Differences in exposure to cigarette smoke constituents in healthy Caucasian and Japanese smokers

Claire Martin Leroy[1], Joerg Diekmann[2], Kohji Takada[3], and Anthony R. Tricker[1].
[1] Philip Morris Products S.A., Neuchâtel, Switzerland.[2] Philip Morris Research Laboratories GmbH, Fuggerstr. 3, D-51149 Köln; [3] Teikyo University, Tokyo, Japan.

Introduction

Differences in lung cancer rates have been observed in different ethnic groups [1] which may be due, in part, to differences in carcinogen exposure [2]. In this context, exposure to cigarette smoke constituents was compared between adult male Caucasian and Japanese smokers in clinically controlled environments in the United Kingdom and Japan, respectively. All smokers smoked the same market brand of cigarettes (6 mg ISO 'tar', 0.5 mg nicotine, 8.0 mg CO). The cigarettes in the United Kingdom had a plain cellulose acetate filter, while in Japan the cigarettes had a cellulose acetate filter containing charcoal.

Methods

Volunteer Caucasian (n=97) and Japanese (n=43) male smokers were confined to two phase I clinical units for the duration of the study. Ethics Committee approval for the studies was obtained in both countries and all subjects gave written consent.

<u>Blood samples</u> were drawn at 17:00 PM for analysis of COHb by oximetry and plasma cotinine by LC-MS/MS.

<u>Urine samples</u> were collected over 24 h for analysis of metabolites of the following mainstream cigarette smoke constituents: Nicotine (nicotine + 5 metabolites [NEq]), NNK (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronide conjugates [total NNAL]), pyrene (1-hydroxypyrene [1-HOP]), acrolein (3-hydroxypropylmercapturic acid [3-HPMA]), benzene (*S*-phenylmercapturic acid [*S*-PMA]), and 1,3-butadiene (mono-hydroxybutenylmercapturic acid [MHBMA]). All metabolites were analysed by LC-MS/MS using methods validated according to FDA criteria by the same analytical contract research organisation.

<u>Mainstream smoke chemistry</u> of both cigarettes was determined according to ISO smoking conditions [3].

Results

Male Caucasian and Japanese volunteers smoked a similar number of cigarettes per day (19.2±4.9 *vs.* 17.9±3.6; p=0.070) during the study and had a similar rating on the **F**agerström **t**est for **n**icotine **d**ependence [4] (FTND sum score: 4.64±1.97 *vs.* 4.47±1.93; p=0.632).

Differences in cigarette mainstream smoke chemistry and the concentrations of the respective biomarkers of exposure in Caucasian and Japanese volunteer smokers are summarized in Table 1. Relative differences in smoke constituent concentrations and the respective biomarkers of exposure are shown in Figure 1.

Conclusions

Reductions in gas vapour phase smoke constituents (acrolein, benzene, 1,3-butadiene) of Japanese cigarettes compared to UK cigarettes were reflected in reductions of the corresponding biomarkers of exposure.

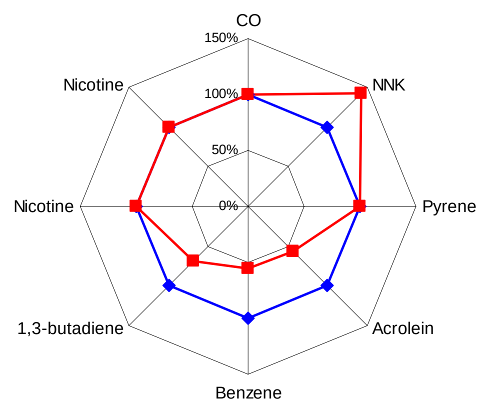
Differences in plasma cotinine concentrations and NEq excretion suggest that Japanese and Caucasians may have different smoking behaviour.

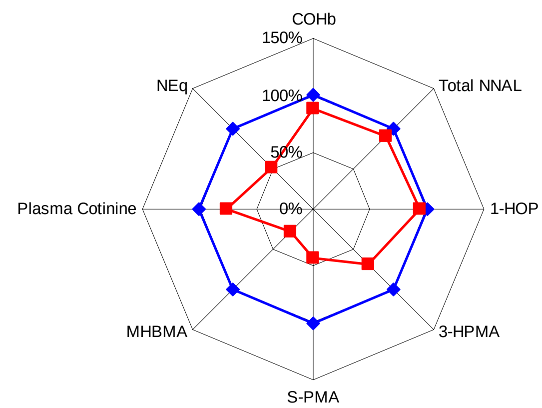
The results of this study provide additional support for the observation that charcoal filters may result in reductions in volatile gas vapour phase smoke constituents.

Table 1: Cigarette smoke chemistry and respective biomarkers of exposure in Caucasians (n=97) and Japanese (n=43)

Mainstream cigarette Smoke constituent	UK Cigarette	Japanese Cigarette	Cigarette smoke constituent biomarker	Caucasian smokers	Japanese smokers	Exposure difference
Tar (mg/cig.)	6.0	6.0	-	-	-	
Nicotine (mg/cig.)	0.5	0.5	NEq (mg/24h)	16.02±6.93	8.24±3.78	p<0.0001
			Plasma cotinine (ng/ml)	252.3±91.3	191.1±91.6	p=0.0004
CO (mg/cig.)	8.0	8.0	COHb (%)	5.73±1.83	5.05±1.82	p=0.045
NNK (ng/cig.)	43.0±3.8	61.9±4.3	Total NNAL (μg/24 h)	0.31±0.16	0.28±0.18	NS
Pyrene (ng/cig.)	28.4±1.0	28.5±0.4	1-HOP (ng/24h)	182.1±81.8	171.1±73.8	NS
Acrolein (ng/cig.)	50.0±3.1	28.0±1.4	3-HPMA (mg/24h)	2.15±1.10	1.47±0.57	p<0.0001
Benzene (ng/cig.)	30.5±0.4	16.9±0.9	*S*-PMA (μg/24h)	5.17±3.05	*2.22*±1.47	p<0.0001
1,3-butadine (ng/cig.)	28.1±0.9	19.1±0.7	MHBMA (μg/24h)	6.20±7.14	1.75±1.35	p<0.0001

Figure 1: Relative differences in smoke constituent concentrations and the respective biomarkers of exposure





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