Frequency of previous head trauma and surgery with general anesthesia in Parkinson's disease and essential tremor

Borislav Ivanov¹, Stefan Peev², Ivan Dimitrov³, Ara Kaprelyan⁴, Kalina Drenska⁴, Vesselina Nestorova⁵, Margarita Grudkova⁴

1. Department of Clinical Medical Sciences, Medical University, Varna, Bulgaria;
2. Department of Periodontology and Dental Implantology, Medical University Varna, Bulgaria;
3. Department of Nursing, Sliven Affiliate, Medical University Varna, Bulgaria;
4. Department of Neurology and Neurosciences, Medical University Varna, Bulgaria;
5. Department of Physiotherapy, Rehabilitation, Thalassotherapy and Occupational Diseases, Medical University Varna, Bulgaria;

Abstract

Introduction
The possible role of head trauma as pathogenic factor in Parkinson’s disease (PD) was first noted by J. Parkinson in his essay in 1817. General anesthesia has also been discussed and considered to be a risk factor for PD. Their role in the etiopathogenesis of essential tremor (ET), the most common movement disorder, has not been studied extensively.
Aim
To assess the frequency of head trauma history and previous surgery with general anesthesia in a clinical setting of PD vs. ET patients.

Material and methods
We analyzed the medical records of 366 PD patients and 613 ET patients, hospitalized during an 8-year period in the First clinic of Neurology, Sveta Marina University Hospital, Varna, Bulgaria.

Results
Twenty (5.46%) PD and 36 (5.87%) ET patients had suffered head trauma with concussion or more severe brain damage prior to their initial movement disorders symptoms. Seventy-four (20.22%) PD and 142 (23.16%) ET patients had undergone 1 or more surgical interventions with general anesthesia prior to their first symptoms. Frequencies of head trauma and general anesthesia did not differ statistically between groups.

Conclusion
Some authors support the hypothesis for association of head injury and general anesthesia with increased risk of developing PD. Our results of similar frequency of head trauma and slightly larger of general anesthesia in the ET group support further research of their potential causal or triggering role in the pathogenesis of ET.

Keywords: Head Trauma, General Anesthesia, Parkinson’s Disease, Essential Tremor

Introduction
Head trauma (HT) and general anesthesia (GA) have been discussed and considered as risk factors for Parkinson’s disease (PD). The potential relationship between HT and PD has been debated since James Parkinson’s original description in 1817 (1). Even to this day, 200 years later, controversial opinions exist regarding the relationship between head trauma and PD.

Recent studies show opposite results. Some authors find no association (2, 3, 4), while others describe a significantly higher frequency of any degree of head trauma history in patients than in controls (5); history of posttraumatic concussion or unconsciousness associated with a higher risk of developing PD (6, 7); association of the number of head injuries and the duration of unconsciousness with increased risk of PD (8); HT resulting in hospitalization more frequently in PD (9); an interval between HT and PD debut from 3 months to 30 years (4, 5, 10).

GA is another potential environmental risk factor implicated in PD pathogenesis (11). Exposure to GA is known to exhibit a significant positive association with PD (12). Occupational exposure to anesthetic gases may cause a two-fold increase in the risk of PD. A study comparing mortality from PD showed a statistically significant predominance in anesthesiologists compared to internists (13).

The role of HT and GA in the etiopathogenesis of essential tremor (ET), the most common movement disorder, has not been studied extensively.
Aim

To assess the frequency of head trauma history and previous surgery with general anesthesia in a clinical setting of PD vs. ET patients.

Materials and methods

We analyzed the medical records of 366 PD patients and 613 ET patients, hospitalized in the First clinic of Neurology, Sveta Marina University Hospital, Varna, Bulgaria, for an 8-year period. The clinical database was searched for HT with concussion or more severe brain damage and for any kind of surgery with GA, all prior to the initial movement disorder symptoms. HT was not divided by subtypes and a total number of cases was calculated.

The diagnosis of PD was based on the UK Brain Bank criteria (14), and ET patients were diagnosed according to Deuschl criteria (15).

Mean age and disease duration did not differ significantly between the groups (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Gender, age and disease duration of studied PD and ET patients</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Number of patients males/females</td>
</tr>
<tr>
<td>Mean age (years) range</td>
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<td>Mean duration (years) range</td>
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</tbody>
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- *p<0,05
- **p=0,34
- ***p=0,065

Statistical analysis included descriptive methods, independent samples t-test, and Pearson’s correlation analysis.
Results

In the PD group, 20 (5.46%) patients suffered at least once from HT, and 74 (20.22%) had undergone 1 or more surgical interventions with GA.

In the ET group, 36 (5.87%) patients suffered at least once from HT, and 142 (23.16%) had undergone 1 or more surgical interventions with GA.

Differences between groups did not reach statistical significance (Table 2).

Table 2. Frequency of HT and GA in PD and ET groups

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>ET</th>
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<tbody>
<tr>
<td>HT n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>males</td>
<td>20 (5.46%)*</td>
<td>36 (5.87%)*</td>
</tr>
<tr>
<td>total HT</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>41</td>
</tr>
<tr>
<td>GA n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>males</td>
<td>74 (20.22%)**</td>
<td>142 (23.16%)**</td>
</tr>
<tr>
<td>total GA</td>
<td>39</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>123</td>
<td>211</td>
</tr>
<tr>
<td>HT+ GA n (%)</td>
<td>91 (24.86%)**</td>
<td>173 (28.22%)**</td>
</tr>
</tbody>
</table>

- *p=0.81
- **p=0.129
- ***p=0.118

Discussion

Our results show insignificantly higher frequency of HT and GA in ET, compared to PD patients.

Traumatic brain injury (TBI) has also been implicated as a risk factor for other neurodegenerative diseases such as Alzheimer’s disease (AD), frontotemporal lobar degeneration, motor neuron disease, progressive supranuclear palsy, and multiple sclerosis (5, 6).

It is possible that HT and GA act as nonspecific modifying environmental factors and trigger a subsequent pathogenetic cascade, specific for each neurodegenerative process. Another explanation could be that patients with chronic disease such as ET and PD tend to look for possible connections between different events and the disease onset, and consider every incident, whether or not a logical relationship could be established. In this regard, the higher frequency of HT may be a nonspecific subjective phenomenon. In a
study of the medical records of patients suffering HT with presumed brain involvement, morbidity ratios were not elevated for PD, AD, parkinsonism, and motor neuron disease (5).

On the other hand, the same characteristics of the inflammatory cascade that is initiated by mild to moderate head injury can be seen in PD brains at autopsy, with impairment of the blood-brain barrier, edema, leukocyte infiltration, microglial activation, excitotoxicity, free radical production, lipid peroxidation, and finally, upregulation and release of inflammatory cytokines, leading to PD over a decade or two (1, 4). In subjects with less severe trauma, clinically silent loss of neurons in the substantia nigra has been reported (5).

Anesthetics depress the central nervous system. Nitrous oxide inactivates vitamin B12, and evidence of B12 deficiency has been reported in PD. Isoflurane increases the production of reactive oxygen species, implicated in the pathogenesis of PD. Isoflurane also inhibits the dopamine active transporter, it can induce neuroinflammation, and reduces NMDA receptors. Sevoflurane increases TNF-alpha and the production of beta-amyloid. Halothane and isoflurane increase cytotoxicity by increasing oligomerization of beta-amyloid. The same mechanism presents itself at the nigro-striatal level, producing dopaminergic neurotoxicity (13).

A study, evaluating the relationship between HT and PD, found a significantly more PD patients reporting head trauma in the past than control subjects (32% of 97 patients vs 11% of 64 controls) (5). Seidler A. et al. reported insignificant differences, but still PD patients having history of GA and HT noticeably more often than controls (16).

Andrew et al. reported eight cases of posttraumatic postural and kinetic tremor treated by stereotactic surgery. The patients had additional focal neurological signs, and midbrain involvement in the genesis of tremor was discussed. Essential tremor was mentioned in one of the cases (17).

The traditional view of ET as a benign, monosymptomatic disorder was recently revised. Growing evidences in the last two decades led most authors to the opinion that ET is rather a chronic progressive neurodegenerative disorder with significant physical and psychosocial disability of the persons affected (18, 19).

ET is the most common movement disorder, but the etiopathogenesis still remains unclear. Some cases of PD and ET share similar pathological findings, and they may share common risk factors as well. Our results of similar frequency of two risk factors in both groups may elucidate some aspects of the nature of ET.

Conclusion

Some authors support the hypothesis for association of head injury and general anesthesia with increased risk of developing PD. The frequency differences for both studied variables do not reach statistical significance between our patient’s settings, but show a trend for a larger frequency of head trauma and
general anesthesia in the ET compared to PD group. This would support further research of their potential causal or triggering role in the pathogenesis of ET.

Conflict of interest:

None declared.

References


**Corresponding author:**

Borislav D Ivanov, MD, PhD,
Associate Professor of Neurology,
Department of Clinical Medical Sciences,
Faculty of Dental Medicine,
Medical University,
Varna, Bulgaria
email: borislav.ivanov@mu-varna.bg