Effects of a Nicotine-Enriched Cigarette on Nicotine Titration, Daily Cigarette Consumption, and Levels of Carbon Monoxide, Cotinine, and Nicotine

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Abstract. To test whether cigarettes with low tar, low carbon monoxide, and medium nicotine yield produce less dangerous effects than cigarettes low in tar and CO but high in nicotine, 12 subjects were recruited to smoke nicotine-enriched cigarettes. The subjects smoked three types of cigarettes in the three experimental conditions: (1) their own brand; (2) cigarettes with 4.8 mg tar, 4.0 mg CO, and 0.5 mg nicotine; (3) cigarettes with 5.8 mg tar, 4.1 mg CO, and 1.1 mg nicotine. Subjects monitored their daily consumption for 12 weeks; 4 weeks for each condition. During laboratory visits, the subjects smoked a cigarette while their heart rate and carbon monoxide in expired air were measured pre- and post-smoking. A blood sample was drawn and analyzed for nicotine and cotinine in each experimental condition. No significant differences in daily cigarette consumption were found, although a trend (P < 0.07) in the direction of fewer nicotine-enriched cigarettes per day was found. Levels of CO varied significantly among the three conditions: The subjects’ own brands yielded the highest level, while the nicotine-enriched cigarette yielded the lowest level. No differences were found for nicotine or cotinine levels. A second purpose of the experiment was to record the degree of nicotine titration displayed by individual smokers; tar and CO levels remained constant in the experimental cigarettes. No general titration effect was observed, although for daily consumption it approached significance. When the subjects’ nicotine dependence, measured with a tolerance questionnaire, was taken into account, a correlation with daily consumption was found (r = .77, P < 0.005). A cigarette with low tar and CO, but medium to high nicotine yield, would seem to produce less hazardous effects and is worthy of further investigation. The controversial question of whether smokers titrate for nicotine is a function of the individual’s nicotine dependence.

Key words: Nicotine-enriched cigarette - Titration - Nicotine dependence - CO - Plasma nicotine - Cotinine

Tobacco companies seem to be aware of smokers’ concern about the hazards of smoking and their health. New and supposedly ‘healthier’ products are constantly introduced into the market. Brown and Williamson, for example, spend 150 million dollars to advertise and promote a low tar-nicotine cigarette (Louis 1980). The idea behind all the new products is to minimize the nominal rates of tar and nicotine obtain through standardized machine smoking. The means available to reduce tar and nicotine yields are by tobacco extraction processes, reblending, use of reconstituted tobacco sheet, selected combinations of filters, smoke dilution devices, and cigarette burning rates.

The tar and nicotine yields of today’s cigarettes, at least in the USA and Western Europe, are certainly much lower than previously. The typical tar rate in England in 1935 was about 33 mg/cigarette, while in 1976 it was 18 mg/cigarette. For nicotine the figures are 3.0 and 1.3, respectively (Russell 1976).

Independent researchers have also suggested the ‘lowering approach’. Concentrating on six substances that are regarded as harmful, i.e., tar, nicotine, carbon monoxide (CO), nitrogen oxides, hydrogen cyanide, and acrolein, Gori and Lynch (1978) tried to guide smokers to cigarettes that did not exceed a critical level of daily smoke intake with regard to all the six constituents. It was supposed that if smokers choose the ‘right’ brand the residual damage to health should not appreciably increase the risk of the smoker over that of the nonsmoker. Their calculations, as they admit, are based on the assumption that the smokers of low tar and nicotine cigarettes will not change their smoking habits. Unfortunately, they neglected to cite a large number of studies that have established the phenomenon of compensation (i.e., regulation of nicotine intake through smoking more or less intensively according to decreased or increased nicotine content of the tobacco), while giving only one reference to support their own view. Compensation, however, both upwards and downwards, seems to be fairly well-established even if no one has argued that smokers can fully compensate a substantially reduced delivery of nicotine, or that all smokers do compensate. The literature on the role of nicotine is well-reviewed by Russell (1978) and Gritz (1980). Recently, it has been found that the physical nicotine dependency of smokers (Fagerström 1978) covaries with degree of compensation (Fagerström and Bates 1981).

When considering nominal nicotine yields of cigarettes and plasma nicotine levels, only 4% of the variance in plasma nicotine could be accounted for by nominal nicotine yield (Russell 1980). For CO hemoglobin (Hb) and cigarette consumption the correlation r was 0.30, which means that 10% of the CO Hb variation can be related to the number of cigarettes smoked (Russell 1980). In the same report it was also found that high nicotine, tar, and CO cigarettes gave somewhat lower levels of CO Hb than cigarettes with lower nominal deliveries. Jaffe et al. (1981), measuring exhaled CO, found no differences across groups of cigarette brands from high nicotine-tar rates to very low nicotine-tar rates. This
indicates that nominal yields or daily consumption of cigarettes are very crude measures and account for little of the variation of CO and nicotine within the smokers' body.

Consequently, some major investigators (Russell et al. 1973; Russel 1980; Goldfarb et al. 1976) have suggested that a low tar-medium nicotine cigarette can offer substantial health gains. With a medium nicotine cigarette the smokers will inhale less smoke to obtain his/her optimal level of nicotine, compared with a low nicotine cigarette. With reduced smoke intake, the level of CO and probably most of the gases to be found in the smoke will be lower. Dunn and Freiesleben (1978) found a decrease in the smokers' level of CO when the nicotine yield of the cigarettes was increased by 30%, while holding CO and tar deliveries nearly constant.

The present study will test the medium nicotine hypothesis as a means to a less hazardous cigarette by varying nicotine content independently of tar and CO through artificial enrichment of nicotine. The independent variation of tar, CO, and nicotine will also provide an excellent opportunity for testing the nicotine compensation hypothesis. The smokers' nicotine dependence will be taken into consideration, since it is likely that compensation varies according to the smokers' dependence.

Data were collected while the smokers smoked the experimental cigarettes in their daily life for 2 months. Number of cigarettes smoked was obtained through self-monitoring, while expired CO and heart rate was measured in a laboratory smoking situation where blood samples were also taken for analysis of nicotine and cotinine.

Materials and Methods

Twelve healthy smokers were recruited for the experiment. All but one subject were on the staff of local hospitals. Five were males and seven were females (age range 22–45 years). They were all regular cigarette smokers with a daily consumption rate of 15–35. The average consumption was 26.9, which is far above the mean Swedish smoking rate of 16 cigarettes/day. They were not paid, but motivated to participate because of the free cigarettes they were given.

Procedure. The experiment consists of three conditions where the order of conditions 2 and 3 was balanced: (1) smoking their own brand for 3 weeks; (2) switching to one of the experimental cigarettes for 4 weeks; (3) switching to the other experimental cigarette for 4 weeks.

During the whole experiment the subjects were required to self-record their daily cigarette consumption and during each condition they came to the laboratory on three occasions to turn in consumption records to the experimenter, smoke a cigarette while expired CO and heart rate (HR) were recorded pre- and postsmoking, and receive cigarettes (condition 2 and 3). In one of the three laboratory visits under conditions 2 and 3, the subjects were asked for a blood sample without any previous warning. The lack of warning was probably a reason for five subjects refusing to give blood. The experiment was started without plans for measuring nicotine and cotinine but, during the experiment, a method for nicotine and cotinine analysis became available from an independent laboratory (M. Curwall, Swedish Tobacco Monopoly, Stockholm).

When arriving at the laboratory for smoking, they had smoked a cigarette 60 min earlier and were first given some minutes of rest to stabilize HR. After the HR was recorded manually at the volar of radial artery, they blew up a balloon for CO measurement. While smoking, they sat alone in a 3 × 3 m room furnished with a table and chairs. They had access to magazines and coffee and were instructed to smoke in their normal fashion. All subjects smoked, on all occasions, down to what was considered a normal butt for them. After extinguishing the cigarette, the subjects who were willing to submit to venopuncture went immediately after recording of CO and HR to an adjoining room where the blood was taken 2.5–3 min later. For each subject, the laboratory visit was at the same time of day across visits.

Experimental Cigarettes. The two types of experimental cigarettes were provided by the Swedish Tobacco Monopoly. One of the cigarettes was a commercially available brand containing 0.53 mg nicotine, 4.8 mg tar, and 4.0 mg CO. The other cigarette had the same tobacco base as the commercially available brand, but was enriched with nicotine by spraying nicotine citrat on the tobacco. The cigarette yielded 1.1 mg nicotine, 5.8 mg tar, and 4.1 mg CO. The cigarettes, as well as the packs, were identical. The subjects were not blind to conditions, since the taste differed. All subjects recognized the change to the other experimental cigarette. Unfortunately, most of the subjects rated the nicotine-enriched cigarette as bad tasting and one subject had to drop out of the study because of problems with his throat, probably due to the enriched cigarette. The subjects' normal brands yielded an average of 1.1 mg nicotine, 12 mg CO, and 14 mg tar.

Measurements. The subjects self-monitored their daily cigarette consumption during the entire experiment. Some made a mark for every cigarette on a small piece of paper attached to the pack, while others counted the cigarettes in the pack in the morning and again at night with all new packs recorded. They were instructed to minimize exchange of cigarettes with other smokers. There was no limit to the number of free cigarettes they could smoke.

CO was analyzed through expired air blown into a balloon which was connected to an Ecolyser 2106 displaying CO content in parts per million (ppm).

Physical dependence on nicotine was approximated by the Tolerance Questionnaire, which consists of eight questions about the smoking habit; e.g., 'How soon after awakening do you start smoking?' The questions, as well as scoring and validity, are described by Fagerström (1978, 1981).

Results

The effects of the different types of cigarettes on average cigarette consumption/day, CO, HR increase, and plasma nicotine and cotinine are displayed in Table 1. The daily cigarette consumption did not vary significantly between any of the three conditions. The strongest trend was between the two experimental cigarettes. The subjects smoked 1.9 cigarettes/day less of the 1.1 mg nicotine cigarettes compared to those with 0.5 mg nicotine ($t = 1.56, P < 0.07$).

The CO levels were significantly different between all three types of cigarettes, with the highest value for their own brand and the lowest in the 1.1 mg nicotine cigarette. Comparing the 0.5 mg and 1.1 mg nicotine cigarettes, 9 of 12 subjects had lower values in the 1.1 mg nicotine cigarette.

HR increase while smoking in the laboratory was significantly higher for their own brand as compared to both of the experimental cigarettes. The greater increase in pulse rate in