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Biochemical Validation of Self-Reported Smokeless Tobacco Abstinence among Smokeless Tobacco Users: Results from A Clinical Trial of Varenicline in India

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Abstract

The validity of self-reported tobacco use is often questioned given the potential for underestimation of use. This study used data from a double-blind placebo-controlled clinical trial of varenicline for smokeless tobacco dependence in India to evaluate the accuracy of self-reported smokeless tobacco cessation using biochemical validation procedures and to evaluate correlates of reporting inaccuracy. Smokeless tobacco users attending a dental clinic at AIIMS were randomized to placebo or varenicline; all participants received counseling. Detailed smokeless tobacco use was recorded and abstinence was defined as cotinine-verified 7-day point prevalence cessation (cotinine <50ng/ml) and breath CO >10ppm at the end of 12 weeks of treatment. One-half of study completers (82/165) self-reported abstinence. Biochemical verification confirmed that (65.9%) subjects provided accurate self-reports while (34.1%) participants under-reported tobacco use. These data indicate poor agreement between self-reported and biochemically confirmed abstinence ($\kappa=-0.191$). Under-reporters of tobacco use had significantly higher baseline cotinine ($p<0.05$), total craving ($p<0.012$), and negative reinforcement craving ($p<0.001$), vs. those whose self-reports were correctly verified. These findings provide evidence to support the need for biochemical validation of self-reported abstinence outcomes among smokeless tobacco users in cessation programs in India and identify high levels of pre-treatment cotinine and craving levels as potential correlates of false reporting.

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Statement of Interest

Dr. Schnoll has served as a consultant to GlaxoSmithKline and Pfizer, and Pfizer provided the study medication and placebo for this study free of charge.

Keywords

Biochemical validation; smokeless tobacco users; varenicline; self-report; urine

Introduction

Tobacco use is a leading cause of premature mortality and preventable morbidity worldwide. The rate of smokeless tobacco (SLT) use is highest in India (Global Adult Tobacco Survey, 2009), in contrast to the United States, where the rate of smokeless tobacco use is less than 5% (Substance Abuse and Mental Health Services Administration 2011). Given the magnitude of SLT use in India, efficient methods are needed to accurately measure the prevalence of use and to monitor and evaluate the potential impact of cessation interventions.

Worldwide, self-reports are a principle measure used to monitor trends in cigarette smoking and the evaluation of treatment outcome studies (Wong et al. 2012). The validity of self-reported tobacco use is often questioned given the potential for under-estimation of use (Boyd et al. 1996; Jarvis et al. 1988; Jarvis et al. 1987). Subject responses regarding their recent tobacco use (smoking practices) are mainly affected by recall bias resulting in inaccurate reporting of current tobacco use. Moreover, self-reports may be unreliable because participants may be unwilling to admit to a health problem or social behavior that many perceive to be undesirable or when there are laws banning certain behaviors (Fendrich et al. 2005). Thus, biochemical validation is recommended in intervention studies, where cessation outcomes need to be assessed (Benowitz et al. 2002). Most literature on SLT from India are based on self-reports with limited use of biochemical validation (Dhavan et al. 2011; Jain et al. 2012; Pattanayak et al. 2012). Given the public health importance and policy implications of these data there is a need for accurate measurement of tobacco use status. Commonly used measures of active smoking status have included expired carbon monoxide, thiocyanate, nicotine and cotinine, a major metabolite of nicotine (Jarvis et al. 1987).

This study used data from a double-blind placebo-controlled clinical trial of varenicline for smokeless tobacco dependence in India to evaluate the accuracy of self-reported smokeless tobacco cessation using biochemical validation procedures and to evaluate correlates of reporting inaccuracy (Jain et al. 2014). This study is the first focusing exclusively on issues of biochemical verification of SLT use in India.

Methods

Participants

The study was conducted at the National Drug Dependence Treatment Center (NDDTC) at the All India Institute of Medical Sciences (AIIMS), New Delhi, India. All the study participants were exclusively smokeless tobacco users, confirmed by breath carbon monoxide assessment. Of the 165 study completers, the present analyses focus on the 82

trial participants who reported cessation from SLT use and provided a sample for biochemical validation of self-report.

Procedures

Details concerning the clinical trial procedures can be found in Jain et al. (2014). With regard to the present study, following the 12-week course of either placebo or varenicline, participant quit rates were assessed at the end of treatment (EOT). Self-reported 7-day point prevalence abstinence was assessed and participants who indicated abstinence were asked to attend clinic for biochemical confirmation with urinary cotinine (cut-off for abstinence < 50 ng/ml) and absence of tobacco smoking using breath CO (<10ppm). At baseline (week 0), demographic (e.g., age, education) and smokeless tobacco use (e.g., rate, years of use) data were collected. The smokeless tobacco version of the Fagerström Test for Nicotine Dependence (FTND-ST; Ebbert et al. 2006) was also administered. Participants also completed measures of nicotine withdrawal (the Minnesota Nicotine Withdrawal Scale [MNWS; Hughes & Hatsukami 1986]), nicotine craving (Questionnaire on Smoking Urges [QSU; Cox et al. 2001]), the hedonic effects of smokeless tobacco (Cigarette Evaluation Scale [CES; Westman et al. 1992]), and affect (the positive and negative affect scale [PANAS; Watson et al. 1988]).

Lab Analysis

Quantitative urinary cotinine was done by using Enzyme-linked immunosorbant assay (ELISA) kits of Calbiotech, Inc., USA, which uses solid phase competitive ELISA. Assay was carried out as directed by the manufacturers. Urinary cotinine concentrations corresponding to the optic densities were calculated by using standard curve and the results were expressed in units of nanogram per milliliter. The sensitivity limit of cotinine assay was 1ng/ml. In the current study, urinary cotinine cut-off for abstinence was < 50 ng/ml (SRNT Subcommittee on Biochemical Verification 2002).

2.4 Statistical Analysis

The validity of the self-reported EOT abstinence from smokeless tobacco use, vs. biochemically-confirmed results, was assessed using chi-square test of association and the Kappa coefficient. ANOVA and chi-square were used to evaluate continuous and categorical correlates of verified abstinence.

Results

Self-report and urinary cotinine were analyzed for 165 completers; 82/165 completers (49.7%) self-reported abstinence at EOT (Table 1). Biochemical verification of self-reported cessation confirmed that only 54 subjects (65.9%) provided accurate self-reports while nearly one-third of participants (n=28) were under-reporting tobacco use ($X^2[1] = 87.27, p < .001$). These data indicate poor agreement between self-reported and biochemically confirmed abstinence ($\kappa = -0.19$). Biochemical verification correctly classified 98% of participants who self-reported tobacco use.

Table 2 shows socio-demographic and tobacco use characteristics of the sample of 82 participants who self-reported abstinence at EOT. The mean age of self-reported quitters was 35.7 [SD = 10] years. The average age at initiation of smokeless tobacco use was 22.51 [SD = 8.8] years and mean duration of regular tobacco use was 12 [SD = 8.2] years. The daily consumption of tobacco was around 5 packets. The number of chews ranged from 4 to 25 times daily with the average chew rate being 10.52 [SD = 4.8]. The CO levels at baseline ranged from 0 to 2 with mean 0.89 [SD = 0.47]. The urine cotinine levels at baseline ranged from 200 ng/ml to 45931 ng/ml with mean 6128.74 [SD = 6628.32] ng/ml.

A one way ANOVA was conducted to compare accurate and inaccurate reported tobacco use on socio-demographic variables (e.g., age, education, income) and tobacco use variables (e.g., FTND, years of tobacco use, age at started using tobacco, average chew rate, average packets, CO at baseline, urine cotinine levels). There was a statistically significant difference in the baseline urine cotinine levels between accurate self-reporters and under-reporters of abstinence ($F[1,80] = 3.955, p = 0.05$). No additional significant differences were seen in demographic and tobacco-related variables.

Under-reporters of tobacco use had significantly higher total craving at baseline ($F[1,80] = 6.58, p = 0.01$) and negative reinforcement craving at baseline ($F[1,80] = 11.27, p = 0.001$) vs. participants whose self-reports were correctly verified. No significant differences were seen between false and verified reports of tobacco use in depression scores and other measures such as reasons for smoking, positive and negative affect, positive reinforcement craving, and withdrawal.

Discussion

Self-report and recall of tobacco use with or without biologic verification is an extensively used method in clinical practice and epidemiological research to collect data for several health-related behaviors including tobacco use. Compared with estimates based on cotinine concentration, smoking prevalence based on self-report is generally lower (Gorber et al. 2009), although the extent of the difference varies by country (West et al. 2007). Biochemical validation of tobacco use status is used in limited studies from India (Jain et al. 2012; Pattnaik et al. 2012; Dhavan et al. 2011). Further, smokeless tobacco remains an under-researched area. This study is the first to examine the validity of self-report of tobacco use among pure smokeless tobacco users participating in a varenicline tobacco cessation trial in India. Urinary cotinine concentration was estimated as a biomarker of recent tobacco use to validate self-reported abstinence from smokeless tobacco use. The results indicated that abstinence from smokeless tobacco use based on self-report alone poorly approximates estimates based on urinary cotinine concentration.

Biochemical verification confirmed that only 54 subjects (65.9%) provided accurate self-reports while nearly one-third (34%) of respondents were classified as “under reporters” (their cotinine concentrations identified them as current users of SLT although they reported that they had quit). Nearly a third of the participants at end of 12 weeks of treatment with varenicline or placebo who reported not using tobacco in the previous 7 days had urinary cotinine levels greater than 50 ng/ml. Other studies have found varying levels of

concordance for self-reported estimates of smoking, depending on the population studied, the type of biological specimen used in the measurement of cotinine, and the cut-points used to identify smokers (Gorber et al, 2009). Only about 2% of respondents were classified as “false positives” (their cotinine concentration classified them as quitters, but they reported that they had used tobacco in last week). This discrepancy may be explained by recall bias. Further, cotinine is a measure of recent exposure to tobacco (SRNT 2002), so it is likely that cotinine levels in some of these cases were too low to identify them as current users.

The mean urinary cotinine concentration at baseline was significantly higher among under reporters than among subjects reporting abstinence. Despite using methods like timeline follow back to increase accuracy of self-report, some under-reporting may be due to social desirability bias as subjects were participants of a tobacco cessation trial. Being participants in a cessation trial, they report abstinence as the expected outcome. Moreover, participants who do not report a recent lapse in timeline follow back records may generate higher urinary cotinine levels on biochemical validation. On other parameters such as age, education, income, FTND total and individual items, years of tobacco use, age at initiation of tobacco use, and daily chew rate and baseline CO levels, no significant difference emerged between the participants accurately reporting abstinence versus those falsely reporting abstinence at the end of treatment.

The time to first cigarette after waking (FTND item 1) has been associated with many aspects of dependence such as smoking cessation (Baker et al. 2007; Kozlowski et al. 1994), smoking relapse (Toll et al. 2007) and tolerance (Pillitteri et al. 2007), and urinary cotinine concentration (Joshua et al, 2009). The current study did not find association between time to first dip in the morning after waking up and urinary cotinine levels (Muscat et al. 2009). Lastly, false reporters of abstinence also have significantly higher baseline total craving and negative reinforcement craving. This again may reflect the notion that heavier smokeless tobacco users, as indexed by current craving level, may be a sub-group who are more likely to yield false self-reports of tobacco cessation.

The present findings may be limited by a relatively small sample and the use of a sample of treatment-seekers who may not represent the general population of smokeless tobacco users in India. The present data do not consider rate of nicotine metabolism, which could influence cotinine values. While there was no self-reported tobacco use within 10 days of cotinine testing across all 82 participants who reported abstinence, 5 participants who self-reported abstinence used tobacco 13–14 days prior to testing and, if they were slow metabolizers of nicotine, the cotinine testing may have been affected. Nevertheless, this study provides evidence to support the need for biochemical validation of self-reported abstinence outcomes among SLT users in cessation programs in India and identifies high levels of pre-treatment cotinine and craving levels as potential correlates of false reporting. Future clinical trials with this population are encouraged to use biochemical verification procedures to validate self-reported cessation outcomes and identify additional correlates of false reporting.

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References

- Baker TB, Piper ME, McCarthy DE, Bolt DM, Smith SS, Kim S, Toll BA. Time to first cigarette in the morning as an index of ability to quit smoking: implications for nicotine dependence. *Nicotine and Tobacco Research*. 2007; 9(Suppl4):S555–570.10.1080/14622200701673480 [PubMed: 18067032]
- Benowitz NL, Jacob P, Ahijevych K, Jarvis MJ, Hall S, LeHouezec J, Velicer W. Biochemical verification of tobacco use and cessation. *Nicotine and Tobacco Research*. 2002; 4(2):149–159. [PubMed: 12028847]
- Boyd NR, Windsor RA, Perkins LL, Lowe JB. Quality of measurement of smoking status by self-report and saliva cotinine among pregnant women. *Maternal Child Health Journal*. 1998; 2(2):77–83. Retrieved from link.springer.com/article/10.1023%2FA%3A1022936705438. [PubMed: 10728263]
- Dhavan P, Bassi S, Stigler MH, Arora M, Gupta VK, Perry CL, Reddy KS. Using Salivary Cotinine to Validate Self-Reports of Tobacco Use by Indian Youth Living in Low-Income Neighborhoods. *Asian Pacific Journal of Cancer Prevention*. 2011; 12(10):2551–2554. Retrieved from europepmc.org/abstract/MED/22320954. [PubMed: 22320954]
- Dolcini MM, Adler NE, Ginsberg D. Factors influencing agreement between self-reports and biological measures of smoking among adolescents. *Journal of Research on Adolescence*. 1996; 6(4):515–542. Retrieved from psycnet.apa.org/psycinfo/1997-02897-006.
- Fendrich M, Mackesy-Amiti ME, Johnson TP, Hubbell A, Wislar JS. Tobacco-reporting validity in an epidemiological drug-use survey. *Addictive Behaviors*. 2005; 30(1):175–181. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15561458>. [PubMed: 15561458]
- Gorber SC, Schofield-Hurwitz S, Hardt J, Levasseur G, Tremblay M. The accuracy of self-reported smoking: a systematic review of the relationship between self-reported and cotinine-assessed smoking status. *Nicotine and Tobacco Research*. 2009; 11(1):12–24.10.1093/ntr/ntn010 [PubMed: 19246437]
- Jain R, Balhara YP, Jhanjee S, Sethi H. Concordance between urinary cotinine levels and self-reported tobacco use among drug-dependent persons: a pilot study. *Substance Abuse*. 2012; 33(2):99–102.10.1080/08897077.2011.630947 [PubMed: 22489581]
- Jain R, Jhanjee S, Jain V, Gupta T, Mittal S, Goelz P, Schnoll RA. A double blind placebo – controlled randomized trial of Varenicline for smokeless tobacco dependence in India. *Nicotine and Tobacco Research*. 2014; 16(1):50–57.10.1093/ntr/ntt115 [PubMed: 23946326]
- Jarvis MJ, Russell MA, Benowitz NL, Feyerabend C. Elimination of cotinine from body fluids: implications for noninvasive measurement of tobacco smoke exposure. *American Journal of Public Health*. 1988; 78(6):696–698. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1350287>. [PubMed: 3369603]
- Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vesey C, Saloojee Y. Comparison of tests used to distinguish smokers from non-smokers. *American Journal of Public Health*. 1987; 77(11):1435–1438.10.2105/AJPH.77.11.1435 [PubMed: 3661797]
- Muscat JE, Stellman SD, Caraballo RS, Richie JP Jr. Time to first cigarette after waking predicts cotinine levels. *Cancer Epidemiology Biomarkers and Prevention*. 2009; 18(12):3415–3420.10.1158/1055-9965.EPI-09-0737

- Kozlowski LT, Porter CQ, Orleans CT, Pope MA, Heatherton T. Predicting smoking cessation with self-reported measures of nicotine dependence: FTQ, FTND, and HSI. *Drug and Alcohol Dependence*. 1994; 34(3):211–216. Retrieved from www.ncbi.nlm.nih.gov/pubmed/8033758. [PubMed: 8033758]
- Parker DR, Lasater TM, Windsor R, Wilkins J, Upegui DI, Heimdal J. The accuracy of self-reported smoking status assessed by cotinine test strips. *Nicotine and Tobacco Research*. 2002; 4(3):305–309. [PubMed: 12215239]
- Patrick DL, Cheadle A, Thompson DC, Diehr P, Koopsell T, Kinne S. The validity of self-reported smoking: a review and meta-analysis. *American Journal of Public Health*. 1994; 84(7):1086–1093. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8017530>. [PubMed: 8017530]
- Pattanayak RD, Jain R, Sagar R. Reliability of self-reported tobacco use in bipolar disorder: an exploratory study of euthymic patients visiting a tertiary care hospital in India. *International Journal of Psychiatry in Medicine*. 2012; 43(2):153–63. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22849037>. [PubMed: 22849037]
- Pillitteri JL, Kozlowski LT, Sweeney CT, Heatherton TF. Individual differences in the subjective effects of the first cigarette of the day: a self-report method for studying tolerance. *Experimental and Clinical Psychopharmacology*. 1997; 5(1):83–90.10.1037/1064-1297.5.1.83 [PubMed: 9234043]
- Society for Research on Nicotine and Tobacco Subcommittee on Biochemical Verification. Subcommittee on Biochemical Verification. Biochemical verification of tobacco use and cessation. *Nicotine and Tobacco Research*. 2002; 4(2):149–59.10.1080/14622200210123581 [PubMed: 12028847]
- Substance Abuse and Mental Health Services Administration. Results from the 2010 national survey on drug use and health: Summary of national findings. Vol. 2012. Rockville, MD, USA: 2011.
- Toll BA, Schepis TS, O'Malley SS, McKee SA, Krishnan-Sarin S. Subjective reactivity to the first cigarette of the day as a predictor of smoking relapse: a preliminary study. *Drug and Alcohol Dependence*. 2007; 89(2–3):302–305.10.1016/j.drugalcdep.2007.01.011 [PubMed: 17320313]
- West R, Zatonski W, Przewonznia K, Jarvis MJ. Can we trust national smoking prevalence figures? Discrepancies between biochemically assessed and self-reported smoking rates in three countries. *Cancer Epidemiology, Biomarkers and Prevention*. 2007; 16(4):820–822.10.1158/1055-9965.EPI-06-0679
- Wong SL, Shields M, Leatherdale S, Malaisson E, Hammond D. Assessment of validity of self-reported smoking status. *Health Reports*. 2012; 23(1):47–53. Retrieved from <http://www.statcan.gc.ca/pub/82-003-x/2012001/article/11625-eng.pdf>. [PubMed: 22590805]

Table 1

Self-report Versus Urinalysis for Completers (N = 165)

Self-report	Biochemical Result		
	Abstinent	Chewing	Total
Abstinent	54 (65.9%)	28 (34.1%)	82 (100%)
Chewing	2 (2.4%)	81 (97.6%)	83 (100%)

Note. $X^2_{[1]} = 87.27$, $p < .001$.

Table 2

Differences between Accurate and Inaccurate Self-Reporters of Tobacco Abstinence (N = 82)

Characteristic	Inaccurate Reporters (n = 28)	Accurate Reporters (n = 54)	Overall (n = 82)
Age (Mean, SD)	35.89 (8.6)	35.54 (10.8)	35.66 (10.0)
Education (Mean, SD)	1.46 (1.138)	1.07 (1.061)	1.21 (1.097)
Income (Mean, SD)	1.36 (0.731)	1.37 (0.681)	1.37 (0.694)
FTND Total (Mean, SD)	6.86 (1.919)	6.57 (2.270)	6.67 (2.149)
Years of use (Mean, SD)	12.11 (7.960)	11.98 (8.460)	12.02 (8.243)
Age started chewing (Mean, SD)	24.36 (12.740)	21.56 (5.758)	22.51 (8.808)
Average Chew Rate (Mean, SD)	10.82 (5.525)	10.37 (4.553)	10.52 (4.877)
Average Packets per day (Mean, SD)	5.12 (5.637)	4.65 (5.562)	4.81 (5.557)
FTND ITEM 1 (Mean, SD)	2.14 (1.044)	2.02 (1.141)	2.06 (1.104)
CO-Baseline (Mean, SD)	0.89 (0.497)	0.89 (0.462)	0.89 (0.472)
Urine cotinine Baseline (Mean, SD)	8114.46 (9161.911)	5099.11 (4606.520)	6128.74 (6628.327)
Urine cotinine EOT (Mean, SD)	4847.65 (7725.48)	16.87 (13.44)	1666.41 (5020.64)
Craving	136.1 (43.4)	113.4 (34.9)	121.1 (39.3)
Craving (Total Positive reinforcement)	68.1 (19.4)	61.7 (17.0)	63.9 (18.0)
Craving (Total Negative Reinforcement)	40.0 (18.0)	28.2 (13.4)	32.3 (16.0)