Levels of biomarkers of exposure and biological effect in smokers switched to reduced toxicant prototype cigarettes compared to smokers of conventional cigarettes and ex-smokers and never smokers

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Introduction:

Development of new tobacco products that result in the substantial reduction in exposure to harmful smoke constituents has been suggested as a possible way to reduce some of the health risks of smoking (1). We have previously shown that it is possible to substantially reduce exposure to a number of smoke toxicants, as determined using biomarkers of exposure (BoE), by switching smokers for 4 weeks to a reduced toxicant prototype (RTP) cigarette with reduced yields of specific smoke toxicants (2). However, the magnitude and duration of exposure reduction required to lead to detectable changes in risk remains unknown.

Study Design:

The study was mainly ambulatory with occasional clinical confinement, when urine and blood samples were collected for biomarker analysis (Figure 2). Study cigarettes were supplied free of charge to smokers who were allowed to smoke ad libitum throughout the study. Daily cigarette consumption was recorded throughout the study. All smokers initially smoked the cork tipped control for two weeks before switching either to the white-tipped or RTP.

Materials and Methods:

Products:

Three types of cigarettes were manufactured for this study, all with target ISO tar and nicotine yields of 7.0 and 0.7mg/cig respectively. Two versions of the conventional king size control cigarette were produced, one with cork and one with white tipping, to maintain some level of blinding after the switch. The visually different RTP was a king size cigarette of reduced circumference, incorporating treated tobacco and a tobacco substitute sheet in the blend and high activity carbon and amine-functionalised resin in the filter (Figure 1). Compared with the control, the yields of TSNAs from the RTP were 55-86% lower, aromatic amines were reduced by 33-50% and the vapour phase toxicants reduced by up to 90-95%.

Endpoints:

BoE for: Nicotine, TSNAs (NNK, NNN, NAB NAT), Aromatic Amines (4-aminobiphenyl, 3-amino biphenyl, o-toluidine, 2-amino naphthalene), vapour phase constituents (crotonaldehyde, acrolein, 1,3-butadiene, acrylonitrile) and PaHs (pyrene, fluorene, naphthalene & phenanthrene). BoBE: F2-isoprostane (8-iso-PGF2 type III & VI), sICAM-1, white blood cell, monocyte and neutrophil counts, 11-dehydroxy thromboxane B2, 8-OHdG, cis-thymidine glycol, SOD activity, Glutathione reductase activity, Catalase activity, malondialdehyde, Ascorbic acid, dehydroascorbic acid, Total antioxidant capacity, hsCRP, total cholesterol, LDL, HDL, Triglycerides, Fibrinogen, MCP-1, neutrophil elastase, LTB4 and oxLDL.

Results:

As previously reported (SRNT 2013, POS3-125), many smokers significantly increased cigarette consumption during the study. Despite this increase, reductions in toxicant BoE for the RTP group were still observed with 28-65% less TSNA BoE, 4-30% less aromatic amines BoE and 30-74% less vapour phase toxicant BoE.

Conclusions:

We have again shown that it is possible to develop Reduced Toxicant Prototype cigarettes that not only have lower smoke yields of specific toxicants but also result in significant and in some cases large reductions in the levels of corresponding BoE in smokers. This exposure reduction was maintained for 6 months. However, these maintained reductions in exposure did not result in many detectable changes in BoBE. This may be due to the utility of the BoBE used, or that the reduction was not substantial enough, or the study long enough, to demonstrate biological effect changes. Further research is required to elucidate this.

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Conflict of Interest Statement:

Funded by British American Tobacco (BAT). All authors except I Meyer are current employees of BAT. I Meyer was the Principle Investigator for the study and employed by Momentum Pharma Services, Hamburg, Germany.

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