

PLASMA COTININE AND NICOTINE METABOLITES IN URINE, A COMPARISON OF CAUCASIAN AND JAPANESE SMOKERS

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AIMS

To analyse plasma cotinine and nicotine equivalents (NEQ) in urine obtained from Caucasian smokers living in the UK and Japanese smokers of 6 mg ISO 'tar' and 0.5 mg ISO nicotine cigarettes.

NEQ is the molar sum of nicotine and five major nicotine metabolites (i.e., nicotine + cotinine + *trans*-3'-hydroxycotinine and their respective glucuronides) excreted in urine over 24 h, expressed in mg nicotine. The determined NEQ represents approximately 80% of nicotine and metabolites excreted in human urine (Figure 1) [1].

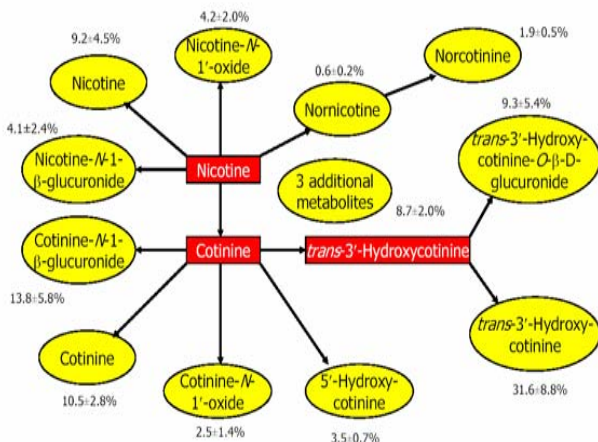
METHODS

140 volunteers (97 Caucasians, 43 Japanese) were confined in a phase 1 clinical unit and 24 h urine samples and blood samples were obtained.

Cigarette supplies were monitored throughout the study to ensure accurate determinations of cigarettes per day (CPD) smoked in the 24 hour urine collection period.

LC-MS-MS was used to determine plasma cotinine (blood sampled at 18:30 h) and NEQ in 24 h urine samples.

Figure 1: Nicotine Metabolism



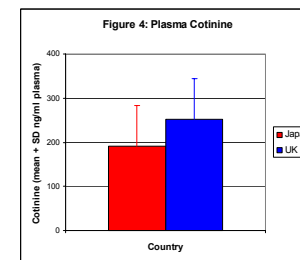
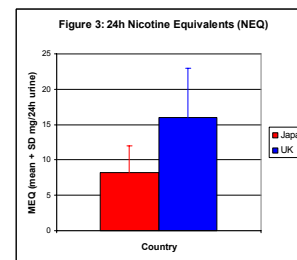
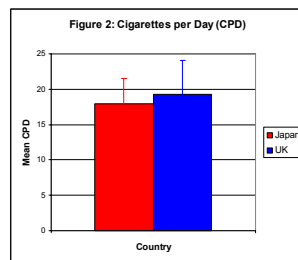
Square boxes indicate metabolites in blood and circles indicate metabolites in urine.

RESULTS

CPD smoked by Caucasian and Japanese smokers were similar (mean±S.D. 19.2±4.9 vs. 17.9±3.6 CPD) as presented in Figure 2.

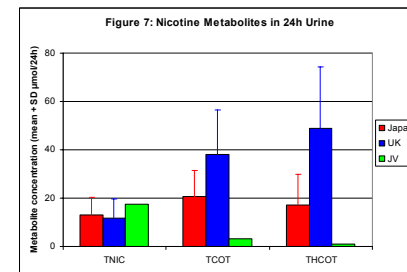
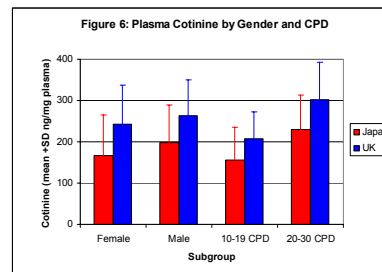
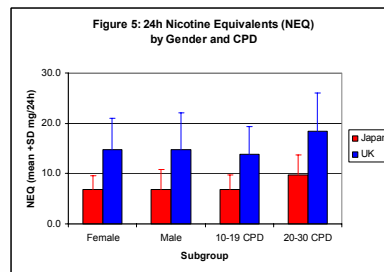
Caucasian smokers had significantly higher levels of NEQ excretion compared to Japanese smokers (mean±S.D. 16.0±6.9 vs. 8.2±3.8 mg/24 h; p<0.0001 as presented in Figure 3).

Plasma cotinine levels in Caucasian smokers were also higher than in Japanese smokers (mean±S.D. 252.3±91.3 vs. 191.0±91.6 ng/ml plasma; p=0.0004) as presented in Figure 4.



Comparison of the Caucasian and Japanese data by subgroups (gender, 10-19 CPD vs. 20-30 CPD) and on a per cigarette basis confirmed the lower levels of urinary NEQ and plasma cotinine in Japanese as compared to Caucasian smokers (Figures 5 and 6).

Analysis of the ratios of urine metabolites identified one Japanese volunteer (JV) who may have had compromised nicotine metabolism (Figure 7). This volunteer excreted very low levels of total cotinine (TCOT) and total *trans*-3'-hydroxycotinine (THCOT) in urine compared to the levels of total nicotine (TNIC).



CONCLUSIONS

Higher levels of plasma cotinine and NEQ were found in Caucasian smokers than in Japanese smokers smoking similar quantities of cigarettes with identical ISO 'tar' and nicotine yields.

REFERENCES

- Demetriou D, Schepers G, Determination of nicotine and its metabolites in urine by HPLC after DETBA derivatization, Biomarkers of Tobacco Exposure. Application to Clinical and Epidemiological Studies. Minneapolis, October 25-26, 2001.