Exposure to cigarette smoke toxicants in smokers who switch to using the glo™ tobacco heating product

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Introduction

Tobacco heating products (THPs) represent a subset of the next-generation nicotine and tobacco product category, in which tobacco is typically heated at temperatures of less than 350°C instead of burning (900°C) and has the potential to significantly reduce the majority of cigarette smoke toxicants. The use of THPs holds great potential for reducing the harm associated with tobacco use but this needs to be scientifically proven.

Objective

To examine changes in biomarkers of exposure (BoE) to cigarette smoke toxicants when smokers switch to using the novel THP, THP1.0 (commercially known as glo™) **(Figure 1)** for 5 days, compared with those seen in smokers who remain smoking combustible tobacco cigarettes.

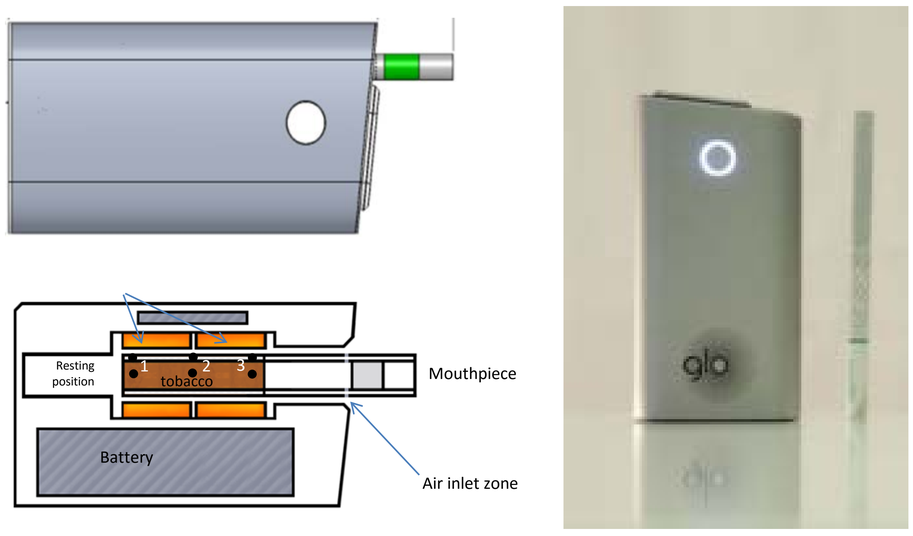

Figure 1. Schematic drawings (left) and picture (right) of THP1.0 with a tobacco consumable.[1]

Approach and Methods

We performed a two-centre, in-clinic (confinement), forced-switching, randomised controlled clinical study in Fukuoka, Japan (UMIN000024988, ISRCTN14301360). Baseline levels of BoE to selected gas and particulate phase cigarette smoke toxicants in the exhaled breath and urine of 180 smokers were compared to those seen when the smokers either remained smoking combustible cigarettes or switched to using a mentholated or non-mentholated THP1.0 for 5 days. The study was IRB approved and run in accordance with ICH-GCP. Subjects provided written informed consent prior to study participation and were deemed healthy following medical examination and clinical laboratory screening. Smoking status was verified by exhaled carbon monoxide (eCO) and urinary cotinine measurements.

Subjects were healthy male or female smokers of Japanese origin aged 23-55. Smoking status was verified by urinary cotinine and eCO at screening and admission. Healthy status was verified by vital signs, clinical laboratory evaluations, physical examination, ECG and lung function tests. Subjects typically smoked 10-30 cigarettes per day, within 6–8 mg ISO tar bands, with at least a 3-year smoking history.

Main exclusion criteria were planning to quit smoking in next 12 months, regular use of nicotine or tobacco products other than cigarettes, and non-inhalers (self-reported or observed at admission). Female subjects were excluded if a positive pregnancy test was performed at screening or admission.

All subjects smoked cigarettes for two consecutive 24-h periods, up to a limit of 120% of their self-reported usual daily consumption. All urine voided by each subject was collected over each 24-h period and the urine tested for BoE. eCO was also measured on both days.

At end of baseline period, subjects were randomised to either continued smoking or THP1.0 use groups. They remained in the clinic for a further 5 days and 24-hour urine samples were collected for BoE analysis. eCO was also measured on each day.

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Results

120 subjects completed the study in the regular cigarette, menthol cigarette, regular THP1.0 and mentholated THP1.0 groups; see **Table 1** for demographics of participants in these groups. Subjects who switched from smoking to exclusive use of either THP1.0 variant (n=30 in each group) for 5 days showed reductions in levels of exhaled carbon monoxide and a range of urinary BoEs, compared to their levels at baseline. In contrast, the continued smoking groups (regular and mentholated; n=30 in each group) showed little change in BoE levels throughout the study. Data from these groups are presented in **Figures 2** and **3**.

	Cigarette N = 30	THP1.0 N = 30	Menthol cigarette N = 30	THP1.0 menthol N = 30
Age, years				
Mean ± SD	32 ± 8.2	34 ± 10.1	33 ± 8.6	31 ± 7.7
Range	23 – 54	23 – 53	23 – 54	23 – 49
Sex, N (%)				
Male	15 (50.0%)	15 (50.0%)	14 (46.7%)	16 (53.3%)
Female	15 (50.0%)	15 (50.0%)	16 (53.3%)	14 (46.7%)
Average daily cigarette consumption				
Mean ± SD	17 ± 5.7	17 ± 4.5	15 ± 3.9	15 ± 4.3
Median	15	18	15	15
Range	10 – 30	10 – 30	10 – 20	10 – 20

Table 1. Subject demographics in the regular and mentholated cigarette and regular and mentholated THP1.0 groups at screening.

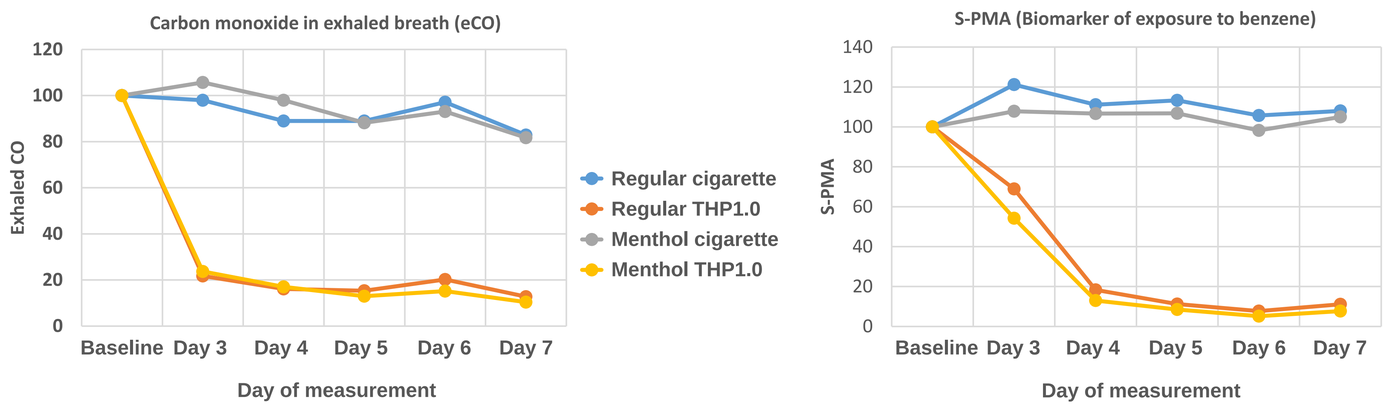

Figure 2. Mean levels (n=30 in each group) of biomarkers of exposure to carbon monoxide (eCO, left) and benzene (S-PMA, right). Baseline data were averaged from the two 24-h periods prior to randomisation.

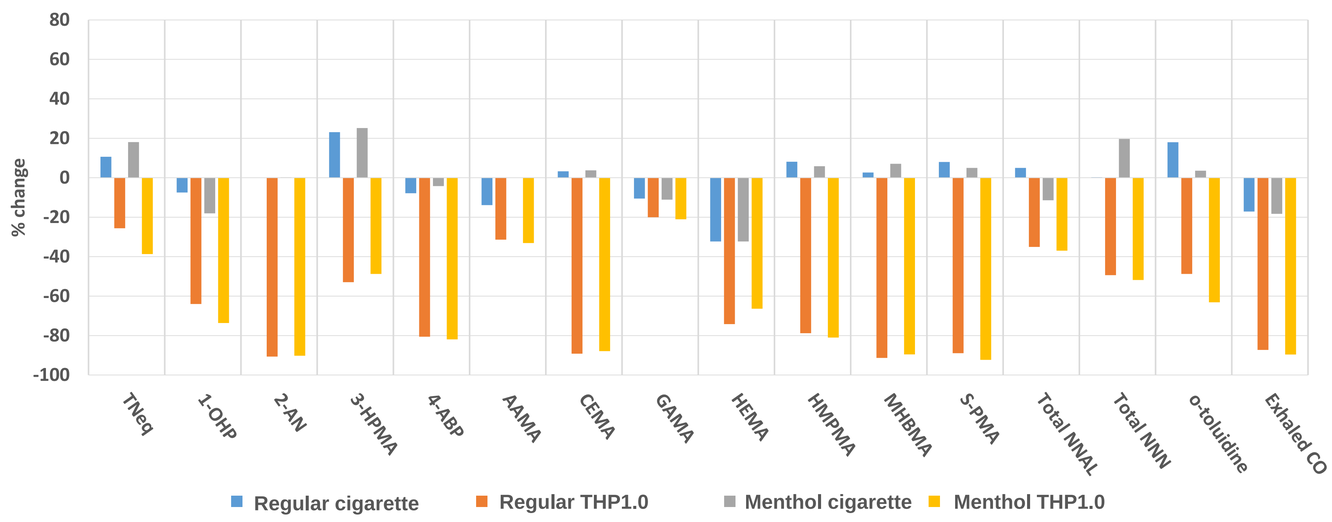

Figure 3. Percentage changes in biomarkers of exposure in subjects who either remained smoking regular or mentholated cigarettes or who switched to using either regular or mentholated THP1.0. Data were obtained by expressing BoE levels after 5 days of switching relative to those seen at baseline.

Conclusions

- In this clinical study, we observed reductions in BoE in subjects who switched to using either regular or mentholated THP1.0.
- These findings are in accordance with the lower levels of toxicants measured in the machine emissions from THP1.0.
- Future studies will examine whether these reductions in exposure are preserved for prolonged, ambulatory periods and also whether these lead to any changes in health effects indicators in smokers.

References

1. Assessment of tobacco heating product THP1.0 Part 2: Product design, operation and thermophysical characterisation. Eaton, D *et al.,* 2017. Reg Tox Pharm. (In press)