ELECTRONIC CIGARETTE – A WAY OF SMOKING CESSATION?

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ELECTRONIC CIGARETTE – A WAY OF SMOKING CESSATION? (Abstract): Specialists have the ethical obligation to promote smoking cessation using evidence-based therapeutic strategies. In the context of the growing popularity of the electronic cigarettes (ECs), the smokers asking us about it and we must be ready to provide expert advice. With the evidence available to date we must be cautious in recommending of the smokers to use ECs for smoking cessation because these have not proven superiority over drugs used for smoking cessation approved by the Food and Drug Administration (FDA), ECs are not FDA approved, short-term safety data shows that they cause airway reactivity and health risk of exposure to ECs in the long term is unknown. Before the ECs to occupy a place in the standard clinical approaches for the treatment of tobacco addiction longer needed more data about their safety clinical and regulatory of their use. Keywords: ELECTRONIC CIGARETTE, SMOKING CESSATION, EXPERT ADVICE.

Complete tobacco cessation is the best outcome for smokers. Electronic cigarettes (ECs) are the newest and most promising products for Tobacco Harm Reduction (THR) (1). ECs are electrically-devices: a lithium battery, attached to a heating element (atomizer) that vaporizes a humectant (propylene glycol, glycerol, distilled water, vegetable glycerin and/or polyethylene glycol), flavorings and liquid nicotine. Consumers (namely "vapors") may choose from several nicotine strengths, non-nicotine liquids, and a more than 7500 unique flavors of e-juice were available in January 2014 (2); this selection is a characteristic feature of ECs from any other THR products. Since they appeared in 2003, there has been constant development of more efficient and appealing ECs (2).

E-cigarettes are attractive because they provide behavioral aspects of smoking (hand-to-mouth movement, vapor that simulates tobacco smoke, flavorings that simulate cigarette taste), address to the sensory stimulation (3), psychopharmacologic (i.e., nicotine) (4) and social aspects. A range of reasons are reported for using ECs, mainly to quit or reduce smoking, to use a product
apparently healthier than tobacco, to overcome smoking restrictions, and to reduce costs related to tobacco dependence (5). All of this explains why ECs is believe to be effective in reducing tobacco smoking (6, 7) and are efficient as long-term substitutes of traditional cigarettes (3).

The use of ECs is apparently booming. It is estimated that in 2014 there were 466 brands (2). Sales are forecasted to increase by a factor of 17 by 2030 (8). Data from the United States, United Kingdom, Canada and Australia suggest that more than three-quarters of current and former smokers consider ECs less harmful than traditional tobacco. In the same study ECs use is higher among non-daily smokers and heavier smokers than among daily-smokers and smokers of fewer cigarettes (9). The number of nonsmoking youth that use ECs is rising and associated with increased intentions to smoke cigarettes (10). Adolescent ECs use it seems to be related much more with adolescent sensation seeking (11), rather to tobacco reduction or cessation behavior. It should be emphasized that this increase in ECs use has emerged despite the concerns raised by public health authorities about the safety and appropriateness of using them as alternatives to smoking (12, 13).

We can divide the studies targeted on safety/risk profile of ECs use into chemical, toxicological and clinical studies (14).

Clinical studies are the most informative, but the relatively recent entry of ECs into the market and the lengthy lag time for onset of many diseases of interest (i.e. cancer), conclusive evidence about the association of ECs use with such diseases will not be available for years or ever decades. Accordingly, most research is now focused on in vitro effects, with clinical studies limited into evaluation of short-term use or pathophysiological mechanisms of smoking-related diseases (14, 15, 16). At present, ECs are highly variable (differing design, materials, utilization, combustion voltage, and liquid cartridge concentration), because the manufacturing and distribution of these products, and also cartridge manufacturing and production is unregulated. This is another barrier to effectively studying the potential adverse and beneficial effects of ECs (17) and adding to the complexity of trying to counsel patients regarding their safety (16).

Chemical studies have two mainly problems: one is fails to address unknown, potentially toxic contaminants because usually focused on the known specific chemicals (investigated concentrations of several substances known to be toxic/carcinogenic in conventional cigarette) (18), and the other one arise from unknown effects when these substances are heated and inhaled, although these chemicals in flavors are approved for use in the food industry (14, 18). Thus makes difficult to appreciate in vivo effects of such substances. Therefore, we would be cautious in conclusions, because this kind of studies does not offered any objective information about effects of use of these substances (14). Many studies found that the product labels did not show the concentrations of solvents and flavorings (18). Much more, some studies showed that nicotine-free products were found to contain nicotine, sometimes in high concentrations (20, 21). In a recent study (22), cancers causing agents, formaldehyde and other toxicants like acrolein have been found into some ECs brands to
be as high as in the smoke produced by some cigarettes.

At present, there are only few toxicological studies, mostly on established cell lines and approach of cytotoxic effects has its deficiency. Patterns of ECs toxicity may fluctuate due to design features in the device, type and source of ingredients, and the manufacturing (including quality control measures) (19). Again, we cannot directly apply the results in vivo situation (14, 19), because a range of results is to be expected from different or the same cell lines and exists the risk of over or under estimating the toxic effects interpretation (23, 24, 25, 26). For example, in a recent study (26), it was found that at least four of their samples were not refills but concentrated flavors. It must be note that, the levels of cinnamaldehyde found to be cytotoxic were about 400 times lower than those currently approved for use (27). Another study of the ECs use cytotoxicity on embryonic and adult cells showed a decreased cellular survival due to the flavoring agents (23), so that maybe these flavors, not the nicotine, are the potentially harmful ingredients in e-juice. It should be done studies that comparing the potential cytotoxicity effects of ECs vapor with those resulting from the exposure of tobacco smoke should be mandatory, but unfortunately standards for vapor production and exposure protocols have not been clearly defined (14).

Data from clinical trial have found no significant differences in adverse events between ECs use and nicotine patches (6). Supporting this, other clinical studies have announced clinically minor adverse events with ECs use (mouth irritation, cough, and nausea) (28) or lower rates of adverse events than tobacco use (7). On the other hand, the Food and Drug Administration (FDA) has received reports related to the ECs use associated of both minor adverse events (headache, chest pain, nausea, cough) and major adverse events (hospitalizations for pneumonia, congestive heart failure, seizure, rapid heart rate, and burns related to routine use) (29). It must be note that, the longest duration of a clinical trial has been 24 months (30). Accordingly, these clinical studies evaluated the adverse effects of short-term EC use. Despite on evidences from these clinical trials of harmful effects of vamping (cardiovascular and respiratory functional outcomes), these are considered milder compared with smoking traditional cigarettes. It is required data from longer-term clinical studies before any clearly conclusions are made because it is difficult to assess the prognostic implications from few and short existing studies (14, 19).

Regarding chemical, toxicological and clinical studies, a recent review about ECs use health effects (18) appreciated that many studies found harmful substances: fine/ultrafine particles, cytotoxicity, metals, carcinogenic tobacco-specific nitrosamines and carbonyls, some in most samples, others in few, some in high concentration, as high as in conventional cigarettes or higher, but mostly slow or trace levels. In November 2014, the FDA reported that has detected levels of carcinogens and toxins, such as diethylene glycol (a harmful ingredient found in antifreeze) in laboratory analyses of 18 flavors and different cartridge types of ECs (31).

**CONCLUSIONS**

At present, on the base of studies per-
formed until now (many methodological problems, few and small studies, inconsistencies and contradictions in results, lack of long-term results), no definite conclusions can be established on the safety of ECs use (16, 18, 19).

It must be note that ECs use can also have adverse health effects on non-users (16). During pregnancy due to the perception that ECs are safer than traditional tobacco, may increase their use (32). A toxicologically study revealed the cytotoxic effects associated with ECs flavoring agents on embryonic cells and this could leading to embryonic loss or developmental defects (23). The risks associated with embryonic exposure to the chemical constituents in ECs in not completely understood. E-cigarettes may be a potential source of third hand exposure to nicotine (33). As ECs use has proliferated, the number of calls to poison centers involving unintentional exposure to ECs and e-juice, ingestion, inhalation, or skin absorption by young children, has markedly increased (34). Importantly, the lethal dose of nicotine to a previously unexposed person is around 0.5 to 1 g (35), and bottles of nicotine solution can be obtained via Internet (home mixing) (16). Some lithium batteries are poorly designed (low-quality materials, manufacturing defects) and improper use can causes fires or explosions (in house, in car, skin burns) (36).

ECs are nicotine-delivery products. As a consequence, the ECs users will always risk associated with nicotine use – the potential disease and related side effects (increased blood pressure, heart rate, micro vascular injury and dependence) (17). All medically approved treatments for smoking, have concentrated on total abstinence from nicotine (37). It must be note that, almost all the health risks come from various substances (tar, chemicals) found in the smoke, not from nicotine (38). Nicotine is considered as harmless by some health professionals, but others do not agree this point of view (39). The existing evidence shows that ECs aerosol is not just “water vapour” as is often claimed in the marketing for these products (15). Much more, ECs use represented serious threats to adolescents (10, 11) and fetuses (23). Additionally, it increases exposure of non-smokers to nicotine and a number of toxicants (15, 16, 33, 35).

Despite the fact that direct claims about cessation efficacy are prohibited by law, the ECs manufacturers make indirect claims about cessation, through product user testimonials (16). For many years ECs have been used as a healthier alternative to smoking or as an aid to smoking cessation (40, 41, 42, 43). The only existing randomized smoking cessation study has showed that ECs were not significantly more effective than nicotine patch therapy (6). Some prospective studies were very promising about ECs' effect as a smoking or as an aid to cut down or quit (7, 44) and a recent ‘real-life’ study showed that ECs increased cessation rates more than no aid/nicotine replacement treatment (45). A meta-analysis found that ECs users were significantly less likely than non-users to have cessation smoking (46) and a study in cancer patients showed that EC-users were twice as likely to be smoking at the time of follow-up as non-users (47, 48).

Specialists have the ethical obligation to promote smoking cessation using evidence-based therapeutic strategies. In the context of the growing popularity of the ECs, the
smokers asking us about it and we must be ready to provide expert advice. With the evidence available to date we must be cautious in recommending of the smokers to use ECs for smoking cessation because these have not proven superiority over drugs used for smoking cessation approved by the FDA, ECs are not FDA approved, short-term safety data shows that they cause airway reactivity and health risk of exposure to e-cigarettes in the long term is unknown. Before the ECs to occupy a place in the standard clinical approaches for the treatment of tobacco addiction longer needed more data about their safety clinical and regulatory of their use.

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