Antiepileptic Agents for Early Seizure Prophylaxis in Traumatic Brain Injury

Su Qiong (Rebecca) Liang, B.Sc.(Pharm); Jennifer Haymond, B.Sc.(Pharm), ACPR, Pharm.D.; Flora Young, B.Sc.(Pharm), ACPR, Pharm.D.

Background
- Posttraumatic seizures (PTS) are among the many complications associated with traumatic brain injury (TBI)\(^1\)
- Early PTS (within 7 days) is thought to be associated with secondary brain injury which may result in worse outcomes\(^2,3\)
- The incidence of early PTS is approximately 1-2%\(^4,5,6\)
- Evidence-based practice guidelines currently support the use of antiepileptic drugs (AED) to reduce the risk of early PTS when overall benefit outweighs the risk of treatment\(^7,8,9\)
- Phenytoin is the drug of choice, with one guideline supporting antiepileptic drugs (AED) to reduce the risk of early PTS when overall benefit outweighs the risk of treatment\(^7,8,9\)
- Current practice at Royal Columbian Hospital (RCH) is variable
- Evidence

Purpose
- To characterize the incidence of PTS and the use of AED for early seizure prophylaxis in patients with TBI at RCH

Methods
- Design: Retrospective chart review, tertiary care trauma centre
- Patients: Random sample of convenience
  - Admitted to RCH April 1, 2015 – August 31, 2017
- Inclusion:
  - ≥18 years of age
  - Diagnosis of TBI within 24h of admission
  - ≥1 risk factor for early PTS
- Exclusion:
  - Death within 48h of injury
  - History of previous TBI or seizure disorder
  - Injury causing TBI >24h prior to admission
  - Transfer out of RCH within 7 days of admission
- Primary outcomes:
  - Proportion that received seizure prophylaxis
  - Proportion that received prophylactic AED
- Secondary outcomes:
  - Incidences of early and late PTS
  - Selection and duration of prophylactic AED
  - Associated monitoring, adverse effects, and drug interactions

Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>54 (19-94)</td>
</tr>
<tr>
<td>Male</td>
<td>77.8%</td>
</tr>
<tr>
<td>Median no. risk factors for early PTS, n (range)</td>
<td>2 (1-5)</td>
</tr>
<tr>
<td>Patients with GCS ≤10</td>
<td>29.6%</td>
</tr>
<tr>
<td>Patients requiring ICU admission</td>
<td>39.5%</td>
</tr>
<tr>
<td>Patients requiring neurosurgical intervention</td>
<td>12.3%</td>
</tr>
<tr>
<td>Patients with history of alcohol abuse</td>
<td>19.8%</td>
</tr>
</tbody>
</table>

Table 2: Outcomes

<table>
<thead>
<tr>
<th>Patients who received seizure prophylaxis</th>
<th>n=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who received phenytoin</td>
<td>80%</td>
</tr>
<tr>
<td>Median no. of levels drawn per patient</td>
<td>1</td>
</tr>
<tr>
<td>No. of corrected levels within therapeutic range</td>
<td>2</td>
</tr>
<tr>
<td>No. of subtherapeutic levels</td>
<td>0</td>
</tr>
<tr>
<td>Patients who received levetiracetam</td>
<td>20%</td>
</tr>
<tr>
<td>Median duration of AED therapy, days (range)</td>
<td>7 (2-14)</td>
</tr>
<tr>
<td>ADRs reported requiring discontinuation</td>
<td>0</td>
</tr>
<tr>
<td>Patients with potentially significant drug interactions</td>
<td>80%</td>
</tr>
</tbody>
</table>

All patients n=81
- Patients who received propofol 38%
- Patients who received benzodiazepine(s) 48%

Figure 1: Proportion of patients that experienced PTS

<table>
<thead>
<tr>
<th>No Seizure</th>
<th>Early Seizure</th>
<th>Late Seizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>94%</td>
<td>5%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Figure 2: Proportion of patients that received seizure prophylaxis

<table>
<thead>
<tr>
<th>AED</th>
<th>No AED</th>
</tr>
</thead>
<tbody>
<tr>
<td>94%</td>
<td>6%</td>
</tr>
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</table>

Risk factors for early PTS
- Glasgow Coma Score (GCS) ≤10
- Posttraumatic amnesia >30 min
- Immediate seizure post trauma
- Depressed skull fracture
- Intracranial hemorrhage
- Penetrating head injury
- Cortical contusion

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Conclusions
- Overall observed incidence of early PTS at RCH was 4.9%
- 6.2% of patients with at least one risk factor for early PTS received seizure prophylaxis
- 80% of these patients received phenytoin
- 50% had a phenytoin level within therapeutic range
- No ADRs requiring discontinuation of AED were reported
- Further research is required to better identify TBI patients at high risk of early PTS that would most benefit from prophylaxis with AED

Limitations
- Retrospective chart review
- Small sample size
- Low event rate
- Use of propofol and benzodiazepines early during admission may have reduced seizure events

References