Effect of chronic and acute cigarette smoking on the pharyngo-upper oesophageal sphincter contractile reflex and reflexive pharyngeal swallow

K Dua, E Bardan, J Ren, Z Sui, R Shaker

Abstract

Background—Cigarette smoking is known to affect adversely the defence mechanisms against gastro-oesophageal reflux. The effect of smoking on the supraoesophageal reflexes that prevent aspiration of gastric contents has not been previously studied.

Aims—To elucidate the effect of cigarette smoking on two of the supraoesophageal reflexes: the pharyngo-upper oesophageal sphincter (UOS) contractile reflex; and the reflexive pharyngeal swallow.

Methods—Ten chronic smokers and 10 non-smokers were studied, before and 10 minutes after real or simulated smoking, respectively. UOS pressure and threshold volume for the reflexes were determined using a UOS sleeve assembly. Two modes of fluid delivery into the pharynx were tested: rapid injection and slow injection.

Results—For both rapid and slow injections, the threshold volume for triggering the pharyngo-UOS contractile reflex was significantly higher in smokers than in non-smokers (rapid: smokers 0.42 (SE 0.07) ml, non-smokers 0.16 (0.04) ml; slow: smokers 0.86 (0.06) ml, non-smokers 0.38 (0.1) ml; p<0.05). During rapid injection, the threshold volume for reflexive pharyngeal swallow was higher in smokers (smokers 0.94 (0.09) ml, non-smokers 0.46 (0.05) ml; p<0.05). Acute smoking further increased the threshold volume for the pharyngo-UOS contractile reflex and reflexive pharyngeal swallow during rapid injection.

Conclusions—Smoking adversely affects stimulation of the pharyngo-UOS contractile reflex and pharyngeal reflexive swallow. These findings may have implications in the development of reflux related respiratory complications among smokers.

(Gut 1998;43:537–541)

Keywords: smoking; supraoesophageal reflexes; pharyngo-upper oesophageal sphincter contractile reflex; reflexive pharyngeal swallow; airway protection; gastro-oesophageal reflux

A number of supraoesophageal reflexes have been proposed to help prevent aspiration of gastric contents. These reflexes enhance the physical barriers against entry of refluxate into the pharynx, such as the oesophageo-upper oesophageal sphincter (UOS) and the pharyngo-UOS contractile reflexes; close the introitus to the trachea, as with oesophagoglottal and pharyngoglottal closure reflexes; or result in pharyngeal volume clearance as well as airway closure, as seen during reflexive pharyngeal swallow. Cigarette smoking is known to affect adversely the defence mechanisms against gastro-oesophageal reflux disease (GORD). However, its effect on the supraoesophageal reflexes described above has not been previously studied. Our aim in the present study was to elucidate the effect of chronic and acute smoking on two of these supraoesophageal reflexes: the pharyngo-UOS contractile reflex, and reflexive pharyngeal swallow.

Methods

We studied 10 healthy chronic smokers (mean age 34 (SD 5) years; six males) and 10 healthy non-smokers (mean age 33 (8) years; five males) in the sitting upright position. The protocol was approved by the Human Research Review Committee of the Medical College of Wisconsin, and study subjects gave informed consent. Smokers were defined as those with a history of smoking one or more packs of cigarettes per day for at least two years. Non-smokers were those who never smoked or occasionally smoked but had stopped over two years ago. Smokers were instructed to abstain from smoking for 12 hours prior to the study. We then studied them before and 10 minutes after smoking two cigarettes. The 10 minute interval after smoking was given to allow the pharyngeal temperature to return to baseline. Non-smokers were studied before and 10 minutes after simulated smoking of two unlit cigarettes. The duration of real/simulated smoking in each volunteer was kept to 15 minutes.

To monitor baseline UOS pressure and UOS response to pharyngeal water stimulation, and to determine the threshold volume for reflexive pharyngeal swallow, we adopted the method described previously. We used an UOS sleeve assembly (6 × 0.6 × 0.4 cm; Dentsleeve, Adelaide, Australia) that had recording ports at the proximal and distal ends of the sleeve for manometric positioning. It also incorporated an injection port located 2 cm proximal to the sleeve device and two oesophageal ports located 5 and 7 cm apart. To prevent the possibility of anaesthetising the pharynx, the nasal passage was lubricated with a non-anaesthetic jelly (Surgilube, E. Fougera & Co., Atlanta Inc., Melville, New York), applied with a cotton swab. The sleeve assembly was passed transnally and positioned within the UOS such that...
the injection port (the distal pharyngeal port, immediately above the sleeve segment) was oriented posteriorly and situated 2 cm above the UOS high pressure zone (fig 1). The pharyngeal, oesophageal, and sleeve ports were connected to pressure transducers in line with a minimally compliant pneumohydraulic system (Arndorfer Medical Specialties, Green-dale, Wisconsin). With this arrangement, the onset and offset of water injection, UOS pressure, and oesophageal pressures were recorded on chart paper that was run at a speed of 25 mm/s. To avoid stimulation of swallowing, the pharyngeal ports (including top of the sleeve) were not perfused after the sleeve assembly was positioned. Studies were then performed following a 10 minute adaptation period. Rate of spontaneous swallowing per minute was then determined by a five minute observation period and this was repeated at the end of the study. The UOS sleeve assembly was used in the present study for several reasons. The shape of the UOS sleeve conforms with that of the UOS opening. Once in position, the sleeve prevents axial rotation of the UOS catheter. As a result of this, the sleeve consistently measures the anterior-posterior pressure within the UOS and the pharyngeal water injection port is always maintained in the posterior orientation. Being 6 cm long, the sleeve can continuously record the UOS pressure, even during longitudinal UOS movement as observed with swallowing. Use of a side hole catheter may have given altered results for the above reasons and therefore was not used. The UOS sleeve assembly does have a slower response rate; in

Figure 1  Diagram of the manometry sleeve catheter positioned across the UOS.
Within and between group comparisons were done using paired and unpaired t tests and analysis of variance. Bonferroni correction was applied for multiple comparisons. Values are given as mean (SE) unless stated otherwise.

Results

RATE OF SPONTANEOUS SWALLOWS

The rate of spontaneous swallows was similar between non-smokers and smokers (1.4 (0.2) and 1.5 (0.2) per minute respectively). However, real, but not simulated smoking of two cigarettes resulted in a significant increase in the spontaneous swallowing rate (p<0.05; fig 2).

PHARYNGO-UOS CONTRACTILE REFLEX

Except for one non-smoker and two smokers, at threshold volume, rapid or slow injection of water into the pharynx directed posteriorly resulted in an increase in UOS pressure (fig 3). Smoking of two cigarettes abolished the pharyngo-UOS contractile reflex in three additional smokers (one during rapid injection and two during slow injection). No similar effect was seen after simulated smoking of two unlit cigarettes by non-smokers. Results presented below exclude those in whom the pharyngo-UOS reflex could not be elicited and comparison is made between those in whom the reflex was triggered before and after smoking.

For both rapid and slow injections, the threshold volume required to trigger the pharyngo-UOS contractile reflex was significantly higher in smokers compared with non-smokers (p<0.05). Acute smoking of two cigarettes by smokers further increased the threshold volume required to trigger the reflex by rapid water injection (before smoking 0.42 (0.07), after smoking 0.68 (0.09) ml; p<0.05). For slow water injection, although the threshold volume further increased following smoking, the difference did not reach statistical significance (before smoking 1.0 (0.13) ml; NS). Simulated smoking of two unlit cigarettes by non-smokers did not significantly change the threshold volume for triggering the pharyngo-UOS contractile reflex by either rapid or slow injections (rapid: before simulated smoking 0.16 (0.04), after simulated smoking 0.24 (0.07) ml; slow: before simulated smoking 0.38 (0.1), after simulated smoking 0.38 (0.07) ml; NS; fig 4).

The threshold volume of water required to trigger the pharyngo-UOS contractile reflex by slow water injection in both non-smokers and chronic smokers, was significantly higher compared with rapid water injection (non-smokers: rapid 0.16 (0.04), slow 0.38 (0.1) ml, p<0.05; smokers: rapid 0.42 (0.07), slow 0.87 (0.05) ml, p<0.05; fig 4).

In non-smokers, the time interval between the onset of water injection and the onset of change in UOS pressure (latent period) was 0.6 (0.07) seconds for rapid, and 6.4 (1.4) seconds for slow water injections. In smokers, although there was a trend for a longer interval period (rapid: 1.4 (0.2), slow 8.2 (1.8) seconds), this difference did not reach statistical significance when compared with non-smokers. For both rapid and slow water injections, the latent period did not change significantly after simulated (in non-smoker group) or real (in smoker group) smoking. However, in both non-smokers and smokers, the latent period was significantly longer for slow injections compared with rapid injections (p<0.05).

The percentage rise over the basal UOS pressure following pharyngeal stimulation by
both rapid and slow water injections was similar in smokers and non-smokers (smokers: rapid—before smoking 31 (13)%, after smoking 44 (19)%; slow—before smoking 31 (12)%, after smoking 47 (14)%; non-smokers: rapid—before simulated smoking 60 (10)%, after simulated smoking 51 (11)%; slow—before simulated smoking 66 (14)%, after simulated smoking 64 (19)%).

REFLEXIVE PHARYNGEAL SWALLOW
As shown in fig 5, in non-smokers and smokers, the threshold volume required to trigger reflexive pharyngeal swallow was significantly higher for slow water injection compared with rapid injection (non-smokers: rapid 0.46 (0.05), slow 1.1 (0.1) ml, p<0.05; smokers: rapid 0.94 (0.09), slow 1.4 (0.1) ml, p<0.05). For rapid water injection, this threshold volume was significantly higher in smokers compared with non-smokers (smokers 0.94 (0.09), non-smokers 0.46 (0.05) ml, p<0.05). After acute smoking of two cigarettes, the threshold volume further increased (after smoking 1.5 (0.09) ml, p<0.05). A similar increase was not seen after simulated smoking by the non-smoker group (post-simulated smoking 0.48 (0.04) ml, NS). However, contrary to rapid water injection, in both smokers and non-smokers, the threshold volume required to trigger reflexive pharyngeal swallow by slow pharyngeal water injection prior to real or simulated smoking was similar to that following real or simulated smoking respectively.

Discussion
In this study we determined the adverse effect of cigarette smoking on the pharyngo-UOS contractile reflex and reflexive pharyngeal swallow. The pharyngo-UOS contractile reflex and reflexive pharyngeal swallow are among a number of supraoesophageal reflexes that have been proposed to help prevent aspiration of gastric contents. These reflexes: enhance the physical barriers against entry of refluxate into the pharynx, namely the oesophago-UOS and pharyngo-UOS contractile reflexes; close the introitus to the trachea, such as the oesophagoglottal and pharyngoglottal closure reflexes; or result in pharyngeal volume clearance as well as airway closure, such as reflexive pharyngeal swallow. The adverse effects of smoking on the defence mechanisms against gastro-oesophageal reflux such as lowering of upper and lower oesophageal sphincter pressures, increased frequency of failed secondary peristalsis, impaired oesophageal acid clearance, and decrease in salivary base output, as well as its negative effect on gastric emptying have been described previously. Findings of the present study elucidate yet another area of the upper gastrointestinal tract on which cigarette smoking exerts a negative effect. The mechanism responsible for these effects of smoking is currently not known. A significantly higher volume of water was required in chronic smokers to trigger the pharyngo-UOS contractile reflex and reflexive pharyngeal swallow compared with non-smokers. Furthermore, acute smoking of two cigarettes by smokers significantly increased the threshold volume required to trigger these reflexes during rapid water injection and abolished the pharyngo-UOS contractile reflex in one subject during rapid water injection and in two subjects during slow water injection. These negative effects of smoking may be due its effect on the sensory afferent branch of these reflexes. However, the possibilities of a central mechanism and/or a motor effect cannot be excluded. It is unlikely that pharyngeal temperature changes during smoking could have caused the above effect, as we allowed a 10 minute interval between completion of smoking and estimation of threshold volumes for the above reflexes. Similarly it is unlikely that the above effect could be secondary to the
subject being more relaxed or adapted to the
manometric catheter during the second half of the
study compared with the first half, as no
significant difference in the threshold volumes
was noted before and after simulated smoking.
It is possible that cigarette smoking may alter
the concentration and/or function of the pha-
ryngeal sensory nerve endings resulting in a
higher threshold volume for pharyngo-UOS
contractile reflex and reflexive pharyngeal
swallow. Nicotine has been shown to affect
adversely the oesophageal mucosa by produc-
ing free radicals, resulting in oxidative stress,
and by inhibiting sodium transport. Ciga-
rette smoking may have similar effects on the
pharyngeal mucosa leading to alteration in the
function of the pharyngeal sensory nerve
endings.
In the present study, the frequency of
spontaneous swallowing was similar between
non-smokers and smokers. Acute real but not
simulated smoking significantly increased the
frequency of spontaneous swallowing. Earlier
studies have suggested that smoking may
decrease salivary output. Although oral
manipulation inherent with cigarette smoking
causes hypersalivation, it is unlikely that
excessive salivation accounted for the
increased frequency of spontaneous
swallowing as this was not observed during
simulated oral manipulation of unlit cigarettes
by non-smokers. Furthermore, swallow
frequency was measured before and after
completion of smoking and not during the act
of smoking. It is possible that the “irritant”
effect of cigarette smoke on the oral/
pharyngeal mucosa may have been responsible for
the observed increase in the frequency of spontaneous swallowing, or, alternatively, this
could be secondary to a central effect of
nicotine.
In summary, in chronic smokers the thresh-
old volume for triggering the pharyngo-UOS
contractile reflex and reflexive pharyngeal
swallow is significantly higher compared with
that in non-smokers. Acute smoking of ciga-
rettes further affects these reflexes adversely.
These findings identify yet another deleterious
effect of cigarette smoking that can further
weaken the airway protective mechanisms
against aspiration. These findings may have
implications in the pathogenesis of reflux
related respiratory complications among
smokers.

This work was supported in part by NIH grant no.
RO1-DC00669, Merit Review Grant from the Department
of Veterans Affairs, and Institutional Research Grant from the
Medical College of Wisconsin. Part of this work was presented
at the Research Forum during Digestive Disease Week in May
1995 and published in abstract form (Gastroenterology

1 Reynolds RPE, Effer GW, Bendeck MP. The upper esophag-
alen sphincter in the cat: the role of central innervation
assessed by transient vagal blockade. Can J Physiol
and quantification of a pharyngo-UES contractile reflex in
and anesthesia on the pharyngo-UES contractile reflex in
pharyngo-UES contractile reflex in humans. Am J Physiol
1997;266:G654–8.
reflex: a mechanism of airway protection. Gastroenterology
6 Shaker R, Ren J, Medda B, et al. Identification and charac-
terization of the esophagoglottal closure reflex in a feline
pharyngeal water stimulation: evidence for a pharyngogl-
tal closure reflex [abstract]. Gastroenterology 1994;106:
A58.
8 Nishino T, Takizawa K, Yokokawa N, et al. Depression of
the swallowing reflex during sedation and/or relative
analgesia produced by inhalation of 50% nitrous oxide in
9 Nishino T. Swallowing as a protective reflex for the upper
10 Shaker R, Ren J, Zamir Z, et al. Effect of aging, position, and
temperature on the threshold volume triggering pharyngeal
11 Tiffin A, Shaker R, Ren J, et al. Inhibition of resting lower
esophageal sphincter pressure by pharyngeal water stimula-
12 Scott AM, Kellow JE, Shuter B, et al. Effect of cigarette
smoking on solid and liquid intragastric distribution and
13 Johnson RD, Horowitz M, Maddox AF, et al. Cigarette
smoking and rate of gastric emptying: effect on alcohol
14 Dua K, Bardan E, Xie P, et al. Effect of chronic and acute
cigarette smoking on upper and lower esophageal sphinc-
ters and on secondary esophageal peristalsis. Gastroenterol-
15 Kahrlas PJ, Gupta RR. Mechanisms of acid reflux
16 Chattopadhyay DK, Greaney MG, Irwin TT. Effect of ciga-
rette smoking on the lower oesophageal sphincter. Gut
17 Stanciu C, Bennett JR. Smoking and gastro-oesophageal
18 Dennish GW, Castell DO. Inhibitory effect of smoking on
the lower esophageal sphincter. N Engl J Med 1971;284:
1136–7.
19 Ralil PS, Wright RA. Transdermal nicotine and gastro-
20 Kahrlas PJ, Gupta RR. The effect of cigarette smoking on
salivation and esophageal acid clearance. J Lab Clin Med
21 Rattan S, Goyal RK. Effect of nicotine on the lower esopha-
esophageal-pharyngeal acid regurgitation [abstract]. Gastro-
enterology 1991;100:A494.
production in rat esophageal mucosa induced by nicotine.
24 Orlando RC, Bryson JC, Powell DW. Effect of cigarette
smoke on esophageal epithelium of the rabbit. Gastroenter-
ology 1986;91:1536–42.
Effect of chronic and acute cigarette smoking on the pharyngo-upper oesophageal sphincter contractile reflex and reflexive pharyngeal swallow

K Dua, E Bardan, J Ren, Z Sui and R Shaker

Gut 1998 43: 537-541
doi: 10.1136/gut.43.4.537

Updated information and services can be found at:
http://gut.bmj.com/content/43/4/537

These include:

References
This article cites 21 articles, 4 of which you can access for free at:
http://gut.bmj.com/content/43/4/537#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Gastro-oesophageal reflux (351)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/