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Original Research Article

Pharmacotherapy for the Treatment of Smokeless Tobacco Users

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Abstract: ***Background:*** Drug therapy for tobacco abstinence has shown limited effect. Though Bupropion was tried in many studies to access the abstinence rate in smokers while limited data is available for smokeless tobacco (ST) users. This study is an attempt to assess the efficacy and safety of bupropion SR for tobacco abstinence among ST users. Methods: Adults using smokeless tobacco were randomized to bupropion SR titrated to 150 mg twice daily (N= 32) for 12 weeks. First assessment done at 6 week was the 7-day point-prevalence tobacco abstinence. Secondary outcomes were assessed at week 8 and week 12 in terms of prolonged and continuous tobacco abstinence rates, craving and nicotine withdrawal. Results: The prevalence of abstinence rates among smokeless tobacco users with bupropion SR at week 6 (28.1%), week 8 (28.1%) and week 12 (28.1%); p = 0.0003). The prolonged and continuous tobacco abstinence rates did not differ at weeks 6, 8, and 12. The treatment response was observed over time with FTND-ST scale. The mean (±SD) FTND-ST score change from baseline among abstinent subjects was a decrease of 2.66 (±1.52) for the bupropion SR group at 12 week. Conclusions: Abstinence rate with Bupropion SR showed significant increase among ST users. It also showed significant decrease in craving during treatment period.

Keywords: Smokeless Tobacco, Bupropion SR, Pharmacotherapy.

1. INTRODUCTION

Smokeless tobacco (ST) refers to tobacco that is consumed without heating or burning at the time of consumption. It can be used orally or nasally. The use of ST is widespread in India and in western countries as well. In India, according to recent epidemiological studies, ST users contribute about 40% of the total tobacco used (rest being constituted by smoking forms including beedi and cigarettes).1 State level prevalence of tobacco chewing as per the national survey in 2003 reported that the prevalence of chewing tobacco in age group above 15 years to be ranging from 7% (in Jammu and Kashmir) to 60% (in Mizoram) in males and 0.2% (in Punjab) to 60.7% (in Mizoram) in females. 2 Amongst young adolescents (age 13-15 years), an average of 14.6% were current smokeless tobacco users. However, the range varied from as low as 2% (in Himachal Pradesh) to as high as 55.6% (in Bihar).3

ST use has been associated with oral mucosal lesions (Little *et al*., 1992; Martin *et al*., 1999; Tomar *et al*., 1997), periodontal disease (Ernster *et al*., 1990), and precancerous oral lesions (Mattson andWinn, 1989). Long term ST use may increase the risk for oral cancer (Stockwell and Lyman, 1986) and cancer of the kidney (Goodman *et al*., 1986; Muscat *et al*., 1995), pancreas (Muscat *et al*., 1997), and digestive system (Henley *et al*., 2005). Associations between ST use and cardiovascular events (Teo *et al*., 2006) and death from coronary artery disease and stroke (Henley *et al*., 2005) have also been observed.

Smokeless tobacco use imposes adverse health consequences, though 64% of ST users express desire to quit (Severson, 1992), and the increasing promotion of ST as a potential harm reduction strategy for cigarette smoking (McNeill, 2004; National Institute of Health, 2006), there is an urgent need to deliver effective behavioral and pharmacological therapies for ST users. Though behavioral therapy for ST users have shown good results but no pharmacological approach has been shown to increase long-term (≥6 months) tobacco abstinence rates among smokeless tobacco users (Ebbert *et al*., 2004). Bupropion sustained-release (SR) has been clearly demonstrated to increase tobacco

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abstinence among cigarettes smokers (Hughes *et al*., 2002). To date, two pilot studies have been conducted suggesting potential efficacy of bupropion SR for increasing tobacco abstinence rates among ST users (Dale *et al*., 2002; Ebbert *et al*., 2003; Glover *et al*., 2002).

This study was planned to evaluate the effectiveness of the pharmacotherapy (bupropion SR) for abstinence among healthy individuals using smokeless tobacco at a tertiary center. The study was conducted in the psychiatry department, IMS, BHU, Varanasi.

2. METHODS

2.1. Study Design

Our study was an open label, clinical trial comprising of a treatment phase of 12 weeks and follow-up at 2, 4, 6, 8 and 12 weeks. The study was conducted at the department of psychiatry IMS, BHU, Varanasi, India in compliance with the ethical principles of the Declaration of Institute of Medical Sciences BHU. Study was conducted between Jan 2012 to June 2013. Study protocol was approved by the institutional review committee prior to recruitment and enrollment.

2.2. Study Population

Subjects were recruited through the patients attending psychiatric OPD BHU, Varanasi. Eligibility criteria for the study: were 18-65 years of age, used ST daily for at least one year, scored 4 or more points in Fagerstrom tolerance questionnaire, were in good general health, willing to complete all study procedures, willing to quit ST, and signed the informed consent.

Exclusion criteria of study was- persons having any predisposition to seizure disorder, history of head injury resulting in loss of consciousness for more than 1 hour, history of stroke or transient ischemic attack, being in poor general health, as the presence of severe and chronic cardiovascular disease, chronic pulmonary disease, renal or hepatic dysfunction, currently on other behavioral or pharmacologic tobacco treatment program; had another member of their household already participating in this study; had a contraindication to the use of bupropion (i.e., personal or family history of seizures, significant closed head injury, bulimia or anorexia nervosa); had an allergy to bupropion; or had been diagnosed with any cancer (except skin cancers) in the year prior to randomization.

2.3. Interventions

Subjects were assigned to receive bupropion SR orally for study period. Bupropion SR was started 150 mg once daily for seven days then titrated to 150 mg twice daily for remaining period of study. The target quit date (TQD) was set after 2 weeks of pharmacotherapy.

During the 12-weeks of medication phase, participants attended study visits at week 2, 4, 6, 8 and 12 for general assessment of vitals, status of tobacco use, adherence to treatment, any adverse effects and concomitant use of any other medication. A plan of follow up at 15, 20 and 24 weeks was made for the subjects who has completed 12-week medication phase. Telephonic follow-up was done at 15 and 20 weeks. Last follow-up was made at institution.

2.4. Screening

Screening was done by taking proper medical history and conducting thorough clinical examination by a resident with measurement of vital signs (blood pressure, heart rate, weight, and height). Detailed history of substance use especially tobacco use was explored and level of dependence was measured using the Fagerström Tolerance Questionnaire-Smokeless Tobacco (Boyle *et al*., 1995).

2.5. Adverse Events

Adverse effects were observed and explored at each visit and were documented properly on case record and followed up until resolution or end of study.

2.6. Statistical Analyses

Current study comprises of 38 participants out of which 32 were smokeless tobacco users and 6 were smokers. From a pilot study, we observed a tobacco abstinence rate of 44% at the end of 12 weeks of medication for ST users receiving bupropion SR compared to 26% for subjects receiving placebo (Dale *et al*., 2002).

Subjects who missed a visit or failed to attend were considered to be using tobacco for that visit. Tobacco abstinence endpoints were analyzed using logistic regression. The analysis was performed using SPSS version 16. Withdrawal symptoms were assessed at each visit as either present (1) or absent (0).

3. RESULTS

3.1. Subjects

Of 60 individuals screened, 38 were eligible and included in the study to receive treatment (32 smokeless and 6 smokers) and only smokeless were included in the final analysis. A total of 3 subjects (2 smokeless, 1 smoker) discontinued study participation prior to the end of the medication phase. Baseline characteristics of enrolled subjects were described in (Table 1). 96.9% subjects were male and 3.1% were female. The mean age was 34.28 years (range 18 to 65 years), and the mean duration of regular ST use was 11.06±7.49 years (range 1 to 30 years). In addition to ST use, 7 subjects (21.88%) reported “ever” cigarette smoking (> 100 cigarettes in lifetime) with a median duration of cigarette abstinence of 2 years, and 6 subjects reported current cigarette smoking at baseline.

The overall, range of the study sample was 18-65 years with mean age 34.28±12.91 years. Study by Keller *et al* also showed that younger and middle-aged adults (18–54 years) are more likely to get enrolled for tobacco cessation in Minnesota State. Mean age of onset tobacco use was 23.16±8.7, baseline mean Fagerstrom score was 6.25±1.44 and mean no. of quit attempt was 1.53±2.51. The overall rates of continuous abstinence at 6, 8 and 12 weeks were 28.12%, 28.12% and 28.12%respectively in pharmacotherapy group.

3.2. Abstinence rates

The study showed tobacco abstinence rates as 28.12%, 28.12% and 28.12% at 6, 8 and 12 weeks. Though the abstinence rate was same at each visit during the medication phase but we observed a significant reduction in Fagertrom score at each visit ($p < 0.05$) reflecting an overall greater likelihood of tobacco abstinence at each study visit.

Table-1: Socio-demographic characteristics of the smokeless tobacco users

Socio-demographic characteristics	Number (N=32)	%
Sex		
Male	31	96.9
Female	1	3.1
Marital status		
Married	20	62.5
Unmarried	12	37.5
Residence		
Urban	8	25.0
Semi-urban	8	25.0
Rural	16	50.0
Religion		
Hindu	28	87.5
Muslim	4	12.5
Occupation		
Govt.	8	25.0
Semi-skilled	7	21.88
Student	5	15.6
Unskilled/agriculture	6	18.8
Unemployed	6	18.8
Education		
Illiterate	3	9.4
Primary	2	6.2
Middle	4	12.5
High school	5	15.6
Intermediate	6	18.8
Graduate	7	21.8
Postgraduate	5	15.6
SES		
Upper	1	3.1
Upper Middle	3	9.4
Middle	15	46.9
Lower Middle	6	18.8
Lower	7	21.8
Family Type		
Nuclear	15	46.9
Joint	17	53.1
Total	**32**	**100.0**

Characteristics	Number (N)	Smokeless (Mean±SD)
Mean age of sample		34.28±12.91
Mean age of onset tobacco use		23.16±8.7
Mean duration of intake of tobacco		11.06±7.49
Baseline mean Fagerstrom score		6.25±1.44
No. of quit attempt		1.53±2.51
Precipitating factors for the intake of tobacco use	**N**	**(%)**
No	0	0
Peer Pressure	23	71.9
Underlying stress	9	28.1
No. of quit attempt		
Nil	21	65.6
1-2	1	3.1
3-4	5	15.6
5+	5	15.6
Total	**32**	**100**

Table-2: Comparision of pharmacotherapy among the smokeless tobacco users on the basis of FTND-ST score (from baseline to each visit)

FTND-ST score for smokeless	TotalFTND score Mean±SD	t-value	p-value
Baseline	6.25±1.437	--	--
Week 2	4.59±1.266	9.051	0.000
Week 4	4.03±1.513	9.557	0.000
Week 6	3.25±1.796	9.960	0.000
Week 8	2.81±1.655	12.114	0.000
Week 12	2.66±1.516	12.677	0.000

This table shows the mean FTND-ST score for smokeless tobacco users in pharmacotherapy group at baseline, week 2, week 4, week 6, week 8, week 12.

The mean reduction of FTND-ST score for smokeless tobacco users from baseline to week 2, week 4, week 6, week 8, week 12 was 1.66, 2.22, 3.0, 3.44 and 3.59 respectively.

The mean reduction rate in FTND-ST score was highest at week 12. There was a significant reduction at every visit from baseline.

4. DISCUSSION

This study was an attempt to assess the efficacy of bupropion for the treatment of ST users. It has been observed that bupropion did significantly increase short-term or long-term tobacco abstinence rates among ST users. Many explanations exist for the efficacy of bupropion for ST users which is evident from literature suggesting that bupropion is clearly efficacious for cigarette smokers (Hughes *et al*., 2002) and may be efficacious for ST users (Ebbert *et al*., 2003).

We found very impressive result of tobacco abstinence in the study group at 12 weeks what was observed in previous two pilot studies of bupropion SR for ST users (Dale *et al*., 2002; Glover *et al*., 2002). Though previous studies have demonstrated the implementation of behavioral modifications are effective for ST users (Severson, 2003). A systematic review showed that behavioral interventions such as Quitline can help in Smokeless tobacco abstinence (Schensu *et al* 2018). It is recommended that a tobacco Quitline should be initiated where trained counselors and health-care providers are available to provide support to people consuming smokeless tobacco (Schensu *et al*. 2018). Studies showed that Bupropion SR does not give good results for long term tobacco abstinence among ST. While efficacy of nicotine patch or nicotine gum for long term abstinence rates is also inconclusive. We found similar consistent result with one of the pervious investigations assessing the effect of bupropion on craving and withdrawal among cigarette smokers (Teneggi *et al*., 2005).

In our study, the overall rates of continuous abstinence in smokeless tobacco users at 6, 8 and 12 weeks were 26.3%, 28.9% and 28.9% respectively in pharmacotherapy group. Participation of females are very less (3.1%) while many studies have indicated that woman have the readiness to quit tobacco but because of lack of family support and household environment influence they have low level of SLT cessation rate (Murthy *et al*. 2018).

In summary, the strengths of our study are the efficacy and dose response demonstrated by point-prevalence rates and the rates of continuous abstinence. However, limitations of our study are small sample size, no control or placebo group, subjects who enroll in

clinical trials are motivated to stop tobacco and so this may not be representative of the general population of smokeless tobacco users.

REFERENCES

1. Indian Council of Medical Research Bulletin, November, 2000.
2. Rani, M., Bonu, S., Jha, P., Nguyen, S. N., & Jamjoum, L. (2003). Tobacco use in India: prevalence and predictors of smoking and chewing in a national cross sectional household survey. Tobacco control, 12(4), e4-e4.
3. Global Youth Tobacco Survey Collaborating Group. (2003). Differences in worldwide tobacco use by gender: findings from the Global Youth Tobacco Survey. Journal of school health, 73(6), 207-215.
4. Little, S. J., Stevens, V. J., LaChance, P. A., Severson, H. H., Bartley, M. H., PhD, E. L., & Leben, J. R. (1992). Smokeless tobacco habits and oral mucosal lesions in dental patients. Journal of Public Health Dentistry, 52(5), 269-276.
5. Martin, G. C., BROWN, J. P., EIFLER, C. W., & HOUSTON, G. D. (1999). Oral leukoplakia status six weeks after cessation of smokeless tobacco use. The Journal of the American Dental Association, 130(7), 945-954.
6. Tomar, S. L., Winn, D. M., Swango, P. A., Giovino, G. A., & Kleinman, D. V. (1997). Oral mucosal smokeless tobacco lesions among adolescents in the United States. Journal of Dental Research, 76(6), 1277-1286.
7. Ernster, V. L., Grady, D. G., Greene, J. C., Walsh, M., Robertson, P., Daniels, T. E., ... & Hauck, W. W. (1990). Smokeless tobacco use and health effects among baseball players. JAMA, 264(2), 218-224.
8. Mattson, M. E., & Winn, D. M. (1989). Smokeless tobacco: association with increased cancer risk. Smokeless Tobacco Use in the, 13-16.
9. Stockwell, H. G., & Lyman, G. H. (1986). Impact of smoking and smokeless tobacco on the risk of cancer of the head and neck. Head & Neck Surgery, 9(2), 104-110.
10. GOODMAN, M. T., MORGENSTERN, H., & WYNDER, E. L. (1986). A case-control study of factors affecting the development of renal cell cancer. American journal of epidemiology, 124(6), 926-941.
11. Muscat, J. E., Hoffmann, D., & Wynder, E. L. (1995). The epidemiology of renal cell carcinoma. A second look. Cancer, 75(10), 2552-2557.
12. Muscat, J. E., Stellman, S. D., Hoffmann, D., & Wynder, E. L. (1997). Smoking and pancreatic cancer in men and women. Cancer Epidemiology and Prevention Biomarkers, 6(1), 15-19.
13. Henley, S. J., Thun, M. J., Connell, C., & Calle, E. E. (2005). Two large prospective studies of mortality among men who use snuff or chewing tobacco (United States). Cancer Causes & Control, 16(4), 347-358.
14. Teo, K. K., Ounpuu, S., Hawken, S., Pandey, M. R., Valentin, V., Hunt, D., ... & INTERHEART Study Investigators. (2006). Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. The lancet, 368(9536), 647-658.
15. Severson, H. H. (1992). Enough snuff: ST Cessation from the behavioral, clinical, and public health perspectives. Pounds (millions), 279.
16. McNeill, A. (2004). Harm reduction. Br Med J, 328: 885–887.
17. National Institutes of Health State-of-the-Science Panel. (2003). National Institutes of Health State-of-the-Science Conference Statement: symptom management in cancer: pain, depression, and fatigue, July 15–17, 2002. Journal of the National Cancer Institute, 95(15), 1110-1117.
18. Ebbert, J. O., Elrashidi, M. Y., & Stead, L. F. (2015). Interventions for smokeless tobacco use cessation. Cochrane Database of Systematic Reviews, (10).
19. Hughes, J. R., Stead, L. F., Hartmann- Boyce, J., Cahill, K., & Lancaster, T. (2014). Antidepressants for smoking cessation. Cochrane database of systematic reviews, (1).
20. Dale, L. C., Ebbert, J. O., Schroeder, D. R., Croghan, I. T., Rasmussen, D. F., Trautman, J. A., ... & Hurt, R. D. (2002). Bupropion for the treatment of nicotine dependence in spit tobacco users: a pilot study. Nicotine & tobacco research, 4(3), 267-274.
21. Ebbert, J., Rowland, L. C., Montori, V. M., Vickers, K. S., Erwin, P. J., & Dale, L. C. (2003). Treatments for spit tobacco use: a quantitative systematicreview. Addiction, 98(5), 569-583.
22. Glover, E. D., Glover, P. N., Sullivan, C. R., Cerullo, C. L., & Hobbs, G. (2002). A comparison of sustained-release bupropion and placebo for smokeless tobacco cessation. American Journal of Health Behavior, 26(5), 386-393.
23. Boyle, R. G., Jensen, J., Hatsukami, D. K., & Severson, H. H. (1995). Measuring dependence in smokeless tobacco users. Addictive behaviors, 20(4), 443-450.
24. Keller, P. A., Boyle, R. G., Lien, R. K., Christiansen, B., & Kobinsky, K. (2021). Engaging smokeless tobacco users in population-based cessation services: Findings from an observational study. Journal of Public Health Management and Practice, 27(4), E173-E176.
25. Severson, H. H. (2003). What have we learned from 20 years of research on smokeless tobacco cessation?. The American journal of the medical sciences, 326(4), 206-211.
26. Nethan, S. T., Sinha, D. N., Chandan, K., & Mehrotra, R. (2018). Smokeless tobacco cessation interventions: A systematic review. The Indian journal of medical research, 148(4), 396.
27. Teneggi, V., Tiffany, S. T., Squassante, L., Milleri,

S., Ziviani, L., & Bye, A. (2005). Effect of sustained-release (SR) bupropion on craving and withdrawal in smokers deprived of cigarettes for 72 h. Psychopharmacology, 183(1), 1-12.

28. Murthy, P., Subodh, B. N., Sinha, D., Aghi, M., & Chaturvedi, P. (2018). Smokeless tobacco (SLT) use and cessation in India: Lessons from user and health care provider perspectives. Asian journal of psychiatry, 32, 137-142.
29. Schensul, J. J., Begum, S., Nair, S., & Oncken, C. (2018). Challenges in Indian women's readiness to quit smokeless tobacco use. Asian Pacific journal of cancer prevention: APJCP, 19(6), 1561.

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