Research Article
Patterns of Nicotine Dependence and Nicotine Withdrawal in newly diagnosed patients of Head and Neck Squamous Cell Carcinoma: experience from a tertiary care centre in eastern India
Authors
Dr Barnini Ghosh1*, Dr Anish Dasgupta2
Department of Radiation Oncology, Medical College & Hospital, Kolkata, India
Corresponding Author
Dr Anish Dasgupta
Email: barninig@gmail.com, Phone No. – 9830843385

Abstract
Context: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide. In India, cancer of the lip and oral cavity is the most common cancer among males. Risk factors for developing HNSCC include genetic background, geographical location, diet, tobacco and alcohol abuse. Cigarette smoking and excessive alcohol consumption, besides being independent risk factors, also have synergistic effect.
Aims: To evaluate the prevalence of nicotine addiction and patterns of nicotine withdrawal in newly diagnosed patients of HNSCC.
Settings and Design: Single institutional, Prospective study in a tertiary care hospital
Methods and Material: Newly diagnosed patients of HNSCC attending the Radiotherapy OPD were evaluated for patterns of nicotine addiction and severity of dependence using the Fagerstrom Test for Nicotine Dependence (FTND). Later, they were evaluated for signs/symptoms of nicotine withdrawal using Minnesota Nicotine Withdrawal Scale – Revised (MNWS-R) when they were admitted for neoadjuvant or concurrent chemotherapy.
Statistical analysis used: IBM SPSS Version 23
Results: Out of the 73 cases (67 males, 6 females) studied, 87.7% had consumed tobacco. 4.1% were active users with high levels of dependence (as per FTND). Significant correlation between duration of tobacco cessation and duration of symptoms was observed. Symptom evaluation with MNWS-R showed 4 out of 10 major determinants of well-being- pain, insomnia, anxiety and headache and correlated with the overall daily symptom score. None of the patients suffered from nicotine withdrawal.
Conclusions: Diagnosis of malignancy is a strong motivation for tobacco cessation. Larger sample size and multicentric studies are required for further validation.
Keywords: nicotine dependence, nicotine withdrawal, Fagerstrom Test, Minnesota Nicotine Withdrawal Score-Revised.

Introduction
Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide[1]. In India, cancer of the lip and oral cavity is the most common cancer among males with 119,992 new cases diagnosed and 72,616 deaths in 2018 so far[2].
The several risk factors for developing HNSCC include genetic background, geographical location, diet, tobacco and alcohol abuse. Cigarette smoking and excessive alcohol consumption, besides being independent risk factors, also have a synergistic effect\textsuperscript{[3,4]}. Apart from these, reverse smoking, that is, the habit of keeping the lighted end of the cigarette in mouth while smoking and chewing of betel quid (paan) consisting of betel leaves, areca nut and slaked lime, are also widespread in India, predisposing the patients to HNSCC. Recently, association of high risk types of Human Papilloma Virus (HPV), particularly HPV-16 has also been implicated in the development of HNSCC\textsuperscript{[5]}. Majority of the HNSCC occur in patients above 50 years of age, with the average age of diagnosis for smoking related HNSCC being 60 years\textsuperscript{[6]}.

Continuing to smoke even after a diagnosis of malignancy contributes to a higher risk of complications during treatment and decreased responses to radiotherapy and chemotherapy. It also increases the risk of recurrence and of developing a second primary tumour, with decreased quality of life and overall survival\textsuperscript{[7-10]}. Our aim was to evaluate the prevalence of nicotine addiction and patterns of nicotine withdrawal in newly diagnosed patients of HNSCC.

**Subjects and Methods**

A single institutional, prospective, observational study was carried out in a tertiary care hospital. Newly diagnosed patients of HNSCC (histologically proven), with good performance status (ECOG performance status 0 to 1) attending the Radiotherapy OPD were selected. Informed consent was obtained from each participant. They were evaluated for patterns of nicotine addiction and severity of dependence using the Fagerstrom Test for Nicotine Dependence (FTND). FTND is a quick, easy to administer tool, to assess Nicotine Dependence, is widely used worldwide and has been validated in several languages and populations\textsuperscript{[11-13]}.

Later, they were evaluated for signs/symptoms of nicotine withdrawal using the Minnesota Nicotine Withdrawal Scale – Revised (MNWS-R) when they were admitted for neoadjuvant or concurrent chemotherapy\textsuperscript{[14,15]}. There are two scales – a self-report and an observer scale. Assessment is done on the basis of these two scales. All the patients were evaluated by the same investigator to avoid inter-observer variation in the results.

**Results**

73 newly diagnosed histologically proven cases of Head and Neck Squamous cell carcinoma (HNSCC) were selected and studied. The patient characteristics were as follows –

| GENDER | FREQUENCY | PERCENT  |
|--------|-----------|----------|
| MALE   | 67        | 91.8     |
| FEMALE | 6         | 8.2      |
| TOTAL  | 73        | 100      |

Hence, we find that the patients were mostly in the sixth decade of their life. There was male preponderance. Majority suffered from oral cancer.

| Site                      | Frequency | Percent |
|---------------------------|-----------|---------|
| Oral Cavity               | 33        | 45.2    |
| Larynx                    | 21        | 28.8    |
| Pharynx                   | 19        | 26      |
| Total                     | 73        | 100     |

| Age            | Frequency | Percent |
|----------------|-----------|---------|
| < 30 yrs       | 2         | 2.7     |
| 30–40 yrs      | 8         | 11      |
| 41– 50 yrs     | 20        | 27.4    |
| 51- 60 yrs     | 17        | 23.3    |
| 61 –70 yrs     | 21        | 28.8    |
| 71– 80 yrs     | 5         | 6.8     |
| Total          | 73        | 100     |

...
Out of the 73 patients, 64 patients (87.7%) had consumed tobacco and rest were non-users. Only 3 out of 73 (4.1%), were active tobacco users with high levels of dependence (as per FTND).

Distribution of the 73 patients, by responses given to the Fagerstrom Test for Nicotine Dependence

| Question                                                                 | Score (points) | Response   |
|------------------------------------------------------------------------|----------------|------------|
| 1. How soon after you wake up do you smoke your first cigarette?       |                |            |
| Within 5 minutes                                                       | 3              | 21 (28.8%) |
| 6 to 30 minutes                                                        | 2              | 33 (45.2%) |
| 31 to 60 minutes                                                       | 1              | 8 (11%)    |
| After 60 minutes                                                       | 0              | 11 (15%)   |
| 2. Do you find it difficult to refrain from smoking in places where it is forbidden (i.e., in church, at the library, etc.)? |                |            |
| Yes                                                                   | 1              | 34 (46.6%) |
| No                                                                    | 0              | 39 (53.4%) |
| 3. Which cigarette would you hate most to give up?                    |                |            |
| The first one in the morning                                          | 1              | 37 (50.7%) |
| Any other                                                             | 0              | 36 (49.3%) |
| 4. How many cigarettes per day do you smoke?                          |                |            |
| 31 or more                                                            | 3              | 3 (4.1%)   |
| 21 to 30                                                               | 2              | 32 (43.8%) |
| 11 to 20                                                               | 1              | 22 (30.1%) |
| 10 or less                                                            | 0              | 16 (21.9%) |
| 5. Do you smoke more frequently during the first hours after waking? |                |            |
| Yes                                                                   | 1              | 3 (4.1%)   |

59 out of 73 (80.8%) patients had moderate to high level of dependence. The mean FTND score was 6.1 ± 2.2 points for the sample as a whole. No significant correlation of nicotine dependence was observed with – stage of disease (p= 0.913), gender (p=0.665) or smoking cessation (p=0.231). No significant difference was noted in symptoms score among users and non-users or between the low/medium/high dependence groups as per FTND.

The Minnesota Nicotine Withdrawal Scale-Revised is shown below, which was used to evaluate the signs/symptoms of nicotine withdrawal among the 73 patients.
Duration of symptoms correlated well with the duration of tobacco cessation (Pearson coefficient – 0.401; p value < 0.002). Symptom evaluation with MNWS-R showed 4 out of 10 major determinants of well-being – pain, insomnia, anxiety and headache and they correlated with the overall daily symptom score (p < 0.05). None of the patients suffered from nicotine withdrawal.

**Discussion**

Majority of the patients suffered from oral cancer and had moderate to high levels of nicotine dependence. Tobacco cessation had significant correlation with the duration of daily symptoms. Diagnosis of malignancy was found to be a strong motivation for tobacco cessation. A limitation of our study was that it was a single institutional study with a small sample size. Larger sample size and multicentric studies are required for further validation.

We hope that further studies will lead to standardisation of interventions based on such patterns of nicotine dependence and withdrawal among head and neck cancer patients in the near future.

Source(s) of support: Nil
Presentation at a meeting: Not Applicable
Conflicting Interest (If present, give more details): Nil

**References**

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55(2):74–108.
2. The Global Cancer Observatory, GLOBOCAN 2018; September 2018
3. Blot WJ, McLaughlin JK, Winn DM, Austin DF, Greenberg RS, Preston-Martin S, Bernstein L, Schoenber J, Stemhagen A, Fraumeni JF Jr. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res. 1988;48(11):3282–3287.
4. Malik G, Dhull AK, Atri R, Kaushal V. A comparative evaluation of neoadjuvant chemotherapy followed by concomitant chemoradiation versus accelerated radiation therapy versus conventional radiation therapy in a locally advanced head and neck carcinoma. Asian J Oncol 2017;3:59-65
5. Kreimer AR, Clifford GM, Boyle P, Franceschini S. Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. Cancer Epidemiol Biomarkers Prev. 2005;14(2):467–475.
6. Vigneswaran N, Tilashalski K, Rodu B, Cole P. Tobacco use and cancer. A reappraisal. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;80(2):178–182.
7. Chen AM, Chen LM, Vaughan A, Sreeraman R, Farwell DG, Luu Q, et al. Tobacco smoking during radiation therapy for head-and-neck cancer is associated with unfavorable outcome. Int J Radiat Oncol Biol Phys. 2011;79(2):414–419.
8. León X, del Prado Venegas M, Orús C, López M, García J, Quer M. Influence of the persistence of tobacco and alcohol use in the appearance of second neoplasm in patients with a head and neck cancer. A case-control study. Cancer Causes Control. 2009;20(5):645–652.
9. Toll BA, Brandon TH, Gritz ER, Warren GW, Herbst RS, AACR Subcommittee on Tobacco and Cancer Assessing tobacco use by cancer patients and facilitating cessation: an American Association for Cancer Research policy statement. Clin Cancer Res. 2013;19(8):1941–1948.
10. Pinto FR, Matos LL, Gumz Segundo W, Vanni CM, Rosa DS, Kanda JL. Tobacco and alcohol use after head and neck cancer treatment: influence of the type of oncological treatment employed. Rev Assoc Med Bras. 2011;57(2):171–176.
11. Gritz ER, Carr CR, Rapkin DA, Chang C, Beumer J, Ward PH. A smoking cessation
intervention for head and neck cancer patients: trial design, patient accrual, and characteristics. Cancer Epidemiol Biomarkers Prev. 1991;1(1):67–73.

12. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict. 1991;86(9):1119–1127.

13. Mikami I, Akechi T, Kugaya A, Okuyama T, Nakano T, Okamura H, et al. Screening for nicotine dependence among smoking-related cancer patients. Jpn J Cancer Res. 1999;90(10):1071–1075.

14. Hughes JR; Hatsukami DK. Signs and symptoms of tobacco withdrawal. Arch Gen Psychiatry 43:289-294, 1986.

15. Toll BA, O'Malley SS, McKee SA, Salovey P, Krishnan-Sarin S: Confirmatory factor analysis of the Minnesota Nicotine Withdrawal Scale. Psychol Addict Behav 2007;21:216-225.