higher number of particulate matter than e-cigarettes [12]. However, six other authors , including three independent studies have reported that e-cigarettes and HNB emission of particulates from e-cigarettes and HNB is almost equal to the level of 25% of cigarette smoke [13–18]. As a matter of fact, e-cigarettes produce more particulates, but dispersing of them in sidestream from ICOs lasts longer. However, a diameter of most particles produced by IQOS is just below 1000 nm, which is regarded as relatively safer than lower mass particles [13]. The number of respirable fraction of particles is higher in GLO and cigarette smoke, however, a global mass of particles in GLO was lower [18].

HPHC in secondhand emission were reported [17, 18]. The methods of assessment differ between independent and company funded studies. This may be an explanation why particulate matter and acrolein in an independent research were detected [14], when in company funded did not [17].

Animal and human studies

Plasma nicotine concentration in people exposed to e-cigarettes and HNB exceeds half of the levels in people exposed to cigarettes. However, expired carbon oxide in e-cigarettes or HNB users constitutes about 25% of a number of parts per milion (ppm) observed in smokers [19]. According to nicotine consumers, smoking gets more satisfaction than an alternative delivery, but smokers do not perceive less satisfacion as unbearable. HNB users reported lower satisfaction than smokers, but a use of HNB suppressed significantly the need for smoking [19].

In people who switched from smoking to ICOS use, there were observed a large reduction of biomarkers concentrations and expression of systemic imflammation, oxidative stress, endothelial dysfunction and a decrease of serum high-density lipoprotein [20–23]. Positive changes of lung lipid profile were also stated [24]. RCT studies confirm expectations that switching from smoking to HNB reduces but does not completely remove exposure to HPHC. Such trials lasted not longer than 90 days and one cannot conclude about a longer influence of switching from smoking dependence to HNB on health effects [25].

In vitro RNA toxicogenomics assessment showed reduced biological effect of HNB when compared to cigarette [26]. MicroRNA expression indicates that HNB aerosol evokes reduced effects on the lung tissue compared to cigarette smoke [27, 28].

The question if HNB products may be useful in the removal of nicotine dependence remains open. No independent study is available. Daily use of HNB in people who switched from smoking remains on the level of a use of conventional cigarettes. Observational studies have showed different results, but conclusions do not allow to regard HNB as a much useful proposal [22, 29, 30]. In an interesting case report from Japan, a man in whom eosinophilic pneumonia developed following a rapid increase of daily HNB use, has been described.

Are HNB products useful in limiting tobacco dependence?

The question has been discussed lately in the US and UK [32, 33]. The most important conclusions from the British Report are the following:

1. Heat- not- burn products still pose a risk to users. There is likely to be a reduction in risk for cigarette smokers who switch to heat- not-burn products but quitting entirely would be more beneficial.
2. People using these products are exposed to between 50 and 90 percent less harmful and potentially harmful compounds, compared with conventional cigarettes.

3. There is a reduction in risk to bystanders where conventional smokers switch to heat-not- burn products.

The FDA has asked if scientific studies have shown that switching from cigarettes to the ICOS system can reduce the risk of tobacco-related diseases. The answer is negative.

Thus, no official statements are convincing with regard to any limitation of nicotine dependence due to the use of HNB products. The most important reason for the cautious opinion is a lack of independent long-term studies into expected effects of HNB products resulting in nicotine dependence limitation. The likelihood that never smokers, particularly youths, will become established HNB users is low. According to the FDA, the probability that former smokers will re-initiate tobacco use with HNB seems to be also low. The chance that smokers will become long-term dual users is usually assessed as high or moderate. This is important in the light of the discussed problem of the possibility of complete switching from conventional smoking to the use of HNB products. Published data have given no answer to this question.

Fundamental question for pneumologists

To the end of 2018 no data about an influence of switching from conventional cigarettes to HNB use in people suffering from chronic airway disease have been published. Human studies are very poor and avoid the answer to many problems concerning advantages and disadvantages of such switching. Very little is known about the persistence of liking for HNB use instead of cigarettes. Neither the FDA/ British Government nor clinicians are able to compare effects of switching to e-cigarretes and HNB. However, suggestions that HNB are only signs of novel tobacco industry strategy to slow progress in tobacco control seems to be exaggerated [34]. Undoubtedly, burned, not combustible cigarettes contain less harmful and potentially harmful products than conventional cigarettes. In opposite to e-cigarettes consumption, a number of people starting their nicotine dependence with HNB is extremally low. The use of HNB does not seem to be convenient in comparison with smoking. Thus, one cannot see an important danger for a wide use of HNB in the general population.

E-cigarettes

Approximately 15 % of adult people in the USA use e-cigarettes occasionally. The number of current e-cigarettes consumers exceeds 7% , and systematically increases [35]. In many countries, the highest rates are reported in adolescents and people below 25 of age [36]. The prevalence of tobacco smoking has fallen lately, but in some countries, users of e-cigarretes exceeded the number of smokers [37]. Among students of Polish non-medical universities, 37% declared as ever using e-cigarettes. This proportion was a little lower in health educated medical students but still exceeded 25% [38]. E-cigarettes both in Poland and in the US are utilized mostly by people parallelly smoking conventional cigarettes (dual users) [39–41]. A typical e-cigarette consumer is a male, poorer, nonmarried, white, young [42].

Devices and liquids

Each e-cigarette consists of an atomizer with a battery heating a metal coil, a reservoir of liquid, a cartridge and a silica wick (Fig. 2).

Electronic cigarettes encompass a variety of products looking like a classical cigarette (first generation, „cigarlikes") or larger devices to hold the liquid. The most popular in the USA system named JUUl seems to be more convenient and probably safer because it is not liable to accidental outburst of a device [43].

The types of cigarettes differ significantly in voltage and resistance of a coil. A variety of metals are used but all contain nickel.

There are a lot of liquids that may be vaped and sucked by the user. In fact all liquids contain nicotine in a variety of concentrations and many flavoring artificial additives [44] (Table 1).

The most important differences between first and third generation devices consist in better control over a liquid stabilisation and the physical features of vaporized aerosol. The power in electrical circuit of coils varies with the age and temperature of metal components [45]. Increased power results in the production of volatile carbonyl compounds, including carbonyl nickel regarded as a very strong carcinogen. Additionally, other metals like chromium, copper, zinc, silver and heavy metals have been found in vaporized liquids [44]. Metal coils of the majority of devices comprise nickel/chromium or kanthal (chromium/aluminium/iron). Even short exposure to metal fumes influences lung immunological system leading to metal fume fever, asthma and cancer [46].

Heating is also responsible for the aldehyde contamination of aerosol, because both glycerine and propylene glycol form aldehydes while heating [47]. E-cigarette liquid may be contami-

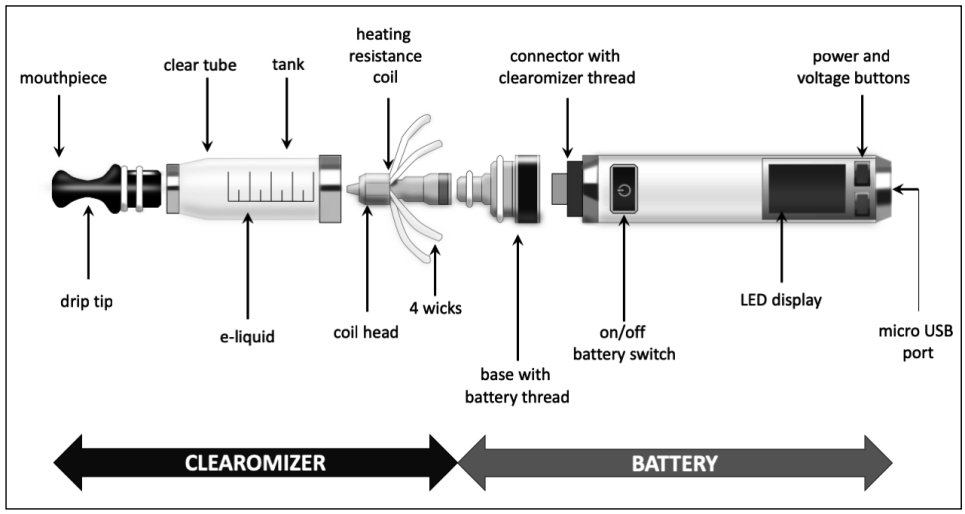

Figure 2. The construction of E-cigarette

Table 1. The most frequent constituents of liquid and heated liquid of e-cigarettes

LIQUID	AEROSOL
Glycerol	Glycerol
Propylene glycol	Propylene glycol
Ethylene glycol	Acrolein
Diethylene glycol	Nicotine
Nicotine	Acetaldehyde
Ethanol	Formaldehyde
Formaldehyde	Glyoxal and methylglyoxal
Nornicotine	Benzene
Cinnamaldehyde	Acetone
Alkaloids	Nitrosonicotine
	Nitroso and methylnitrosoamines
	Toluene
	Nickel and nickel carbonylate
	Chromium, lead, copper, cadmium, tin
	Silica

nated with ethylene glycol as a result of inappropiate manufacturing. Ethylene glycol has not been approved in any products for humans [48]. A temperature of aerosol is very often out of control and cases of airway scalding were described [49]. The highest power the biggest production of particulates, thus the resistance of coil plays a vital role in toxicity. The resistance of coil influences the manufacturing of different contents of aerosol. Moreover, the higher power and resistance the more particles are deposited in the alveolar space [44].

The lithium battery is responsible for explosions both while charging and aerosol heating [50]. Many accidents with the mouth and eye injuries were reported. Explosions and their consequences are so common that a special classification has been proposed [51].

Liquid pH plays a role in the toxicity of aerosol [52, 53]. Apart from nicotine, which is affected by pH , some liquids contain nicotyrine that inhibits nicotine metabolism and increases nicotine toxicity [54, 55]. All ingredients in e-cigarettes contain nicotine, propylene glycol or vegetable glycerine and flavors. Nicotine concentrations in liquids range from 15 to 25 mg/ml but in some cases exceed 25 mg/ml. The nicotine contents in liquids is not repeatable and evidence of quality assurance is usually absent. A conventional cigarette delivers only about 2 mg of nicotine, which is one thirty of nicotine LD50 value [56]. Thus, an ingestion of the liquid can be fatal, especially for children [57]. The total calls for house single unintended exposures in the US exceed 1 milion per year [58].

JUUL device uses protonated nicotine formulations derived from loose-leaf tobacco. It contains up to 10 times more nicotine than other e-cigarettes [43]. Consciousness of nicotine dependence among people is very low. Two thirds of young Americans do not know that nicotine is present in all JUUL products [43].

Apart from variable nicotine contents, also other components have been found by many investigators as differering from what was indicated on a label. No manufacturer inform about the presence of metals, arsenic and other toxic agents in liquids.

Although glycerine and propylene glycol have been regarded by the FDA as safe, they form toxic agents while heated [59]. Aldehydes produced in a heating process are responsible

for airway irritation, symptoms and a decrease of FEV_1. Cinnamaldehyde has been shown as a mutagenic agent [60, 61]. Moreover, aldehydes are also very strong carcinogens. They are detected in a variety of e-liquids in concentrations of 10–40 mg/ml — enough to be of toxic relevance when inhaling [62].

Flavoring components, especially cinnamon and diacetyl (a buttery flavoring) preferred by many adolescents, produce airway discomfort. In the past, such flavoring agents were reported as a cause of bronchiolitis obliterans [63].

Also, a puffing behavior influences the toxicity of e-cigarettes. Flow rate probably does not impact the nicotine absorption but a time of puffing do, because a coil is heated for a longer time [64]. The e-cigarrete puff duration is longer than a puff during smoking [65].

Indoor air quality

Both e-cigarettes and HNB diminish indoor air quality. Safety of non-users in the field of general health or nicotine dependence is unacceptable and more hazardous than nicotine replacement products. E-cigarette vapors influence particulates $PM_{2.5}$ and ultrafine particles (UFP) concentrations/counts at close proximity distances indoors. The levels of $PM_{2.5}$ increased 160-fold at a distance of 0.5 m, and 103-fold at 1 m. The corresponding growths in UFP counts were 5.2, and 3.0-fold higher, respectively [66]. However, chemical quality of indoor air according to the presence of benzene, toluene or aldehydes is much better than in homes of smokers [67].

Direct and indirect influence on airway and alveolar epithelium

An *in vitro* study on airway and alveolar epithelium deliver undoubted evidence that cells exposed to e-cigarettes are strongly affected. A cellular metabolism of amino acids decreases, a cell viability is reduced, but a production of inflammatory cytokines, especially IL-8 and IL-6, and also reactive oxygen species increase as a result of exposure to both the entire liquid and flavoring compounds [68–70]. Oxidative stress develops following direct action of toxic compounds on the airways and alveolar epithelial cells [71]. Moreover, e-liquid decreases antioxidant activity [72]. Neutrophils and macrophages are probably the largest source of reactive oxygen species.

Many tested compounds cause a destruction of epithelial barrier, especially when an exposure lasts longer. One interesting experiment described an influence of e-cigarettes on epithelial antivirus defense. Exposed cells produced a decreased amount of antiviral proteins, and the load of viruses inside cells was highly increased [73].

In vitro models of e-cigarette exposure of alveolar epithelium should be treated very cautiously. Investigators have used the cell line of human adenocarcinoma that unlike natural alveolar epithelium, do not form a tight junctions in culture [74]. In adenocarcinoma cells, a dose-dependent increase of lactate dehydrogenase according to necrotic cell death was observed. Moreover, antimicrobial defense was affected by an exaggerated growth of methicillin-resistant Staphylococcus bacteria and diminished effectiveness of endogenous antibacterial peptides [75].

It is important that e-cigarette exposure on adenocarconoma cells cause cell death and decrease cell viability [71]. It is well established that these cells are highly resistant to death affecting agents. Thus, one can judge that e-liquids might be extremely toxic.

Not only epithelium, but also endothelial cells are strongly affected following e-cigarette exposure in a dose-dependent manner [76].

Animals exposure

The lungs in animals exposed during experiments to e-cigarettes are directly strongly affected.

In mice exposed to aerosol from e-cigarettes for 5 hours in each of 3 days, an increase of the concentration of several cytokines in bronchoalveolar lavage was observed [77]. Mice developed oxidative stress with a significant reduction of glutathione. Another group of investigators confirmed oxidative stress with a different parameter [78].

Interesting data were showed by authors dealing with experimental models of lung emphysema. Mice exposed to a nebulization machine developed histological pictures of emphysema, an increased mucin production, airway resistance and airway inflammation [79].

Also, in mice exposed separately to aerosol inspired by nose, BAL content of inflammatory cytokine associated with emphysema or interstitial lung diseases was recorded [71, 75].

Undoubtedly, mice exposed to e-cigarettes are more succeptible to infections. Destroyed defense mechanisms leading to increased bacterial colonization including *Streptococcus pneumoniae* and MRSA strains in the airways seem to be especially harmful. Both innate and adoptive

defense mechanisms, local and systemic, are affected [75, 80].

Murine exposure just after a birth impairs their development [81]. This observation corresponds with many evidences of an influence of nicotine-induced neonatal impairment in humans. Although no human data on pregnant women are available, these suggestions force to act with due caution as far as recommendations for alternative method of smoking in pregnancy are concerned [82].

Lung toxicity in humans

There is no data from studies lasting longer than one year on effects of exposure to e-cigarettes or HNB. A cross-sectional study including 45 thousand of adolescents reported coughing and sputum production, both in former or dual smokers and never smokers [83]. In comparison to never smokers, current e-cigarettes users developed more asthma symptoms, wheezing and full bronchitic symptoms [84]. A short exposure *ad libitum* in former smokers produced an increase of airway resistance and a decrease of exhaled nitric oxide, which suggests a growth of oxidative stress [85]).

Considering particular agents of e-liquid, we cannot cleary point to one component responsible for deleterious effect in the lungs. A recent study with the use of both murine and human epithelial cells exposed to nicotine alone, nicotine-containing and nicotine-free condensate has revealed that even nicotine alone causes disruption of lung epithelial barrier, lung inflammation and diminished cell proliferation. A pro-inflammatory effects of e-cigarette vapor condensate also depend on induction of apoptosis and necrosis of human alveolar macrophages [86]. Disrupted function of these cells leads to succeptibility to infection and probably cancerogenesis as well. An experiment with wholly nebulized nicotine, acrolein, propylene glycol and glycerol has produced lung inflammation. The effect of acute exposure to these aerolized agents lasts shorter than changes induced by combustible tobacco smoke. Moreover, lung inflammation develops due to defective local and systemic immunological reactions to bacteria and viruses in exposure to e-cigarettes.

Cardiovascular effects of e-cigarettes

E-cigarettes use and smoking have been responsible for many cardiovascular changes. Both have resulted in defects of heart development and malformation and cardiac dysfunction following a decrease of expression of cardiac transcription factors [76].

Similarly to smoke, e-cigarettes have elevated nicotine-depending blood presure and heart rate in acute observational or experimental studies [87]. Some authors have postulated activation of sympathetic central outflow as a part of „splenocardiac axis" [72]. However, the influence of these cardiac parameters is weaker than acute smoke exposure [87]. In one study, cigarette smoke increased arterial stiffeness but e-cigarette did not [88]. Thus, acute effect of a e-cigarette use seems to be less harmful than cigarette smoking, but effects of a long-lasting exposure have never been described. In a limited number of epidemiologic studies, no risk of myocardial infarction was observed [89].

Are e-cigarettes really less toxic?

E-cigarettes are commonly regarded as less toxic than smoking. Acute experiments on cell cultures in both whole body murine and in humans have suggested that lung and cardiovascular toxicity in e-cigarette exposed subjects is less harmful. Cold e-liquid contains less carcinogens and cardiovascular toxic agents than cigarette smoke. However, heated liquid is a source of potential strong carcinogens, including benzene [90–92]. The heating of liquid leads to formation of a wide range of degradation products, including carcinogens. Benzene formation was detected in all devices except JUUl [90]. Exposure to this agent exceeded 100 mcg/m^3 and is not a negligible risk factor of carcinogenesis, though is lower than produced by combustible tobacco cigarettes. Heated coils and wicks create metals and silica fumes containing toxic and carcinogenic products that may be responsible for neoplasms development, inflammation and silicosis.

In opposition to commonly accepted view about minimal toxicity, some authors observed that bone-derived mesenchymal stem cells exhibit overproduction of reactive oxygen species on higher level than cells exposed to cigarette smoke [93]. Moreover, e-cigarette changes morphology, cell-cell communication and mesenchymal cells proliferation more strongly than a traditional cigarette.

E-cigarettes influence nicotine yield and increase a plasma nicotine concentration. One study suggests that 10 puffs of e-cigarette gives higher nicotine plasma concentration than one tobacco cigarette [94]. It is well established that

a regular use of high doses of an addictive substance leads to greater dependence.

In adolescents, nicotine dependence starts from the use of e-cigarettes. Most of young people become dual users in a short time or even change their likings to smoking [95, 96]. Nicotine abstinence symptoms are well described and consist of anxiety, depression, concentration difficulties, decreased heart rate with diminished general capacity to exercise, irritability and insomnia, weight gain.

Importantly, women of childbearing age start to use e-cigarettes, because they are convinced that they do no harm. Nicotine crosses the placenta and actively influences neonates development [97]. It is well known that children of women smoking during pregnancy or passively exposed to smoking are characterized by cognitive impairment, anxiety, irritability and some other somatic symptoms. Nicotine acts on acetylocholine receptors detectable on very early stages of neonatal development and are situated not only in central nervous system but in a whole body [97]. This may explain an increased risk of some future disorders such as type II diabetes, hypertension, obesity and chronic airway diseases.

Acute poisoning and accidental events

E-liquid poisoning has been reported many times. The routes of poisoning comprise not only the mouth but also skin and eyes. Poison centers have noted thousands of cases mostly among children [98]. Liquid in suicide attempts has been used intravenously and orally.

The FDA have collected reports of cases of adverse events probably related to e-cigarettes use, including burns of the airways and faces from device explosions, severe pneumonia, liquid pneumonia, eosinophilic pneumonitis, heart failure, ulcerative colitis, chronic neutrophilia, ischemic stroke [99–102]. On the other hand, switching from smoking to e-cigarettes use improves asthmatic symptoms, hemoglobin oxygenation and blood saturation, coughing and sputum production.

Is it time recommendation?

The question to what extent e-cigarettes might be useful for quitting smoking remains open. Many authors believe that e-cigarettes effectively replace smoking, especially in COPD patients [103]. However, observation time in many studies encompassed from 3 to 12 months. Some investigators have found no effect on long-term cessation of smoking [104].

National experts point to a lack of results of long-term epidemiological studies. Analyses according to EBM criteria are troublesome because there have been showed only few RCT studies in rather small populations.

On the other hand, the use of e-cigarettes and HNB still rise sharply. The consciousness of many disadvantages, including dependence is very low. Many young people start to use these products as never smokers. In a short time they become dual or polyusers.

It is true that final decisions should be delayed, but in many countries national experts groups published recommendations based on available data. The FDA has delayed a comprehensive plan for tobacco and nicotine regulation until 2022. In Europe, recommendations described cautious suggestions, especially when comparing different products. The British Department of Health & Social Care pronounces: „heat-not-burn products still pose a risk to users... experts were unable to precisely quantify the risk from heat-not-burn products compared with conventional cigarettes because limited data is available".

Opinions have changed lately from explicitly negative to more cautious. Yet, in 2015, e-cigarettes were regarded as a Trojan horse that would slow the process of smoking denormalization, reducing the number of people trying to quit, and seducing young smokers. Changes have been observed from „guilty until proven innocent" to „could be beneficial for adult smokers seeking to quit" [105].

However, countries differ according to demography, number of smoking people, especially adolescents and even a smoking manner. In Eastern Europe, the custom of offering one another cigarettes is very popular. Formulation of HNB practically excluded this behavior and seems to be a way to limit smoking . The number of smoking women and the number of dual or polyusers influence non only the effectiveness, but also foreseen ways of smoking cessation. Both nicotine dependence and withdrawal symptoms varied as a function of gender.

E-cigarettes and HNB products are only one of many ways to limit smoking. Whilst e-cigarettes and HNB have been characterized as being less harmful than combustible tobacco, only a minority of current smokers, around 15%, are going to use these devices [106]. Smokers principally explain it in terms of pleasure they derive from smoking [106]. In some recent guidance for

primary care, neither e-cigarettes nor HNB exists [107]. It seems, however, that actual knowledge allows physicians to take into account both methods individually recommended and applied in smokers. These modern proposals ought to be an additional way of smoking cessation in people, in whom traditional methods occurred ineffective. Switching cannot finish the process of quitting smoking, but should be only one of the stages of eliminating nicotine dependence. It seems that in the Polish population, HNB systems are more effective in smoking cessation. According to a report of an independent institute of opinion polls (CBOS), in the group of 1000 adults using e-cigarettes or HNB that have been trying to stop smoking, half of HNB users achieved the purpose while among e-cigarette users only one quarter succeeded [108]. On the other hand, in randomly assigned adults in the UK, e-cigarettes occurred more effective at smoking cessation than nicotine -replacement therapy, when both products were accompanied by behavioral support [109].

However, the most important question that might be considered in individuals is a balance between expected success of antinicotine treatment and disadvantages from the management. Prolonged application of e-cigarettes associated with a significant exposure to many harmful substances, especially non standardized contents of flavoring agents is unacceptable. Many opinion leaders postulate that national health care decision-making institutions should simply ban the sale of flavored nicotine products for use in e-cigarettes [110]. Physicians ought to remember that both smoking and alternative methods, including e-cigarettes or HNB use are disadvantageous to human health.

Conflict of interest

The authors declare no conflict of interest.

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