Effects of Different Cigarette Smoke Yields on Puffing and Inhalation: Is the Measurement of Inhalation Volumes Relevant for Smoke Absorption?

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NIL, R, R BUZZI AND K BATTIG *Effects of different cigarette smoke yields on puffing and inhalation Is the* measurement of inhalation volumes relevant for smoke absorption⁹ PHARMACOL BIOCHEM BEHAV 24(3) 587-595, 1986 -Puffing patterns (number of puffs, puff volume, puff duration, puff interval, peak pressure, peak flow, peak latency), respiratory smoke inhalation (postpuff inspiratory latency, volume and time and postpuff expiratory volume and time), and the pre- to postsmoking boost of tidal air CO concentration were analyzed in 117 regular smokers They smoked both a cigarette of the habitual brand and a second cigarette of a brand with about 40 to 50% lower machine standard smoke yields and the most similar taste quality The pre- to postsmoking CO boost remained unrelated to the smoke deliveries of the cigarettes in both comparisons (interindividual and switching) Estimated mouth intake of nicotine was strongly dependent on the smoke yield variables of the cigarettes but remained uncorrelated with CO absorption The discrepancy between mouth smoke intake and alveolar smoke absorption could not be explained by the volumes or durations of the postpuff respiratory cycle Multiple regression analyses suggested differential modes of control for the daily number of cigarettes smoked, for the patterns of puffing, for respiratory inhalation, and finally for alveolar CO absorption The results are discussed m relation to the dynamics of puffing and inhalation and their possible relevance for tobacco-related diseases

Cigarette smoke yields Ogarette puffing Cigarette smoke inhalation Nicotine titration COHb

OVER the last years most industrialized countries have witnessed a pronounced shift toward the use of lighter cigarettes Today the net effect of these changes on mouth intake of smoke and on alveolar resorption of CO and mcotine appears to be rather different A series of studies [2, 3, 4] has documented that CO and nicotine absorption remained nearly unaffected by these changes even when Including "ultra" light cigarettes Further, smoke yield measures do not or only modestly affect the dally frequency of cigarette smoking [23,27] On the other hand, although a series of studies has revealed compensation in puff volumes for differences in smoke vield, it also appears that such compensations are incomplete, accounting in general for no more than about 20% of the differences m smoke yields This fact has been estabhshed both with the puff flowmeter method and with the butt analysis technique [2,22]

Therefore, respiratory inhalation can reasonably be expected to be a better candidate for explaining CO and mcotine absorption than measures of mouth intake of smoke [11] However, so far only a limited number of small sample studies has attempted to analyze the respiratory mechanisms of smoke inhalation

The present study involved the analysis of puffing patterns and each subsequent postpuff respiratory cycle in 117

regular smokers The respiratory traces, obtained by the transthoracic impedance method and calibrated with a spirometer, were analyzed for each single puff with respect to time latencies and volume Two types of comparisons were then made, namely (a) interindividually across all subjects when they smoked their own habitual brand cigarette and (b) intraindividually for acute switching to a cigarette brand with a smoke dehvery lowered by about 50%

METHOD

Subje~ ts

Sixty-nine men and forty-eight women aged between 17 and 64 years were recruited by newspaper advertisement They were all regular smokers and reported themselves to be m good health They received contemporary per hour salaries for participating in this study

Apparatus

A puff flowmeter consisting of a cigarette holder connected with a precision pressure transducer system [7] was purchased from Projects CGC Ltd This holder did not occlude ventilations of the cigarettes, but it might have re-

FIG 1 Pattern of a single puff with the concomitant respiratory trace of a subject

duced the possibility of a manual occlusion of the ventilation holes by the subjects A digital analyzer built at the laboratory was used to transform the analog signals of the pressure transducers into digital printouts for puff volume, puff duration, puff interval, peak pressure, latency to peak pressure, and peak flow

The estimation of CO and nicotine mouth intake was computed by means of the standard machine smoking data (International Standard Organization Norm 30308), the resulting CO/nicotine yield and the total puff volume per cigarette of the subject It represents thus an extrapolation of the CO/nicotine yield by multiplying it with the relation subject's puff volume/machine puff volume

The CO analyzer, Beckman Instruments model 866, was used for measuring CO concentration in the expiratory tidal air, The expiratory air, which ts a mixture of alveolar and dead-space air, was collected m a Teflon bag during normal breathing and simultaneously analyzed with the instrument until stable CO readings were obtained This was mostly achieved within 3 to 5 min This procedure of CO analysis, First described by Rawbone *et al* [18] has the advantage of highly precise and stable CO readings which are independent of breathmg techniques It implies, however, the consequence of smaller absolute CO values than obtained with the more often used end tidal air CO analysis Respiratory movements were recorded by the transthoracic impedance method Two electrodes were fixed at the right thorax (one at the frontal thorax near the 6th rib and the second at the lateral thorax at a 90° angle to the first electrode) which continuously recorded changes in transthoracic impedance These signals were amplified and then transformed by a laboratory built analyzer into digital printouts for the latency to the first respiratory movement after a puff and for the latencies and amphtudes of both the lnspiratory and expiratory parts of the first complete respiratory cycle following a puff (Fig 1)

A dry spirometer (Hospal-Calculalr, Sandoz Pharmaceutical Dept , Hospital Supply, Basel) was used to calibrate quantitatively the inspiratory and expiratory amplitudes of the thorax Impedance signals This calibration involved the comparison of the Impedance amphtudes with the spirometer respiratory volumes across 15 breathing cycles This procedure was carried out before smoking each of the two cigarettes and served as the basis for calculating the mspiratory and expiratory volumes for each postpuff respiratory cycle All values were rounded off to 100 ml units, and all data for which the impedance/volume product moment correlation

 $*_{p}$ <0 05, $\nmid p$ <0 01, $\nmid p$ <0 001

did not reach at least 0 8 in the calibration procedure were omitted from further analysis Under these condinons, values of postpuff inspiratory latency, postpuff inspiratory volume and duration could be obtained for 97 subjects and corresponding expiratory values for 67 subjects Blood pressure and pulse rate were obtained with the module Elag Be-207-S (Cologne, FRG)

Testmg Pro~ edure

The sample of the subjects was divided Into two groups One group first smoked a cigarette of the personal brand and then the cigarette with lowered smoke yields For the other group this sequence was reversed In each case the cigarette with the lower smoke yield was also a commercial brand cigarette and was selected to be as similar as possible to the personal brand cigarette with respect to blend and taste but

Men				Women			Men vs women	
	Mean \pm SD			Mean \pm SD			t -test	
Vanable	Habitual cig	Light cig	t-test	Habitual cig	Light cig	t -test	Habitual cıg	Light cig
Total puff volume/ cig (ml)	5116 ± 2201	664 5 ± 3051	3 9‡	509 8 \pm 224 4	6191 ± 2912	$21*$		
Puff volume (ml) Peak pressure (cm H, O)	42 3 14 ₅ 士 21 2 86 \pm	50 2 16 ₃ \pm 78 22 6 \pm	30 [†]	133 414 \pm 81 234 \pm	158 470 \pm 21 6 \pm 85			
Peak flow (ml/sec) Peak latency (sec) Puff duration (sec)	348 106 \pm 0.75 \pm 024 2 18 \pm 071	106 35 ₅ \pm $0.81 \pm$ 024 $259 \pm$ 0 79	31 [†]	84 362 \pm 0.67 \pm 014 $202 \pm$ 0.52	99 37.9 \pm $0.68 \pm$ 016 $221 \pm$ 0 59		$21*$	33 [†]
Puff interval (sec) Number of puffs Postpuff inspir	$229 \pm$ 128 12.6 \pm 45 $0.39 \pm$ 048	$200 \pm$ 109 137 \pm 47 $0.35 \pm$ 0 38		$217 \pm$ 107 12 ₅ 48 \pm 0 17 \pm 0 26	$202 \pm$ 111 13 4 \pm 52 019 $016 \pm$		$2.6*$	30 [†]
latency (sec) Postpuff inspir time (sec)	$125 \pm$ 043	$128 \pm$ 0.53		1 17 \pm 042	$114 \pm$ 046			
Postpuff expir time (sec)	$187 \pm$ 066	$196 \pm$ 0 59		$182 \pm$ 084	091 $195 \pm$			
Postpuff inspir volume (1) Postpuff expir	0 ₃ 0 ₅ \pm $06 \pm$ 0 ₄	0 ₅ 06 \pm 04 06 \pm		0 ₃ 04 \pm 0 ₅ 0 ₃ \pm	0 ₃ $04 \pm$ $06 \pm$ 0 ₄			$2.5*$
volume(1) Est nicotine	08 $15 \pm$	$11 \pm$ 0 ₅	361	$12 \pm$ 0 ₆	$08 \pm$ 06	3 13 +	$2.6*$	$27+$
mouth intake (mg) Inhalation efficiency	0 18 \pm 0 27	$0.23 \pm$ 0 23		0 17 \pm 0 17	$0.32 \pm$ 023	28 ₁		
Δ tidal CO boost (ppm)	26 20 \pm	1 ₅ 24 \pm		21 \pm 14	19 20 \pm			
Subjective smoking need (mm)	\pm 25 51	47 22 \pm		48 30 \pm	41 26 \pm			
Subjective smoking satisfaction (mm)	60 28 $+$	36 21 \pm	$55+$	49 31 士	31 23 $+$	31 [†]		
Presmoking tidal inspir vol (1)	0 ₅ 0 ₂ 土	0.5 0 ₂ 士		0 ₂ 04 \pm	0 ₂ 04 \pm			

TABLE 2 AVERAGE PUFFING BEHAVIOR AND t-TEST COMPARISONS

 $*_{p}$ < 0 05, $\models p$ < 0 01, $\models p$ < 0 001

to differ from the personal brand by a 50% lower machine smoking yield of nicotine Together with a questionnaire for assessing smoking habits and alcohol and coffee consumption three packs of these lower yield cigarettes were sent to the subjects in advance to allow familianzation with the different brand For control, the subjects were required to bring 10 butts of these cigarettes to the testing session In addition, the subjects also received in advance a form to protocol time for the cigarettes smoked on the test day before arriving at the laboratory

The time protocol of the testing session which lasted 90 min was identical for all subjects and fixed as follows-Collection of the cigarette butts smoked on the test day with the corresponding time protocol,—Fixation of the thorax
impedance electrodes,—Coronary prone behavior impedance electrodes,--Coronary questionnaire,—CO analysis of tidal air,—Calibration of the thorax impedance amplitudes,—Measurement of pulse rate and blood pressure,-Assessment of the subjective need for smoking,--Smoking the first cigarette,--Subjective assessment of smoking satisfaction,—Measurement of pulse rate and blood pressure (immediately after the last putf), -CO analysis of tidal air $(5 \text{ min after the last pdf})$,--Pause $(30 \text{ min of the left})$ min),--CO analysis of tidal air,--Calibration of the thorax impedance amplitudes,-Measurement of pulse rate and blood pressure,-Assessment of the subjective need to smoke,-Smoking the second cigarette (45 min after the first cigarette),-Subjective assessment of smoking satisfaction,—Measurement of pulse rate and blood pressure,— CO analysis of tidal air $(5 \text{ min after the last pdf})$

To assess the subjective need for smokmg, a 100 mm analog scale was presented, marked at the two ends with "no need to smoke at all" and "very strong need to smoke The assessment of smoking satisfaction was correspondingly achieved with the presentation of an analog scale marked at

FIG 2 Puffing vanables averaged separately for the female, male, and whole subject sample The subjects have been classified into groups according to the machine standard nicotine yield of their habitual cigarette (left) and the lighter test cigarette (right)

the ends with "the cigarette tasted very good" and "the cigarette tasted very bad '

Data Analysis

All experimental data were punched on cards and statistically analyzed on a large-scale CDC computer using the SPSS and BMDP software systems The statistical analyses included cross-sectional correlations and comparisons of means by the *t*-test method (two-tailed) Multiple regression analyses were performed in order to evaluate the main determinants of cigarette consumption, mouth-level and alveolar-level smoke uptake The analyses were performed separately for each sex

RESULTS

Table 1 shows for each sex the averages for the smoking habit and physiological data The female subjects differed from the male subjects by significantly lower blood pressure and by smoking lighter cigarettes In all other aspects, including the daily frequency of cigarette smoking, the two sexes did not differ from each other

Means of Smoking Variables and Switching Effects

For quantitative comparisons, all puffing and respiratory data are presented in Table 2 as averages for both sexes and both types of cigarettes Switching to the lighter cigarette with about 50% less smoke yield produced in both sexes an increase of the puff volumes by about 20%, but no significant changes for any of the measures of respiratory inhalation The net decrease in mouth intake of CO and nicotine per cigarette thereby amounted to about 30% Both sexes recognized the low delivery cigarette immediately and rated it significantly less satisfactory than the habitual cigarette

Cross-Sectional Analyses

The results of the cross-sectional analyses (Kendall τ) are presented in Figs 2 and 3 For illustrative purposes the subjects have been classified into groups of equal size according

FIG 3 Inhalation variables and pre- to postsmoking heart rate difference, averaged separately for the female, male, and whole sample The subjects have been classified into groups according to the machine standard nicotine yield of their habitual cigarette (left) and the lighter test cigarette (right)

Dependent vanable	Original set of independent variables	Sample	Subset of independent variables for best regression	Γ	\mathbf{R}	F
Cig /day	Nicotine yield Condensate yield	$male + female$				
	CO yield Smoke pH	male				
		female	Smoke $pH(0.56†)$ CO yield $(0.68*)$ Nicotine yield (-0.36)	0 53	022	$(3,38)=4.95\dagger$
CO baseline	Nicotine yield Condensate yield CO yield	$male + female$	$Cig / day (0.52+)$ Nicotine yield $(0.20*)$	0 53	0 27	$(2\;112)=22\;34\ddagger$
	Smoke pH Cig /day	male	$Cig / day (0.41\dagger)$ Condensate yield (0 35†)	0 50	0 21	$(2,60)=9.47\overline{z}$
		female	$Cig / day (0.40+)$ CO yield (0.49) Condensate yield (-0.35)	0 51	020	$(3,38)=4.50+$
Puff volume/ cig	Nicotine yield Condensate yield CO yield	$male + female$	CO baseline $(0\ 31\ddagger)$ CO yield $(-0.23*)$	0 36	011	$(2,102)=7$ 42‡
	Smoke pH Cig /day CO baseline	male	CO baseline $(0.48\ddagger)$ CO yield $(-0.34*)$ Smoke pH (-0.22) $Cig / day (-0.18)$	047	0 17	$(4,58) = 4.08\dagger$
		female	Nicotine yield (-0.31^*)	0 3 1	0 0 7	$(1,40)=4$ 31*
Postpuff inspiratory volume/cig (PPIV)	Nicotine yield Condensate yield CO yield Smoke pH Cig /day	$male + female$	Puff vol / cig (0 46‡) CO yield $(0.30*)$ Smoke pH (-0.19) CO baseline (-0.16)	0 55	0 26	$(4,78)=8$ 34‡
	CO baseline Puff volume/cig Nicotine mouth intake	male	CO mouth intake (0 50‡) Smoke pH (-0.26)	064	0 39	$(2,49) = 1733\ddagger$
	CO mouth intake	female				
Δ tidal CO	Nicotine yield Condensate yield CO vield Smoke pH Cig /day CO baseline	$male + female$	CO baseline $(0.40\ddagger)$ Nicotine yield (-0.25) PPIV (0 19) Nicotine mouth intake (0 23) Cig /day $(0 15)$	050	0 20	$(5,85)=5,62\ddagger$
	Puff volume/cig Nicotine mouth intake CO mouth intake PPIV	male	CO baseline $(0.51†)$ PPIV (0 42 ⁺) $Cig / day (-0.28)$ Condensate yield (-0.25) Smoke $pH(022)$	0 56	0 25	$(5.47) = 4.40^+$
		female	Puff volume/cig (0.36^*) CO baseline (0 26)	048	0 19	$(2,44)=6,54\dagger$

TABLE 3 MULTIPLE REGRESSION ANALYSES

 $*_{p}<0$ 05, $\nmid p<0$ 01, $\nmid p<0$ 001

to the nicotine yield of their habitual brand (left panel) and reclassified according to the nicotine yield of the lighter cigarette (right panel) smoked for comparison The correlation coefficients shown m the figures give evidence for some compensation for differing nicotine yields, mainly among the puffing variables However, mouth nicotine intake, mouth CO intake, and the total puff volumes per cigarette still correlated significantly with the smoke yield measures of the cigarettes as shown in the bottom panel of Fig 2

The volumes of the first postpuff respiratory cycle (mhalation volumes) are shown in Fig 3 for the same sample splits Inhalation volumes were smaller for decreasing cigarette strength, but this trend was evident only across the habitual cigarettes and not across the lighter cigarettes smoked for comparison The postpuff expirations (smoke exhalation volumes) were also smaller for lighter cigarettes, but in this case the relation became significant for both cigarette types The pre- to postsmoklng differences in tidal air $CO (= \Delta$ tidal CO) were nearly identical for all subsamples As a result "inhalation efficiency" defined as Δ tidal CO in ppm per unit of CO mouth intake [27] increased rather consistently and strongly with decreasing smoke yields

Multiple Regression Analwe~

A series of multiple correlation analyses were computed In order to delineate more closely the interdependence of the main variables of smoking behavior This was achieved with the BMDP 9R software program, which allows to search for the combination of independent variables producing the most appropriate multiple regressions As criteria for the best multiple regressions, both small Cp values and high amounts of explained variance were adopted [28]

Table 3 lists the different multiple regressions in a hierarchical order beginning with the evaluation of the determinants of daily cigarette consumption and ending with determinants of alveolar CO uptake by including in each step all variables already used in the previous steps

According to this analysis dally cigarette consumption was rather independent of the smoke yield variables in men but not in women For pretest baseline tidal air CO a rather consistent dependence on both the smoke yields and daily consumption was obtained The variations in total puff volume per cigarette were relatively poorly determined with only small amounts of variance being explained by any of the multiple regressions It was best predicted by tidal air CO basehne and the smoke CO yields in the whole sample and in the male subsample, while, interestingly, nicotine yield seemed to play a role among the female subsample only

The postpuff inspiratory volumes (PPIV) were statistically related to different subsets of variables in the whole sample and the male subsample Positive correlations were obtained with cigarette smoke yield measures in the whole sample and in the male subsample, but not in women

 Δ Tidal CO was correlated again in a sex differentiated manner CO baseline played a significant role in the whole sample and in the male subsample The postpuff inspiratory volumes, which were expected to play an important role, did so in a significant manner in the males only, but neither in the females nor in the whole sample In contrast, in the females the puff volumes and to a lesser extent CO baseline were the only variables contributing to the explanation of Δ tidal CO

In addition, a limited set of univariate Kendall correlations were computed across the different inhalation measures Subjective depth of inhalation correlated positively

with Δ tidal CO (t=0 27), $p<0$ 01) but not with PPIV, and PPIV did not correlate with Δ tidal CO

DISCUSSION

The aim of this study was to evaluate in a cross-sectional and switching paradigm the interactions of cigarette smoke yields with puffing and lnhalatory patterns by using a rather large subject sample The analyses of puffing patterns were based on the cigarette holder flowmeter method [7] Although this method has been validated by comparisons with a pyrometer method [10], It was shown to intensify puffing behavior [26] However, changes in cigarette design resulted in comparable changes in puffing behavior when measured with a holder or an inductive plethysmographic cheek coil [26] Statistical analyses were performed separately for the two sexes Although puffing and inhalation patterns seemed to be differentially influenced in the two sexes as suggested earlier [2], the differences are rather difficult to interpret

The present study mdlcates that alveolar absorption of CO is generally independent of cigarette strength as determined by smoke yields for CO, nicotine, and condensate This was the case both for the cross-sectional comparison between smokers of different cigarettes, including also a rather large proportion of smokers with "ultra" light cigarettes, and when these smokers switched within the same test session to a cigarette with smoke yields lowered by about 40 to 50% This is in general agreement with a number of previous studies [2, 3, 17, 19]

A different picture was obtained for the estimated mouth smoke intake These measures do not take into account modulatory effects of puffing intensity on smoke deliveries [6,21], however, on the average they turned out to be highly dependent on the smoke yields of the cigarettes in the crosssectional comparison and they also decreased significantly when the smokers switched to the lighter cigarettes Therefore. the observed compensatory increases of puffing volumes in response to decreasing smoke dehverles were by far not complete and thus cannot explain the near complete compensation seen for alveolar CO uptake or heart rate elevation as a relative index of nicotine intake [15,25]

Similar dissociations between mouth intake of smoke and alveolar intake have been observed in other switching studies [12,20] In the Russell *et a/* study [20], postsmoking COHb levels seemed to be unaffected by switching to hghter cigarettes, as seen in the present study, while plasma nicotine levels and estimated mouth nicotine intake obtained by butt analyses were diminished

Interestingly, inhalation volumes, although considered as a main factor in alveolar smoke uptake [11,18], were not changed In a compensatory manner by switching to the lighter cigarette Furthermore, the failure of such a compensatory change also became apparent considering the development of the postpuff inspiratory volumes (inhalation volume) in the cross-sectional comparison

The observed trend toward a positive relation between inhalation volumes and smoke yields of the cigarettes may at first glance be directly opposite to what one might expect However, in a speculative manner, one could also expect that the smoker tends to dilute concentrated smoke by increasing postpuff inspiration volumes At this stage it should also be remembered that mouth intake of smoke and subsequent inhalation are two highly independent steps [5,26] This is also particularly evident from the multiple regression analysis presented in this study and might thus be one reason

for the observed differential effect of varying smoke deliveries on puffing, respiratory inhalation patterns and alveolar CO absorption According to this two-step hypothesis. the smoker fills his mouth with a variable amount of smoke, thereby manipulating smoke concentrations to some extent by means of an appropriate puffing pattern (to fulfill his gustatory needs²), and subsequently inhales a variable bolus of this smoke adequately diluted by air (to control for sensory $irritation$ of the tracheobronchial mucosa^{2}) Finally, the positioning of the smoke into the inspiratory air bolus might further determme whether the smoke reaches merely the upper dead space or also the lower alveolar space of the respiratory system where nicotine and CO are efficiently absorbed [8]

Only a few attempts have been made so far to measure and estimate the depth of inhalation by using different techniques for the registration of respiratory movements Strain gauge pneumograms were used by Rawbone *et al* [18] and Herning *et al* [13], yielding spirometrically calibrated values of the mhalatton volumes, and by Nil *et al* [17], using a qualitative score as a measure of puff positioning within the ventilatory cycle Guillerm and Radziszewski [10] and Herning *et al* [13] measured inhalation volumes by spirometer calibration of transthoracic impedance signals, as in the present experiment, and Tobin and Sackner [26] used the method of inductive plethysmography in a similar way The most precise and also most elaborate method for the concomitant registration of puffing and respiration has recently been descrtbed by Adams *et al* [1] using a head and arm-out whole body volume displacement plethysmogram The results obtained in the above mentioned studies generally showed highly stable individual patterns of puffing and inhalation but also showed only relatively weak positive relations between the measures of the inhalation volumes and indexes of alveolar smoke uptake, such as plasma mcotme or COHb boosts As in the present experiment, Adams et al [1] showed that the depth of inhalation was much less predic-

tive in a multiple regression analysis for alveolar CO uptake than expected Switching studies using only a limited number of subjects have also failed so far to show significant compensatory adaptions of the depth of inhalation [14,26] or did not analyze the data in this direction [13] This is in general agreement wtth the fatlure of this large scale study to find significant switching effects on any of the inhalatory parameters measured This study further showed that inhalation efficiency could not be explamed by the depth of inhalatton, and thus, as suggested by Adams *et al* [1], the relevance of inhalation volume measures has to be questioned with respect to their predictive value for alveolar smoke uptake

However, although the dynamics of smoke inhalation are sttll poorly understood, they remam of particular relevance for their presumed relation to tobacco-related diseases So far epidemiological studies relied, for this particular aspect of smokmg, on self-reports rather than on objective measures such as mouth intake of smoke, CO or mcotine absorption, and the outcomes of such studies are equivocal Some epidemiological studies reported increased risks for lung carcinoma in inhalers [16], whereas other reported risk increases for noninhalers $[9,14]$ These discrepancies might be understood m the hght of the well-documented fact, also observed in the present study, that self-assessments of inhalatlon tend to be rather poorly related to the outcome of objective measures [24]

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