Prevalence and Severity of Smoking among Patients with Schizophrenia and Bipolar Disorder and the Effectiveness of Nicotine Replacement Therapy – An Observational Study

Dissertation submitted by

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In partial fulfillment of the regulations required for the degree of
DOCTOR OF MEDICINE IN PSYCHIATRY

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**Prevalence and Severity of Smoking among Patients with Schizophrenia and Bipolar Disorder and the Effectiveness of Nicotine Replacement Therapy – An Observational Study"** is a bonafide and genuine research work carried by me under the guidance of Dr. G. Raghuthaman, Professor in the Department of Psychiatry, PSGIMS & R, Coimbatore.

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ABSTRACT

Prevalence and Severity of Smoking among Patients with Schizophrenia and Bipolar Disorder and the Effectiveness of Nicotine Replacement Therapy – An Observational Study

INTRODUCTION

People with mental illness are twice as likely to smoke, so there is a need to establish clarity regarding association of smoking and mental illness. Further, studies on effectiveness of nicotine replacement therapy yielded conflicting results. Hence, we studied the prevalence and severity of nicotine dependence suffering from schizophrenia and bipolar disorder and offered nicotine replacements to study it's effectiveness in the follow up.

AIM

1) To assess prevalence and severity of nicotine dependence in patients suffering with schizophrenia and bipolar disorder

2) To study the effectiveness of nicotine replacements

METHODOLOGY

We recruited consecutive inpatients with schizophrenia or bipolar disorder and measured severity of illness using BPRS/YMRS/HDRS as suitable at baseline, 4^{th} and 12^{th} week. Fagerstrom test for nicotine dependence was used

to assess severity of smoking at baseline, 4th and 12th week. Nicotine replacements were given to those who were willing.

RESULTS

The percentage of smokers among patients with schizophrenia and bipolar disorder were 44.2 % (n=19) and 34.0% (n=16) respectively. The severity of nicotine dependence fell in the mild to moderate category. At 4th week, 17.6 % of those who were diagnosed with schizophrenia and 58.3 % of those with bipolar disorder were abstinent. While at the 12th week, 26.7 % of schizophrenia and 63.7 % of bipolar disorder patients were abstinent($X^2(1)=3.534, p=0.059$). 53.8% of those who continued nicotine replacement therapy at 4th week were abstinent [$X^2(1)=3.589, p=0.058$] and 88.9% at 12th week [$X^2(1)=10.77, p=0.01$]. The number of smokes showed a statistical significant reduction at 4th and 12th week when compared to baseline ($Z=-3.519, p=0.00$; $Z=-2.498, p=0.013$).

CONCLUSION

The prevalence of smoking among male schizophrenia and bipolar affective disorder patients is higher than that of the general population. Greater number of patients with bipolar affective disorder had remained abstinent from smoking at 4th and 12th week. More number of patients who continued nicotine gum at 4th and 12th weeks remained abstinent from smoking.

Keywords

Smoking, Schizophrenia, Bipolar

INTRODUCTION

The global burden of tobacco use in its myriad forms is enormous, given that it adversely affects the physical, mental and social aspects of living. It is estimated that nearly 450 million deaths shall be reported in the next 50 years as a result of cigarette smoking[1] . It was further suggested in the same study that 20 to 30 million premature deaths can be avoided in the first quarter of the century and 150 million in the second quarter by reducing 50 % of the current smoking trends. Tobacco, consumed by means of smoking, remains the leading cause of avoidable morbidity and pre-mature mortality across the world[2].

While the prevalence of smoking appears on the decline in high income countries, the habit in developing countries appear to be on the ascendancy. The rise in population and income in low and middle income countries, has subsequently caused an elevation in their smoking tendencies and presently constitute a major public health issue[4].Hence, the major battleground for the global fight against tobacco consumption has shifted from the developed nations to the developing nations, particularly India and China.

THE INDIAN SCENARIO

India has the dubious distinction of being second in the world when it comes to tobacco consumption and third in terms of manufacturing of tobacco products worldwide. It has also been reported that nearly 900,000 people succumb to illnesses related to tobacco per year in India[5]. Although tobacco can be consumed both through smoked and smokeless forms, smoking is reported to be the predominant habit among males in India constituting more than 50 % of the tobacco users.

TOBACCO USE IN PATIENTS WITH SEVERE MENTAL DISORDERS

It is suggested that people with mental illness are twice as likely as non psychiatric controls to smoke[3] and that in the US estimates of smoking prevalence among individuals receiving psychiatric care indicate that between 50% to 80% psychiatric patients smoke,[4-6] compared to 24% of the general population.[7] Some studies show that patients with schizophrenia who smoke score higher on psychotic rating scales when compared to their non smoking peers.[4,8] and that when comparing the severity of psychotic symptoms in

patients with bipolar affective disorder increased severity in patients who smoke is seen.[9]

But research also indicates that nicotine may be particularly effective in relieving negative symptoms associated with schizophrenia relative to other psychiatric symptoms.[10,11] Thus a need to establish clarity regarding the association of smoking with severe mental illness appeared vital in the treatment of the disorder itself.

Studies in India about nicotine use in psychiatric patients are few and far in between. One study done in India among 510 male psychiatric patients, reported that the prevalence of smoking was 38% among patients with schizophrenia, 24% among patients with mood disorders, and 23% among those with a non-psychotic disorder.[12]

HOW EFFECTIVE IS NICOTINE REPLACEMENT THERAPY(NRT)?

Studies have given conflicting reports on the effectiveness of nicotine replacement therapy on smoking cessation with one concluding that 'NRT is no more effective in helping people stop smoking cigarettes in the long-term than trying to quit on one's own'[14] and another study confirmed that nicotine assisted

reduction to stop programmes can be effective in achieving sustained abstinence from smoking for up to six months.[15]

In controlled trials in smokers with schizophrenia,abstinence rates have been 4% to 19% at 3- to 6-month follow-up with single preparation NRT and 0% to 6% with placebo.[16]

To our knowledge, no study has looked into the effectiveness of nicotine replacement therapy in the Indian setup.

Hence a study that looked into the prevalence and severity of nicotine dependence in Indian patients suffering with schizophrenia and bipolar disorder and following them from acute stage to remission stage seems prudent. We provided 3 educational sessions about quitting smoking and Nicotine replacement therapy and gave nicotine gums to patients who are willing to try and studied its effectiveness.

REVIEW OF LITERATURE

The World Health Organisation has given an estimate that nearly 5 million deaths occur annually worldwide as a result of tobacco use[3]. Other than smoking, tobacco can also be chewed, inhaled, or applied on oral mucosa with the unconventional methods of tobacco consumption finding immense popularity in South Asia and South-east Asia. However, worldwide 90 % of tobacco consumption is accounted for by cigarettes.

In addition to cigarettes, *beedis* appear to be a popular form of smoking tobacco. *Beedis* consist of finely ground, sun – dried tobacco hand rolled in a brown, broad leaf locally known as *tendu* (*Diospyrusmelanoxylon* or *Diospyrusebemum*). *Beedis* remain popular, especially among the rural and low socio-economic strata given it's cheaper cost and association with tradition. *Beedis* are said to account for 48 % (750 billion to 1.2 trillion) of tobacco consumption in India whereas cigarettes account for 14%, making *beedis* the most preferred form of tobacco consumption among Indians[13].

Toxicological analysis suggest that the smoke of beedis, like regular cigarettes, contain phenol, hydrogen cyanide, and benzo(a)pyrenes[6] and total particulate matter, a measure directly related to the amount of carcinogenic material[7] . Nair and colleagues identified carcinogenic tobacco specific nitrosamines from the smoke of *beedis* in concentrations similar to regular cigarettes[8]. When compared to an unfiltered cigarette, *beedi* smoke contains more tar, carbon monoxide, ammonia, hydrogen cyanide, phenol, volatile phenols and benz(a)anthracene.

[13]Gutkha and Zarda constitute the main form of tobacco consumption by means of chewing. Gutkha is a mixture of crushed areca nut, tobacco and catechu, available in both sweet and savoury flavourings. It's usually chewed and spit out. It is commonly used by women and children as well, in a culture where smoking by the fairer sex is still looked down upon. Zarda is a dried and coloured residual tobacco, obtained by boiling leaves with spices and lime.

Ever since the publication of the Doll and Hill study of smoking and lung carcinoma in 1950, the dire consequences of tobacco consumption have been well established. The following years saw several other studies report on the adverse effects to health as a result of tobacco consumption. Presently, the consumption of tobacco is recognised as a major health hazard and cause for

premature morbidity and mortality across the world. As a result, measures to tackle tobacco intake forms the mainstay of all major health programmes across the world.

To look into the epidemic of smoking in India, a study was done by Venkat Narayan et al[22] in 1996 in Delhi by surveying a random sample of adults that were living in urban Delhi. Out of the 13,558 subjects surveyed, 24.5% (95 % confidence interval 23.8 to 25.2) were smokers. Men had a significantly higher prevalence rate of smoking with 2,799 (45.0%) of the 6,221 male subjects studied being smokers. Among the women who were involved in the study only 516 (7.0%) of the 7,337 women admitted to smoking.

Subramanian et al[23] looked into the patterns and distribution of tobacco consumption in India from the 1998 – 9 national family health survey. The analysis included 3,01,984 adults aged 18 and older, from 92,447 households from 26 Indian states. The overall prevalence for the consumption of tobacco by means of smoking was 18.4 % and for chewing was 21.0 % with a combined prevalence of 32.9 %.

In another study conducted at NIMHANS, Bangalore, Chandra et al screened consecutive psychiatric patients who got admitted and found that 36% of them use some form of tobacco products.[13] But both these studies were cross sectional studies which didn't look into the severity of mental illness with smoking and didn't follow up the patients to study any changes in the pattern of cigarette use.

In a study done by Jayakrishnan et al[24] in a rural population in Kerala, the overall prevalence of current daily smokers was 28.1 % (mean age 44.4 years, SD ; 9.2 years). The study design is a community based randomised intervention trial in 4 community development blocks in Thiruvananthapuram district. Ward is the lowest level of administrative system of community development blocks. A total of 11 wards (5 from intervention and 6 from control area) were selected from the CDBs using random sampling method. A smoking cessation programme was being conducted for those in the intervention area. Among the 3,304 males in the intervention and control arm, a total of 928 'current daily smokers' were identified from house to house survey.

Of the 928 smokers, 474 subjects were in the intervention area (mean age: 44.56 years, SD: 9.66 years) and 454 in the control area (mean age: 44.47 years, SD: 10.30 years). The average number of cigarettes and *beedis* consumed per

day corresponds to 13.19 (SD: 8.4) in the intervention and 10.90 (SD: 6.8) in the control groups.

Cigarette smoking was the most common habit among both groups representing 62.5% in the control and 53.8% in the intervention areas. The mean duration of smoking was 15.05 years in the control area (SD: 8.28) and 15.78 years (SD: 9.09) in the intervention area.

The overall FTND score among current daily smokers was 5.04 (SD: 5.05). FTND scores in the control and intervention areas were 4.75 (SD: 2.57) and 4.92 (SD: 2.51) respectively. In conclusion, the study reported moderate level of nicotine dependence in the rural population in Thiruvananthapuram, Kerala.

In a study, [26]Grant et al estimated the burden of all US tobacco consumption carried by nicotine dependent and psychiatrically ill individuals. Among US adults, 12.8 % (95 % confidence interval, 12.0 – 13.6) were nicotine dependent. Associations between nicotine dependence and specific axis I and II disorders were strong and significant ($p<0.05$) in the total population among both men and women.

Nicotine dependent individuals with co-morbid psychiatric disorder constituted 7.1% of the population only and yet they consumed 34.2 % of the total tobacco consumed in the United States. The authors conclude that patients who are nicotine dependent and has a psychiatric disorder would fall into a vulnerable category for tobacco consumption and hence de-addiction treatment in them needs to be actively pursued.

A similar study evaluated the findings of the national survey done in Britain in 1995[25]. Among those surveyed, 32 % were reported to be current smokers, with 8 % classified as light smokers (less than 10 a day), 13 % moderate smokers (10 – 20 a day) and 11 % were heavy smokers (more than 20 a day). No gender difference in patterns of cigarette smoking was noted unlike among the Indian population. Among those who were classed as having psychiatric disorder, 33 % (3,329) were classed as having nicotine dependence as well.

The authors further suggested that there was a clear relationship between dependence on nicotine, alcohol and drugs and psychological morbidity. They also added that smoking nicotine is associated significantly with increased psychiatric disorders.

Studies have shown that the prevalence of smoking is significantly higher among psychiatric outpatients than the general population[27]. The more severely afflicted patients like those with schizophrenia and mania, showed high prevalence rates of 88% and 70% respectively.

Another study sought to study the prevalence of smoking among French psychiatric patients. The prevalence of smoking among 711 patients with mental illness was significantly higher than the French general population[30]

The relatively high prevalence of nicotine dependency in persons with mental illnesses and substance abuse disorders reflects biological, psychosocial, and cultural factors in addition to targeting by the tobacco industry. Some mental illnesses have associated neurobiological features that increase their tendency to use nicotine, make it more difficult to quit, and complicate the withdrawal phase of tobacco cessation.

Genetic linkage studies have found associations between both schizophrenia and bipolar disorder and chromosome 15 in a location at the alpha 7-nicotinic receptor subunit gene[28,29], and the alpha-7 nicotinic receptor gene has been implicated in impaired sensory processing in individuals with schizophrenia and

schizoaffective disorder[31]. Individuals with this gene have auditory sensory-gating deficits and diminished suppression of the auditory evoked P50 response. Nicotine briefly normalizes this deficit, suggesting an association with diminished P50 response and decreased alpha-7 subunits of nicotinic receptors for persons with these psychiatric illnesses[29.]

Gene studies have also found that adolescents with at least one A1 allele have increased impairment of dopaminergic functioning, symptoms of depression, and smoking[32]. These genetic linkages and receptor abnormalities are one of many factors explaining heavy levels of smoking in these individuals, as nicotine might normalize associated deficits in sensory processing, attention, cognition and mood[29].

Nicotine may also offer brief relief from medication side-effects, since tobacco use significantly decreases blood levels of common psychiatric medications[8]. For persons with substance abuse disorders, tobacco use affects the same neural pathway— the meso-limbic dopamine system—as do alcohol, opiates, cocaine, and marijuana[33]. The effects of nicotine and opiates on the brain's reward system are equally potent in a key pleasure-sensing area of the brain: the nucleus accumbens[34].

Persons with mental illnesses and substance abuse disorders also use tobacco for the same reasons as the general population: as part of a daily routine to relieve stress and anxiety. Tobacco use is perceived as a way to fit in and to cope with boredom when social and vocational options are limited.

When coming to the management of these patients, unfortunately the culture of mental health and substance abuse care reinforces tobacco use in treatment settings, residential facilities, and housing[35]. Mental health and substance abuse providers also have high smoking prevalence rates—30%–35% [36]— thereby impeding tobacco cessation efforts[37]. By contrast smoking rates among primary care physicians are only 1%[38].

[12]A study done in India on 286 urban male outpatients with schizophrenia showed that only 38% were found to be smoking presently. This was said to be significantly more than patients who were studied with other psychiatric diagnosis (major affective disorders and non-psychotic disorders) but not medically ill controls and not higher than the rates for the general male population in India. In this study, the use of the smokeless form of the tobacco

appeared to be insignificant. The study also reported that more than half of the responders reported no positive effects from usage of tobacco.

[13]Chandra et al screened 988 consecutive admissions to a major psychiatric hospital in South India. Information was obtained about their use of tobacco products, and participated in the Fagerstrom Test for Nicotine Dependence as well as measures of other substance use. Three hundred and fifty-one patients (36%) reported to be using tobacco currently, with two hundred and twenty seven (65% of tobacco consumers) reporting moderate to severe nicotine dependence. The major diagnosis among tobacco users was that of bipolar affective disorder.

The authors suggested that the smoking epidemic among the psychiatric patients in India has not reached the same level as those in the west. After cautioning for difficulties in interpreting cross-cultural variations, the authors postulated that a presence of a strong family system in India even for the mentally afflicted patients could be a possible explanation for the same. Also, restrictions imposed by family and society on smoking and lower income for patients to afford tobacco-related products were some of the other reasons listed.

A study[39] recruited male patients with schizophrenia and their non-psychotic brothers. Detailed information about tobacco consumption was obtained through Fagerstrom Test for Nicotine Dependence (FTND)for smoked tobacco and FTND – smokeless tobacco.

Investigators also administered University of Pennsylvania Computerized Neurocognitive battery (CNB) for a sub-group of patients. Results showed that schizophrenia patients began using tobacco earlier than their non-psychotic brothers. Also, patients with schizophrenia who were current smokers scored higher on positive symptoms of schizophrenia than non-smokers. No significant difference between nicotine dependent patients and non dependent patients were seen in CNB domains except for attention.

[40]A study in Bangladesh on an urban population of 510 male psychiatric patients (Schizophrenia = 286, Major affective disorders = 84, Non psychotic disorder = 140) showed that prevalence of smoking in psychiatric patients is no greater, if not lesser, than that of the control group of medically ill patients with no psychiatric diagnosis (n=177) or the general population. More number of psychiatric patients had reported to have quit smoking than the medically ill.

The reasons for the absence of high prevalence of smoking among the psychiatric patients were said to be socio-cultural and economic.

In a study[4] done on seventy eight outpatients with schizophrenia, who were assessed by a single rater using the Brief Psychiatric Rating Scale (BPRS), it was found that current smokers tend to have a younger age of onset, more number of previous hospitalisation, require higher mean neuroleptic doses and scored higher in the BPRS. The study implicated that smoking adversely affected symptoms of schizophrenia.

A meta-analysis of worldwide studies showed that forty-two of them across 20 nations consistently showed an association between schizophrenia and current smoking with odds ratio (OR) at 5.9, 95% confidence interval (CI) at 4.9--5.7. Even when controlled for other variables, the association between schizophrenia and current smoking patterns remained. Heavy smoking and high nicotine dependence were more witnessed in patients with schizophrenia when compared to the general population. When compared to the general population, patients with schizophrenia had a greater prevalence of having ever smoked a cigarette (OR=3.1, CI 2.4--3.8). Further, two studies, when adjusted for confounders, showed that patients with schizophrenia showed an increased risk

of smoking everyday compared to control groups. Hence, this study concluded that people with schizophrenia have more risk to start smoking.

In another study, Beck et al[41] recruited 16 patients with schizophrenia or schizo-affective disorder and 12 community controls participated in experimental sessions. Cognitive assessment was done through observations on three cognitive indices - visual spatial working memory (VSWM), sustained attention (Continuous Performance Test – Identical Pairs – CPT-IP) and prepulse inhibition (PPI) after 'typical' smoking and overnight abstinence. They were compared with self reported smoking motivation (Modified reasons for Smoking Scale that included 'cognitive motivators'). Smokers among patients with schizophrenia (but not controls) showed significant less error on the VSWM task in the smoking relative to the abstinent condition. Thus, this preliminary study showed that differential effects of nicotine on cognition may improve the so called negative effects of schizophrenia.

This study throws an interesting conundrum about the role of nicotine in patients with schizophrenia. On the one hand, it's effects are said to be detrimental in schizophrenia, with apparent greater severity of symptoms in schizophrenia patients who smoke. On the other hand, nicotine is said to

improve the negative symptoms of schizophrenia and particularly small studies have shown enhanced cognitive performance in patients with schizophrenia who use nicotine.

Data from National Co-morbidity Survey done in 92-93 showed that the prevalence of smoking in bipolar affective disorder was 69% but a 2007 National Health Interview Survey suggested a prevalence rate of 46%. A study which attempted to address this variability was done by Diaz et al[42] by studying 424 psychiatric patients and 402 volunteer controls at Central Kentucky. Of the 424 psychiatric patients, 99 were diagnosed as bipolar, 258 had a diagnosis of schizophrenia and 67 of major depression. Prevalence of daily smoking patterns currently for patients with major depression, bipolar and schizophrenia were 57%, 66% and 74% respectively.

Data on smoking in patients with bipolar affective disorder are conflicting, with some studies suggesting that bipolar affective disorder patients are prone to increased smoking while other studies found that instances of smoking among bipolar disorder patients were lesser than previously reported. The reasoning behind this was suggested to be that in the latter sample there was a preponderance of patients with unipolar depression. It was hypothesised that the

presence of psychotic symptoms was more likely to induce smoking tendencies in patients.

Yet the study found no evidence of a link between the severity of psychosis and the severity of smoking, as there was no difference in the severity of psychosis between the moderate and heavy smoking groups. This was attributed to the insufficient sample size and the relatively small groups that were involved making it difficult to distinguish if such a difference existed.

The relationship with nicotine and bipolar disorder also appears to be complex from studies. Some suggest that smoking could lead to depression and other affective disorders, with others suggesting that among smokers, cessation of smoking has been associated with development of an affective episode.

[43]A review done by Balfour et al suggested that chronic exposure to nicotine causes changes in serotonin formation and release in the hippocampus which are depressogenic. The authors further postulate that smokers are protected from the consequences of the aforementioned impacts, as long as they continue to smoke. This is explained through the purported anti-depressant properties of nicotine. Further, it is said that these changes contribute to the symptoms

suggestive of depression that smokers go through while attempting to quit the habit.

Hitsman et al[44] in their review address the dilemma some psychiatrists might face in treating nicotine dependence given the conflicting role of nicotine in various studies in reference to psychiatric illness. In their review, the authors report that quite often psychiatry care givers do not address the issue of nicotine dependence as they feel that their clients might not be able to quit completely or might even be adversely affected in their psychiatric status.

They suggested that not only do psychiatric symptoms not worsen upon quitting smoking, some may even improve in their psychiatric symptoms upon quitting tobacco. Therefore, the authors concluded that clinicians should not refrain from treating the nicotine dependence in patients with comorbid psychiatric disorders, but should instead encourage cessation and provide support as they would with any other smoker.

Many mental health and substance abuse providers believe tobacco cessation is unrealistic for their clients. Smoking is often seen as one of the last freedoms and chances to execute free will in patients with psychiatric illness, making

clinicians apprehensive about pursuing it's cessation. Tobacco use is viewed by many providers as a lesser problem than the immediate consequences of other substance abuse[45].

Despite opinions to the contrary, the smoking cessation rates of persons with mental illnesses and substance abuse disorders who desire to quit are comparable to the general population[46]. Several studies have found that 77%–79% of these individuals intend to quit, many in the next month. Although these clients may desire to quit, most are not afforded the same cessation opportunities as the general population.

Behavioural health specialists, in contrast to primary care providers, rarely assess for smoking status or provide cessation counselling. Psychiatric patients receive cessation counselling in only 38% of their visits to primary care physicians and 12% of their visits to psychiatrists[47]. The situation appears even worse in inpatient settings, where—among 250 psychiatric inpatients—only 1% were assessed for smoking status, nicotine dependency was not assessed, and smoking status was never included in treatment plans.

Providers and administrators warn that forbidding smoking will disrupt the treatment milieu, dramatically increase behavioral problems, and result in premature or irregular discharges. But, studies from multiple countries did not find smoking bans had a negative effect on psychiatric symptoms or management in treatment units.

A survey of 158 U.S. state psychiatric facilities found that 41% did not permit smoking at their facility or grounds[48]. Of the remaining 59% still allowing smoking, half planned to go tobacco-free in the near future. The sites that had gone tobacco-free reported improved health of patients and cleaner grounds/environment. Banning smoking reduced seclusion and restraint, decreased coercion and threats among patients and staff, and increased availability of tobacco cessation medication.

The tobacco industry has long targeted individuals with mental illnesses and substance abuse disorders, labelling these populations as “downscale markets.” Prochaska[49] analyzed tobacco industry documents from 1955 to 2004 and found that the industry monitored or directly funded research supporting the concept that persons with schizophrenia were less susceptible to the harms of tobacco and needed tobacco as self-medication. The industry promoted smoking in

psychiatric settings by providing free cigarettes and aiding efforts to block hospital smoking bans.

A study[50] done in the US randomised 123 patients with psychiatric diagnosis and who identified themselves as smokers, at 4 community mental health clinics at both rural and urban areas. 61 participants were randomised to quitline services alone and 62 to both quitline and services of a community tobacco cessation group of upto 10 sessions. In addition to this, they received treatment as usual for their psychiatric diagnoses and were offered free nicotine replacement patches for 12 weeks to all interested participants. Outcome measures were administered at baseline and 6-months with results showing a 50% or greater reduction in smoking and a 10% abstinence rate. This study showed the effectiveness of the nicotine replacement therapy.

In the UK, [51]Moore et al did a systematic review and meta-analysis to study the effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking. This review found that nicotine assisted reduction to stop programmes can be effective in achieving sustained abstinence from smoking of six months. Further, they also added that there was no evidence of an increase in life threatening complications as a result of nicotine replacement use. The

therapy was well tolerated with almost no difference in discontinuation because of side effects in those receiving nicotine replacement therapy compared with those receiving placebo.

A randomized study of persons treated in public mental health systems showed that quit-line counselling plus nicotine replacement therapy led to a significant reduction in self-reported number of cigarettes smoked per day.[17]

Another randomized study of smokers with mental illness showed that NRT was effective in bringing down the self reported number of cigarettes smoked per day and tobacco dependency.

[18] Cochrane review of over 90 trials found that nicotine replacement helps people to stop smoking.[19] Overall, it increased the chances of quitting about one and a half to two times (1.71, 1.60 to 1.83), whatever may be the level of additional support and encouragement.

Another Cochrane review[52] on the effectiveness of Nicotine Replacement Therapy (NRT) included 136 trials of NRT, with 64,640 people in the main

analysis. It indicated that all forms of NRT studied increased the chance of the patient quitting tobacco by about 50 to 60% with or without any counselling. The risk ratio (RR) of abstinence of any form of NRT relative to control was 1.55 with a 95% confidence interval (CI) of 1.49 to 1.61.

Hence, nicotine replacement therapy was said to increase the chances of quitting by about one and half to two times, irrespective of the manner of additional support or encouragement received by the patients. The quit rate was higher in both placebo and treatment arms of trials that included intensive support. Therefore nicotine replacement therapy seemed to increase the rate of quitting from whatever baseline was set by a previous intervention.

All the trials studied had included at least a brief advice on how to quit smoking and hence that was suggested as the minimum additional treatment to be offered in addition to the nicotine replacements.

Meat-analysis of the effect of nicotine replacement therapy on smoking cessation showed there was no direct evidence to show that one form of nicotine treatment was superior to the other. The odds ratio with 95% confidence interval was found to be 1.63 (1.49 to 1.79) for nicotine gums, 1.75 (1.57 to

1.94) in nicotine patches, 2.27 (1.61 to 3.20) in the intranasal spray form of nicotine replacement, 2.08 (1.43 to 3.04) in nicotine inhalers, 1.73 01.07 to 2.80) in sublingual nicotine tablets and 1.71(1.60 to 1.83) among all formulations of nicotine replacements. Hence, it was noted that the type of nicotine replacement used should be primarily decided by the choice and comfort of the patient. This review suggested that no form of NRT was superior to the other in addition to showing their general effectiveness and safety in smoking cessation.

Further, a study done by Hajek et al[53] compared different forms of nicotine replacement in 504 smokers who volunteered for the study. They were randomised to 4 groups based on their type of nicotine replacement and assessed at quit date, 1, 4 and 12 weeks later. There was no difference noted by the authors among the effects the products had on withdrawal discomfort, urges to smoke or rates of abstinence. 20%, 21%, 24% and 24% were the continuous validated abstinence rates in the gum, patch, spray and inhaler groups respectively at 12 weeks.

In the same study, compliance was shown to be good for nicotine patch, low for nicotine gum and very low for the spray and inhaler. The spray appeared to

have lesser than desirable usage as a result of adverse effects, while the less usage associated with inhaler was more due to embarrassment.

The large population-based [54]California Tobacco Surveys of 1992, 1996 and 1999 including 5247 (71.3% response rate), 9725 (72.9% response rate) and 6412 (68.4% response rate) respondents respectively were studied by Pierce et al to look into the long term effectiveness of Nicotine Replacement Therapy. Results indicated that NRT use increased short-term cessation success in moderate to heavy smokers in each survey year. However, a long-term cessation effectiveness among the residents of California appeared to be no greater than before.

Thus, the effective of Nicotine Replacement Therapy as a long-term treatment option for smoking appears controversial and not substantiated yet. Further, to our knowledge, no Indian study on the effectiveness of NRT had yet been published which seems critical given the peculiar socio-cultural and economic issues related with tobacco consumption in the nation.

AIMS :

To study the prevalence and severity of smoking among patients with schizophrenia and bipolar disorder and also to study the effectiveness of nicotine replacement therapy.

OBJECTIVES :

1. To estimate the prevalence of smoking among patients with schizophrenia and bipolar disorder.
2. To study the association of smoking and severity of illness by following the patients from acute stage to remission stage.
3. To prospectively evaluate the effectiveness of Nicotine Replacement Therapy (nicotine gums) among smokers in both schizophrenia and bipolar disorder groups.

METHODOLOGY :

Study Design:

This is a prospective and observational study.

Sample Recruitment:

We screened all the male patients admitted in the psychiatry department and we recruited consecutive patients who were diagnosed as having schizophrenia or bipolar disorder, according to the ICD-10 Classification of Mental and Behavioural Disorders criteria

Inclusion Criteria:

All male patients > 18 years of age with a clinical diagnosis of schizophrenia or bipolar affective disorder as per ICD 10 diagnostic criteria who received in-patient treatment during the period between June 2017 and May 2018 were included.

Exclusion Criteria:

1. Patients who had co-morbid substance use except alcohol and tobacco.
2. Patients who had mental retardation.

Materials used in the study:

1. Patient proforma
2. Brief Psychiatric Rating Scale (BPRS)
3. Young's Mania Rating Scale (YMRS)
4. Hamilton's Depression Rating Scale (HAM-D)
5. Fagerstrom Test for Nicotine Dependence – Tamil version (FTND - Tamil)

Patient Proforma:

a. Socio-demographic details of the patient
b. Diagnosis
c. Clinical details – Duration of illness, number of previous hospitalizations, duration of current episode/exacerbation
d. Details of substance use (tobacco, hans and alcohol)
e. Smoking details – type of smoking, duration of use, daily usage pattern

f. Nicotine gum use – willingness for nicotine gum, dosage of gum, mean number of gums per day, percentage of nicotine gums consumption days, continuation at 4^{th} and 12^{th} week, reason for discontinuation.

Brief Psychiatric Rating Scale (BPRS):

The Brief Psychiatric Rating Scale (BPRS) is a rating scale which a clinician or researcher may use to measure psychiatric symptoms particularly in relation to psychosis or schizophrenia. It evaluates symptoms like thought content, suspisciousness, uncooperativeness, depression, anxiety, hallucinations and unusual behaviour. Each symptom is rated 1- 7 and a total of 21 items are scored. It was first published in 1962 and is one of the most widely used scale to measure psychotic symptoms.

This scale was used to measure the severity of psychotic symptoms in our patient and it was ascertained that they had improved if the score had improved >20%.

Young's Mania Rating Scale(YMRS):

The Young's Mania Rating Scale (YMRS) is used frequently to assess manic symptoms. It is a clinician rated scale. It takes about 10 to 15 minutes to

administer. The scale consists of 11 items out of which a few of the items are rated on a 0 to 8 scale (thought content, irritability, speech and disruptive/aggressive behaviour), while the remaining seven items are graded on a 0 to 4 scale.

This scale was used in our study to assess the symptom severity of manic episode and we ascertained that patient had reached euthymic state if the score was <6.

Hamilton Depression Rating Scale (HAM-D):

The Hamilton Depression Rating Scale (HAM-D or HDRS) is also a clinician rating scale. It takes 20 to 30 minutes to be administered. It's administration serves the purpose to assess the severity of depressive symptoms and also to gauge the difference in depressive symptoms progressively. The original version contains 17 items (HDRS17) related to depressive symptoms that were experienced in the past week. A 21 item version (HDRS21) included four extra items, which is intended to further classify the depression. A limitation of this scale is that it does not assess the atypical symptoms of depression (e.g. hypersomnia, hyperphagia)

This scale was used in our study to assess the severity of the symptoms occurring in the depressive episode and we ascertained that that patient had reached euthymic state if HDRS score <6 in the 17 items scale.

Fagerstrom Test for Nicotine Dependence (Tamil Version):

The Fagerstorm Test for Nicotine Dependence is a standard instrument used to assess the intensity of physical addiction to nicotine. It was designed to provide an objective measure of nicotine dependence related to cigarette smoking. It has six items that evaluate the quantity of cigarette consumption, the compulsion to use and the dependence.

It was originally developed as the Fagerstrom Tolerance Questionnaire by Karl-OlovFagerstrom and modified to the Fagerstrom Test for Nicotine dependence by Heatherton et al in 1991.

This scale has been adapted and validated in Tamil, in order to overcome any linguistic barriers in the assessment of the severity of nicotine dependence among patients in their native language.

We obtained informed consent from the recruited patients and their caregivers. At baseline, we measured the severity of the mental illness, using BPRS for

schizophrenia and using YMRS and HDRS for bipolar disorder. Using a semi-structured proforma we collected the socio-demographic details, clinical data, smoking status and number of cigarettes smoked among smokers. Among patients who smoke, we used Fagerstrom Test for Nicotine Dependence scale to assess the severity of smoking.

To patients who were dependent on smoking, we suggested them to take nicotine gum to manage withdrawal symptoms as well as to help in maintaining abstinence while in the hospital.

We suggested : Nicotine gum – 2mg 3 per day for those who smoke >10 but <20 cigarettes a day and 4 mg 3 per day for those who smoke ≥20 cigarettes per day

As happening with all patients, we expected that patients might or might not accept nicotine replacement for various reasons. In our study, we had planned to do naturalistic observations among our patient groups to estimate how many accepted nicotine replacement and to study the effects on their smoking status.

Once the mental state of the patients improved, we provided 3 educational sessions to motivate them to give up smoking and suggested them to take oral nicotine replacement for at least 3 months.

Educational sessions involved the 5As, evaluating the stage of readiness to change and motivational interviewing as per the 2005 NSW Australia Health booklet[21]

The 5 As

- Asking about tobacco use
- Assessing willingness to change and nicotine dependence
- Advise on tobacco cessation
- Assist in tobacco cessation
- Arrange follow up

Stage of Readiness to Change

Stage of Change is a valuable model for assessing a person's readiness to change a variety of behaviours including tobacco smoking. Cessation is explained as a process rather than a discrete event and smokers cycle through the stages of being ready, quitting and relapsing on an average of three to four times. Readiness to change can be fluid so some smokers will have moved groups when seen at different times.

Key questions to ask are “How do you feel about your smoking at the moment?” – Stage of readiness to change can be assessed by asking this key question. Clarify whether the smoker is ready to make a quit attempt at this time or in the near future. Ask “Are you ready to quit now?”

People who smoke broadly fall into the following categories:

• Not ready (pre-contemplation) – not seriously thinking of quitting in the next 6 months

• Unsure (contemplation) – considering quitting in the next 6 months

• Ready (preparation) – planning to quit in the next 30 days

• Action – people who have quit in the last six months • Maintenance – smokers who have been abstinent for more than 6 months.

Tailored assistance to the stage of readiness to change is given.

Not ready group – Show interest and encourage the patient to think about the issues

Unsure – Motivate change and offer help to identify and overcome barriers to cessation

Ready – Provide assistance

– to develop a quit plan

– Suggest coping strategies

– Delay, Deep breathe, Drink water, Do something else

– Assist with pharmacotherapy where indicated

– Encourage social support

Action – Congratulate on progress

- Check for problems and if present advise or refer appropriately

Maintenance – Congratulate and reinforce benefits of being a non-smoker.

Brief Motivational Interviewing

Motivational interviewing is a key skill for assisting the unsure group of smokers. It involves asking open-ended questions, reflective listening and summarising. Ambivalence about smoking (likes and dislikes) should be acknowledged and discrepancies in the person's beliefs and personal goals such as health and fitness can be discussed.

The following approach can be used to explore ambivalence and to motivate the patient to consider the need to change. It is important to start with the positives of smoking for the patient, as these are frequently not acknowledged.

Step 1: Ask: "What do you like about smoking?"

Step 2: Ask: "What are the things you don't like about smoking?"

Step 3: Summarise – your understanding of the patient's pros and cons

Step 4: Ask: “Where does this leave you now?” This can be used as a written take home exercise or during the consultation. Ask the patient to list both their likes and dislikes about smoking and their likes and dislikes of quitting.

At the time of discharge, we assessed the severity of illness using BPRS, YMRS and HDRS appropriately and we repeated this 4 weeks and 12 weeks after discharge from the hospital. We also assessed the smoking status and the severity of smoking using Fagerstrom Test for Nicotine Dependence scale 4 weeks and 12 weeks after discharge from the hospital. Patients who did not come for outpatient follow-up treatment, both patients and their caregivers were contacted separately over the phone to get the details about their current smoking status and adherence to oral nicotine replacement therapy.

Sample size calculation:

Among male psychiatric in-patients, Chandra et al found the prevalence of smoking as 44%. Using this estimate, we calculated sample size with the formula $n=(Z_{1-\alpha})^2(P(1-P)/D^2)$, keeping confidence interval as 95% and absolute precision as 10%; we needed 90 patients to estimate the prevalence of smoking among male patients suffering with schizophrenia or bipolar disorder

STATISTICAL ANALYSIS

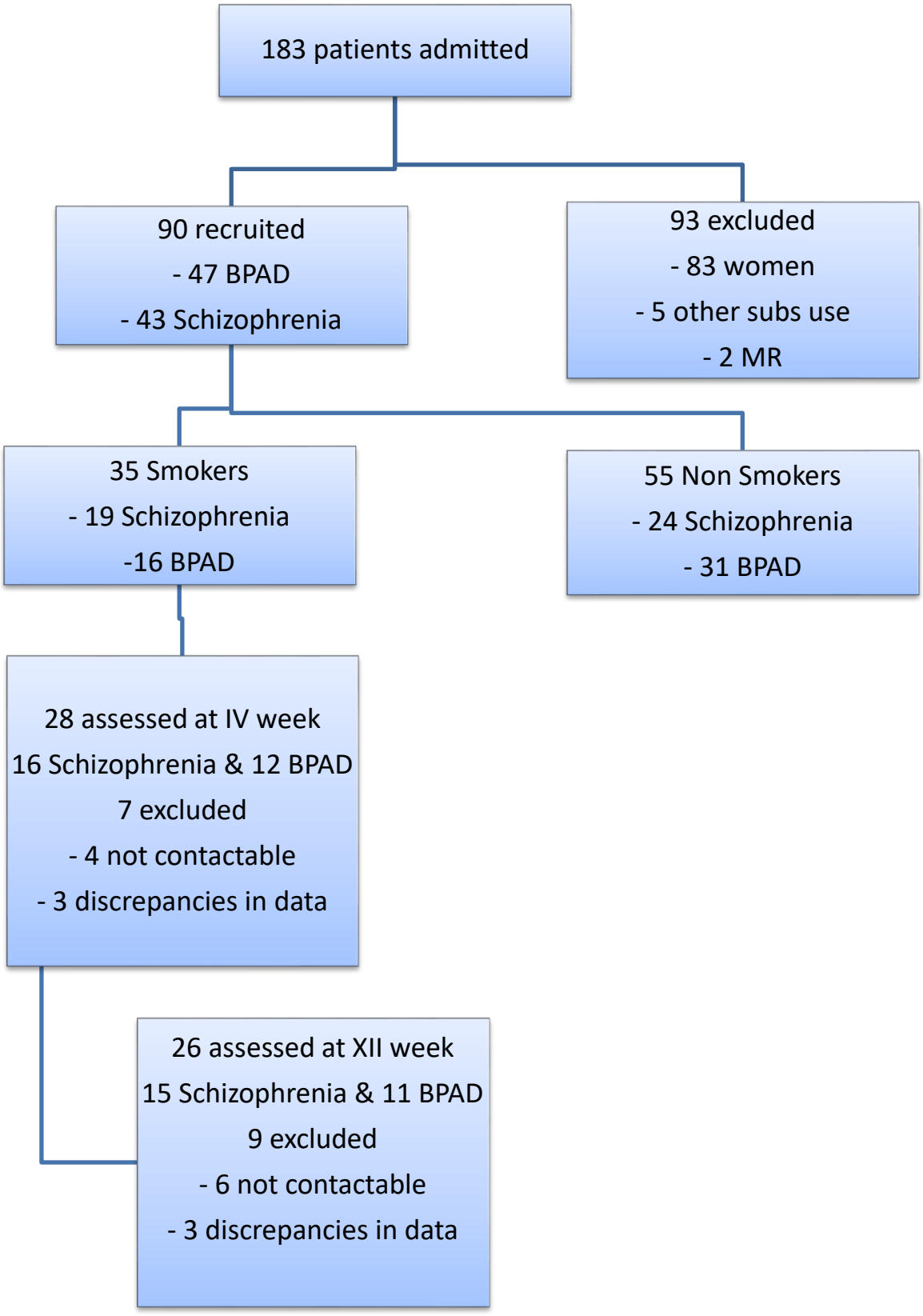
We carried out the statistical analysis using the software SPSS (IBM SPSS - Statistical Product and Service Solutions, version 19.0). We tested for normality of all continuous variables using Shapiro-Wilks test. We used descriptive statistics to get the mean, median and standard deviation of following variables: age, monthly income, duration of illness, duration of current episode/exacerbation, number of hospitalization, scores obtained in the rating scales at baseline, IV week and XII week (BPRS, YMRS, HAMD), duration of smoking, number of cigarettes/beedis, and score obtained in Fagerstrom nicotine dependence test. We got frequencies of the following variables: education of patients and their caregivers, marital status, occupation, smoking status at baseline, IV week and XII week, number of smokes at baseline, IV week and XII week, and number of nicotine gum used per day.

Using chi-square test, we studied the strength of relationship of following variables in schizophrenia and bipolar disorder groups: smoking status at baseline, IV week and XII week, willingness to use nicotine gum, and compliance with nicotine gum and other medications. We used student t test, to study the significance of differences between schizophrenia group and bipolar

disorder group in the following variables: duration of smoking, number of nicotine gum used per day, and percentage of nicotine consumption per day.

As the variable number of smoke per day was not normally distributed, we used Mann-Whitney U test to study the difference in the median of that variable between schizophrenia group and bipolar disorder group. As number of smokes per day variable was not normally distributed, we used Wilcoxon Signed Ranks Test to study the significance of difference between schizophrenia and bipolar disorder groups.

RESULTS


183 patients admitted
90 recruited
- 47 BPAD
- 43 Schizophrenia
93 excluded
- 83 women
- 5 other subs use
- 2 MR
35 Smokers
- 19 Schizophrenia
-16 BPAD
55 Non Smokers
- 24 Schizophrenia
- 31 BPAD
28 assessed at IV week
16 Schizophrenia & 12 BPAD
7 excluded
- 4 not contactable
- 3 discrepancies in data
26 assessed at XII week
15 Schizophrenia & 11 BPAD
9 excluded
- 6 not contactable
- 3 discrepancies in data

During our study period from June 2017 to May 2018, 183 patients were admitted in our ward for schizophrenia or bipolar disorder. Ninety of those met our inclusion criteria and hence was included in our study. Twelve among the 90 patients did not come for follow up and they were contacted over the phone and details about their smoking status and use of nicotine gums were obtained. Four participants at 4^{th} week and 6 at 12^{th} week were unreachable and hence not included in the data. We have made errors in entering data in 3 participants; hence they were excluded from the analysis.

Among 90 patients, 43 were diagnosed to have schizophrenia and 47 were suffering from bipolar affective disorder(46 patients were admitted for manic episode and one patient was admitted for depressive episode). The mean age of the participants with schizophrenia was 39.49 (SD – 9.740) years and that of those with bipolar affective disorder was 39.53 (SD – 12.34) years.

Table 1. Socio-demographic profile of patients with Schizophrenia and Bipolar Affective Disorder

		Schizophrenia N=43	**BPAD N=47**
Age in years Mean (SD)		39.49 (9.740)	39.53 (12.337)
Family Income in rupees Mean (SD)		16,465.12 (8,732.394)	25,531.91 (14,555.518)
Education N (%)	I to V	6 (14 %)	5 (10.6%)
	V to X	13 (30.2%)	11 (23.4%)
	Higher Secondary	17 (39.5%)	16 (34.0%)
	Graduate	7 (16.3%)	15 (31.9%)
Marital Status N (%)	Unmarried	18 (41.9%)	12 (25.5%)
	Married	16 (37.2%)	29 (61.7%)
	Separated	9 (20.9%)	6 (12.8%)
Occupation N (%)	Unemployed	22 (51.2%)	3 (6.4%)
	Unskilled	13 (30.2%)	16 (34.0%)
	Skilled/Professional	8 (18.6%)	28 (59.6%)

BPAD - Bipolar Affective Disorder SD Standard Deviation

Table 1 presents the socio-demographic profile of the male patients admitted in our ward.

The monthly family income of patients with schizophrenia had a mean of 16,558.14 (SD – 8688.532) and the mean of the monthly family income among patients with bipolar affective disorder was 25,404.26 (SD - 14,678.674).

Majority of the patients with schizophrenia fell into the secondary to higher secondary category in education while among the bipolar disorder patients, most had done their higher secondary or graduation.

When looking into the marital status of the participants, most [41.9%(n=18)] of the patients with schizophrenia were unmarried while a majority [61.7% (n=29)] of those with bipolar affective disorder were married.

More than half, 51.2%(n=22) of the schizophrenia patients were unemployed. Unskilled form of employment was being done by 30.2%(n=13) among the schizophrenia subset while 34.0%(n=16) of the bipolar disorder were

engaged in unskilled labour. 59.6%(n=28) were involved in skilled or professional line of work for the bipolar affective disorder group.

Table 2. Severity of illness among patients with Schizophrenia and Bipolar Affective Disorder

	Schizophrenia Mean (SD)	**BPAD Mean (SD)**
Duration of Illness (years)	14.19(8.063)	12.89 (9.286)
Duration of Current Episode (weeks)	9.86 (6.472)	5.15 (3.155)
Number of Previous Hospitalisations	1.95 (1.731)	1.85 (1.351)
Number of Previous Hospitalisations	1.95 (1.731)	1.87 (1.361)

BPAD- Bipolar Affective Disorder SD- Standard Deviation

The duration of illness appeared to be long in both the groups with mean duration of illness in years being 14.19(SD – 8.063) years for patients with schizophrenia and 12.89(SD – 9.286) years for those with bipolar affective disorders. The mean duration of the current exacerbation was 9.86(SD – 6.47) weeks for patients with schizophrenia and the mean duration of the current

episode was 5.15(SD – 3.16) weeks for the bipolar affective disorder patients. The number of previous hospitalisations appeared to be similar across the two groups with the mean being 1.95(SD-1.731) in the schizophrenia section and 1.87(SD-1.361) in the bipolar affective disorder section.

Table 3. Baseline data of patients with Schizophrenia and Bipolar Affective Disorder

	Schizophrenia Mean (SD)	**BPAD Mean (SD)**
BPRS *(Baseline) n=43	28.90 (3.987)	-
YMRS# (Baseline) n=46	-	37.26 (2.970)
HAMD^ (Baseline) n=1	-	22.00
BPRS (4th week) n=12	8.10 (4.175)	-
YMRS (4th week) n=10	-	6.38 (5.755)
HAMD (4th week) n=0	-	-
BPRS (12th week) n=11	5.56 (2.651)	-
YMRS (12th week) n=9	-	3.38 (4.955)
HAMD (12th week) n=0	-	-

*Brief Psychiatric Rating Scale BPAD -Bipolar Affective Disorder

#Young's Mania Rating Scale ^Hamilton's Depression Rating Scale

SD Standard Deviation

The mean baseline score on the Brief Psychiatric Scale among schizophrenia patients gradually improved over 12 weeks. The mean baseline score on the Young's Mania Rating Scale improved from 37.26(SD-2.970) to 3.38(SD-4.955) at 12^{th} week. There was only a single bipolar affective disorder patient admitted with a depressive episode and his HAMD baseline score was 22.

Table 4. Details of smoking among patients with Schizophrenia and Bipolar Affective Disorder

		Schizophrenia N=43	**BPAD N=47**	**Total**	**Statistics Schizophrenia Vs BPAD**
Smoking Status N (%)	Yes	19 (44.2%)	16 (34.0%)	35 (38.9%)	$X^2(1) = 0.972$ $P = 0.324$
	No	24 (55.8%)	31 (66.0%)	55 (61.1%)	
Duration of Smoking in years Mean SD		18.79 (8.772)	16.06(9.270)		$t(33) = 0.893$ $p = 0.378$
Type of Smoking N (%)	Cigarettes	10 (52.6%)	9 (56.3%)	19(54.3%)	
	Beedis	6 (31.6%)	4 (25.0%)	10 (28.6%)	
	Both	3 (15.8%)	3 (18.8%)	6 (17.1%)	
No. of cigarettes Mean (SD)		10.58 (6.487)	12.75 (8.092)	11.67 (7.257)	
No. of beedis Mean(SD)		8.22 (5.178)	12.43 (13.501)	10.06 (9.747)	
No. of smokes Median		10.00	12.00	10.00	$Z = -1.384$ $p = 0.166$
Other	Hans	4 (9.3%)	2 (4.3%)	6 (6.7%)	

substances N (%)					
	Alcohol	7 (16.3%)	7 (17.0%)	14 (16.7%)	
	Both	-	2 (4.3%)	2 (2.2%)	
FTND Mean (SD)		3.06 (2.772)	3.86 (2.445)		t(29)=-841 p=0.407

X^2 Pearson Chi Square Test BPAD Bipolar Affective Disorder

t T test Z Mann Whitney Test

SD Standard Deviation FTND Fagerstrom Test for Nicotine Dependence

Of all the schizophrenia patients evaluated, 44.2%(n=19) identified themselves as smokers and 34.0%(n=16) of the bipolar affective disorder patients were known to be smokers. Although, the number was slightly lesser in the bipolar affective disorder group, the difference was not statistically significant (p=0.324). The mean duration of smoking also didn't differ among the 2 diagnostic groups (p=0.378).

Cigarettes appeared to be the predominant mode of smoking tobacco with 52.6%(n=10) of patients with schizophrenia and 56.3%(n=9) of patients with bipolar affective disorder reported to be using them.

The median of number of smokes was lesser in the schizophrenia group at 10.00 as compared to 12.00 for bipolar affective disorder group but the difference was not statistically significant(Z=-1.384,p=0.166).

9.3%(n=4) patients with schizophrenia admitted to using hans as well, while 16.3%(n=7) of them reported to alcohol use as well. 4.3%(n=2) of the recruits with bipolar affective disorder reported using hans as well, with a similar percentage reporting using both hans and alcohol in addition to smoking. 17%(n=7) of the bipolar affective disorder patients had alcohol use as well.

At the baseline, Fagerstrom Test for Nicotine Dependence had a mean of 3.06(SD-2.772) for schizophrenia patients and 3.86(SD-2.445) for bipolar affective disorder patients.

Table 5. Details of NRT at Baseline

	Total N=35	**Schizophrenia N=19**	**BPAD N=16**	**Statistics Schizophrenia Vs BPAD**
Wiiling for NRT N (%)	24 (68.6%)	13 (68.4%)	11 (68.8%)	$X^2(1)$= 0.00 P = 0.983
Not willing for NRT N (%)	11 (31.4%)	6 (31.6%)	5 (31.3%)	
Mean no. of nicotine gums per day Mean(SD)	1.92 (0.88)	1.85 (0.97)	2.00 (0.78)	t(22)=-436 p=0.667
% of nicotine consumption days Mean (SD)	90.02(20.32)	87.82 (24.68)	92.64 (14.31)	
No. of patients who used 2mg Nicotine gum N (%)	17 (70.8%)	10 (76.9%)	7 (63.6%)	
No. of patients who used 4mg Nicotine gum N (%)	7 (29.2%)	3 (23.1%)	4 (36.4%)	

X^2 Pearson Chi Square Test SD Standard Deviation

BPAD Bipolar Affective Disorder

Majority of the patients were willing for nicotine replacement therapy across the two groups – 68.4%(n=13) of people with schizophrenia and 68.8%(n=11) of patients with bipolar affective disorder.

The mean number of nicotine gums used per day was 1.85(SD-0.97) for schizophrenia patients and 2.00(SD-0.78) for those with bipolar affective disorder. The percentage of nicotine consumption days was high for both the groups, 87.82 (SD-24.68) for patients with schizophrenia and 92.64(SD-14.31) for patients with bipolar affective disorder. Most of the patients, 76.9%(n=10) and 63.6%(n=7) in schizophrenia and bipolar affective disorder respectively, required only 2mg dosage of nicotine gums.

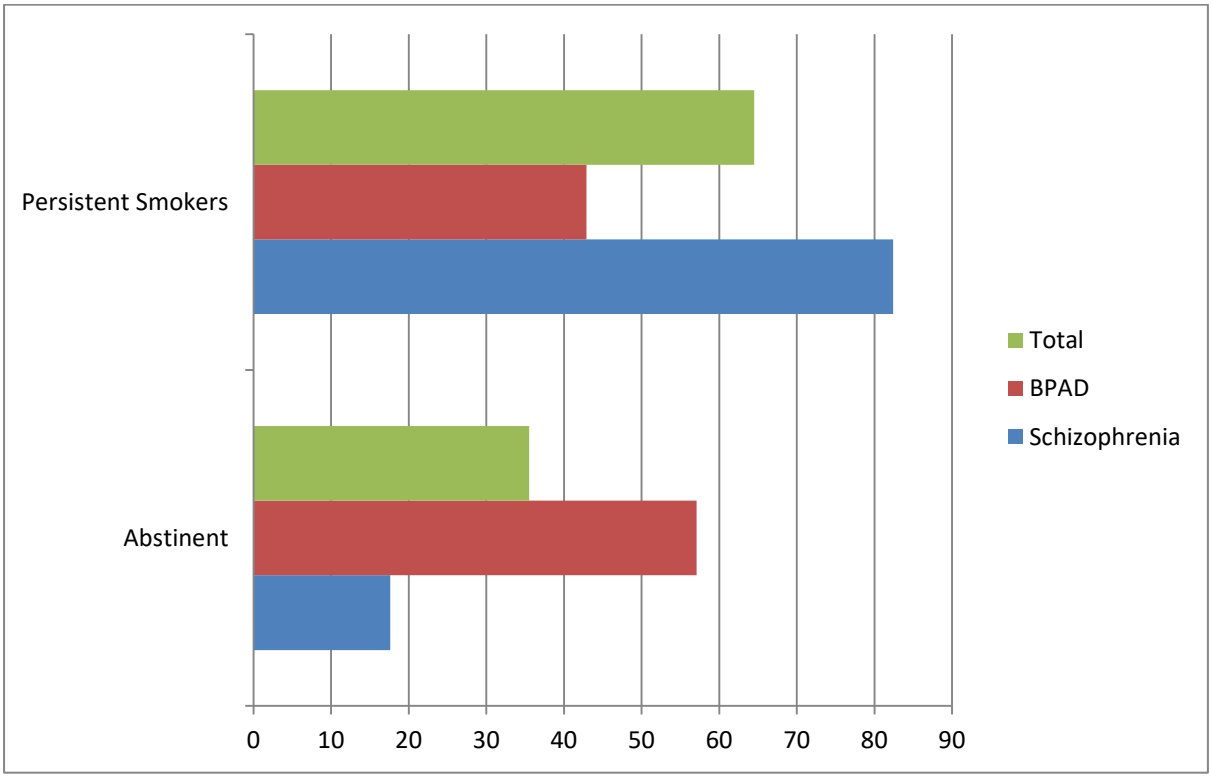
Table 6. Abstinence at 4th week

	Total N=28	**Schizophrenia N=16**	**BPAD N=12**	**Statistics Schizophrenia Vs BPAD**
Abstinent N(%)	10 (35.7%)	3 (18.8%)	7 (58.3%)	$X^2(1)$= 3.590 P = 0.058
Not abstinent N (%)	18 (64.3%)	13 (81.2%)	5 (41.7%)	
No of smokes Mean (SD)	6.08 (5.60)	7.27 (5.96)	4.30 (4.76)	
No. of cigarettes Mean (SD)	4.55 (4.92)	4.82 (5.04)	4.22 (5.04)	
No. of beedis Mean (SD)	5.08 (5.99)	7.00 (6.41)	1.25 (2.50)	
FTND (4th week) Mean (SD)	2.61 (2.33)	2.80 (2.44)	2.38 (2.33)	t(16)=0.375 p=0.713

X^2 Pearson Chi Square Test SD Standard Deviation NRT

Nicotine Replacement Therapy

Fig 1 Abstinence at 4th week



Out of the 28 smokers, who were followed up and evaluated at 4th week, 35.7% were abstinent, with 18.8%(n=3) of the schizophrenia patients and 58.3%(n=7) of the bipolar affective disorder patients. More number of patients in the BPAD group remained abstinent than in the schizophrenia group, which showed a trend towards statistical significance ($X^2(1)=3.590, p=0.058$). The mean number of smokes was 6.08(SD-5.60) among all patients followed up,

with it being 7.27(SD-5.96) among those with schizophrenia and 4.30(SD-4.76) for those with bipolar affective disorder.

Table7. Compliance to NRT at 4th week

	Total N=28	**Schizophrenia N=16**	**BPAD N=12**	**Statistics Schizophrenia Vs BPAD**
Continuing NRT N (%)	13 (61.9%)	6 (50.0%)	7 (77.8%)	X^2 *(1)*= 1.683 *P* = 0.195
Discontinued NRT N (%)	8 (38.1%)	6 (50.0%)	2 (22.2%)	

Among the smokers,61.9%(n=13) of patients continued nicotine replacements, with 50.0%(n=6) of them in the schizophrenia group and 77.8%(n=7) in the bipolar affective disorder group. This difference was not statistically significant ($X^2(1)=2.561$,p=0.110).

The mean Fagerstrom nicotine dependence scale remained similar between the two groups and it was not statistically significant (t(16)=0.375,p=0.713).

Table8. Regularity to follow up and medication at 4th week

	Total N=28	**Schizophrenia N=16**	**BPAD N=12**	**Statistics Schizophrenia Vs BPAD**
Regular to Follow up 4th week N (%)	19 (67.9%)	11 (68.8%)	8 (66.7%)	$X^2(1)=.014$ P=0.907
Compliant with medication 4th week N(%)	26	15 (94.1%)	11 (92.9%)	$X^2(2)=1.473$ P=0.479

Both showed similar compliance and follow up rates as well, with the results being statistically similar ($X^2(1)=.014$,p=0.907; $X^2(2)=1.473$,p=0.479).

Table 9. Abstinence at 12th week

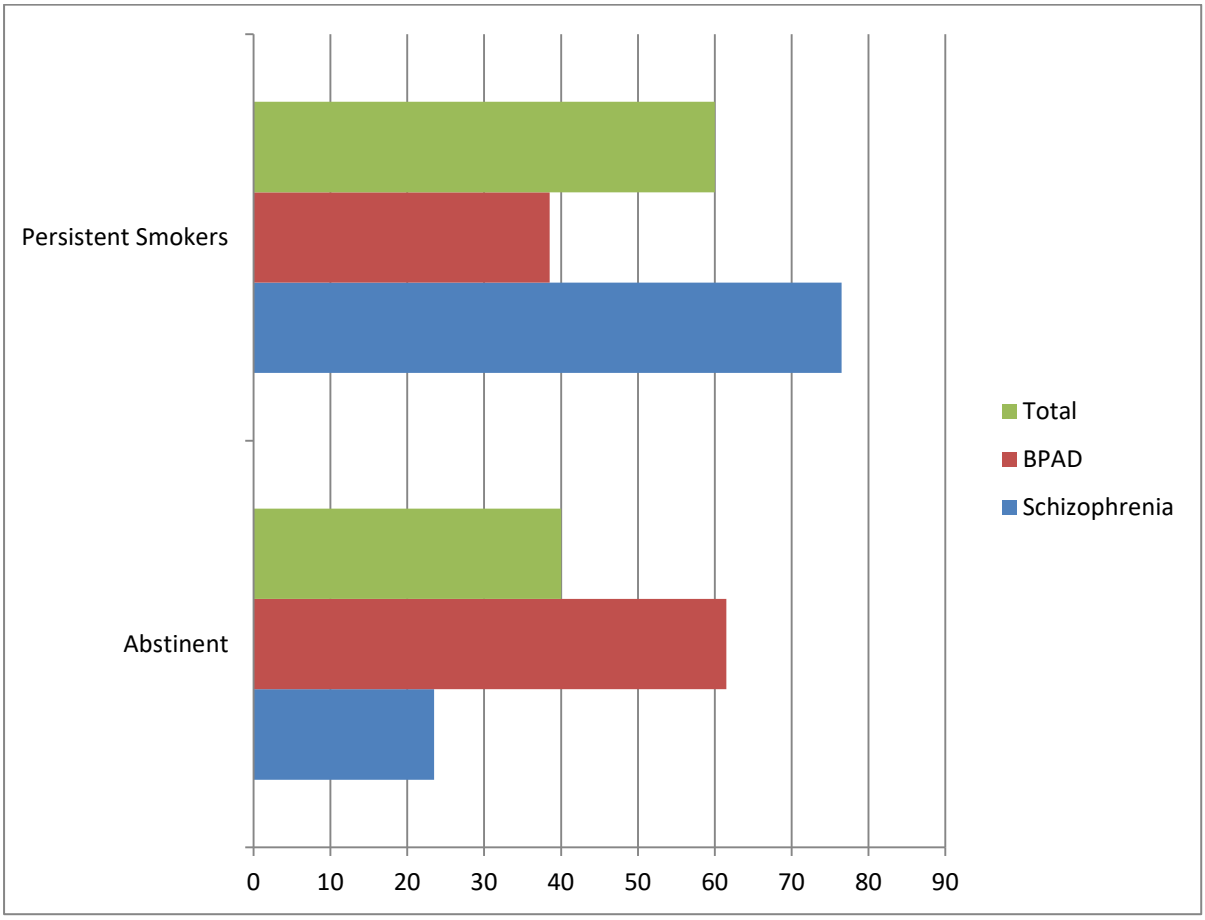
	Total N=26	**Schizophrenia N=15**	**BPAD N=11**	**Statistics Schizophrenia Vs BPAD**
Abstinent N (%)	11(42.3%)	4 (26.7%)	7 (63.6%)	$X^2(1) = 3.554$ $p=0.059$
Non abstinent N(%)	15 (57.7%)	11 (73.3%)	4 (36.4%)	
Number of smokes 12th week Mean (SD)	7.11 (6.57)	7.73 (5.71)	6.25 (7.91)	
FTND (12th week) Mean (SD)	1.94 (2.04)	2.36 (1.912)	2.00 (2.867)	

X^2 Pearson Chi Square Test BPAD Bipolar Affective Disorder

Z Mann Whitney Test SD Standard Deviation

FTND Fagerstorm Test for Nicotine Dependence

Fig 3. Abstinence at 12th week



42.9%(n=9) of all patients followed up were abstinent, of which 63.6% were from the bipolar affective disorder group and 26.7% from the schizophrenia group. More abstinence rate in the BPAD group than the schizophrenia group is showing a trend towards statistical significance (X^2=3.554,p=0.059).

The score on Fagerstrom Nicotine Dependence Scale also remained similar between the two groups at 2.36(SD-1.912) for schizophrenia patients and 2.00(SD-2.867) for patients with bipolar affective disorder

Table10. Continuing NRT at 12th week

	Total N=26	**Schizophrenia N=15**	**BPAD N=11**	**Statistics Schizophrenia Vs BPAD**
Continues NRT 12th week N(%)	9 (42.9%)	3 (25.0%)	6 (66.7%)	$X^2(1) = 3.646$ $p = 0.056$
Discontinued NRT 12th week N(%)	12 (57.1%)	9 (75%)	3 (33%)	

NRT Nicotine Replacement Therapy

66.7% of the patients with bipolar affective disorder continued their nicotine replacement therapy while only 25.0% of the schizophrenia patients and this difference was statistically significant(X^2=5.239,p=0.0022).

Table 11. Regular to follow up and medication at 12th week

	Total N=26	**Schizophrenia N=15**	**BPAD N=11**
Regular to Follow up 12th week N(%)	16 (59.3%)	9 (56.3%)	7 (63.6%)
Complaint with medication 12th week N(%)	22 (81.5%)	13 (81.3%)	9 (81.8%)

A majority(59.3%) of our patients were regular to follow up with 56.3%(n=9) of the schizophrenia patients and 63.6%(n=11) of the bipolar affective disorder patients. Around 80% of our total patients were complaint with our medication and the figure was similar among our schizophrenia and bipolar disorder group patients.

Table 12. Effectiveness of NRT: Patients on NRT vs Patients not on NRT at 4th and 12th week

NRT	Abstinent	Not abstinent	Statistics
On NRT 4th week	7 (53.8%)	6 (46.2%)	$X^2(1)=3.590$ p=0.058
Not on NRT 4th week	1 (12.5%)	7 (87.5%)	
On NRT 12th week	8 (88.9%)	1 (11.1%)	$X^2(1)=10.755$ p=0.01
Not on NRT 12th week	2 (16.7%)	10 (83.3%)	

NRT Nicotine Replacement Therapy

Among those who continued NRT at 4th week, half [53.8%(n=7)] remained abstinent while a majority [87.5%(n=7)] of those who were not on NRT continued to smoke. These results were trending towards significance[$X^2(1)=3.590$,p=0.058]. At 12th week, nearly 90%(n=8) of those on NRT remained abstinent while 83.3% of those who were not on NRT continued

to smoke. This result was found to be highly statistically significant [$X^2(1)=10.755, p=0.01$].

Fig 2. NRT vs Abstinence at 4^{th} and 12^{th} week

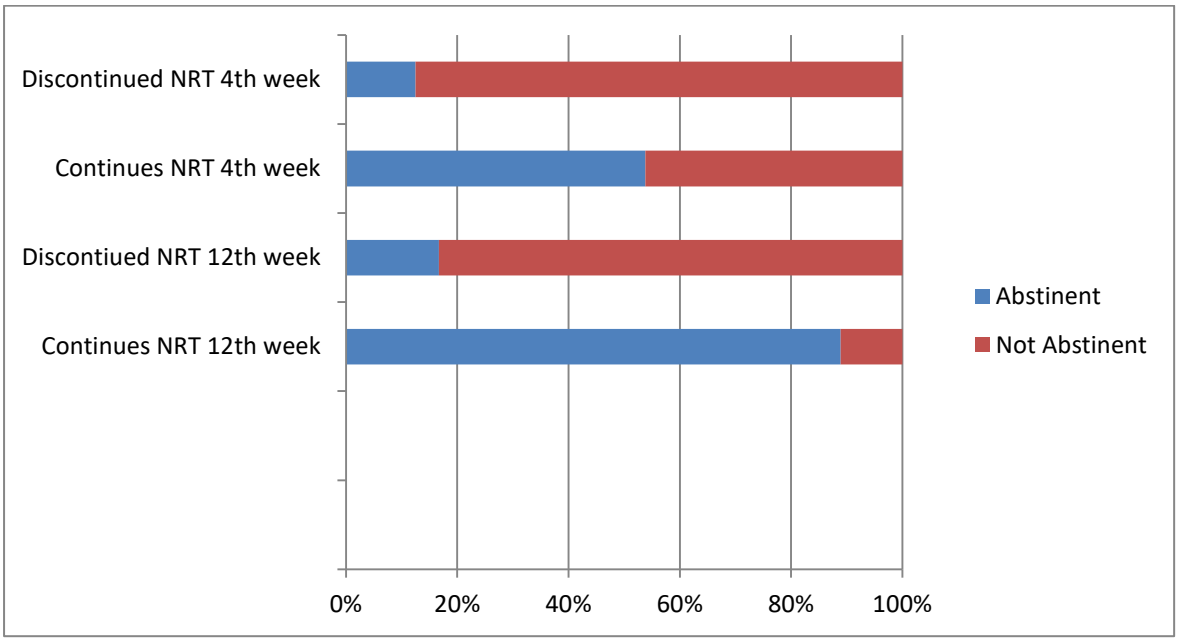


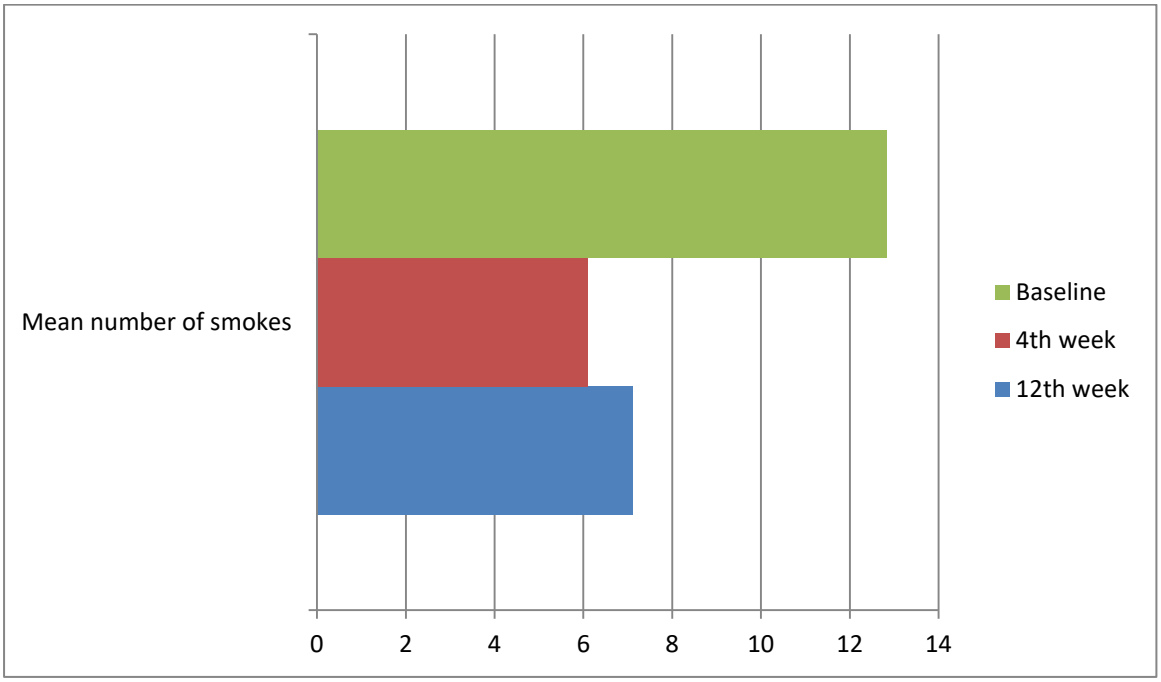
Table 13. Comparison of the number of smokes from baseline to 12th week

Number of smokes	**Mean (SD)**	**Median**	**Statistics 4th week Vs Baseline, 12th week Vs Baseline**
Baseline	12.82 (7.96)	10.00	
4th week	6.08 (5.60)	5.00	Z = -3.519 *P* < 0.0001
12th week	7.11 (6.56)	5.00	Z = -2.498 *P* = 0.013

Z Wilcoxon Signed Ranks Test SD Standard Deviation

The mean number of smokes at baseline was 12.82(SD-7.96) for all patients who were smoking, which at 4th week was at 6.08(SD-5.60). At 12th week the mean was at 7.11(SD-6.56). Both at 4th and 12th week, number of smokes had reduced statistically significantly as compared to baseline.

Fig 3. Mean number of smokes in baseline, 4th and 12th week



DISCUSSION:

Among the 90 patients whom we recruited for our study, the **prevalence of smoking was 38.9%**. While the prevalence of smoking was **44.2% in schizophrenia group**, it was **34% for patients with bipolar affective disorder group.** At 4th week, 58.3% of the bipolar affective disorder patients were abstinent as compared to 18.8% of schizophrenia patients and this result was heading towards statistical significance *($X^2(1)$*= 3.590,*P* = 0.058). Similarly at 12th week, 63.6% of the bipolar affective disorder patients and 26.7% of schizophrenia patients were abstinent and this difference was showing a trend towards statistical significance *($X^2(1)$* = 3.534,*P* = 0.059). **The median number of smokes reduced from 10 at baseline to 5 at 4th week and to 5 at 12th week** and this reduction was statistically significant. While analysing the effectiveness of NRT, comparing to patients who were not on NRT, **53.8% of those who were on NRT at the 4th week and 88.9% of those who were on NRT at 12the week were abstinent** and this was statistically significant.

In our study, the rates of tobacco use across the sample was 38.9% which is similar to the 36% rate of tobacco use among psychiatric in-patients in the study conducted by Chandra et al at NIMHANS, Bangalore[13]. 44.2% of the male schizophrenia patients admitted had tobacco use while 34.0% of the patients

with bipolar affective disorder had reported to be using tobacco. In another study[12] done in India, 38% of the recruited urban male outpatients with schizophrenia reported to have tobacco use, which is similar to our findings.

While the NIMHANS study evaluated tobacco use in both the smoked and smokeless form, our study was primarily focussed on the smoking type of tobacco use alone. While their study evaluated tobacco use among both sexes, we assessed tobacco use in male patients alone. Yet both our studies had a similar total prevalence of smoking indicating that perhaps tobacco use in females continues to be much below the male population.

Our study findings and that of similar studies in India would suggest that smoking among psychiatric patients is at a rate higher than that of the general population. This is in much lesser than the findings of studies in the west, with one study[27] reporting a prevalence rate of smoking at 88% in schizophrenia and 76% in mania. Another study[30] from France also reported that smoking among psychiatric patients were at a rate higher than the general French population.

In the study[23] done by Subramanian et al the overall prevalence of smoking all over India was said to be at 18.4 % while the combined prevalence of

tobacco use (including smokeless tobacco) was at 32.1%. This would suggest that smoking is perhaps more prevalent among patients with major mental disorders.

However, these results need to be interpreted with caution, as the above mentioned study was done from a survey conducted nearly 20 years ago. Further, our study was concentrated in a city in Tamil Nadu while the aforementioned study looked into overall prevalence across the nation. India being a diverse country with socio- economic and cultural differences across states, a comparison between a highly localised population and that of the whole nation would seem difficult.

In a more recent study[24] done in rural Kerala, the overall prevalence of smoking among males surveyed was at 28.1%. Hence, these studies would suggest that smoking may be slightly more prevalent than the general population among patients with major mental disorders but the proportion is much lesser than what is experienced in the developed world.

This would suggest that the ill of smoking among psychiatric patients in India has not reached the same magnitude as in the west. This finding is perhaps

extendable to other developing nations too, as a study from Bangladesh[40] concluded that smoking among psychiatric patients was no greater, or even lesser than that of the general population.

The reason for this difference could be socio-cultural and economic. Firstly, in developing nations like India, a good family support system exists for the psychiatric patients. Secondly, a social taboo related to smoking still persists in such developing nations, where that habit is frowned upon and even discouraged, perhaps unlike the west where individual choice attains primacy. Thirdly, most of our patients might still find the cost of the tobacco products to be prohibitive and hence is unable to indulge in the behaviour.

Our study neither showed any relation between the diagnosis and smoking status nor duration of smoking with the illness. This is again in contrast with a study done in the west which showed a greater duration of smoking among schizophrenia patients. The number of smokes had per day also was not affected by the diagnosis of the patient. The severity of nicotine dependence also appeared to be similar across the two groups as measured by the Fagerstrom test for nicotine dependence.

Most of our patients reported mild to moderate nicotine dependence which is in contrast to the study[13] done by Chandra et al where 65% of the patients were in the moderate to severe nicotine dependence range. The contradiction could be as a result of a numerous factors. We used a modified Tamil version of the Fagerstrom test for nicotine dependence that has been validated as well while in their study the test was clinician administered instead of self reported like ours. In the study[24] done by Jayakrishnan et al in Kerala, the severity of nicotine dependence was reported to be of mild to moderate dependence which is similar to our study. In their study too, the Fagerstorm test for nicotine dependence was translated into the local language and then re-translated to English to check for accuracy. Although, we expected a higher severity of nicotine dependence in samples with self reportage, perhaps patients were under reporting their levels of dependence.

Also, the Chandra et al study[13] modified the Fagerstrom test for nicotine dependence to look into the severity of dependence in the smokeless form as well but this modification though innovative has not been validated to our knowledge.

No relationship was seen between diagnosis (schizophrenia and bipolar affective disorder) and willingness to start nicotine replacement therapy. At 4th week, 58.3%(n=7) of the bipolar affective disorder patients and 18.8%(n=3) of the schizophrenia group were abstinent. This increase abstinence rate in bipolar group was trending towards significance (X^2 = 3.590,p=0.058).

Similalry more patients with bipolar affective disorder (63.6%) than patients with schizophrenia (26.7%) were abstinent at the end of 12th week as well and this difference also moving tending towards statistical significance.(X^2=3.554,p=0.059).

More abstinence rate in bipolar disorder could be attributed to the remission of manic phase as it is generally seen that patients initiate and indulge in smoking during this phase. However, the duration of smoking was similar in both the groups suggesting chronic addiction. Perhaps education about smoking cessation and NRT has helped more for our bipolar disorder patients than schizophrenia patients.

Discontinuation of nicotine replacement therapy was seen more in patients with schizophrenia than in bipolar affective disorder. Some of the reasons given

for discontinuation was strong burning taste of the gum, headache, nausea and hiccups. This was despite the chew and park technique being taught to all patients on nicotine gum. Further, upon changing the flavour of the nicotine gum certain participants reported improvement in the burning sensation.

The mean number of smokes per day showed a statistically significant reduction when evaluated both at 4^{th} week and at 12^{th} week. This reduction shows that nicotine replacement therapy is effective in reducing the frequency of smokes even at the 4^{th} week which is in keeping with a study done in the US which shows that nicotine replacement therapy is effective in reducing the severity of smoking immediately[15].

Abstinence rates were higher in our study – 53.8%(n=7) and 88.9%(n=8) for patients among both samples who continued nicotine replacement therapy at both 4^{th} week and 12^{th} week. Among those who discontinued at 4^{th} week, only 12,5%(n=1) patient was abstinent and the number was 16.7%(n=2) at 12^{th} week. These values were trending towards statistical significance for 4^{th} week [X^2 (1)=3.590,p=0.058] and significant for 12^{th} week [X^2 (1)= 10.755, p=0.01]. As all patients received 3 educational sessions irrespective of their compliance to nicotine gum, it is fair to assume the added benefit of nicotine gum in addition

to educational sessions. Further as suggested by Thorndlike et al[47] nictoine replacement therapy is more effective in helping patients remain abstinent if had over a three month period.

Further schizophrenia patients may find it harder to quit smoking completely perhaps due to the nicotine improving attention deficits seen as suggested by Vats et al study[39] done in the US. There was no difference between the two groups when it came to regularity of follow up and medication, suggesting that it had no role to play in the results.

STRENGTHS:

1. To our knowledge, this is the first prospective study done on smoking in India. All other previously done studies on smoking among psychiatric patients in India were cross – sectional studies. This allowed us to have a better understanding of the patterns of cigarette use from acute to remission stage of the illness.

2. We used a Tamil version of the Fagerstrom Nicotine Dependence Scale which has been validated and locally adapted. This allowed us to overcome the linguistic barriers that would have risen in the self reporting of the severity of nicotine dependence. Previous studies have used the English version of the Fagerstom Test for Nicotine Dependence and administered by a clinician.

3. We sought to look into the effectiveness of the nicotine replacement therapy in a natural setting. This would provide better clinical understanding of the role of nicotine replacement therapy in stopping nicotine usage. This plays a major role in countries like India where the cost remains a crucial factor in stopping certain medications.

LIMITATIONS:

1. Our study was limited to an urban tertiary setting and may not represent the whole population.

2. We studied only male psychiatric patients

3. We didn't analyse the severity of nicotine dependence in those using smokeless means of tobacco consumption.

4. Less focus was given on the psychological technique involved in quitting smoking

5. We relied on self report to assess smoking and didn't have an objective measure for smoking like conitine level

6. We relied on care giver report for regularity of medication.

7. We didn't compare effectiveness of nicotine gum across brands or flavours.

CONCLUSION:

Our study highlights various important findings about the prevalence of smoking in patients with schizophrenia and bipolar affective disorder and the effectiveness of nicotine replacement therapy

1. The prevalence of smoking among male schizophrenia and bipolar affective disorder patients is higher than the general population, yet lesser than the rates of smoking reported among patients with mental illness in the west.

2. Effectiveness of nicotine replacement therapy in causing abstinence from smoking appeared to be more at the 12^{th} week although an immediate reduction in the frequency of smoking was seen at the 4^{th} week itself.

3. Abstinence from smoking seemed more possible in patients with bipolar affective disorder than those with schizophrenia.

FUTURE DIRECTIONS:

1. To have studies with higher sample size

2. To measure nicotine dependence among patients with the smokeless variety of tobacco consumption as well.

3. To follow up patients for a longer duration of time to check if the effects of nicotine replacement therapy are beneficial in the long run as well.

4. To compare effectiveness of other forms of nicotine replacement therapy in a naturalized setting.

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PROFORMA

Name : OP No :

Age : IP No :

Sex :

Education : Illiterate/1 – V grade/V – X grade/Higher Secondary/Graduate/Postgraduate

Marital status: Unmarried/Married/Divorced or Separated/widow/er

Occupation: Unskilled/skilled/professional/unemployed

Total monthly income (in rupees):

Diagnosis:

Duration of smoking (in years):

Type of smoking (cigarette/beedi/both):

No.of .cigarettes/beedis per day:

Any other substance use: Hans/Betel nut/ Alcohol

Willing for NRT :

	Baseline	4 weeks	12 weeks
BPRS/YMRS/HDRS			
Severity of smoking as per Fagerstrom Rating scale			

Mean number of nicotine gums :

% of nicotine consumption days :

Number of Educational Sessions : 1)

2)

3)

	4th week	12th week
Abstinent from smoking		
If no, no. of cigarettes/day		
No. of beedis/day		
Continuing NRT		
If no reason for discontinuing		
Regular to follow up		
Regular on medication		

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS
(strike off items that are not applicable)

I (write name of the investigator(s) here), Dr.Vineet Sukumar
am carrying out a study on the topic: Prevalence and Severity of Nicotine Dependence on Patients with Schizophrenia and Bipolar Affective Disorder and the Effectiveness of Nicotine Replacement Therapy – An Observational Study
as part of my / our research project being carried out under the aegis of the Department of:
(*Applicable to students only*): My / our research guide is: Dr.G.Raghuthaman
The justification for this study is:

The objectives of this study are:

Primary objectives:

1. To study the prevalence and severity of smoking among patients with schizophrenia and bipolar disorder and also to study the effectiveness of nicotine replacement therapy.

Secondary objectives:

1. To study the association of smoking and severity of illness by following the patients from acute stage to remission stage.

Sample size:. 90
Study volunteers / participants are (specify population group & age group):
Location: PSG Hospital, Peelamedu.
We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:
Initial interview (specify approximate duration): 45 minutes.
Data collected will be stored for a period of 3 years. We will / will not use the data as part of another study.
Health education sessions: Number of sessions: 3
Clinical examination (Specify details and purpose): Nil
Blood sample collection: Specify quantity of blood being drawn: _ml : Nil
No. of times it will be collected: _____.
Whether blood sample collection is part of routine procedure or for research (study) purpose:
1. Routine procedure 2. Research purpose
Specify **purpose**, discomfort likely to be felt and side effects, if any: Nil
Whether blood sample collected will be stored after study period: Yes / No, it will be destroyed
Whether blood sample collected will be sold: Yes / No
Whether blood sample collected will be shared with persons from another institution: Yes / No
Medication given, if any, duration, side effects, purpose, benefits: Nil
Whether medication given is part of routine procedure: Yes / No (If not, state reasons for giving this medication)
Whether alternatives are available for medication given: Yes / No (If not, state reasons for giving this particular
medication)
Final interview (specify approximate duration):_____ mts. If **photograph** is taken, purpose: Nil
Benefits from this study: Nil
Risks involved by participating in this study: Nil
How the **results** will be used: It will be used for research purpose.
If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.**

You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 0422 4345230

Contact number of Ethics Committee Office: 0422 4345818