E-cigarettes are becoming an increasingly popular alternative to conventional tobacco cigarettes among smokers worldwide. The concentration of toxicants (including many Harmful and Potentially Harmful Constituents (HPHCs)) in e-cigarettes has been found to be generally tens to thousands of times lower than in tobacco smoke; many toxicants, simply not present or at detectable levels (eg, Fig 1). As a result, e-cigarette aerosols elicited minimal biological responses in comparison to their tobacco counterparts, even at close to toxic levels (eg, Fig 2). While such reduction is expected for some chemical classes, other e-cigarette aerosols might not be as harmless. For instance, e-cigarette use in isolation does give a very good indication of the potential for the inhalation of e-cigarette aerosols. There is relatively little information available on consumer exposure to HPHCs resulting from the use of e-cigarettes compared to conventional cigarettes. In this study, the objective of this study was to compare changes in selected urine, blood and exhaled biomarkers of exposure to HPHCs among different user groups following a 5-day forced-switch from usual cigarette brand to: (i) a commercially available blu™ e-cigarette; (ii) a commercially available blu™ e-cigarette and the subject’s usual cigarette brand; or (iii) a commercially available tobacco product.

The biomarkers of exposure to the HPHCs selected included a number of cigarette smoke constituents representing classes of compounds believed to be the most significant contributors to smoking-associated disease risks as reported by the FDA.

1. Introduction

Reduced formation of toxicants in blu™ e-cigarette aerosol vs. conventional cigarette smoke...

Reducing consumption of conventional cigarettes over 5 days according to the requirements of the study resulted in a decrease in exposure to a number of HPHCs (Figures 4 and 5).

• Smoking cessation lead to a 66% to 98% reduction in excretion of the urinary biomarkers cotinine, 1-OH-cotinine, and 3-OH-cotinine among the participants in the study group (Figures 4 to 6). The reduction in urinary cotinine levels by 85% to 98% compared to baseline levels was observed in all study groups (Figures 4 to 6). The changes in cotinine concentrations in the urine were similar to the results obtained with urinary cotinine (Figures 4 to 6).

• Individual biomarker responses to the excise and exclusive use blu™ e-cigarettes were comparable to those seen in the consumption group (Figures 4 to 6). The reduction in urinary cotinine levels was observed in all study groups (Figures 4 to 6). The changes in cotinine concentrations in the urine were similar to the results obtained with urinary cotinine (Figures 4 to 6).

• Dual users smoked 52% lower conventional cigarettes compared to smoking their e-cigarette (Figure 4). Dual users smoked 20% less than their usual e-cigarette compared to smoking their usual e-cigarette (Figure 4). Dual users smoked 20% less than their usual e-cigarette compared to smoking their usual e-cigarette (Figure 4). Dual users smoked 20% less than their usual e-cigarette compared to smoking their usual e-cigarette (Figure 4). Dual users smoked 20% less than their usual e-cigarette compared to smoking their usual e-cigarette (Figure 4).

• Overall, measurable nicotine and cotinine were present in the samples from all participants. For both groups of biomarkers for HPHCs were significantly lower and many were indistinguishable, from those of subjects who had ceased to use any nicotine product (Figures 4 to 6). The excretion and concentration of all exhaled biomarkers evaluated in this study were higher in the dual use group at Day 5 compared to the cessation group (Figures 4 to 6). The excretion and concentration of all exhaled biomarkers evaluated in this study were higher in the dual use group at Day 5 compared to the cessation group (Figures 4 to 6).

2. Study Design

3. Reductions in Blood and Urine Biomarkers of HPHC Exposure from Day -1 to Day 5

% change in biomarkers of exposure after 5 days

4. Changes in Exhaled CO and NO Levels

Physiological changes associated with smoking reductions were noted in both blu™ e-cigarette nicotine (CO) and nitric oxide (NO) end points. CO exposure is often estimated from exhaled CO concentrations in exhaled breath or from CO bound to haemoglobin (Figures 4 and 5).

• All groups experienced decreases in exhaled CO at Day 5 compared to Day -1, with decreases in the cessation and exclusive e-cigarette groups of 24% to 32% and 30% to 31% in the dual use group (Figure 5). Further, there were no differences between the cessation and exclusive use group measurements on Day 5 whereas the dual use group had higher exhaled CO compared to cessation, as expected since this group still consumed conventional cigarettes.

• Smoking has been reported to decrease CO production but the mechanism remains incompletely understood. Exhaled CO is used as a noninvasive biomarker of exposure in the airways, and can be be detected in exhaled breath. In this study, no CO was observed to increase from Day -1 to Day 5 in the cessation (40%) and exclusive e-cigarette (56%), whereas the dual use group experienced a 90% reduction in exhaled CO (Figure 4).

• The findings associated with exhaled biomarkers in the cessation and exclusive e-cigarette use groups are consistent with other research findings associated with reductions in exhaled CO and increases in exhaled NO following smoking cessation (Figures 7 to 8).

5. Conclusions

The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6). The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6). The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6). The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6). The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6). The data presented here demonstrate that smokers who completely substituted conventional cigarettes with e-cigarettes for 5 days experienced reductions in exposure to a number of HPHCs as measured by urine, blood and exhaled biomarkers of exposure. Moreover, the data show that smokers who switched to e-cigarettes experienced significantly reduced HPHC exposures after partially replacing conventional with the blu™ e-cigarette product, albeit to a lesser extent. The data are consistent with the findings of other investigations which have demonstrated that e-cigarette use results in a decrease in biomarkers of tobacco exposure (Figures 4 to 6).

• The present study extends the findings of [1] (summarised in Figure 1), which showed the e-cigarette aerosol levels of HPHCs such as carbonyl compounds, tobacco-specific nitrosamines, polyalcoholic amines and other contaminants are often in the 100s of times lower than those found in the smoke of conventional tobacco cigarettes. We observed a blu™-dosed system e-cigarette produced markedly lower levels of exhaled biomarkers when used by smokers in lieu of their usual cigarette brand style for a period of 5 days.

• It has been suggested that dual use may be a public health concern because of the possibility that it exposes smokers to higher levels of aerosolized smoking-related toxicants (Figure 1). Furthermore, a recent study reported that dual use of e-cigarettes while continuing to smoke did not result in reduced exposure to known carcinogens and toxicants (Figure 1). The study presented here found a decrease in daily reduction in exhaled CO on the dual use group as an initial indication of the non-increasiveness of the measured exhaled biomarkers to other smoking biomarkers. In this study, the reduction in biomarkers of exposure to HPHCs in this group and the reduction in conventional cigarettes smoked. The impact of longer term exposure and dual use e-cigarette on biomarkers of exposure to HPHCs is still not clear.

• Whether the reductions in toxic and carcinogenic constituent exposure such as those observed here may have the potential to reduce risks for chronic, smoking-caused diseases for long-term e-cigarette users who partially or completely abandoned their use of conventional cigarettes.

• Overall, the present study shows the great potential that the blu™-dosed system e-cigarette may provide for smokers seeking an alternative to tobacco products; the role that biomarkers of exposure may play in risk assessment and comparing exposure to HPHCs across different product categories, and supports the case for regulating e-cigarettes differently from tobacco-containing products.

References