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Nicotine and carbon monoxide intake from high- and low-yield cigarettes

We measured daily nicotine intake in 11 habitual smokers who smoked their usual brand or commercial high-yield (Federal Trade Commission [FTC] yield 1.2 mg nicotine, 16 mg tar) or low-yield (0.4 mg nicotine, 5 mg tar) cigarettes. Daily nicotine intake was measured from metabolic clearance data in conjunction with blood and urinary concentrations of nicotine during 24-hr smoking periods. On the average, subjects consumed 35 mg nicotine while smoking their usual cigarettes and 26 mg while smoking either high- or low-yield commercial cigarettes different from their usual brand. This level of nicotine consumption from low-yield cigarettes was because smokers obtained 60% more nicotine per cigarette than predicted by FTC yield and they smoked 25% more cigarettes a day. Although there was considerable variability in nicotine intake between subjects, there was a correlation within subjects between intake while smoking their usual brand and experimental cigarettes. Nicotine intake between the two commerical high- or low-yield cigarettes also correlated (r = 0.86). These findings are consistent with a minimal level of acceptable daily intake of nicotine for individuals that is related to usual intake. We suggest that our protocol provides a better quantitative estimate of the yield of different cigarette brands and potential health hazards than those currently provided by the FTC.

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People who are unable to stop smoking are often advised to switch to cigarettes that yield less nicotine and tar, on the assumption that low-yield cigarettes are less hazardous. The yield of American cigarettes is taken from results of United States Federal Trade Commission (FTC) smoking machine tests.[5] It is well known that people do not smoke cigarettes like machines and that their intake of nicotine and other combustion products of tobacco differs considerably from yields predicted by smoking machines. The most direct way to assess relative hazards of different brands of cigarettes is to measure the smoker's intake of tobacco smoke constituents. We recently described a method for determining daily nicotine intake, a method similar to that used in drug bioavailability studies.[4] Metabolic clearance of nicotine is determined after intravenous injection; data

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Table I. *Nicotine, carbon monoxide, and tar yields of cigarettes as determined by the FTC*

Brand	FTC smoking machine yield		
	Nicotine (mg)	Carbon monoxide (mg)	Tar (mg)
Usual (N = 11)	1.0 ± 0.15 (0.87 – 1.48)	15.1 ± 1.3 (12.3 – 16.5)	16.3 ± 2.7 (11.0 – 23.1)
Camel (85 mm, filtered)	1.18	16.0	16.0
True (85 mm, filtered)	0.43	4.3	4.9

Data are $\bar{X}$ ± SD (range).

are then used in conjunction with blood and urinary nicotine concentrations during a 24-hr smoking period to estimate 24-hr nicotine intake. Concentrations of carboxyhemoglobin (COHb) during the 24-hr smoking period are used to estimate daily carbon monoxide intake.

With these methods, we studied nicotine and carbon monoxide intake in smokers who switched from their usual brand of cigarettes to popular commercial brands of cigarettes in the high- (15 mg) and low- (5 mg) tar classes. We asked the following questions: Is there any difference in nicotine and carbon monoxide intake while smoking high- and low-yield commercial cigarettes? If there is regulation of nicotine intake, how is it accomplished—how much compensation occurs by smoking a different number of cigarettes and how much by adjusting nicotine intake per cigarette?

Methods

Our subjects were six men and five women 22 to 55 yr old (30 ± 10; $\bar{X}$ ± SD). All were habitual cigarette smokers who smoked at least one pack a day ($\bar{X}$ = 28 ± 7 cigarettes; range 20 to 40 cigarettes a day) of medium- to high-yield cigarettes and had smoked for an average of 13.5 yr (range 6 to 40 yr). Subjects were hospitalized in the General Clinical Research Center at San Francisco General Hospital Medical Center. They ate a normal diet, except beverages with caffeine and alcohol were prohibited.

On the second hospital day after overnight abstinence from smoking, nicotine was infused intravenously for determination of metabolic clearance. Subjects were then studied in three experimental smoking blocks. For the first block (2 days), subjects smoked their own brand of cigarettes as desired. In each of the next two blocks (four days each), subjects smoked either Camel (R. J. Reynolds) filter (85 mm) or True (Lorillard) filter (85 mm) cigarettes. These cigarettes were chosen as popular cigarettes in the 15- and 5-mg tar classes. Cigarettes were purchased from local supermarkets. The order of smoking high- and low-yield cigarettes was balanced and was similar for men and women. FTC yields of subjects' own brand, Camel, and True cigarettes are shown in Table I. All cigarette butts were collected. Grams of tobacco smoked were estimated by subtracting the weight of all butts from the weight of a comparable number of unburned cigarettes. This measure was considered important because True cigarettes contain less tobacco than Camel or the usual brand cigarettes (True, 0.63 gm; Camel, 0.81 gm; usual brand, 0.80 ± 0.08 gm). Urine was collected every 24 hr for measurement of daily nicotine excretion. A circadian blood sampling study was performed on the last day of each smoking block. Nicotine was infused after overnight abstinence from smoking.[4] *l*-Nicotine bitartrate, 1.5 μg base/kg/min, was infused for 60 min. Blood samples were collected at frequent intervals and urine was collected for 5 hr after the end of the infusion.

On smoking days, subjects were given three or four packs of their usual brand of cigarettes each morning and were instructed to smoke them in any manner they wished. On the day of blood sampling, an indwelling butterfly catheter was inserted in a forearm vein for collection of blood for nicotine, cotinine, and COHb concentration determinations. Blood samples were collected every 2 hr from 8 A.M. to midnight and then at 4 and 8 A.M. the next day. Blood sampling was independent of when subjects smoked

their last cigarette. To assess the effect of blood collection on smoking behavior, counts of the number of cigarettes smoked and urinary excretion of nicotine on the day before sampling were compared with those measured on the day of circadian blood sampling. Concentrations of nicotine and cotinine in blood and urine were measured by GLC with a nitrogen-phosphorus detector.[9] COHb was measured with an Instrumentation Laboratories Model 280 Co-oximeter. On the fourth day of smoking Camel or True cigarettes, subjects were given a questionnaire (adapted from Adams[1]) that inquired about the characteristics of the cigarette.

Computations of renal and nonrenal clearance of nicotine, AUC, and daily consumption of nicotine have been described.[4] Differences between experimental blocks and days within blocks were analyzed by repeated measures analysis of variance considering effects of sex and order of treatment. Significant differences were assumed when $P < 0.05$.

Results

There were no significant differences in number of cigarettes smoked on the blood sampling day and the nonsampling day (measured day before the day of blood sampling). Average blood concentrations of nicotine and COHb at various times of the day for all subjects in different experimental conditions are shown in Fig. 1. Blood concentrations of nicotine analyzed as AUC were higher while smoking the usual brand cigarettes (478 ± 155 ng · ml^{-1} · hr) than when smoking Camel and True cigarettes (349 ± 158 and 336 ± 115 ng · ml^{-1} · hr). True and Camel cigarettes did not differ from each other; both differed from the usual brand cigarettes. COHb levels tended to be higher while subjects smoked Camel cigarettes but were the same while smoking the usual brand or True cigarettes.

On average, subjects received 35 mg nicotine a day while smoking their own cigarettes and 26 mg a day while smoking True or Camel cigarettes (Fig. 2, *A*). Rank order of nicotine intake comparing brands across subjects was similar (correlation coefficients: Camel and True, $r = 0.86$; usual brand and Camel, $r = 0.55$; usual brand and True, $r = 0.81$; all $P < 0.05$).

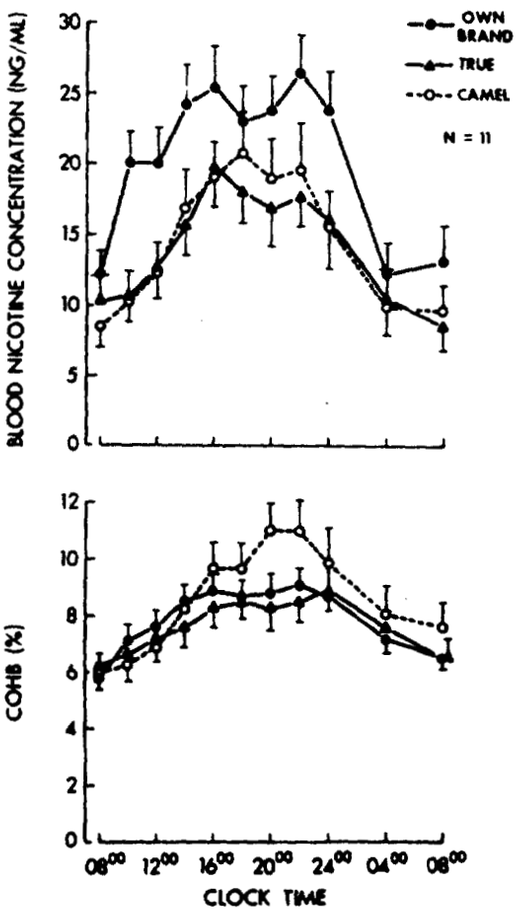

Fig. 1. Mean blood nicotine and COHb concentrations throughout the day while smoking usual brand, Camel, or True cigarettes.

Subjects smoked more cigarettes a day while smoking True cigarettes (39 ± 10) but smoked the same number of their usual brand (29 ± 7) and of Camel (30 ± 10) cigarettes. Although subjects smoked more True cigarettes, the amount of tobacco burned per day did not differ between brands (18.5 ± 4.7, 18.2 ± 6.8, and 19.1 ± 6.6 gm a day for usual brand, Camel, and True cigarettes). This is consistent with the fact that True contained less tobacco per cigarette, so that although subjects smoked more True cigarettes, smokers were in fact smoking the same amount of tobacco.

Estimated nicotine intake per cigarette was highest for the usual brand ($\bar{X} = 1.2 \pm 0.2$ mg), next highest for Camel (0.9 ± 0.4 mg),

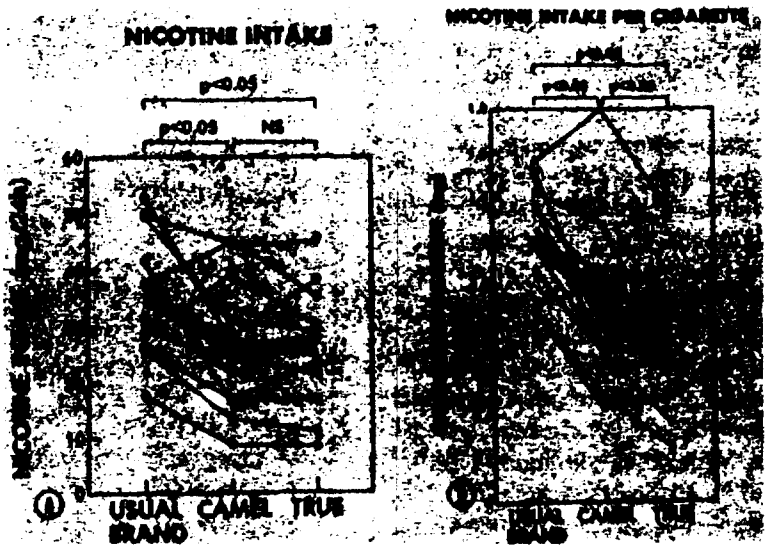

Fig. 2. Daily intake of nicotine *(A)* and average nicotine intake per cigarette *(B)* while smoking usual brand, Camel, or True cigarettes. *Stippled* areas indicate average ($\bar{X}$) values.

and lowest for True (0.7 ± 0.3 mg) cigarettes (Fig. 2, *B*). The quantity of nicotine consumed per gram of tobacco burned was greater for the usual brand (1.9 ± 0.5 mg/gm) than for Camel (1.5 ± 0.6 mg/gm) and True (1.4 ± 0.6 mg/gm) cigarettes. Comparing the ratio of nicotine intake to FTC yield, smokers smoked True cigarettes most efficiently (ratio 1.61 ± 0.70), their usual brand next most efficiently (1.11 ± 0.27), and tended to undersmoke Camel cigarettes (0.76 ± 0.33).

There were no sex differences in any of the measured variables, although women tended to consume less nicotine a day (overall $\bar{X}$: women, 23.4 ± 11.6 mg/day; men, 34.1 ± 10.7 mg/day) and less nicotine per cigarette (0.82 ± 0.35 and 1.03 ± 0.37 mg/cigarette). There was no difference in AUC between the sexes, because women on the average metabolize nicotine more slowly than do men,[4] which results in higher average blood concentrations of nicotine in women at any given intake level. Differences in daily intake of nicotine between usual and experimental brands were greater for women than for men, which suggests that men may regulate nicotine intake more efficiently than women.

Subjects reported differences between Camel and True cigarettes in strength, satisfaction, and overall quality. Camel cigarettes, which were similar in FTC-determined yield of nicotine and tar to the usual brand cigarettes of most subjects, were rated "about right" in strength, whereas True cigarettes were rated "too mild." Camel cigarettes were rated from "sufficiently satisfying" to "very satisfying," whereas True cigarettes were rated "slightly satisfying" to "fairly satisfying." The overall quality of Camel cigarettes was rated "fair" to "good," whereas the quality of True cigarettes was rated "poor." Camel cigarettes were rated "not quite as good" to "about the same" and True cigarettes were rated "not nearly as good" as the usual brand cigarettes.

Discussion

We found that our subjects maintained the same blood level of nicotine and carbon monoxide while they were smoking popular high- and low-yield commercial cigarettes, despite the fact that the low-yield cigarettes were rated as being of much poorer quality than the usual brand cigarettes. Consumption of desired nicotine dose was accomplished primarily by obtaining 60% more nicotine per low-yield cigarette than the yield predicted by FTC smoking machine assays. High-yield cigarettes were smoked less efficiently; intake was 76% of

that predicted. Also, more (25%) of the low-yield cigarettes were smoked a day. It is noteworthy that although more low-yield cigarettes were smoked a day, the same total weight of tobacco of all brands was smoked. As we have reported,[3] there is no difference in percent nicotine per gram tobacco in these brands, so it is not surprising that smoking the same weight of tobacco results in the same nicotine delivery.

Subjects' higher nicotine levels while smoking the usual brand of cigarettes may relate in part to the pleasure of smoking a cigarette with which one is familiar and enjoys and in part to maintaining a particular nicotine blood level. Other brands were judged not as pleasurable and were smoked in such a way that the nicotine blood level was about 70% of that while smoking their usual brand cigarettes. The findings that nicotine intake while smoking the usual brand of cigarettes correlated strongly with that from high- or low-yield brands within subjects and that intake levels were the same for high- and low-yield cigarettes suggest that each individual has his or her own acceptable lower limit for nicotine. We speculate that intake below this level might be associated with manifestations of nicotine abstinence.

Others have reported that smokers studied in the laboratory smoke more low-yield cigarettes than their usual brand, puff more deeply, and inhale more often.[7, 8] Longer-term studies of switching to low-yield brands have generally indicated that smokers maintain nicotine and carbon monoxide at higher levels than those predicted by machine yields, but most investigators report incomplete compensation while smoking low-yield cigarettes.[3, 10–12] Our study differs from others in that we have more directly determined daily intake of nicotine and carbon monoxide. Important methodologic issues in our study were that the subjects were studied in a hospital and that the smokers smoked different brands for only 4 days. The finding that cotinine concentrations in seven subjects in whom we had the data were of the same order on the day of admission and on the day of the circadian study while smoking their own cigarettes supports the assumption that the hospital environment did not affect nicotine intake. This is also supported by the finding that the number of their own brand of cigarettes smoked a day in the hospital was of the same order as that reported by subjects as their usual cigarette consumption outside the hospital. We cannot exclude the possibility that subsequent hospitalization influenced smoking behavior, but we do know there was no significant order effect for high-low comparisons.

Whether nicotine and carbon monoxide intake measured after 4 days of smoking a new brand is maintained at the same level when that brand is continued longer in a more natural environment needs further study. It is also important to recognize that our subjects were not trying to quit smoking. It is possible that people who are motivated to stop smoking, unlike our present subjects, would be less likely to smoke the low-yield cigarettes more often or more intensively than the high-yield cigarettes. However, we believe that the comparison between high- and low-yield cigarettes is valid in the assessment of relative nicotine and carbon monoxide intake for the general population of habitual smokers.

We studied only one brand of low-yield cigarettes that was in the 5-mg tar class. There is recent evidence that the smoking of ultra-low-yield cigarettes in the 1-mg tar class results in reduced nicotine intake, although much less than that predicted by the FTC.[6]

In summary, our study indicates that smokers consume as much nicotine and carbon monoxide from low- as from high-yield commercial cigarettes and that this compensation occurs primarily from smoking low-yield cigarettes more efficiently than predicted by the FTC smoking machine assay. These data are consistent with our recent report that nicotine intake as estimated by blood concentration of cotinine was no different in a cross-sectional sample of people who smoked FTC-determined low-yield compared to high-yield cigarettes.[3] We suggest that our method provides a better quantitative estimate of yields of different cigarette brands and associated health hazards than those currently provided by the FTC assay.

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References

1. Adams PI: The influence of cigarette smoke yields on smoking habits, *in* Thornton RE, editor: Smoking behaviour—Physiological and psychological influences. London, 1978, Churchill-Livingstone, pp 349-360.
2. Ashton H, Stepney R, Thompson JW: Self-titration by cigarette smokers. Br Med J 2:357-360, 1979.
3. Benowitz NL, Hall SM, Herning RI, Jacob P III, Jones RT, Osman A-L: Smokers of low-yield cigarettes do not consume less nicotine. N Engl J Med 309:139-142, 1983.
4. Benowitz NL, Jacob P III: Daily intake of nicotine during cigarette smoking. CLIN PHARMACOL THER 35:499-504, 1984.
5. Federal Trade Commission: Report of "tar," nicotine and carbon monoxide of the smoke of 200 varieties of cigarettes. Washington, D. C., 1981, Federal Trade Commission.
6. Gori BG, Lynch CJ: Smoker intake from cigarettes in the 1-mg Federal Trade Commission tar class. Reg Toxicol Pharmacol 3:110-120, 1983.
7. Gritz ER: Smoking behavior and tobacco abuse, *in* Mello N, editor: Advances in substance abuse: Behavioral and biological research. Greenwich, Conn., 1980, JAI Press, pp 91-158.
8. Herning RI, Jones RT, Bachman J, Mines AH: Puff volume increases when low nicotine cigarettes are smoked. Br Med J 283:187-193, 1981.
9. Jacob P III, Wilson M, Benowitz NL: Improved gas chromatographic method for the determination of nicotine and cotinine in biologic fluids. J Chromatogr 222:61-70, 1981.
10. Robinson JC, Young JC, Rickert WS, Fey G, Kozlowski LT: A comparative study of the amount of smoke absorbed from low yield ('less hazardous') cigarettes. Part 2: Invasive measures. Br J Addict 78:79-87, 1983.
11. Russell MAH, Wilson C, Patel UA, Feyerabend C, Cole PV: Plasma nicotine levels after smoking cigarettes with high, medium, and low nicotine yields. Br Med J 2:414-416, 1975.
12. Turner JAM, Sillett RW, Ball KP: Some effects of changing to low-tar and low-nicotine cigarettes. Lancet 2:737-739, 1974.