Inverted U shaped effect of nicotine on the severity of depressive symptoms: A population-based survey

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A R T I C L E   I N F O

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A B S T R A C T

Objectives: To investigate whether that nicotine concentration represented by the degree of smoking dependence variably influence the rate and severity of depressive symptoms.

Methods: Cross-sectional, analytical study, involving 300 medical students selected by random sampling techniques were asked to complete a questionnaire contains three parts: demographic information, Beck Depression Inventory with cutoff point for depression is 17 and the Fagerström Test for Nicotine dependence with cutoff point for severe dependence is five.

Results: A total of 233 medical students completed the questionnaire; their mean age was (21.38 ± 1.74).

The rate of smoking was 22.7% while that of depression was 32.2%. Low dependent smokers in contrast to other groups of smokers and non-smokers display the lowest rate of depressive symptoms (15%), while the highest rate recorded among severely dependent smokers (71.4%, \(p = 0.0001\)). After adjustment of other risk factors, regression analysis reveal that severe dependent smokers associated with 12.5 odds of depressive symptoms than non-smokers (\(p = 0.0001, \text{C.I. 4.10 e}^{38.29}\)).

Conclusion: In comparison with light and moderate smokers, heavy smokers demonstrate higher risk of depressive symptoms in medical students.

1. Introduction

Many epidemiological studies have shown a strong association of smoking with depression,\(^1,^2\) it has been found that about 50% of the individuals suffering from depression reported to be smokers, on the other hand, regular smokers display more depressive symptoms, more frequent and severe episodes of depression and higher rate of suicidal ideation.\(^3\)

The common explanation of this association is the self-medication hypothesis, which state that depressed patients smoke to relieve their symptoms.\(^4\) This hypothesis was constructed on the reports of smokers who experience an improved sense of well-being, greater calm, better attention, and superior ability to concentrate after smoking.\(^5\) Additionally, nicotine increases the secretion of dopamine in the limbic system which may also contribute to the euphoria and addictive potential of nicotine.\(^6\)

However, recently the self-medication hypothesis undergoes significant criticism because of the many published prospective studies which prove that smoking increase the risk of depression and not the reverse.\(^7,^8\) These studies explain the previous reported improvement among smokers as following: smoking only generates mood changes in nicotine-deprived smokers, but these only represents the restoration of normal moods, and it’s found that when non-deprived smokers had a cigarette, their mood ratings remain unaltered.\(^9\)

Many factors implicated in the variability of nicotine effects in the brain like nicotine dose, duration and frequency of administration.\(^10\) In the present study, we propose that there is diverse influence of nicotine on mood according to the level of dependence; it means that low nicotine exposure may produce positive effects while high dose of nicotine (severe nicotine dependence) associated with negative emotional effect and depressive symptoms.

The aim of the present study is to investigate whether nicotine concentration represented by the degree of smoking dependence has variable influence on the rate and severity of depressive symptoms among medical students.

2. Methods

Study design: a cross-sectional analytical study, conducted on medical students in the college of medicine, University of Al-Mustansiriyah, Baghdad, Iraq from October to December 2011. The study follows the Helsinki Declaration regarding humans involved.
in clinical trials and was approved by the local scientific and ethical committee in the medical college.

Participants: students were voluntarily invited to participate during their attendance in the laboratory, sessions, or lectures. First, students informed about the anonymity of the questionnaire and that the information is confidential, then verbal consent were taken from those who were willing to participate.

Measures: the questionnaire composed of three parts:

- **General demographic questions**: this part contains general information about students (age, sex, stage of study).
- **Beck Depression Inventory-II**: this questionnaire composed of 21 items, assessing many symptoms that occur in depressive patients like (sadness, pessimism, guilt, fatigue, anorexia, crying, suicidal thoughts, etc.); these symptoms were phrased in four alternative descriptions (four statements). Every set of statements was written in the order of increasing distress. The participants had to select, for each item, the response alternative that correspond best to their situation for now and the past week. The total score was obtained by adding the values of all items, each ranged from 0 to 3, with the total score ranged from 0 to 63,\textsuperscript{11} and a cut score of either 17 or 18 provide the best balance between sensitivity and specificity.\textsuperscript{14}
- **Fagerström test for nicotine dependence (FTND)**: those were reported to be smokers then fill the FTND questionnaire in addition to questioning their age of starting to smoke. Recent systemic review of the FTND questionnaire found that the reliability of this scale ranged from 0.65 to 0.91 with sensitivity (0.75) and specificity of (0.80) and the Cronbach’s alpha of internal consistency ranged 0.55 to 0.74.\textsuperscript{15} The FTND scale composed of six items questions (time taken for the first cigarette after waking up, ability to refrain from smoking in forbidden places, how many cigarettes smoked per day, etc.). The total score for the FTND ranged between 0 and 10; a score ranged from 0 to 3 regarded as mild dependence, while score of 4–5 as moderate dependence and scoring higher than 5 considered as severe smoking dependence.

2.1. Statistical analysis

Analyses of the results were done by using PASW Statistics 18 software (SPSS Inc., Chicago, IL). The numerical variables expressed as mean ± SD and analyzed by using independent sample t-test for the comparison of two independent groups or the Analysis of Variance test (ANOVA) for the comparison of more than two groups (Tukey test for post hoc analysis). Categorical variables expressed as number (%) and analyzed with Pearson’s chi-squared test for univariate analysis, and multivariable analysis done to find the association between groups in adjustment for sex, age, and stage of the students using logistic regression analysis, Odd ratio and its class interval were reported; in all the above tests a p value less than 0.05 were considered as statistically significant.

3. Results

Two hundred and thirty three medical students participated in the study; their age ranged from 18 to 26 with a mean of (21.38 ± 1.74), female represents (43.6%) of all the students. Smoking prevalence was (22.7%), their age of onset of smoking ranged from 14 to 23 years. The range of the students score on Beck Depression Inventory ranged between 2 and 41, and (32.2%) of all medical students demonstrate depressive symptoms. The distribution of the participants regarding years of study and their smoking status with other parameters presented in Table 1 below.

### Table 1

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Number (% [total number of participants = 233])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (21.38 ± 1.74)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>131 (56.2)</td>
</tr>
<tr>
<td>Female</td>
<td>102 (43.6)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>34 (14.6)</td>
</tr>
<tr>
<td>Second</td>
<td>44 (18.9)</td>
</tr>
<tr>
<td>Third</td>
<td>44 (18.9)</td>
</tr>
<tr>
<td>Fourth</td>
<td>36 (15.5)</td>
</tr>
<tr>
<td>Fifth</td>
<td>39 (16.7)</td>
</tr>
<tr>
<td>Sixth</td>
<td>36 (15.5)</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>180 (77.3)</td>
</tr>
<tr>
<td>Smokers</td>
<td>53 (22.7)</td>
</tr>
<tr>
<td>Low dependence</td>
<td>20 (8.6)</td>
</tr>
<tr>
<td>Moderate dependence</td>
<td>12 (5.2)</td>
</tr>
<tr>
<td>Severe dependence</td>
<td>21 (9.0)</td>
</tr>
<tr>
<td>Age of start smoking (17.36 ± 2.43)</td>
<td></td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>(13.63 ± 7.93)</td>
</tr>
<tr>
<td>&lt;17</td>
<td>158 (67.8)</td>
</tr>
<tr>
<td>≥17</td>
<td>75 (32.2)</td>
</tr>
</tbody>
</table>

Depressed students significantly older, start smoking at earlier age, having higher FTND score than non-depressed (see Table 2). Female students demonstrate significantly higher rate of depression than male students (42.2% vs. 24.4% for females and males respectively, p = 0.004).

Table 3 demonstrate that severe dependent smokers start smoking at earlier age (p = 0.001) and have higher mean depression score (p = 0.001) than other groups. Low dependent smokers (Fig. 1) in contrast to other groups of smokers and non-smokers demonstrate the lower rate (15%) of depressive symptoms (p = 0.0001), while the highest rate seen among severely dependent smokers (71.4%).

In Table 4, univariate logistic regression analysis done using depression as dependent variable, demonstrate that age, sex, age of onset of smoking and the FTND score significantly associated with depression. Female students display 2.25 times higher odds of depressive symptoms than their male peer students. In the same table mentioned before, severe smoking dependence has 6.15 times higher odds of depressive symptoms than non-smokers.

Multivariate logistic regression analysis using depression as dependent variable with age, age of smoking and sex as covariate, demonstrate that severe smoking dependence significantly associated with depression with odds of 12.33 (p = 0.007, C.I: 1.98–76.61) in comparison with non-smokers.

### Table 2

Comparison between non-depressed and depressed students regarding their age, Beck Depression Inventory (BDI), age of start smoking and their Fagerström test for nicotine dependence (FTND).

<table>
<thead>
<tr>
<th></th>
<th>Non-depressed (n = 158) mean ± SD</th>
<th>Depressed (n = 75) mean ± SD</th>
<th>P value</th>
<th>Class interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>21.21 ± 1.73</td>
<td>21.75 ± 1.72</td>
<td>0.027*</td>
<td>0.061–1.015</td>
</tr>
<tr>
<td>BDI</td>
<td>9.03 ± 3.82</td>
<td>23.33 ± 5.07</td>
<td>0.038*</td>
<td>13.12–15.62</td>
</tr>
<tr>
<td>Age of smoking</td>
<td>18.00 ± 2.30</td>
<td>16.52 ± 2.37</td>
<td>0.026*</td>
<td>0.180–2.777</td>
</tr>
<tr>
<td>FTND score</td>
<td>3.50 ± 2.68</td>
<td>6.26 ± 2.76</td>
<td>0.001*</td>
<td>1.246–4.276</td>
</tr>
</tbody>
</table>

*Significant difference between groups using independent sample t-test.
effects of other drugs of abuse such as cocaine and alcohol, creates a sense of euphoria that is hard to distinguish from the tine concentration similar to those found in the plasma of habitual of dopamine, while injecting nicotine to animals with blood nico
dence. First, nicotine injected to animals with low circulating levels nicotine concentration represented by severe smoking depen
dence and depression enclose many problems like subjectivity and bias in reporting. Third, small sample size which is not represen
tobacco dependence and depressive symptoms dif
sectional study, therefore causal association between the degree of smoking dependence and depression, these studies required to be more objective by measuring serum cotinine between the degree of smoking dependence and depression, these
studies required to be more objective by measuring serum cotinine
levels on generalization of the results.

Prospective studies are vital to further elucidate the relationship between the degree of smoking dependence and depression, these studies required to be more objective by measuring serum cotinine level as well as implementing diagnostic interview as a mean for diagnosis and follow up of depressed patients.

5. Conclusions

Despite the above limitations, the present study may partially explain the controversy regarding the relationship between smoking and depression by adoptin

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References