available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Collaborative Review – Bladder Cancer

Editorial by XXX on pp. x–y of this issue

E-cigarettes and Urologic Health: A Collaborative Review of Toxicology, Epidemiology, and Potential Risks

Liam Bourke[a,*], *Linda Bauld*[b], *Christopher Bullen*[c], *Marcus Cumberbatch*[d], *Edward Giovannucci*[e], *Farhad Islami*[f], *Hayden McRobbie*[g], *Debra T. Silverman*[h], *James W.F. Catto*[d]

[a] *Faculty of Health and Wellbeing, Sheffield Hallam University, Sheffield, UK;* [b] *Institute for Social Marketing and UK Centre for Tobacco and Alcohol Studies, University of Stirling, Stirling, UK;* [c] *National Institute for Health Innovation, University of Auckland, Auckland, New Zealand;* [d] *Academic Urology Unit, Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK;* [e] *Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA;* [f] *Surveillance and Health Services Research, American Cancer Society, Atlanta, GA, USA;* [g] *Wolfson Institute of Preventative Medicine and UK Centre for Tobacco and Alcohol Studies, Queen Mary University of London, London, UK;* [h] *Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA*

Article info

Article history:
Accepted December 21, 2016

Associate Editor:
Stephen Boorjian

Keywords:
Electronic cigarettes
Smoking cessation
Toxicology
Urologic health

Abstract

Context: Use of electronic cigarettes (ECs) is on the rise in most high-income countries. Smoking conventional cigarettes is a known risk factor for urologic malignancy incidence, progression, and mortality, as well as for other urologic health indicators. The potential impact of EC use on urologic health is therefore of clinical interest to the urology community.
Objective: To review the available data on current EC use, including potential benefits in urologic patients, potential issues linked to toxicology of EC constituents, and how this might translate into urologic health risks.
Evidence acquisition: A Medline search was carried out in August 2016 for studies reporting urologic health outcomes and EC use. Snowballing techniques were also used to identify relevant studies from recent systematic reviews. A narrative synthesis of data around EC health outcomes, toxicology, and potential use in smoking cessation and health policy was carried out.
Evidence synthesis: We found no studies to date that have been specifically designed to prospectively assess urologic health risks, even in an observational setting. Generating such data would be an important contribution to the debate on the role of ECs in public health and clinical practice. There is evidence from a recent Cochrane review of RCTs that ECs can support smoking cessation. There are emerging data indicating that potentially harmful components of ECs such as tobacco-specific nitrosamines, polyaromatic hydrocarbons, and heavy metals could be linked to possible urologic health risks.
Conclusions: ECs might be a useful tool to encourage cessation of conventional cigarette smoking. However, data collection around the specific impact of ECs on urologic health is needed to clarify the possible patient benefits, outcomes, and adverse events.
Patient summary: While electronic cigarettes might help some people to stop smoking, their overall impact on urologic health is not clear.

* Corresponding author. Faculty of Health and Wellbeing, Sheffield Hallam University, Collegiate Crescent, Sheffield S10 2BP, UK. Tel. +44 114 2255396.
E-mail address: l.bourke@shu.ac.uk (L. Bourke).

http://dx.doi.org/10.1016/j.eururo.2016.12.022
0302-2838/

1. Introduction

Tobacco smoking is an established cause of bladder and kidney cancers (50% and 20% of incident cases, respectively [1]). For people who smoke, there are clear benefits of quitting. For people who do not smoke, or would never have started smoking in the absence of electronic cigarettes (ECs), there are potential risks. Thus, it is important for urologists and urologic health researchers to understand the possible implications of EC use in urology patients [2].

1.1. What are ECs?

ECs are battery-powered devices that work by heating a liquid (*e-liquid*) to create an aerosol that is then inhaled. The aerosol produced is more commonly referred to as *vapour*, and the use of the device as *vaping*. Some are designed to resemble traditional cigarettes (*cigalikes* or first-generation products), whereas newer-generation products (tank systems) are modular and can be personalised. The cigalike devices are closed systems and are generally not refillable. They may be made for single use (ie, disposable) or they can have a rechargeable battery and replaceable cartridges that contain the heating coil (or atomiser) and liquid. The newer-generation products are generally greater in size and consist of a high-capacity lithium battery, sometimes with variable power, an atomiser, and a tank that the user fills with liquid. The atomiser is usually manually activated, which gives greater control over vapour production than the automated systems. Most people start out using a cigalike device, but regular vapers generally use tank-system ECs [3].

There are three main components of the e-liquid: propylene glycol or/and glycerol; nicotine; and flavouring. The propylene glycol/glycerol mix is important for user satisfaction (eg, a high propylene glycol content gives a greater throat hit), but may also be important for nicotine delivery [4]. Nicotine concentrations vary from 0 to 36 mg/ml, with 18 mg/ml being the most commonly used [5,6]. However the European Tobacco Products Directive, which came into effect on May 20, 2016, now limits the concentration to a maximum of 20 mg/ml. The directive also restricts the volume of bottles of e-liquid to 10 ml and the volume of EC tanks to 2 ml, and contains a number of other measures, including restrictions on advertising and promotions, and packaging and labelling requirements. EC liquid (e-liquid) is available in numerous flavours, which are important for user satisfaction. In Great Britain, the most commonly used flavour by current vapers is tobacco, followed by fruit and mint/menthol flavours [3]. The flavours used are considered safe for oral ingestion, but the effects of heating these and then inhaling them are unknown. Some flavours appear to be more cytotoxic than others (eg, strawberry [7] and cinnamon [8]) and associated with higher risk of respiratory disease (eg, diacetyl [9], which gives a buttery flavour).

Heating nicotine-containing e-liquid produces nicotine-containing vapour; however, the association between the concentration of nicotine in the e-liquid and in vapour is inconsistent. Other factors such as heating of the liquid, voltage and amperage resistance, and how the user inhales on the EC also have a role to play. ECs also do not deliver as much nicotine on a puff-by-puff basis as standard cigarettes [10]. Therefore, vapers typically take longer puffs than with standard cigarettes (eg, a mean of 2.4 s for conventional cigarettes vs 4.3 s for ECs) [11].

1.2. Epidemiology/demographics around EC use

Since being introduced, the prevalence of EC use has seen a relatively rapid increase in many high-income countries from which national longitudinal data are available, notably North American and European countries. For example, the prevalence of ever-use among individuals aged ≥15 yr in 27 states of the EU increased from 7.2% in 2012 to 11.9% in 2014 (Table 1) [12]. On average, 15.3% of ever EC users became current users in 2014. The greatest increases in the EU occurred in Malta (5.5% increase), Ireland (5.1%), Sweden (4.5%), and France (4.3%). In that survey, the lowest prevalence in 2014 was reported from Portugal (5.7%), whereas the prevalence was ≥10% in 15 countries, with the

Table 1 – Selected representative prevalence data for electronic cigarette use

Study and setting	Age, no. of participants	Prevalence		
		E-cigarette use	Overall, %	Never tobacco smokers, %
Filippidis et al [12];*	≥15 yr	Ever use, 2012	7.2	
EU (27 countries), 2012–2014	2012: 26 751	Ever use, 2014	11.9	
	2014: 26 792	Transition of ever to current users	15.3 (F 14.2; M 17.7)	
Eastwood et al [14];	11–18 yr	<monthly, 2013	3.7	0.6
Great Britain, 2013–2014	2013: 2062	Monthly or more, 2013	0.9[ʃ]	0.1
	2014: 1952	<monthly, 2014	6.5	1.5
		Monthly or more, 2014	1.7[ʃ]	0.2
Hu et al [16];	≥18 yr	Every or some days		
USA, 2013–2014	75 233	All	3.3 (F 2.8, M 4.0)	
		18–24 yr	5.5	
		25–44	4.4	
		45–64	2.8	
		≥65	0.9	
		Every/some days or rarely	6.6 (F 7.9, M 5.5)	

Please cite this article in press as: Bourke L, et al. E-cigarettes and Urologic Health: A Collaborative Review of Toxicology, Epidemiology, and Potential Risks. Eur Urol (2017), http://dx.doi.org/10.1016/j.eururo.2016.12.022