An Audit of the Treatment of Essential Tremor: Report on 200 patients

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Clinical Features of ET

- Prevalence estimates: 0.4% - 3.9% of population
- Postural tremor (dominant)
- Intention tremor (less common)
- Rest tremor (rare)
- Affects predominantly upper limbs but tremor can spread to affect the head, legs, face, jaw, voice and trunk.
- Other neurological signs can sometimes be seen (e.g. gait abnormalities, reduced arm swing)
Clinical assessment of ET severity

Specimen of spiral drawing

e.g. Left Upper Limb tremor

Bain PG & Findley LJ, 1993
Treatment of ET

**Pharmacotherapy**
- Alcohol
- Propranolol
- Primidone
- Topiramate
- Gabapentin
- Clonazepam
- Mirtazapine

First line treatments
- Second line treatments
- Third line treatments

**Surgical treatment**
- Thalamotomy
- Deep brain stimulation (DBS)
Aim of study

- To assess the effects and adverse effects of treatments prescribed to patients with Essential Tremor
- 200 consecutive patients with ET seen in Dr Bain’s tremor clinic.
- Review anti-tremor treatments in terms of:
  - Benefits
  - Adverse events
Demographics

♀ (55%); ♂ (45%)

Mean duration of tremor: 17.0 ± 16.7

Mean age of onset: 40.2 ± 21.3
## Family history

<table>
<thead>
<tr>
<th>FH &amp; affected relative</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic ET</td>
<td>65</td>
<td>33% - 37%</td>
</tr>
<tr>
<td>Unknown FH</td>
<td>25</td>
<td>12.5%</td>
</tr>
<tr>
<td>Positive FH of ET</td>
<td>110</td>
<td>55%-63%</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; degree</td>
<td>96</td>
<td>48% - 55%</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; degree</td>
<td>33</td>
<td>17% - 19%</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; degree</td>
<td>2</td>
<td>1.0% - 1.1%</td>
</tr>
<tr>
<td>PD</td>
<td>17</td>
<td>8.5% - 9.7%</td>
</tr>
<tr>
<td>RLS</td>
<td>2</td>
<td>1.0% - 1.1%</td>
</tr>
</tbody>
</table>

FH = Family History; PD = Parkinson’s Disease; RLS = Restless Leg Syndrome
Observed Physical Signs

- Head: 35%
- Face: 0.5%
  - Jaw: 11%
  - Tongue: 3.0%
- Lower Limbs: 14%
- Voice: 6.5%
- Upper Limb: 98%
  - Postural tremor: 98%
  - Intention tremor: 75%
  - Rest Tremor: 22%
Tremor severity (mean)

Upper Limb tremor

Lower Limb tremor

Severity

RUL-intention
RUL-posture
RUL-rest
LUL-rest
LUL-posture
LUL-intention
Spiral score

RLL-intention
RLL-posture
RLL-rest
LLL-rest
LLL-posture
LLL-intention

Spiral score

0 0.5 1 1.5 2 2.5 3 3.5
## Treatment

### Response to Alcohol

<table>
<thead>
<tr>
<th>Response to alcohol</th>
<th>No. of patients</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unknown/ Unsure</strong></td>
<td></td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td><strong>Alcohol Responsive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tremor relief (1-4 units)</td>
<td>51</td>
<td>69</td>
<td>65.7%</td>
</tr>
<tr>
<td>Rebounds in couple of hrs</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebounds the next day</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol Non-responsive</strong></td>
<td></td>
<td>36</td>
<td>34.3%</td>
</tr>
<tr>
<td>No relief</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used to be alcohol responsive</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Effects of Treatment

**Response to most common anti-tremor drugs**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Positive effects</th>
<th>Adverse events</th>
<th>Drug withdrawn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Propranolol (n=99)</td>
<td>25</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Primidone (n=70)</td>
<td>11</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Topiramate (n=40)</td>
<td>9</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Mirtazapine (n=30)</td>
<td>12</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Clonazepam (n=20)</td>
<td>8</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Gabapentin (n=19)</td>
<td>8</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
Quality of treatment Index

(Q.T.I) = % responding / % withdrawing from a drug

![Graph showing the Quality of treatment Index for different drugs. The graph compares the Q.T.I values for Propranolol, Primidone, Topiramate, Mirtazapine, Clonazepam, and Gabapentin. The Q.T.I values range from 0 to 0.9, with Propranolol having the highest Q.T.I value.]
Weighted Q.T.I = \frac{(% \text{Mild R} \times 1) + (% \text{Moderate R} \times 2) + (% \text{Good R} \times 3)}{(% \text{Mild AE} \times 1) + (% \text{Moderate AE} \times 2) + (% \text{Severe AE} \times 3)}

<table>
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<tr>
<th>Drugs</th>
<th>Positive effects</th>
<th>Adverse events</th>
<th>Drug withdrawn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 %R</td>
<td>0 1 2 3 %AE</td>
<td></td>
</tr>
<tr>
<td>Propranolol (n=99)</td>
<td>25 17 18 8 43%</td>
<td>2 15 25 2 52%</td>
<td>54 (55%)</td>
</tr>
<tr>
<td>Primidone (n=70)</td>
<td>11 12 7 4 33%</td>
<td>2 16 19 6 73%</td>
<td>48 (69%)</td>
</tr>
<tr>
<td>Topiramate (n=40)</td>
<td>9 5 6 3 35%</td>
<td>1 11 16 1 75%</td>
<td>32 (80%)</td>
</tr>
<tr>
<td>Mirtazapine (n=30)</td>
<td>12 3 4 0 23%</td>
<td>1 5 6 0 47%</td>
<td>20 (67%)</td>
</tr>
<tr>
<td>Clonazepam (n=20)</td>
<td>8 5 1 0 30%</td>
<td>1 4 1 0 35%</td>
<td>14 (70%)</td>
</tr>
<tr>
<td>Gabapentin (n=19)</td>
<td>8 3 1 0 21%</td>
<td>0 3 3 1 53%</td>
<td>14 (74%)</td>
</tr>
</tbody>
</table>
\[
\text{Weighted Q.T.I} = \frac{\left( \% \text{ Mild } R \times 1 \right) + \left( \% \text{ Moderate } R \times 2 \right) + \left( \% \text{ Good } R \times 3 \right)}{\left( \% \text{ Mild } AE \times 1 \right) + \left( \% \text{ Moderate } AE \times 2 \right) + \left( \% \text{ Severe } AE \times 3 \right)}
\]

* R = Response; AE = Adverse Event
Relationship between tremor severity and effect of treatments:

As tremor severity ↑, response to drug treatments ↓.
Effect of stereotactic surgery on ET

3 patients undergone thalamotomy
7 patients undergone DBS surgeries

- Mean age: 68.1 ± 7.42 years
- Mean tremor severity = 6.3 ± 2.0
- Tremor amplitude reduced dramatically (in some cases tremor abolished).
- DBS patients benefited from flexibility of adjusting stimulator settings and fewer adverse events (QTI excellent (10/0))
Conclusions

- Benefits from pharmacotherapy are limited for ET Patients. **Propranolol** should be the first line treatment.
- Adverse events are frequent with all the anti-tremor drugs and cause distress to the patients, who should be monitored.
- Overall the quality of the drug treatments used for ET is poor, with withdrawal rates of > 50% & Q.T.I < 1.
- Drug treatments are usually ineffective in patients with severe tremors (>6/10)
- Stereotactic surgical therapies are reliable at reducing tremor amplitude but carry a risk of serious complications (not encountered in this study)
  - 1/1000 of death
  - 2-3% of intracranial haemorrhage
How can treatment of ET be improved?

- Current medical therapies are barely satisfactory
- Pharmacogenetic studies are needed to improve drug targeting
- Patients with ET should be followed-up for adverse effects from treatment
- Further long term follow up studies are required to assess the effects & adverse effects of anti-tremor medications
- Surgery should be considered earlier for patients with severe tremors, as medication is usually ineffective.