

Response to “Comment on *E-Cigarettes and Cardiovascular Risk: Beyond Science and Mysticism*”

Giuseppe Lippi, MD¹ Gianfranco Cervellin, MD² Emmanuel J. Falavolo, PhD, FFSc (RCPA)³

¹Laboratory of Clinical Chemistry and Hematology, Academic Hospital of Parma, Parma, Italy

²Emergency Department, Academic Hospital of Parma, Parma, Italy

³Department of Haematology, Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, New South Wales, Australia

Address for correspondence Giuseppe Lippi, MD, U.O. Diagnostica Ematochimica, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci, 14, 43126 Parma, Italy (e-mail: glippi@ao.pr.it; ulippi@tin.it).

Semin Thromb Hemost 2014;40:519–520.

The letter referring to our article¹ on the effect of electronic cigarettes (e-cigarette) on human health by Farsalinos et al is both interesting and of value.² The authors basically argue against two issues that we discussed in our previous narrative review, that is, the cardiovascular risk attributable to nicotine and the effective toxicity of liquid nicotine present in e-cigarettes. Besides the fact that the biological evidence available on e-cigarette smoking remains to date rather limited, some aspects need to be highlighted.

As regard the effect of nicotine on cardiovascular risk, two of the articles used by Farsalinos et al² in support of a lack of plausible connection are fairly dated, being respectively published in 1996 and 1998.^{3,4} A more recent meta-analysis on smokeless tobacco and risk of myocardial infarction and stroke published by Boffetta and Straif in 2009 concluded that the relative risk for ever use of smokeless tobacco products was 1.13 (95% confidence interval [95% CI], 1.06–1.21) for myocardial infarction and 1.40 (95% CI, 1.28–1.54) for fatal stroke.⁵ Also, at variance with what is stated in their correspondence,² data about the cardiovascular potential of nicotine are contradictory. Besides episodic case reports of patients developing acute myocardial infarction while using nicotine patches,^{6,7} additional population studies described a high rate of cardiovascular complications in patients using these sticking plasters.^{8,9} Even from a biological perspective, the statement that nicotine has minimal effects in initiating and propagating atherosclerosis is questionable, as recent studies have shown that this compound binds to nicotinic acetylcholine receptors and accelerates the atherogenic process.¹⁰ Therefore, although we would agree

that nicotine replacement therapies (NRTs) present a lesser hazard than continuing to smoke because there exists unquestionable data supporting that use of NRTs carries much lower risks than traditional tobacco smoking, our leading concern relates to the potential health effects of these devices on adolescent and nonsmokers.¹¹ After decades of effective work to reduce cigarette smoking, the widespread availability of e-cigarettes raises the question of whether these devices are reintroducing a form of smoking to many adolescents, who may respond positively to advertising claims that e-cigarettes are safe.¹² Once accustomed to e-cigarettes use, they may then be subjected to adverse side effects of these devices or, even worse, prompted to shift to traditional tobacco smoking.

We also dispute the statement by the authors² that we have exaggerated the toxicity of liquid nicotine present in e-cigarettes. The number of case reports regarding toxicity of nicotine-containing solutions is constantly growing in the scientific literature.^{13–16} Moreover, a recent study investigating the nicotine concentration of several nicotine-containing solutions has concluded that these mixtures could be toxic or lethal if taken other than as directed, even at potentially lower levels of nicotine than expected using manufacturer specifications.^{17,18}

In conclusion, although we respect the points of view raised by Farsalinos et al,² at this point in time it seems premature and potentially hazardous to conclude that e-cigarette use and/or nicotine intake are unlikely to significantly elevate harm. Major caution should be observed until the outcome of randomized, perspective studies on e-cigarette use become available.

published online
May 6, 2014

Issue Theme An Update on the Thrombotic Microangiopathies Hemolytic Uremic Syndrome (HUS) and Thrombotic Thrombocytopenic Purpura (TTP); Guest Editors, Magdalena Riedl, MD, Dorothea Orth-Höller, MD, and Reinhard Würzner, MD, PhD.

Copyright © 2014 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
Tel: +1(212) 584-4662.

DOI <http://dx.doi.org/10.1055/s-0034-1375703>.
ISSN 0094-6176.

Conflict of Interest

One of the authors (E.J.F.) is the Editor in Chief of this journal. There are no other conflicts of interest. None of the authors have received any funding support from manufacturers of tobacco or “smokeless-tobacco” or associated products.

References

- 1 Lippi G, Favaloro EJ, Meschi T, Mattiuzzi C, Borghi L, Cervellin G. E-cigarettes and cardiovascular risk: beyond science and mysticism. *Semin Thromb Hemost* 2014;40:60–65
- 2 Farsalinos KE, Romagna G, Le Houezec J. Comment on *E-Cigarettes and Cardiovascular Risk: Beyond Science and Mysticism*. *Semin Thromb Hemost* 2014;40(4):517–518
- 3 Waldum HL, Nilsen OG, Nilsen T, et al. Long-term effects of inhaled nicotine. *Life Sci* 1996;58(16):1339–1346
- 4 Greenland S, Satterfield MH, Lanes SF. A meta-analysis to assess the incidence of adverse effects associated with the transdermal nicotine patch. *Drug Saf* 1998;18(4):297–308
- 5 Boffetta P, Straif K. Use of smokeless tobacco and risk of myocardial infarction and stroke: systematic review with meta-analysis. *BMJ* 2009;339:b3060
- 6 Ottervanger JP, Festen JM, de Vries AG, Stricker BH. Acute myocardial infarction while using the nicotine patch. *Chest* 1995;107:1765–1766
- 7 Arnaot MR. Treating heart disease. Nicotine patches may not be safe. *BMJ* 1995;310:663–664
- 8 Ottervanger JP, Wilson JH, Stricker BH. Drug-induced chest pain and myocardial infarction. Reports to a national centre and review of the literature. *Eur J Clin Pharmacol* 1997;53:105–110
- 9 Lee AH, Afessa B. The association of nicotine replacement therapy with mortality in a medical intensive care unit. *Crit Care Med* 2007;35:1517–1521
- 10 Santanam N, Thornhill BA, Lau JK, et al. Nicotinic acetylcholine receptor signaling in atherogenesis. *Atherosclerosis* 2012; 225:264–273
- 11 O'Brien SH. Contraception-related venous thromboembolism in adolescents. *Semin Thromb Hemost* 2014;40:66–71
- 12 Hsu R, Myers AE, Ribisl KM, Marteau TM. An observational study of retail availability and in-store marketing of e-cigarettes in London: potential to undermine recent tobacco control gains? *BMJ Open* 2013;3:e004085
- 13 Solarino B, Rosenbaum F, Riesselmann B, Buschmann CT, Tsokos M. Death due to ingestion of nicotine-containing solution: case report and review of the literature. *Forensic Sci Int* 2010;195: e19–e22
- 14 Cervellin G, Luci M, Bellini C, Lippi G. Bad news about an old poison. A case of nicotine poisoning due to both ingestion and injection of the content of an electronic cigarette refill. *Emerg Care J* 2013;9(2): doi: e1810.4081/ecj.2013.e18
- 15 Chen IL. FDA summary of adverse events on electronic cigarettes. *Nicotine Tob Res* 2013;15:615–616
- 16 Cantrell FL. Adverse effects of e-cigarette exposures. *J Community Health* 2013; doi: 10.1007/s10900-013-9807-5
- 17 Cameron JM, Howell DN, White JR, Andrenyak DM, Layton ME, Roll JM. Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions. *Tob Control* 2014;23:77–78
- 18 Connolly GN, Richter P, Aleguas A Jr, Pechacek TF, Stanfill SB, Alpert HR. Unintentional child poisonings through ingestion of conventional and novel tobacco products. *Pediatrics* 2010;125:896–899