The Journal of Laryngology & Otology

cambridge.org/jlo

Effect of bidi smoking on nasal mucociliary clearance: a comparative study

B Paul[1], S S Menon[2], R Vasthare[1], R Balakrishnan[2] and S Acharya[1]

[1]Department of Public Health Dentistry, Manipal College of Dental Sciences, Manipal, Mahe, India and [2]Department of Otorhinolaryngology, Kasturba Medical College, Manipal, Mahe, India

Main Article

Dr S Acharya takes responsibility for the integrity of the content of the paper

Cite this article: Paul B, Menon SS, Vasthare R, Balakrishnan R, Acharya S. Effect of bidi smoking on nasal mucociliary clearance: a comparative study. *J Laryngol Otol* 2019;**132**: 1077–1082. https://doi.org/10.1017/S0022215118002049

Accepted: 17 July 2018
First published online: 20 November 2018

Key words:
Mucociliary Clearance; Nose; Methylene Blue; Tobacco

Author for correspondence:
Dr Shashidhar Acharya,
Department of Public Health Dentistry,
Manipal College of Dental Sciences,
Manipal Academy of Higher Education(Mahe),
Manipal, Karnataka,
India 576104
E-mail: sh.acharya@manipal.edu
Fax: +91 820 257 1966

Abstract

Objective. To compare nasal mucociliary clearance in adult non-smokers, cigarette smokers and bidi smokers using the methylene blue dye test.

Methods. The study sample consisted of 20 non-smokers, 20 cigarette smokers and 20 bidi smokers (age range, 20–40 years). A single drop of the methylene blue dye was placed at the anterior end of the inferior turbinate of the participants' nasal cavity. The distance travelled by the methylene blue in 15 minutes inside the nasal cavity was measured. Nasal mucociliary clearance of the three groups was compared using the Kruskal Wallis test.

Results. Nasal mucociliary clearance was significantly decreased in bidi smokers as compared to cigarette smokers and non-smokers ($p < 0.05$). Multivariate analysis revealed a significant association between nasal mucociliary clearance and bidi smoking, number of cigarettes or bidis smoked per day, and pack-years (all $p < 0.05$).

Conclusion. Nasal mucociliary clearance measurement is a simple and useful index for assessing the effect of smoking on the mucociliary activity of nasal mucosa.

Introduction

Tobacco, in both smoking and smokeless form, is a major cause of morbidity and mortality worldwide.[1] India has a substantial share of the global burden of tobacco-induced disease and death, accounting for over a million deaths per year.[2] In India, approximately half of tobacco consumption is in the form of bidis.[3] At present, India is the fourth largest producer of tobacco, and second largest cigarette and bidi producer in the world, after China.[4]

The prevalence of smoking bidi or the Indian cigar is quite high in rural India and among the lower socioeconomic status population.[5] A bidi contains about 0.2 g sun-dried and processed tobacco flakes, rolled in a tendu leaf (*Diospyros melanoxylon*) and tied together by a cotton thread.[6] Apart from causing an incredible number of diseases, including oral and lung cancer, chronic bronchitis, emphysema, cerebrovascular accidents, and numerous potentially malignant diseases, the components of smoke, such as nicotine, hexamine, ammonia and formaldehyde, are held to be widely responsible for the phenomenon of cilia toxicity.[7–9]

Cilia are rod-shaped organelles that are present in almost all the cells in the human body, primarily in the respiratory tract, lungs and middle ear. They are only about 0.1 mm in length, and possess a rhythmic waving or beating motion, with a frequency of 7–16 Hz.[10] Nasal mucociliary clearance is essentially a protective feature, in which the cilia present in the nasal mucosa are instrumental in eliminating dust particles and other foreign bodies from the nasal cavity towards the nasopharynx. They work successfully to keep the airways free of mucus and dirt, allowing individuals to breathe easily without irritation.

Apart from smoking, disruption in nasal mucociliary clearance is seen in those with diseases such as chronic obstructive pulmonary disease (COPD), bronchial asthma, cystic fibrosis, rhinosinusitis and deviated nasal septum. It is also known that tobacco smoke alters the viscoelastic nature of mucus and further decreases nasal mucociliary clearance.[11]

Studies by Stanley *et al.*[12] and Baby *et al.*[13] observed the mean nasal mucociliary clearance time (saccharine transit time) as 12 minutes. A nasal mucociliary clearance time of over 30 minutes was considered abnormal and signalled an increased chance of morbidity. Ewert[14] observed a decreased rate of dye transportation across a specified area of anterior septal mucosa in healthy smokers compared to non-smokers. However, Quinlan *et al.*[15] reported no distinction between smokers and non-smokers in the mucociliary clearance of insoluble radiolabelled resin particles placed on the inferior nasal turbinate.

The existing literature does not show any conclusive evidence of the effect of bidi smoke on nasal mucociliary clearance. This study aimed to compare nasal mucociliary clearance in adult non-smokers, cigarette smokers and bidi smokers using the methylene blue dye test.

Table 1. Demographic, socioeconomic and tobacco exposure data, by group

Parameters	Non-smoker*	Cigarette smoker†	Bidi smoker‡	*P*-value
Age (mean (SD); years)	29.3 (6.25)	31.2 (5.42)	30.2 (6.77)	0.625
Number of years' formal education (mean (SD))	16.5 (4.2)	18.05 (2.14)	11.6 (2.01)	<0.05**
Marital status (*n*)				0.755
– Unmarried	12	12	6	
– Married	8	8	14	
– Widowed	0	0	0	
– Separated or divorced	0	0	0	
Occupation (*n*)				<0.05**
– Professional or semi-professional	9	16	0	
– Semi-skilled or unskilled	4	0	20	
– Student	7	4	0	
– Other	0	0	0	
Bidis or cigarettes smoked per day (*n*)				<0.05**
– ≤5	20	0	0	
– 6–10	0	16	10	
– 11–20	0	4	9	
– ≥21	0	0	1	
Pack-years (mean (SD))	0 (0)	4.63 (2.74)	7.5 (5.1)	<0.05**
Mean nasal mucociliary clearance (mean (SD); mm)	67.89 (4.10)	67 (5.48)	59.25 (12.38)	<0.05**

SD = standard deviation. *n = 20; †n = 20; ‡n = 20. **P < 0.05 considered statistically significant

Materials and methods

This cross-sectional study was carried out in the Department of Otorhinolaryngology at Kasturba Medical College, Manipal, in India, between August 2016 and September 2017. Participants were classified into three categories depending on whether they were a non-smoker, cigarette smoker or bidi smoker.

Sample size calculation was determined by estimating a 10 per cent difference in the nasal mucociliary clearance values of each group, as evident from previous studies.[12] Based on a power of 0.80 and a 0.05 type I error, a sample size of 60 participants (20 each in the non-smoker, cigarette smoker and bidi smoker groups) was deemed adequate to detect a statistically significant difference between the groups.

The study protocol was reviewed and approved by the Institutional Ethics Committee of Manipal Academy of Higher Education in accordance with the Helsinki declaration.[16] Participants were included only after providing informed written consent.

Sixty male participants aged 20–40 years, residing in the Udupi district, Karnataka, were incorporated into our study. The primary reason for including only males was because smoking is more prevalent among males in the study region than in females.[17] It was also assumed that male participants would be more forthcoming about their tobacco addiction history than females.

Participants taking medications such as decongestants, anti-histamines, saline drops and anticholinergics were excluded. Participants were screened for related nasal and systemic pathologies, such as rhinosinusitis, nasal polyps, allergic rhinitis and COPD, to rule out any confounding effect. A detailed case history and spirometry were used to screen for COPD. The clinical examination was conducted by an ENT specialist with a speculum and a nasal endoscope. Participants were excluded if any of these pathologies were clinically present.

The addiction history of participants was assessed with the help of a standard proforma, which recorded age, education, marital status and occupation, and included a detailed column on tobacco habits.[18]

Nasal mucociliary clearance was measured with methylene blue dye, in accordance with the procedure described by Ewert.[14] The tests were performed in an air-conditioned room (temperature, 24.9 ± 0.30 °C) between 4:00 pm and 5:00 pm. The participants were asked to rest for 30 minutes before the procedure commenced. One drop of the methylene blue dye was applied, with a 24-gauge needle, to the anterior end of the inferior turbinate of the participants' nasal cavity, with the help of a nasal speculum. After application of the dye, participants were instructed not to sniff or sneeze, and to maintain a sitting posture for a period of 15 minutes, following which the participants were asked to recline on a bed. The distance that the methylene blue dye traversed inside the nasal cavity was recorded in millimetres with a nasal endoscope and a standard 6 inch (15.24 cm) metal scale.

Statistical analysis

The SPSS statistical software program, version 20.0 (SPSS, Chicago, Illinois, USA), was used for data analysis. Demographic data were stated as numbers, while the quantitative data were presented as means ± standard deviations. The distribution of the residuals corresponding to nasal mucociliary clearance was considered non-parametric, and the Kruskal Wallis test was used to examine the difference between the nasal mucociliary clearance readings of the three groups.

https://doi.org/10.1017/S0022215118002049 Published online by Cambridge University Press

A p-value of less than 0.05 was considered as statistically significant.

The variables of smoking status, number of years' formal education, marital status, occupation, and number of bidis or cigarettes smoked in a day were categorised according to their distribution in the sample, whereas age, age of smoking onset and pack-years were treated as continuous variables. The dependent variable nasal mucociliary clearance was dichotomised according to the distance covered by the dye inside the nasal cavity (less than 70 mm was scored as 0, and equal to 70 mm was scored as 1). Initially, a bivariate log regression analysis was conducted to assess the effects of the various parameters on nasal mucociliary clearance. Following this, all variables that indicated associations (wherein $p < 0.20$) were considered for multivariate binomial log regression analysis. Crude and adjusted odds ratios and 95 per cent confidence intervals (CIs) were calculated and reported.

Results

The demographic and socioeconomic characteristics and tobacco exposure history of the 60 participants are shown in Table 1. The mean age of participants was 30.23 ± 6.12 years, with an age range of 20–40 years. The mean age of non-smokers, cigarette smokers and bidi smokers was 29.3 ± 6.25 years, 31.2 ± 5.42 years and 30.2 ± 6.77 years, respectively. The mean number of years of formal education ($n = 60$) was 15.38 ± 4.02 years. The mean number of years of formal education of non-smokers, cigarette smokers and bidi smokers was 16.5 ± 4.2 years, 18.05 ± 2.14 years and 11.6 ± 2.01 years, respectively. Among the participants, 30 were married and 30 were unmarried; 25 were professionals or semi-professionals, 24 were semi-skilled or unskilled workers, and 11 were students. The mean age of smoking onset was 18.55 ± 1.76 years for cigarette smokers and 16.25 ± 1.29 years for bidi smokers, while the mean pack-years among these groups were 4.63 ± 2.74 and 7.5 ± 5.1 respectively. The mean nasal mucociliary clearance for the non-smokers, cigarette smokers and bidi smokers was 67.89 ± 4.10 mm, 67 ± 5.48 mm and 59.25 ± 12.38 mm, respectively. Among all the variables compared, only age and marital status were not found to be statistically significantly different between groups.

As the data were not normally distributed, the medians were derived. The median nasal mucociliary clearance of the 60 participants was 70 mm (95 per cent CI = 65.00–70.00), with a range of 35 mm. The median nasal mucociliary clearance of non-smokers and cigarette smokers was 70 mm each, whereas it was 65 mm for bidi smokers. The difference in nasal mucociliary clearance between bidi smokers, non-smokers and cigarette smokers was found to be statistically significant ($p < 0.05$, Kruskal Wallis test).

Table 2 shows the association, on bivariate analysis, between nasal mucociliary clearance and the demographic, socioeconomic and tobacco exposure variables recorded. In the bivariate analysis, a variable with a p-value of less than 0.2 was considered for inclusion in the adjusted model. Smoking status, number of years' formal education, occupation, number of cigarettes or bidis smoked per day, and number of pack-years were thus included.

Table 3 shows the association, on multivariate regression analysis, between nasal mucociliary clearance and the covariates included from the bivariate analysis. In the unadjusted multivariate regression analysis, a statistically significant association ($p < 0.05$) was seen between nasal mucociliary clearance and smoking status, number of cigarettes or bidis smoked per day, and pack-years. However, when adjusted for age, number of years' formal education, marital status and occupation, a statistically significant association ($p < 0.05$) was only seen between nasal mucociliary clearance and smoking status and number of pack-years.

Table 2. Bivariate regression analysis results*

Variables	OR (95% CI)	*P*-value
Smoking status		
– Non-smoker	Reference	
– Cigarette smoker	0.62 (0.16–2.43)	0.492
– Bidi smoker	0.14 (0.04–0.58)	0.006†
Age		
– ≤29 years	Reference	
– >29 years	0.98 (0.90–1.06)	0.550
Number of years' formal education		
– ≤14 years	Reference	
– 15–18 years	2.5 (0.74–8.46)	0.14†
– >18 years	1.85 (0.48–7.06)	0.37
Marital status		
– Unmarried	Reference	
– Married	0.76 (0.27–2.12)	0.603
Occupation		
– Professional or semi-professional	Reference	
– Semi-skilled or unskilled	0.34 (0.11–1.08)	0.067†
– Student	0.82 (0.19–3.65)	0.798
Bidis or cigarettes smoked per day (*n*)		
– ≤5	Reference	
– 6–10	0.39 (0.12–1.39)	0.146†
– 11–20	0.21 (0.05–0.94)	0.041†
– ≥21	0.26 (0.04–1.31)	0.065†
Pack-years (*n*)		
– ≤3	Reference	
– >3	0.82 (0.71–0.95)	0.006†

*Examining the association between nasal mucociliary clearance and demographic, socioeconomic and tobacco exposure variables. †Variables where $p < 0.20$ were considered for inclusion in the adjusted model. The dependent variable nasal mucociliary clearance was dichotomised according to the distance covered by the dye inside the nasal cavity (less than 70 mm scored as '0' and equal to 70 mm as '1'). OR = odds ratio; CI = confidence interval

Discussion

This cross-sectional study determined the nasal mucociliary clearance values of non-smokers, cigarette smokers and bidi smokers, and evaluated the association with demographic, socioeconomic and tobacco exposure variables. The results indicated that nasal mucociliary clearance after 15 minutes was significantly decreased among bidi smokers, in comparison to cigarette smokers and non-smokers. A significant inverse association was also seen between bidi smoking, number of pack-years and nasal mucociliary clearance.

https://doi.org/10.1017/S0022215118002049 Published online by Cambridge University Press

Table 3. Crude and adjusted multivariate regression analysis results*

Variables	Crude OR (95% CI)	*P*-value	Adjusted OR† (95% CI)	*P*-value
Smoking status				
– Non-smoker	Reference			
– Cigarette smoker	0.82 (0.11–3.57)	0.619	0.97 (0.36–4.52)	0.826
– Bidi smoker	0.13 (0.04–0.68)	0.041‡	0.18 (0.07–0.77)	0.049‡
Number of years' formal education				
– ≤14 years	Reference			
– 15–18 years	1.19 (0.09–16.12)	0.894	1.37 (0.05–19.39)	0.971
– >18 years	0.71 (0.05–8.71)	0.799	0.81 (0.07–8.79)	0.833
Occupation				
– Professional or semi-professional	Reference			
– Semi-skilled or unskilled	0.25 (0.09–1.02)	0.083	0.43 (0.11–1.53)	0.091
– Student	0.46 (0.08–2.53)	0.461	0.67 (0.15–3.12)	0.571
Bidis or cigarettes smoked per day (*n*)				
– ≤5	Reference			
– 6–10	0.40 (0.14–2.11)	0.217	0.43 (0.18–2.45)	0.217
– 11–20	0.33 (0.07–0.93)	0.047‡	0.59 (0.15–1.29)	0.141
– ≥21	0.34 (0.06–1.58)	0.073	0.41 (0.09–1.72)	0.089
Pack-years (*n*)				
– ≤3	Reference			
– >3	0.72 (0.63–0.88)	0.011‡	0.87 (0.59–0.94)	0.025‡

*Examining the association between nasal mucociliary clearance and demographic, socioeconomic and tobacco exposure variables. The dependent variable nasal mucociliary clearance was dichotomised according to the distance covered by the dye inside the nasal cavity (less than 70 mm scored as '0' and equal to 70 mm as '1'). †Adjusted for age, number of years' formal education, marital status and occupation. ‡$P < 0.05$ considered statistically significant. OR = odds ratio; CI = confidence interval

- The components of cigarette tobacco smoke cause cilia toxicity
- Nasal mucociliary clearance is a protective feature for eliminating dust particles and foreign bodies from the nasal cavity towards the nasopharynx
- The prevalence of smoking bidi or the Indian cigar is quite high in rural India
- Bidi smoking is more harmful to ciliary movement in the nasal mucosa than cigarette smoking
- Bidi smoking was associated with a higher number of pack-years as compared to cigarette smoking
- Bidi smokers mainly belonged to the lower socioeconomic strata of society

Various factors might have played a role in the outcome. The true biological reasons for the findings are yet to be ascertained; however, the most important explanation could be the chronicity or duration of the smoking habit, denoted by the number of pack-years. As the bidi smokers had a significantly higher number of pack-years, it was assumed that cilia toxicity would develop much earlier relative to cigarette smokers and non-smokers.

One factor that could have affected the results is the nature of the bidi sticks. Bidis are traditionally hand rolled and they are devoid of a filter, unlike cigarettes. The filter of a cigarette functions as a barrier, by preventing the noxious fumes from reaching the nasal cavity. Although a bidi contains a lower amount of tobacco compared to a cigarette, when tested on a standard smoking machine, it produces higher levels of nicotine, carbon monoxide, tar, phenols and ammonia, resulting in a higher degree of addiction. It has been shown that bidis produce three times the amount of carbon monoxide and nicotine, and five times the amount of tar, than cigarettes.[19] Given the low combustibility of the tendu leaf wrapper, bidi smokers must take more frequent and deeper puffs, resulting in the inhalation of more smoke, which is disseminated deeper into the lungs.[20] Unlike the thin, single-layer paper wrapper used in Western-style cigarettes, leaf wrappers add considerably to the total mass of a bidi and contribute significantly to the amount of total particulate matter produced during smoking.[21]

As with all tobacco products, bidis are carcinogenic and mutagenic. Bidi smokers have an increased risk of: coronary heart disease, and cancers of the larynx, pharynx, oral cavity, oesophagus, liver, stomach and lungs. Bidi use during pregnancy is associated with high perinatal mortality.[22–24] Given its relatively lower cost and widespread availability, it is widely perceived that a bidi causes more harm to the respiratory system than a cigarette.

The socioeconomic status of the participants, as denoted by the number of years' formal education and occupation, though not statistically significant, could have played a mediatory role in the difference observed between the bidi smokers and the other two groups. In our study, bidi smokers predominantly belonged to the lower socioeconomic strata; hence, it is possible there was a lack of awareness about the deleterious effects of bidi smoking, as indicated by the significantly higher number of pack-years.

The results obtained from our study are comparable to those of various other studies. Kim *et al.*,[25] observed a

https://doi.org/10.1017/S0022215118002049 Published online by Cambridge University Press

significant increase in methylene blue nasal mucociliary clearance time in smokers compared with non-smokers. Ewert[14] also demonstrated a significant reduction in nasal mucociliary clearance in cigarette smokers compared with non-smokers. However, Quinlan *et al.*,[15] observed no such distinction between smokers and non-smokers in the mucociliary clearance of insoluble radiolabelled resin particles placed on the inferior nasal turbinate. We too could not demonstrate a statistically significant difference in nasal mucociliary clearance between non-smokers and cigarette smokers. It is possible that ciliary damage was less among smokers given the relatively younger age of the study participants (21–40 years). Another possible reason could be the time interval (15 minutes) used to assess nasal mucociliary clearance. It has been postulated that nasal mucociliary clearance time (the time taken for the dye to travel the length of the nasopharynx) could be as low as 12 minutes among healthy people.[12] It is possible that given the longer interval used in our study, the difference in distance travelled by the methylene blue in both groups was reduced, thus affecting the findings.

Few studies utilising saccharin crystals as the nasal mucociliary clearance time indicator showed similar outcomes.[13,26] The primary advantage of the methylene blue test over a saccharin test is the objectivity in study design and the shorter time required to perform the test. The need for objectivity is important; not all participants will have the same level of susceptibility towards the sweet sensation of saccharin, which is mandatory to calculate the nasal mucociliary clearance time.

Nasal mucociliary clearance is affected by various diseases and pathologies.[27–29] Hence, careful screening was required to rule out those participants considered unsuitable for inclusion in the study. The main limitation of our study is that participants' age ranged only from 20 to 40 years. In addition, the extent of passive smoking that each of the three groups of participants might have been subjected to was not explored. The methylene blue dye occasionally caused a mild burning sensation, adding to participants' discomfort.

As we observed a significant association between pack-years and nasal mucociliary clearance, in the future participants with a wider age range (of more than 40 years) should be recruited to explore the effects of bidi and cigarette smoking on nasal mucociliary clearance. In order to arrive at more accurate results, the beating frequency of cilia and the viscoelastic nature of mucus secretion should also be considered.[30]

Nasal mucociliary clearance measurement is an elementary and precise procedure for evaluating the effect of smoking on the mucociliary activity of nasal mucosa. The decreased nasal mucociliary clearance detected in the bidi smokers of our study may be due to reduced ciliary beat frequency, a decline in the number of cilia or alterations in the viscoelastic properties of mucus. Our study emphasises the vital contribution of nasal mucociliary clearance as an indicator of respiratory system health and the general health of an individual.

Acknowledgements. The authors wish to acknowledge Dr Vasudeva Gudattu and Ms Maria Matthews for their commendable contribution towards the sample size calculation and statistical analysis.

Competing interests. None declared

References

1 World Health Organization. *WHO Report on the Global Tobacco Epidemic: Warning about the Dangers of Tobacco*. Geneva: World Health Organization, 2011;50–3

2 World Health Organization. *WHO Global Report on Trends in Prevalence of Tobacco Smoking*. Geneva: World Health Organization, 2015

3 Chaudhry K, Rath GK. *Multisectoral and Intersectoral Approach to National Tobacco Control*. Paper commissioned by the World Health Organization on the occasion of the WHO International Conference on Global Tobacco Control Law: 'Towards a WHO Framework Convention on Tobacco Control', 7-9 January 2000, New Delhi, India

4 GATS-2: Global Adult Tobacco Survey. Fact sheet: India 2016-17. In: https://www.mohfw.gov.in/sites/default/files/GATS-2%20FactSheet.pdf [26 October 2018]

5 Gupta PC, Ray CS, Narake SS, Palipudi KM, Sinha DN, Asma S *et al.* Profile of dual tobacco users in India: an analysis from Global Adult Tobacco Survey, 2009-10. *Indian J Cancer* 2012;**49**:393–400

6 Prabhakar B, Narake SS, Pednekar MS. Social disparities in tobacco use in India: the roles of occupation, education and gender. *Indian J Cancer* 2012;**49**:401–9

7 Bombick DW, Bombick BR, Ayres PH, Putnam K, Avalos J, Borgerding MF *et al.* Evaluation of the genotoxic and cytotoxic potential of mainstream whole smoke and smoke condensate from a cigarette containing a novel carbon filter. *Fundam Appl Toxicol* 1997;**39**:11–17

8 IARC. *Tobacco Smoke and Involuntary Smoking, IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans*, vol. 83. Lyon: International Agency for Research on Cancer, 2004

9 Hecht SS. Tobacco smoke carcinogens and lung cancer. *J Natl Cancer Inst* 1999;**91**:1194–210

10 Satir P, Sleigh MA. The physiology of cilia and mucociliary interactions. *Annu Rev Physiol* 1990;**52**:137–55

11 Navarrette CR, Sisson JH, Nance E, Gipson DA, Hanes J, Wyatt TA. Particulate matter in cigarette smoke increases ciliary axoneme beating through mechanical stimulation. *J Aerosol Med Pulm Drug Deliv* 2012;**25**:159–68

12 Stanley PJ, Wilson R, Greenstone MA, MacWilliam L, Cole PJ. Effect of cigarette smoking on nasal mucociliary clearance and ciliary beat frequency. *Thorax* 1986;**41**:519–23

13 Baby MK, Muthu PK, Johnson P, Kannan S. Effect of cigarette smoking on nasal mucociliary clearance: a comparative analysis using saccharin test. *Lung India* 2014;**31**:39–42

14 Ewert G. On the mucus flow rate in the human nose. *Acta Otolaryngol Suppl* 1965;**200**:1–62

15 Quinlan MF, Salman SD, Swift DL, Wagner HN, Proctor DF. Measurement of mucociliary function in man. *Am Rev Respir Dis* 1969;**99**:13–23

16 General Assembly of the World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *J Am Coll Dent* 2014;**81**:14–18

17 Jha P, Jacob B, Gajalakshmi V, Gupta PC, Dhingra N, Kumar R *et al.*; RGI-CGHR Investigators. A nationally representative case-control study of smoking and death in India. *N Engl J Med* 2008;**358**:1137–47

18 Heatherton TF, Kozlowski LT, Fagerström KO. The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 1991;**86**:1119–27

19 Jayant K, Pakhale SS. Toxic constituents in bidi smoke. In: LD Sanghwi LD, Notani P, eds. *Tobacco and Health: The Indian Scene*. Bombay: Tata Memorial Centre, 1989;101–10

20 Bhonsle RD, Murti PR, Gupta PC. Tobacco habits in India. In: Gupta PC, Hamner JE, Murti PR, eds. *Control of Tobacco Related Cancers and Other Diseases. Proceedings of an International Symposium; 1990 Jan 15–19; Bombay, India*. Bombay: Oxford University Press, 1992;25–46

21 Pakhale SS, Dolas SS, Maru GB. The distribution of total particulate matter (TPM) and nicotine between mainstream and sidestream smoke in bidis and cigarettes. *Anal Lett* 1997;**30**:383–94

22 Malson JL, Sims K, Murty R, Pickworth W. Comparison of the nicotine content of tobacco used in bidis and conventional cigarettes. *Tob Control* 2001;**10**:181–3

23 Abel EL. Smoking during pregnancy: a review of effects on growth and development of offspring. *Hum Biol* 1980;**52**:593–625

24 Dempsey DA, Benowitz NL. Risks and benefits of nicotine to aid smoking cessation in pregnancy. *Drug Saf* 2001;**24**:277–322

25 Kim YH, Kim YJ, Lee SE, Kim YH, Lim SH, Lee JH *et al.* Effect of smoking on bronchial mucus transport velocity under total intravenous anesthesia. *Korean J Anesthesiol* 2008;**55**:52–6

26 Proenca M, Xavier RF, Ramos D, Cavalheri V, Pitta F, Cipulo Ramos EM. Immediate and short term effects of smoking on nasal mucociliary clearance in smokers [in Portuguese]. *Rev Port Pneumol* 2011;**17**:172–6

https://doi.org/10.1017/S0022215118002049 Published online by Cambridge University Press

27 Karnitzki G, Mlynski G, Mlynski B. Nasal mucociliary transport time and ciliary beat frequency in healthy probands and patients with sinusitis [in German]. *Laryngorhinootologie* 1993;**72**:595–8

28 Corbo GM, Foresi A, Bonfitto P, Mugnano A, Agabiti A, Cole PJ. Measurement of nasal mucociliary clearance. *Arch Dis Child* 1989;**64**:546–50

29 Altuntas EE, Kaya A, Uysal IÖ, Cevit Ö, Içağasioğlu D, Müderris S. Anterior rhinomanometry and determination of nasal mucociliary clearance time with the saccharin test in children with Crimean-Congo hemorrhagic fever. *J Craniofac Surg* 2013;**24**:239–42

30 Liote H, Zahm JM, Pierrot D, Puchelle E. Role of mucus and cilia in nasal mucociliary clearance in healthy subjects. *Am Rev Respir Dis* 1989;**140**:132–6