Migraine is a common, primary, chronic-intermittent neurovascular headache disorder characterized by episodic severe headache accompanied by autonomic nervous system dysfunction and in some patients, transient neurologic symptoms known as migraine aura.[1,2] The word migraine is derived from the term hemicrania, and is defined as a paroxysmal headache, commonly but not invariably unilateral, recurrent at irregular intervals and often associated with visual disturbances and other disorders of cerebral function and vomiting.[3] Autonomic functions have been found to be distinctly disturbed in migraine. There are numerous studies done in the past to suggest that there is an autonomic dysfunction in patients of migraine, sympathetic hyperfunction, sympathetic hypofunction and parasympathetic dysfunction have all been noticed. In the American migraine study, Migraine prevalence was 17.6% for women and 6% for men paralleling the Rasmussen et al. estimates.[4]

During headache-free periods, migraineurs may have a reduction in sympathetic function compared to non-migraineurs. Migraine shares significant diagnostic and clinical features with both pure autonomic failure and multiple system atrophy, yet represents a distinct subtype of chronic sympathetic dysfunction. Migraine is most similar to pure autonomic failure in terms of reduced supine plasma norepinephrine levels, peripheral adrenergic receptor supersensitivity, and clinical symptomatology directly related to sympathetic nervous system dysfunction. However, the sympathetic nervous system dysfunction in migraine differs from pure autonomic failure and multiple system atrophy in that it occurs in an anatomically intact system. It is proposed that the sympathetic dysfunction in migraine relates to an imbalance of sympathetic co-transmitters. An enhanced understanding of the sympathetic dysfunction in migraine may help to more effectively diagnose, prevent, and/or treat migraine and other types of headache.[5]
subjects included in the control group were obtained from Maulana Azad Medical College, New Delhi. After taking informed consent from all the participants and the ethical clearance was obtained from the college the subjects were categorized into two groups: Group A: Controls; and Group B: Cases

**Inclusion Criteria:** All adult patients of either sex, in the age group of 20 to 40 years, presenting with a history of headache satisfying the International Headache Society criteria-2 for primary episodic migraine were enrolled for the study.

**Exclusion Criteria:** Migraine patients with diabetes mellitus, hypercholesterolemia disorders, patients taking blood pressure medications and oral contraceptives. Migraine patients with history of any illness known to affect ANS system. All secondary causes of headache were excluded by appropriate clinical and radiological examinations.

All Subjects were tested under similar laboratory conditions and were allowed to acclimatize themselves to experimental and environmental conditions for one hour so that they were relaxed and rested, as anxiety and stress can affect autonomic functions. The procedure of each and every test was explained to the subjects before conducting the tests.

**Autonomic Function Tests:** The autonomic function tests were conducted with the help of a Polyrite-D machine manufactured by RMS. The following autonomic function tests were performed in all the participants:

**Parasympathetic Function Tests:** Resting Heart Rate, Standing to Lying Ratio, 30: 15 Ratio, Valsalva Ratio and Tachycardia Ratio.

**Sympathetic Function Tests:** Handgrip Test (HGT), Cold Pressor Test (CPT) and Sympathetic Skin Response (SSR).

**Statistics:** Results of the study were analysed statistically using ANOVA.

**RESULTS**

In table 1, the mean SBP of the cases was 122.70 ± 9.23 and the median was 125, while the mean and median SBP of the controls is 122.87 ± 6.80 and 123 respectively. The mean SBP of the cases is less than that of the controls and the difference between cases and controls is statistically insignificant as suggested by the p value of 0.933 derived applying ANOVA. The same table 1 shows the DBP of cases and controls which are 77.44 ± 7.062 and 74.97 ± 3.97, median is 78 for cases and 74 for controls. Although the mean DBP of cases is more when compared to the mean DBP of controls there is no statistical significance between the two groups using the parametric test.

During hand grip test the mean value for change in systolic blood pressure (SBP) in cases was 21.48 ± 3.89, median is 20 and that of controls was 22.13 ± 3.67 while median is 22 respectively as shown in table 1. The same table shows that the mean change in diastolic blood pressure (DBP) in cases to be 17.22 ± 3.35 and median to be 16 as compared to mean change in diastolic blood pressure of 17.47 ± 2.10 in controls, who had a median of 18. But none of the values were significant statistically using ANOVA.

During cold pressor test the mean value for change in systolic blood pressure (SBP) in cases was 16.47 ± 2.74 and median was 16, that of controls was 16.46 ± 1.72 while their median was 16 as shown in table no.(1), p value is 0.863 applying ANOVA. The same table shows that the mean change in diastolic blood pressure (DBP) in cases to be 12.11 ± 5.20 and median was 12 as compared to mean change in diastolic blood pressure of 12.20 ± 4.23 in controls, while the median was 12, p value is 0.859. None of the values were significant statistically.

As shown in table 1 controls had a mean value for latency of SSR as 1.55 ± 0.08, median was 1.55 when compared to a mean of 1.44 ± 0.16 and median of 1.50 in cases. The difference in the values was found to be statistically significant. The p value was 0.0004. The mean value and median for resting heart rate in cases were 78.63 ± 8.71 and 76 beats per minute respectively as compared to 79.33 ± 4.44 and 80 beats per minute respectively in control group as shown in table 2. The mean value for resting heart rate was less in cases in comparison to that of controls. But this difference was statistically insignificant as the p value is 0.681 applying ANOVA.

The mean value for the S/L ratio in controls was 1.06 ± 0.02 where as in cases it was 1.08± 0.04, median was 1.07 in both cases and controls as shown in table 2. We could not find any statistical significance for these values of controls and cases using ANOVA. As shown in table 2, the mean value for the lying to standing ratio (30:15) in controls was 1.06 ± 0.02 as compared to 1.08 ± 0.04 in cases. The median value for the parameter was 1.06 in controls compared to 1.07 cases, though, this increase when compared statistically with controls is found to be
out of the five parameters of the parasympathetic function tests none of them had any significant difference when the values of cases and controls were compared. Hence the parasympathetic nervous system of our study group is functioning normally in patients of episodic migraine during interictal period.

**DISCUSSION**

Numerous studies have said that a disturbance of the autonomic nervous system is a primary characteristic of migraine. Although evaluations of autonomic function in migraine have been reported, the results are conflicting. The most common findings are sympathetic hypofunction but higher sympathetic tone or parasympathetic dysfunction had also been reported. There is a major finding from our study involving migraineurs. The autonomic nervous system has been found to be functioning abnormally.

The resting heart rate, Valsalva ratio, standing to lying ratio, 30:15 ratio and tachycardia ratio are all representatives for analyzing the functioning of the parasympathetic system. In our study none of them showed any statistical difference when the values of those ratios for migraineurs were compared with that of healthy individual controls. Hence we concluded that the parasympathetic nervous system in the group of migraineurs that were enrolled in our study to be functioning normally. Previous studies by Pierangeli G et al. had also shown an intact and normal parasympathetic system which is in acceptance with our study.

The systolic blood pressure between cases and controls showed no statistical significance while the diastolic blood pressure has been found to be higher in migraineurs although statistical difference could not be found when compared to that of controls and this increased diastolic blood pressure could be secondary to sympathetic hyperfunction or due to reflex response to sympathetic hypofunction. Similar results were also shown in previous studies done by Aaron Shechter BA et al. to assess the autonomic nervous system.

In the handgrip test, the rise in diastolic blood pressure just before the release of hand grip was considered for evaluation. Studies done by Pogacnik T et al. had revealed that HGT showed a statistically significant decrease in response in migraineurs. In our study we found out that the migraineurs showed a slightly decreased rise in the diastolic blood pressure just before the release of the handgrip when compared to that of healthy controls. In accordance with this finding we may contemplate that there is a sympathetic hypofunction in migraineurs but the small difference between the two groups was not insignificant using ANOVA.

### Table 1: Sympathetic Function Tests

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases (n=54)</th>
<th>Controls (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting SBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>122.70 ± 9.23</td>
<td>122.87 ± 6.80</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>125</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>96 – 136</td>
<td>110 – 132</td>
</tr>
<tr>
<td>Resting DBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>77.44 ± 7.062</td>
<td>74.97 ± 3.97</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>78.00</td>
<td>74.50</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>60 – 92</td>
<td>68 – 84</td>
</tr>
<tr>
<td>HGT SBP – Resting SBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>21.48 ± 3.89</td>
<td>22.13 ± 3.67</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>14 – 32</td>
<td>16 – 30</td>
</tr>
<tr>
<td>HGT DBP – Resting DBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>17.22 ± 3.35</td>
<td>17.47 ± 2.10</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>16.00</td>
<td>18.00</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>12 – 28</td>
<td>14 – 22</td>
</tr>
<tr>
<td>CPT SBP – Resting SBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>16.47 ± 2.74</td>
<td>16.46 ± 1.72</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>16.00</td>
<td>16.00</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>10 – 24</td>
<td>14 – 20</td>
</tr>
<tr>
<td>CPT DBP – Resting DBP (mm Hg)</td>
<td>Mean ± S.D.</td>
<td>12.11 ± 5.20</td>
<td>12.20 ± 4.23</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>12.00</td>
<td>12.00</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>80 – 18</td>
<td>10 – 24</td>
</tr>
</tbody>
</table>
| Sympathetic Skin Response  | Mean ± S.D.  | 1.44 ± 0.16     | 1.55 ± 0.08 | 0.0004(
|                           | Median       | 1.50            | 1.55    |
|                           | Range        | 1.00 – 1.70     | 1.26 – 1.69|

The mean value of Valsalva ratio in controls was 1.49 ± 0.35 and while in cases it was 1.48 ± 0.71, as shown in table 2, median was 1.48 and 1.49 for controls respectively. Though the mean value for Valsalva ratio was lower in patients of migraine cases as compared to Controls, however the statistical significance could not be established. p value was 0.515 using ANOVA. The mean value for tachycardia ratio for both controls and cases were found to be very close. The mean value of Tachycardia ratio in controls was 0.75 ± 0.04 and while in cases it was 0.74 ± 0.06, both groups had a median of 0.75 as shown in table 2. The difference in the values was found to be negligible and statistically insignificant as the p value was 0.827 applying ANOVA. Out of the five parameters of the parasympathetic function tests none of them had any significant difference when the values of cases and controls were compared. Hence the...
proved to be statistically significant.

Cold Pressor test is also done to assess the status of the sympathetic system of an individual. Here cold acted as a painful stimuli. In the studies done in the past no differences were found between the case and control groups when comparing blood pressure response to a psychological stressor. In our study we found no significant difference when the values of normal controls were compared to that of migraineurs.

The sympathetic skin response is a very good indicator of the integrity of peripheral sympathetic cholinergic function. In the study conducted by Yildiz SK et al. the mean latencies were longer and the maximum amplitudes were smaller on the symptomatic side compared with the asymptomatic side in attack and in interictal periods.

In the study that we conducted, we observed that the latencies in the patients of migraine were found to be shorter than normal healthy individuals and the results showed a significant statistical difference between the case and the control groups. Seeking justification for this contradictory appearance of latencies in our study we decided that such a difference might have occurred due to the highly unpredictable and capricious behaviour of the autonomic nervous system in migraineurs. Hence, after assessing the sympathetic skin response, we found out that the sympathetic nervous system showed hyperfunction in the group of migraine patients in our study.

**CONCLUSION**

1. Assessment of the sympathetic system showed no statistical significance for hand grip test and cold pressor test but sympathetic skin response showed statistical significance, the latencies of cases were shorter than that of controls and hence we conclude that migraineurs in our study had sympathetic hyperfunction during headache free state.

2. Assessment of the parasympathetic system showed statistical significance for none of the 5 parameters viz. resting heart rate, standing to lying ratio, 30:15 ratio, Valsalva ratio and tachycardia ratio and therefore we conclude a normal parasympathetic function in the migraineurs of our study group during headache free state.

3. An enhanced understanding of the sympathetic dysfunction in migraine may help to more effectively diagnose, prevent, and or treat migraine and other types of headache.

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