Original article

Effect of smoking on cardiovascular autonomic function test and nerve conduction velocity: Cross sectional study in Indian population

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Abstract:

Introduction: In recent years, study of cardiac autonomic modulation as well as nerve conduction studies has been greatly facilitated by the development of various computer based methods. Present work was planned to study the correlation between smoking and cardiovascular autonomic functions and nerve conduction velocity among smokers.

Material & Methods: 100 male subjects in the age group 25 years to 40 years comprising of 50 smokers and 50 nonsmokers as control group were selected for present study. Cardiovascular autonomic function tests were assessed by using Canwin autonomic analyser. Median nerve conduction velocities were measured by using clarity Medicare’s octopus-2 Channel EMG Machine.

Observations & Results: After applying ‘Z’ test of difference between two sample means, it was observed that there is a highly significant difference between mean values of autonomic function tests in the smokers and non-smokers group. It was also found that there is highly significant difference between mean values of sensory nerve conduction velocity in the smokers as compared to non-smokers group. However no significant difference was observed in the motor nerve conduction velocity in smokers as compared to nonsmokers.

Conclusion: From present study we present evidence that the relative involvement of large and small nerve fiber damage due to smoking is not uniform.

Keywords: autonomic function tests, nerve conduction velocity, smoking, smoking index

Introduction:

Smoking is a worldwide major cause of preventable morbidity and mortality. (1) It is a prime factor in heart disease, stroke and chronic lung disease. Smoking has been identified as a major coronary heart disease risk factor. (2) The degree of risk of developing coronary heart disease is directly related to the number of cigarettes smoked per day. (3) Smoking also induces subclinical changes in myelin sheath leading to demyelination of nerves and consequent decrease in conduction velocity. (4) In recent years, study of cardiac autonomic modulation as well as nerve conduction studies has been greatly facilitated by the development of various computer based methods. With this background in mind it was planned to compare the effects of smoking on autonomic nervous system and somatic nervous system among smokers and nonsmokers.

Materials and Methods:

The present study was conducted at Pravara Institute of Medical sciences, Loni. The study was approved by Institutional ethical committee from our university. The sample size was calculated with help of expert from our university using online sample...
The study was completed using strobe guidelines. 100 male subjects in the age group 25 years to 40 years comprising of 50 smokers and 50 nonsmokers as control group were selected for present study. The subjects were selected by simple random sampling method. Participant subjects were from staff members, residents and patients from routine OPD. Prior informed written consent was obtained after explaining the procedure and purpose of study tests. Smokers with history of smoking for more than 5 years with no history of any major illness like hypertension, diabetes mellitus, and peripheral neuropathy in past or present were considered as case group for present study. Subjects who had never smoked in life and not having any other addiction related to tobacco and with no history of any major illness were considered as control group for present study. The detailed personal history of the participants like type of diet, habits, addictions, occupation and past history was recorded. The study was approved by Institutional Ethical committee. Here smoking Index was calculated by multiplying average number of cigarettes smoked per day & duration of smoking in years. According to Smoking Index the smokers were classified into:

1. Light smokers: Smoking intake (1-100)
2. Moderate smokers: Smoking intake (101-200)
3. Heavy smokers: Smoking intake (>201)

Subjects were called in the morning 9.00 a.m. The blood pressure was measured in lying down position. Cardiovascular autonomic function tests were assessed by using canwin autonomic analyser machine.

**Autonomic Functions Tests:**

1. **Resting heart rate:** Subject was asked to lie comfortably for 15 minutes. ECG was recorded continuously for 1 minute. Resting heart rate was calculated from ECG.

2. **Expiration –Inspiration ratio (E: I ratio):** Subject was asked to take deep inspiration for 5 seconds followed by deep expiration for 5 seconds. ECG was recorded for 3 such cycles. This test is based on sinus arrhythmia during each respiratory cycle which depends upon variation of vagal tone.

3. **30:15 ratio : (Response to standing )** Subject was asked to lie down comfortably over the couch, then he was asked to stand up. Heart rate was recorded at 15th & 30th beat immediately after standing.

4. **Valsalva ratio:** Subject was asked to sit comfortably. Heart rate was recorded at rest with ECG. Subject’s nose was clipped with nose clip and a mouth piece was inserted between teeth and lips. The other end of mouthpiece was connected to mercury manometer. Subject was asked to blow air into the mouthpiece and maintain the pressure at 40 mmHg for 15 seconds. ECG was continuously recorded.

5. **Sustained Handgrip Test:** The subject was asked to hold spring dynamometer in left hand and compress it maximally and the value was noted. Then he was asked to hold spring dynamometer in left hand and compress it to up to 30% of maximum and hold it for 4 minutes. The rise in Diastolic blood pressure at the point just before the release of handgrip was noted. This test is an indicator of sympathetic insufficiency.
In present study motor and sensory nerve conduction velocity of median nerve was measured. Measurement of median nerve conduction velocity was done by using clarity medicare’s octopus-2 Channel EMG Machine. It is a device manufactured by Clarity Medicare Pvt.Ltd, Mohali, India. It has an extensive data base to keep tract of subjects history. Being fully automatic calculation errors are eliminated and easy to use.

**Motor nerve conduction velocity:**

1. For motor nerve conduction velocity, median nerve was stimulated supramaximally at two points along its course respectively at wrist and antecubital fossa (elbow).
2. The stimulating electrodes were placed with anode 3 centimeters proximal to cathode.
3. Recording and reference electrodes were placed over abductor pollicis brevis along thenar muscle border.
4. Ground electrode was placed over forearm.

**B. Sensory nerve conduction velocity:**

1. For sensory nerve conduction velocity, ring electrodes were placed at the index finger.
2. The cathode is placed at proximal interphalangeal joint and anode 3 cm distal.
3. Ground electrode was placed over the palm.

4. With the help of stimulating electrodes a submaximal stimulation is given at wrist and conduction velocity was recorded.

**Motor nerve conduction study setting:**

- Sensitivity: 2-5 mv/mm,
- Low frequency filter: 2-5 Hz,
- High frequency filter: 10 KHz,
- Sweep speed: 2-7 ms/cm,
- Supramaximal stimulation range: 30-45 mv.

**Sensory nerve conduction study setting:**

- Sensitivity: 2-5 mv/mm,
- Low frequency filter: 2-5 Hz,
- High frequency filter: 10 KHz,
- Sweep speed: 2-7 ms/cm.
- Submaximal stimulation range: 10-15 mv.

In the present study we recorded sensory and motor nerve conduction velocities using surface electrodes which require less precision in placement and are therefore quicker to use. Also using low noise amplifier and signal averaging minute potentials can be recorded from nerve trunks by using these electrodes. By using computerised technique, majority of errors can be eliminated giving more reliable and reproducible results. The data was tabulated and statistical analysis was done by using SPSS, Version 11. Comparison between two groups was done by using Z test. P value was calculated.
Observations & Results:

Table No.1: Comparison of mean values of autonomic function tests in smokers and non-smokers:

<table>
<thead>
<tr>
<th>Autonomic function tests</th>
<th>Smokers (n=50)</th>
<th>Non-smokers (n=50)</th>
<th>Z test value</th>
<th>‘p’ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting Heart Rate (/min)</td>
<td>78.36 ± 5.55</td>
<td>70.54 ± 4.68</td>
<td>7.62</td>
<td>0.0987</td>
</tr>
<tr>
<td>Expiration : Inspiration Ratio</td>
<td>1.16 ± 0.14</td>
<td>1.39 ± 0.16</td>
<td>7.66</td>
<td>0.0991</td>
</tr>
<tr>
<td>30:15 Ratio (Response to standing)</td>
<td>0.99 ± 0.12</td>
<td>1.09 ± 0.13</td>
<td>4.0</td>
<td>0.0897</td>
</tr>
<tr>
<td>Valsalva Ratio</td>
<td>2.87 ± 1.09</td>
<td>4.89 ± 1.24</td>
<td>8.66</td>
<td>0.0999</td>
</tr>
<tr>
<td>Sustained handgrip Test (Rise in diastolic Pressure) (mmHg)</td>
<td>6.12±2.8</td>
<td>9.06±3.64</td>
<td>4.53</td>
<td>0.0987</td>
</tr>
</tbody>
</table>

(Table 1: Z test was applied as test of significance, P value showing significant difference between two groups)

After applying ‘Z’ test of difference between two sample means there was a highly significant difference between mean values of autonomic function tests in the smokers and non-smokers group (i.e. p<0.01) It was seen that Resting Heart Rate had significantly increased, Expiration: Inspiration Ratio, 30:15 Ratio (Response to standing) and Valsalva Ratio had significantly decreased in Smokers as compared to nonsmokers. Rise in diastolic pressure was found significantly more in smokers than nonsmokers using sustained handgrip test.

Table No. 2: Comparison of mean values of Nerve conduction velocity in smokers and non-smokers:

<table>
<thead>
<tr>
<th>Nerve conduction velocity</th>
<th>Smokers (n=50)</th>
<th>Non-smokers (n=50)</th>
<th>Z test value</th>
<th>‘p’ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor NCV (mt/sec)</td>
<td>57.41± 4.21</td>
<td>57.58 ± 4.50</td>
<td>0.19</td>
<td>0.278</td>
</tr>
<tr>
<td>Sensory NCV (mt/sec)</td>
<td>50.26 ± 4.70</td>
<td>53.38 ± 3.90</td>
<td>4.54</td>
<td>0.0983</td>
</tr>
</tbody>
</table>

(Table 2: Z test was applied as test of significance)
It showed mean and SD values of motor NCV and sensory NCV in smokers and nonsmokers. After applying ‘Z’ test of difference between two sample means there was a highly significant difference between mean values of sensory nerve conduction velocity in the smokers as compared to non-smokers group (i.e. p<0.01) while there was no significant difference in the motor nerve conduction velocity in smokers as compared to nonsmokers.

Table No. 3: Correlation of Smoking index and autonomic function tests in Smokers:

<table>
<thead>
<tr>
<th>Smoking Index</th>
<th>Resting Heart Rate (/min)</th>
<th>E : I Ratio</th>
<th>30:15 Ratio</th>
<th>Valsalva Ratio</th>
<th>Sustained Handgrip Test (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-100 (Light smokers) (n=31)</td>
<td>Median</td>
<td>77.28</td>
<td>1.22</td>
<td>1.03</td>
<td>3.66</td>
</tr>
<tr>
<td>101- 200 (Moderate smokers) (n=11)</td>
<td>Median</td>
<td>79.38</td>
<td>1.09</td>
<td>0.91</td>
<td>3.15</td>
</tr>
<tr>
<td>Above 200 (Heavy smokers) (n=8)</td>
<td>Median</td>
<td>81.10</td>
<td>1.03</td>
<td>0.94</td>
<td>1.82</td>
</tr>
</tbody>
</table>

Increases indicating greater damage to parasympathetic system. Also Resting heart rate values go on increasing with severity of smoking suggesting similar effect. Increased in diastolic pressure was found significantly more in smokers than in nonsmokers using sustained handgrip test (Sympathetic function test)

Table No.4 : Correlation of Smoking index and Motor N.C.V. and Sensory N.C.V. in smokers:

<table>
<thead>
<tr>
<th>Smoking Index</th>
<th>Motor N.C.V.(mt/sec)</th>
<th>Sensory N.C.V.(mt/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-100 (Light smokers) (n=31)</td>
<td>Median</td>
<td>59.99</td>
</tr>
<tr>
<td>101- 200 (Moderate smokers) (n=11)</td>
<td>Median</td>
<td>58.76</td>
</tr>
<tr>
<td>Above 200 (Heavy smokers) (n=8)</td>
<td>Median</td>
<td>56.43</td>
</tr>
</tbody>
</table>

From table no.4, it was seen that, there was decrease in motor N.C.V. as well as sensory N.C.V. as the severity of smoking (Smoking index) goes on increasing.
Table no.5: Comparison of effects of smoking on Autonomic nervous system and Somatic nervous system:

(Percent change in comparison to nonsmokers)

<table>
<thead>
<tr>
<th>Smoking Index</th>
<th>Resting Heart Rate (/min)</th>
<th>E: I Ratio</th>
<th>30:15 Ratio</th>
<th>Valsalva Ratio</th>
<th>Sustained Handgrip Test (mmHg)</th>
<th>Motor NCV (mt/sec)</th>
<th>Sensory NCV (mt/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers (n=50)</td>
<td>70.54 ± 4.68</td>
<td>1.39 ± 0.16</td>
<td>1.09 ± 0.13</td>
<td>4.89 ± 1.24</td>
<td>9.06±3.64</td>
<td>57.58 ± 4.50</td>
<td>53.38 ± 3.90</td>
</tr>
<tr>
<td>1-100 (Light smokers ) (n=31)</td>
<td></td>
<td>+9.56%</td>
<td>-12.23%</td>
<td>-5.50%</td>
<td>-24.38%</td>
<td>-32.00 %</td>
<td>+4.18%</td>
</tr>
<tr>
<td>101- 200 (Moderate smokers) (n=11)</td>
<td></td>
<td>+12.50%</td>
<td>-12.96%</td>
<td>-17.43%</td>
<td>-35.12%</td>
<td>-31.78%</td>
<td>+2.10%</td>
</tr>
<tr>
<td>Above 200 (Heavy smokers) (n=8)</td>
<td></td>
<td>+14.99%</td>
<td>-17.30%</td>
<td>-14.67%</td>
<td>-62.60%</td>
<td>-35.20%</td>
<td>-2.01%</td>
</tr>
</tbody>
</table>

[ (+ = Increase, - = Decrease) : Deviation is calculated in percentage by comparison between smokers and nonsmokers.]

**Discussion:**

Smoking affects cardiovascular system by several mechanisms. Heavy smoking is the commonest cause of ischemic heart disease and death in 30 years -40yrs of age group who are likely to be free from other myocardial risk factors. (6) Hemodynamic effects of smoking appear to be mediated by nicotine. Such effects cause increase in myocardial work. Nicotine increases cardiac output by increasing both heart rate and myocardial contractility. (1) Autonomic alterations may contribute to the increased cardiovascular risk present in smokers. The pressor and tachycardial effects of cigarette smoking are associated with an increase in plasma catecholamines , suggesting the dependence of these effects on adrenergic stimulation. Smoking is accompanied by a marked and prolonged increase in heart rate and blood pressure. (7) Smoking also impairs baroreflex sensitivity in humans which may contribute to the smoking induced increase in blood pressure and heart rate as well as to the concomitant alterations in their variability. (8) The autonomic neurohumoral response evoked by smoking results in down regulation of beta-adrenergic receptors in long term smokers. (9) Resting heart rate is an easy counting measurable parameter with high prognostic implications. (10)
Chemicals in cigarette smoke are also toxic to peripheral nerves.\(^{(11)}\) Smoking represents an important problematic factor concerning the age dependency of peripheral nerve function.\(^{(12)}\) Smoking affects nerves by several mechanisms. Smoking decreases blood supply to nerves.\(^{(11)}\) Smoking also induces subclinical changes in myelin sheath leading to demyelination of nerves and consequent decrease in conduction velocity.\(^{(4)}\) The demyelinated axon has poor electrotonic conduction.\(^{(13)}\)

In our present study, from statistical results of cardiovascular autonomic function tests, it was found that smoking directly affects these tests, which were found statistically significant. Similarly from statistical results of nerve conduction velocities, it was seen that significant changes were found in conduction velocity of sensory nerves but not in motor nerves. When smokers were classified according to smoking index criteria, changes were observed directly proportional in all cardiovascular tests with smoking index. Changes were observed in sensory nerve conduction velocity in moderate and heavy smokers only; however such changes were not seen in light smokers.

In our present study, we found that overall percentage change in autonomic function is more than overall percentage change in somatic function. It was also noted that these changes increase along with increasing smoking index i.e. with severity of smoking. Therefore it appears that involvement of autonomic nervous system occurs earlier and to a greater extent than somatic nervous system in smokers. We could not find similar comparison in previous studies among smokers. However, very similar results were found in earlier studies involving diabetic neuropathy,\(^{(14)}\) nutritional neuropathy\(^{(15)}\) as well as alcoholic neuropathy.\(^{(16)}\) In our study, we tried to assess the effects of smoking on autonomic functions and somatic functions and tried to correlate them with severity of smoking expressed as Smoking Index. Robert Young reported relationship between peripheral somatic and autonomic neuropathy in patients with diabetic polyneuropathy.\(^{(17)}\) He found early involvement of autonomic nerves as compared to somatic nerves and attributed this to greater susceptibility of small fibers of autonomic nerves to damaging influences than large fibers of somatic nerves. He explains his hypothesis with reference to Behse study\(^{(18)}\) stating that there is usually a disproportionate and faster involvement of unmyelinated and small myelinated fibers than large nerve fibers. (Morphometric study pattern) There are many studies that explain a broad overall relationship between large myelinated and small autonomic fibers dysfunction with etiological influences.\(^{(16,17,18)}\)

In conclusion, we present evidence that the relative involvement of large and small nerve fiber damage due to smoking is not uniform. Understanding of details of large and small fiber damage may advance this explanation further.

**Conclusion:**
In present study, comparing the effects of smoking on autonomic nervous system and somatic nervous system, it is observed that there is early involvement of autonomic nervous system as compared to somatic nervous system. From this work we presents evidence that the relative involvement of large and small nerve fiber damage due to smoking is not uniform.

**Limitations of Present study:**
In this study, baseline activities of parasympathetic & sympathetic systems were studied excluding the acute effects of smoking as well as passive smoking.
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www.ijbamr.com  P ISSN: 2250-284X , E ISSN : 2250-2858