Pharmacology Biochemistry and Behavior, Vol. 60, No. 4, pp. 817–821, 1998

0091-3057/98 $19.00 + .00

ELSEVIER

PII S0091-3057(98)00042-2

Effects of Cigarette Smoking Through a Partially Occluded Filter

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Received 27 July 1997; Revised 5 December 1997; Accepted 16 December 1997

PICKWORTH, W. B., R. V. FANT, R. A. NELSON AND J. E. HENNINGFIELD. *Effects of cigarette smoking through a partially occluded filter.* PHARMACOL BIOCHEM BEHAV **60**(4) 817–821, 1998.—The effects of a commercially available corn syrup solution that is applied to the filter end of a cigarette causing an occlusive barrier to cigarette smoke were evaluated. The manufacturer claims that the solution reduces exposure to nicotine, carbon monoxide (CO), and other constituents of tobacco smoke and may aid in smoking cessation by providing a means of gradual nicotine dose reduction. Nineteen volunteers (10 men) smoked commercial cigarettes treated with 0, 1, 2, or 3 drops of the corn syrup solution in a double-blind, crossover experiment. Increases in plasma nicotine after smoking averaged 13.3, 10.5, 9.7, and 6.0 ng/ml in the 0, 1, 2, and 3 drop conditions, respectively. In the 3 drop condition, there was a significant reduction in exhaled CO levels. Subjects reported increased difficulty in cigarette draw and a trend toward decreased strength as a function of the number of drops applied. Cardiovascular and EEG measures of smoking were not significantly affected by the application of the drops. Cigarettes treated with 0, 1, 2, or 3 drops of the solution were machine smoked using methods of the Federal Trade Commission (FTC); nicotine yields were 1.0, 1.0, 0.78, and 0.73 mg of nicotine. These results indicate that Take Out drops reduce exposure to nicotine and other constituents of tobacco smoke from a single cigarette. © 1998 Elsevier Science Inc.

Nicotine EEG Carbon monoxide Tobacco smoke exposure

MANY smokers who attempt to quit do so by gradually reducing their daily exposure to nicotine, carbon monoxide (CO), and other constituents of tobacco smoke. Some people simply reduce the number of cigarettes smoked per day until abstinence is achieved. About 26% of former smokers who quit without medical assistance did so by gradual cessation methods (3). Another method of gradually reducing exposure to constituents of tobacco smoke is by brand switching or nicotine fading. Smokers using this technique substitute their usual brand of cigarettes with brands that have lower yields of tar and nicotine (4). A major problem with brand fading strategies is that smokers can sustain their preferred level of nicotine from nearly any brand of cigarette by increasing their smoking intensity of brands that have lower yields of nicotine and tar (8).

Some smokers use devices to reduce their exposure to nicotine, which may aid in achieving tobacco abstinence. Ventilated filters dilute mainstream smoke with air. Martin et al. (11) reported that a ventilated filter (One Step at a Time®) reduced CO exposure by 78%. However, compensatory smoking can defeat the intent of these filters as well (7). Similarly, Stitzer et al. (18) reported that Phase Out®, a device that produced dilution of mainstream smoke by perforating the filters of commercial cigarettes, significantly reduced nicotine and CO intake to levels predicted from machine smoking of the perforated cigarettes.

A recently marketed program advertised to control, reduce, and eliminate smoking uses a corn syrup solution to reduce exposure to nicotine and other constituents of tobacco smoke. One to 3 drops of the solution are placed on the filter end of a cigarette prior to smoking. As the drops dry, they form a barrier (an occlusive filter) to the delivery of nicotine, tar, and other products of tobacco smoke. As part of a smoking cessation program lasting several weeks, smokers are instructed to place increasing numbers of drops (first week—1 drop; second week—2 drops, third week and thereafter—3 drops) to the filter end of the cigarette. Based on machine-smoking data, the manufacturer claims that 3 drops reduced

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exposure to tar and nicotine by more than 95%. Recent preliminary results from an open-label clinical trial appear to support the beneficial effects of using the drops in a smoking cessation program (5).

The primary purpose of the study was to determine if the solution reduces exposure to constituents of tobacco smoke in research volunteers. Smoking parameters and effects of the corn syrup solution were compared in men and women smokers to determine if gender affected these variables. Cigarettes treated with the solution were tested using the methods of the Federal Trade Commission (FTC) smoking procedures to determine the extent that the solution affected machine yields of nicotine, tar, and CO. Nicotine and CO exposure as measured by the FTC test could be directly compared to values obtained from smokers.

METHOD

Machine-Smoking Test

Marlboro® cigarettes from the same batch and lot as those smoked by the subjects were treated with 0, 1, 2, or 3 drops of the corn syrup solution according to the instructions of the manufacturer. The cigarettes were machine smoked using the parameters and specifications of the FTC, Cambridge Method, (2,16) by an independent testing laboratory (Labstat, Kitchener, Ontario, Canada). This analysis gives the machine yield of nicotine, tar, and CO delivery.

Subjects

Nineteen subjects participated in this outpatient study. All of the subjects were African-American; 10 were men. The subjects were recruited from the community and were paid $350 for participation. To be included in the study it was required that subjects smoke >20 cigarettes/day for at least 2 years of a brand of cigarettes that delivers >1 mg of nicotine (FTC ratings). The mean age of the subjects was 34.8 years. They weighed an average of 68.2 kg and smoked (mean ± SD) 26 ± 6.2 cigarettes a day for an average of 18.3 years. The nicotine yield of their cigarettes averaged 1.2 mg. All of the subjects were smokers of mentholated cigarettes. Their score on a test for nicotine dependence (1) averaged 7.0; on this test, scores of 6 or above indicate a high level of nicotine dependence. On a day before beginning the study, the experimental procedures were explained and subjects gave informed consent in accordance with guidelines of the Department of Health and Human Services and the local Institutional Review Board.

Procedures

Experimental design. Subjects participated in four experimental sessions that were separated by at least 48 h. Each subject was exposed to all experimental conditions, and the order of presentation of the conditions was randomized. The study was conducted in a double-blind manner; neither the subject nor the research personnel knew the treatment condition.

Cigarette preparation. Only Marlboro® cigarettes (King Size, Filter Soft Pack; Philip Morris Inc., Richmond, VA) were used in this study. By the standards of the FTC, this brand of cigarette delivers: 1.1 mg nicotine, 16 mg tar, and 14 mg CO. These cigarettes were treated with 0, 1, 2, or 3 drops of the corn syrup solution, Take Out® (UltraTech Corp., Lafayette Hill, PA). To disguise the presence of the corn syrup solution (a light pink solution) the filter ends of the cigarettes were colored pink before the application of the drops. The solution was applied according to the manufacturer's suggestion—a small cavity was made in the filter end of the cigarette and the drops were added into the cavity and over the entire tip of the filter. About 1 min after application of the drops, the subject smoked the cigarette ad lib to a line 3 mm above the edge of the filter wrap.

Nicotine analysis. Blood samples were placed in an ice bath immediately after their collection. At the end of the session, the blood samples were centrifuged for 10 min at 3500 rpm and the plasma was drawn off, placed in tubes, and stored in a freezer until the nicotine analysis was performed. Nicotine concentrations were determined using gas chromatography-thermoionic specific detector (Labstat Inc. Kitchener, Ontario, Canada). The limit of detection was 1 ng/ml.

Experimental procedure. On the day the subjects signed the consent document, they smoked a single untreated cigarette outside the experimental room. The time to smoke and the number of puffs were recorded as "natural" smoking. Smoking during the experimental sessions was completed in a small well-ventilated chamber adjacent to the experimental room.

On days of experimental sessions, subjects reported to the clinical laboratory after at least 3 h of tobacco abstinence. Exhaled CO concentrations were obtained using a Breathco monitor (Vitalograph, Lexena, KA). A cannula was inserted into a forearm vein to obtain blood samples. Gold-plated electrodes were applied to three scalp locations, Fz, Cz, and Pz, and connected to a BioLogic (Chicago, IL) automated EEG acquisition and analysis system. Blood pressure and heart rate were recorded using an automated monitor (IVAC Inc, San Diego, CA). Before smoking the experimental cigarette, baseline measures of heart rate, blood pressure, resting EEG, exhaled CO, and a venous blood sample that was later analyzed for nicotine levels were collected. Cardiovascular measures and blood samples were obtained 2, 5, 10, 15, 30, and 60 min after smoking. Exhaled CO was measured at 15 and 60 min after smoking. One-minute samples of resting (eyes closed, relaxed) electroencephalogram (EEG) were collected 10 and 30 min after smoking. EEG samples were analyzed as previously described (15) for power and spectral edge frequency in the following EEG bands: delta (0–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta1 (13–24 Hz), and beta2 (24–32 Hz).

At 20 min after smoking, the subjects responded to computer-delivered visual analog questions about the experimental cigarette smoking. Subject responded by placing the cursor along a 100 mm horizontal line to index their endorsement of the following phrases (anchors at the extremes of the visual analog line appeared on the screen): "Rate your overall SATISFACTION from the cigarette (not satisfying . . . very satisfying);" "Rate the overall TASTE of the cigarette (very bad . . . very good);" "Rate the STRENGTH of the cigarette (very weak . . . very strong);" "Rate the DRAW from the cigarette (very hard . . . very easy);" "Rate the HOTNESS of the cigarette (not at all . . . very hot);" "How much did you LIKE the cigarette (not at all . . . very much);" "Rate the HARSHNESS of the cigarette (very harsh . . . very smooth)."

Data Analysis

The machine-smoking data on nicotine, tar, and CO yield were subjected to a one-way analysis of variance, ANOVA, (20) by drop condition. For behavioral measures (number of puffs, time to smoke), data were subjected to two-way, repeated-measures ANOVAs by condition (five levels: "natural"

smoking, and 0, 1, 2, and 3 drops) and gender. Data on subjective measures were similarly analyzed but only four levels of condition (0, 1, 2, and 3 drops) were considered. Plasma nicotine and cardiovascular data were subjected to three-way ANOVAs by condition (four levels: 0, 1, 2, and 3 drops), time (seven levels: baseline, 2, 5, 10, 15, 30, and 60 min postsmoking), and gender. Carbon monoxide data were similarly analyzed with only three levels of time (baseline, and 15 and 60 min postsmoking). EEG data collected at 10 min were expressed as a percentage of the baseline score. These percentage scores were subjected to two-way ANOVA by condition and gender. When the ANOVA indicated significant main effects or interactions, post hoc analyses were performed using Tukey's honestly significant difference test.

RESULTS

Machine Smoking

The corn syrup solution significantly reduced nicotine yield when cigarettes were machine smoked using the methods of the FTC, $F(3, 12) = 8.2$, $p < 0.005$. As illustrated in Fig. 1, mean nicotine yield per cigarette was 1.0, 1.0, 0.78, and 0.73 mg when treated with 0, 1, 2, and 3 drops, respectively. Post hoc analyses indicated that the nicotine yield using 0 or 1 drops was significantly greater than yields following 2 or 3 drops.

Tar yield with machine smoking was also significantly reduced by the corn syrup solution, $F(3, 12) = 7.4$, $p < 0.005$. Average tar yield per cigarette was 14.9, 14.2, 12.0, and 11.5 mg after treatment with 0, 1, 2, and 3 drops, respectively. Post hoc analyses indicated that the tar yield using 0 or 1 drops was significantly greater than yields following 2 or 3 drops.

Although the CO boost in the 3 drop condition was greater than in other conditions, the overall analysis of variance comparing drop conditions indicated no significant difference between drop conditions on the CO delivery, $F(3, 12) = 2.6$, NS.

Behavioral Measures

There was a significant difference in the number of puffs taken, $F(4, 68) = 9.1$, $p < 0.001$, to smoke the cigarette. Subjects took significantly fewer puffs of the untreated cigarette (0 drop condition) in the "natural" setting compared to smoking an untreated cigarette in the smoking chamber. However, there were no overall differences in number of puffs taken in the smoking chamber as a function of the number of drops placed on the filter. Furthermore, this effect was related to gender, $F(4, 68) = 4.0$, $p < 0.01$. Women averaged 11.4 puffs in the "natural" condition and took between 14.3 and 16.1 puffs in the chamber. Men averaged 11.4 puffs in the "natural" condition and averaged between 11.3 and 13 puffs in the chamber. Thus, the difference between "natural" smoking and "chamber" smoking was greater for the women. There were no differences as a function of condition on the amount of time taken to smoke. Time to smoke the cigarette averaged 269 s across all conditions.

Subjective Measures

Of the seven measures rating qualities of smoking (Table 1), "draw" was the only one on which condition had a significant effect, $F(3, 51) = 9.5$, $p < 0.001$. On a scale of 0 (very hard) to 100 (very easy), subjects rated the cigarette draw with 0 drops as 66, and 56, 42, and 23 after 1, 2, and 3 drops, respectively. Post hoc analyses indicated that it was significantly more difficult to draw smoke in the 2 and 3 drop condition than in the 0 drop condition. It was also significantly harder to draw in the 3 drop condition than in the 1 drop condition. This effect was not related to gender. As shown in Table 1, ratings of drug strength decreased with increasing numbers of drops of the corn syrup solution; however, this effect did not reach the 0.05 level of significance, $F(3, 51) = 1.67$, $p < 0.10$.

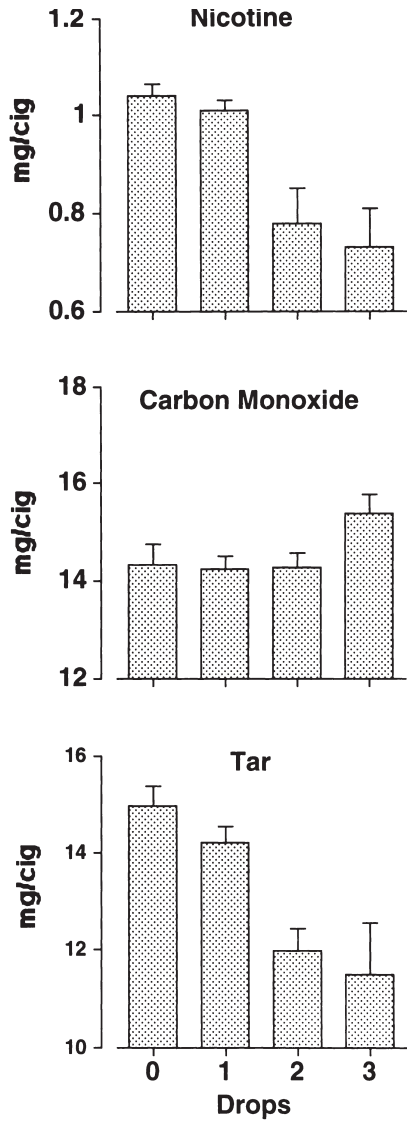

FIG. 1. Effects of corn syrup solution drops on nicotine, carbon monoxide, and tar from machine smoking a single Marlboro cigarette by methods of the Federal Trade Commission (FTC).

Biochemical Measures

As shown in Fig. 2, there was a significant dose by time interaction on plasma nicotine levels, $F(18, 306) = 4.3$, $p < 0.001$. The nicotine boost in plasma was progressively reduced as the drops of corn syrup solution increased. The mean peak increase from pre- to postsmoking was 13.3, 10.5, 9.7, and 6.0 ng/ml in the 0, 1, 2, and 3 drop conditions, respectively. Post hoc analyses showed that the nicotine boost was significantly greater in the 0 drop condition than in all drop conditions.

TABLE 1

VISUAL ANALOGS SCORES AFTER SMOKING EXPERIMENTAL CIGARETTES TREATED WITH DROPS OF CORN SYRUP SOLUTION

	Number of Drops			
Question	0	1	2	3
Satisfaction	55	51	51	49
Taste	54	45	52	44
Strength	56	51	47	36
Draw	66	56	42	23
Hotness	29	26	26	27
Like	49	41	51	38
Harshness	52	38	37	45

The table shows mean (n = 19) rating on the visual analog scales of seven subjective questions.

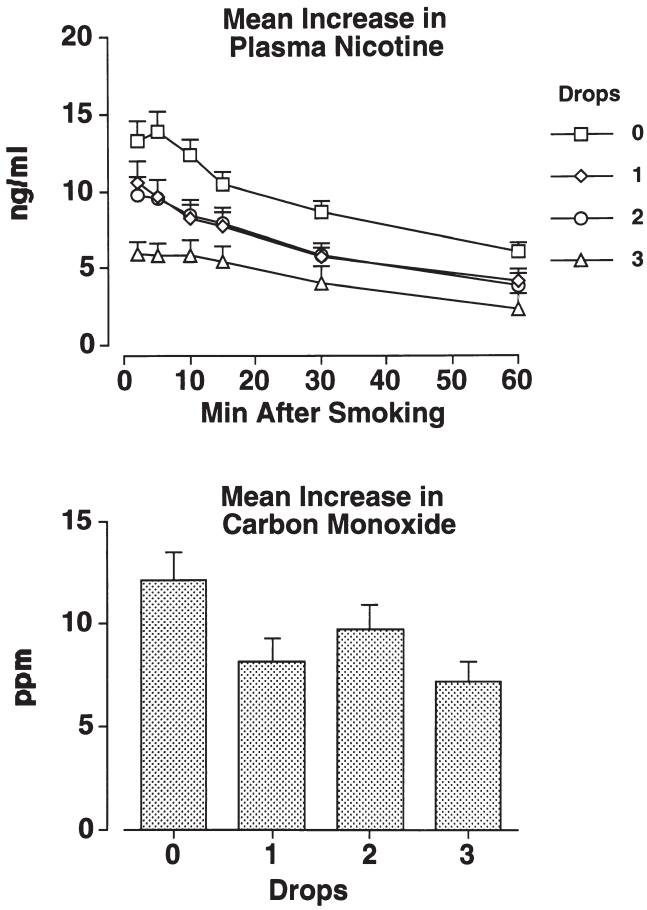

FIG. 2. Effects of corn syrup solution drops on smoking-induced increases in plasma nicotine and exhaled carbon monoxide.

Additionally, the nicotine boost in the 3 drop condition was significantly less than in the 1 and 2 drop conditions. Compared to the 0 drop condition, plasma nicotine levels remained higher for 30 min in the 1 and 2 drop conditions, and throughout the entire 60 min in the 3 drop condition. There were no gender-related effects.

There was a significant difference in exhaled CO as a function of drop condition, $F(6, 102) = 3.8$, $p < 0.01$. The CO boost from pre- to postsmoking was 12.2, 8.9, 9.7, and 7.2 ppm in the 0, 1, 2, and 3 drop conditions, respectively. Post hoc analyses showed that the CO boost was greater in the 0 drop condition than in all conditions in which drops were applied. The boost was also significantly greater in the 2 than the 3 drop condition. There were no gender related effects.

Cardiovascular Measures

Heart rate, systolic blood pressure, and diastolic blood pressure were all increased by smoking. However, no condition by time effects were found on cardiovascular measures. Heart rate increased 9.3 beats per min in the 0 drop condition and from between 5.5 and 6.6 beats per min in the 1, 2, and 3 drop conditions. Systolic blood pressure increased 8.4 mmHg in the 0 drop condition and from between 4.5 and 6.6 mmHg in the conditions in which drops were applied. Diastolic blood pressure increased 8.8 mmHg in the 0 drop condition and from between 6.9 and 8.4 mmHg in other conditions. There were no dose-related changes in cardiovascular measures as a function of gender.

Electroencephalographic Measures

None of the EEG measures examined were significantly changed as a function of drop condition. However, smoking did produce an effect on theta power at Fz that was related to gender, $F(1, 10) = 9.1$, $p < 9.05$, but was unrelated to drop condition. Theta power increased 29.9% from pre- to postsmoking among females and decreased 23.8% among males.

DISCUSSION

In the present study, the maximum filter occlusion condition (3 drops) reduced the plasma nicotine and CO boosts by 45 and 59%, respectively, as determined by biochemical measures in the subjects. In other studies where smoke dilution devices have been used nicotine and CO exposure have been systematically reduced to up to 80% (7,18). In those studies, the reduction in smoke exposure resulted in changes in smoking behavior to compensate for the reduction in nicotine delivery. For example, Henningfield and Griffiths (7) reported increased rate of puffing and total number of puffs when smoke was diluted with a ventilated filter. Similarly, Zacny and Stitzer (21) reported smoking more cigarettes, taking larger and more closely spaced puffs when nicotine exposure was reduced through brand switching. In the present study, the number of puffs taken and the time to smoke did not differ as a function of the drop condition. Several explanations for the discrepancy between our results and those of other studies are tenable. The subjects smoked a prescribed length of the cigarette (57 mm), and it may be difficult to demonstrate compensation when smoking a single cigarette. In addition, it may be difficult to adjust smoking behavior in the presence of an occlusive filter where difficulty in draw was significantly increased. The period of tobacco abstinence preceding the smoking may have been too short to engender serious attempts to regulate nicotine intake. Furthermore, the subjects knew they could smoke their own brand of cigarette immediately after the 1 h session, and they may not have been adequately motivated to obtain nicotine from the experimental cigarette. Finally, the experimental cigarette was not mentholated, but all of the subjects ordinarily smoked mentholated cigarettes. It is possible that the taste of the cigarette

was not appealing enough to induce efforts to obtain more nicotine.

Although the corn syrup solution reduced nicotine plasma levels and exhaled CO, there were orderly but not significant changes in cardiovascular measures in this study. In the 3 drop condition, there were smaller increases in heart rate and blood pressure than after smoking the untreated cigarette. Stitzer et al. (18) reported a similar result in a smoke dilution experiment. In an experimental condition that reduced nicotine and CO exposure by about 50%, the level obtained in the present study, there was a small but not significant decrease in pulse rate. Cigarette smoking by abstinent smokers typically increases EEG alpha frequency and decreases theta power (15). No such changes were observed after smoking the untreated (0 drops) cigarette or those treated with the corn syrup solution. It is possible that the 3-h tobacco deprivation that preceded the experimental session was not long enough to engender the increase in EEG theta power and decrease in alpha frequency associated with tobacco deprivation (10,15,19). The results of these studies indicate that the EEG effects of tobacco abstinence reliably appear after 12 h (overnight) tobacco deprivation although Herning et al. (9) reported some EEG changes (increased theta power) that were present within 3 h after the last cigarette.

There were few significant gender differences on the biochemical, physiological, or subjective measures of the present study. One gender related finding was that women smoked the untreated cigarette faster in the "natural" smoking situation than in the experimental smoking chamber. Another finding related to gender was the effects of the cigarettes on the production of theta power at the Fz electrode. Smoking caused the expected decrease in theta power in men but increased theta power in women. In a study of the EEG and performance effects of short-term smoking abstinence in women, Gilbert (6) reported that smoking increased theta power in the frontal midline area during a cognitive task, an area proposed to be involved in executive function (17). The gender differences in EEG activity observed in the present study may represent a functional physiological distinction between smoking in men and women. Usually, tobacco abstinence is associated with increased theta power (9,15) that is reversed by cigarette smoking (15), nicotine gum (13,14), or transdermal nicotine delivery (12).

In summary, our results indicate that the occlusive filter reduced exposure to nicotine, CO and other components of tobacco smoke. Further studies will be required to determine the general utility of this approach either as an aid to smoking cessation or relief of tobacco withdrawal symptoms. For example, the effects of the occlusive filter in a more naturalistic experimental paradigm is critically important to determine if patients would increase the number of cigarettes smoked to compensate for the reduced nicotine delivery.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the help of Marianne Chenoweth for her nursing skills and administrative contribution to this study. Special thanks for the technical help of Melissa Rohrer, Kelly Stephenson, and Kristin Liebig and to William Rosen of UltraTech Inc. for supplying the Take Out solution.

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