Author’s response to reviews

Title: Successfull smoking cessation with e-cigarettes in smokers with a documented history of recurring relapses: case report

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Author’s response to reviews: see over
Dear Sir.

Thank you for giving us the opportunity to respond to the comments and suggestions raised by your referees and yourself.

We hope we have responded adequately to criticisms/suggestions (see below) and improved the overall quality of our manuscript. Please note that corrections are marked up in the text. We would be therefore very grateful if you would consider this re-submission for publication in the JMCR.

RESPONSE TO THE JOURNAL OF MEDICAL CASE REPORTS EDITORIAL TEAM

1) Authors should address the concerns by the reviewers.
   We have carefully addressed reviewers’ concerns.

2) Specifically include in the discussion section, the status of e-cigarettes approval in the Europe and the US. Consider including an image of e-cigarette. Also review the manuscript for language.
   As per your request, we have included in the Discussion a section addressing in detail the current regulatory status and safety of e-cigarettes. We have also included an image of e-cig (plus legend) and checked grammar and language.

3) Page 4, Line 4: Psychologist, 3 years (instead of yr) experience.
   Amended in the text.

RESPONSE TO REVIEWER 1

A few limitations must be highlighted in the text. There is a likely explanation that those who used E-cigarettes are more likely to have quit anyway without it. The more quitting attempts a smoker makes the more likely the smoker will eventually succeed in quitting. In such case reports, a question should have been asked of the cases if they took up E-cigarettes with the intention to quit or not. Do the cases believe they would not have quit if it weren’t for the E-cigarettes?

It is possible that these success stories may be due to the repeated number of quit attempts and not necessarily to the E-cigarette. However, when we contacted these patients and asked if they took up the E-cigarette with the intention to quit and if they believed that they would not have quit if it weren’t for the E-cigarettes, answers were both positive for all three patients. Of note, Patient 3 informed us that due to repeated technical problems with his E-cigarette he resumed tobacco smoking. Technical defects should be reduced by increasing manufacturing standards in order to improve device acceptability and use.

We have addressed this in the Discussion section (page 6).

Another important aspect that needs to be highlighted by the authors is the risk of E-cigarettes. New studies show that there are other harmful substances in E-cigarettes such as the anti-freeze diethylene glycol and tobacco-specific nitrosamines. In the US, the FDA has publicly requested from Americans not to smoke the E-cigarette pending further evidence about its safety. The authors should weigh in on the benefits and harms of using E-cigarettes and the risk that non-smokers might end up using it and get addicted to nicotine and being to smoke tobacco cigarettes.

A number of reports available over the internet have characterized, quite extensively, the components contained in E-cigs liquid and vapour using gas chromatography mass spectrometry (GC-MS). They demonstrate that the primary components of E-cig cartridges are propylene glycol.
In an independent study, Laugesen tested E-cig mist for over 50 priority-listed cigarette smoke toxicants and found none. This report only revealed traces (8.2 ng/g) of Tobacco-specific Nitrosamines (TSNAs) in the “high” nicotine cartridge of a Ruyan brand E-cig. However, it must be noted that this amount is equal to the quantity reported to be present in a nicotine medicinal patch.

In contrast, the US Food and Drug Administration (FDA) announced in a press conference that “a laboratory analysis of electronic cigarette samples has found that they contain carcinogens and toxic chemicals such as diethylene glycol, an ingredient used in antifreeze” (3). The actual lab report revealed that the “carcinogens” referred to in the FDA’s press conference were TSNAs, but failed to specify the quantity detected. The FDA’s report did state that the quantity of diethylene glycol (DEG) detected in the liquid in one of the 18 samples was 1% (0.01 ml), but did not point out that this is a non-toxic quantity (4). The FDA did not report finding DEG, or any other harmful chemical, in the vapour.

Recently, Cahn and Siegel have reviewed the results of 16 laboratory analyses of E-cig liquid, including the FDA’s “Final Report” (5). TSNAs were reported in two studies, but at trace levels, which are similar to those found in a nicotine patch, and, most importantly, about 500-fold to 1400-fold lower than TSNA levels measured in regular cigarettes (E-cigs containing only 0.07–0.2% of the TSNAs present in cigarettes). The presence of DEG was reported in the FDA’s report in one of the 18 cartridges, yet none of the other 15 studies found any DEG. The authors stated, “Other than TSNAs and DEG, few, if any, chemicals at levels detected in E-cigs raise serious health concerns. Although the current data is insufficient to conclude that E-cigs are safe in absolute terms and that further studies are needed to comprehensively assess their safety, these products appear to be much safer than tobacco cigarettes and comparable in toxicity to conventional nicotine replacement products” (5).

In a recent prospective proof-of-concept study, we monitored possible modifications in smoking habits of 40 smokers not willing to quit experimenting with a 7.4 mg nicotine/cartridge E-cig (6). Combined sustained smoking reduction and smoking abstinence was shown in 22/40 (55%) participants, with an overall 88% fall in cigs/day. Mouth and throat irritation, and dry cough were common, but diminished substantially by the end of the study. Participants’ perception and acceptance of the product was good.

Retailers all over the world have already sold hundreds of thousands of E-cigs, yet there is no evidence that these products have endangered anyone, and no indication that E-cigs are any more an immediate threat to public health and safety than traditional cigarettes, which are readily available to the public.

This reviewer is also concerned that the non-smokers taking up an e-cig might end up using it and get addicted to nicotine and eventually starting to smoke tobacco cigarettes. Judging from the relationship between smoking and the use of snus, in Sweden, Norway, and the U.S., snus appears to be a gateway away from smoking. We have addressed this in the Discussion section.

RESPONSE TO REVIEWER 2

The report would be strengthened if there were cotinine measurements for the period that the e-cigarettes were used as there is also considerable controversy as to whether they actually deliver nicotine in substantial amounts to the user, but the report is valuable even without that information.

This reviewer is absolutely correct. We are currently measuring nicotine in our ongoing clinical trials with E-cig.

http://clinicaltrials.gov/ct2/show/NCT01164072?term=electronic+cigarette&rank=1

The report also needs some English language editing. We have checked grammar and language, as per this reviewer’s indication.