REDUCED ANESTHESIA EFFECT OF SODIUM AMYTAL DURING THE INTRACAROTID AMOBARBITAL PROCEDURE IN PEDIATRIC PATIENTS TAKING TOPIRAMATE OR ZONISAMIDE

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REVISED ABSTRACT

RATIONALE: A recent report (Bookheimer, et al. 2005) suggested that patients taking carbonic anhydrase inhibiting drugs have an increased rate of anesthesia failures during the Intracarotid Amobarbital Procedure (IAP). This study aims to clarify the interaction between the carbonic anhydrase inhibiting drugs topiramate (TPM) and zonisamide (ZNS), and sodium amobarbital during the IAP in pediatric patients.

METHODS: A retrospective chart review was performed on pediatric patients with intractable epilepsy who underwent the IAP between 2002 and the present at the Minnesota Epilepsy Group. Fifteen patients were identified who were taking TPM or ZNS at the time of the IAP and 20 were identified who were on other anticonvulsants at the time of the procedure. Independent samples t-tests were conducted to determine whether the groups differed with respect to amobarbital dose, time to first motor return, and time to first verbalization.

RESULTS: The two groups did not differ with respect to age (mean age = 12.53 for TPM/ZNS patients and 12.15 for other AEDs), IQ (mean IQ = 82.4 for TPM/ZNS patients and 87.8 for other AEDs), or total number of AEDs (mean number of AEDs = 2.5 for TPM/ZNS patients and 2.1 for other AEDs). Patients taking TPM or ZNS were 5 times more likely to require an additional bolus of amobarbital to achieve sufficient motor loss and required a statistically significantly higher total dose of amobarbital to achieve complete anesthetization for both left (p<0.05) and right (p<0.05) injections than patients taking other AEDs. Five patients (33%) taking TPM or ZNS did not achieve complete motor loss despite additional Amytal, while only one patient (5%) taking other AEDs experienced anesthesia failure. Following left injection, patients taking TPM or ZNS experienced a shorter recovery time for both motor and verbal functions, although these results did not reach statistical significance. For the right injection, the differences on these variables were not significant. Language lateralization and hemispheric memory capacity findings were similar between the two groups.

CONCLUSIONS: These results suggest reduced anesthesia effect of sodium amobarbital during the IAP in pediatric patients taking TPM or ZNS. Pediatric patients taking these drugs were more likely to require an additional bolus of amobarbital, received a greater total dose of amobarbital, were more likely to experience anesthesia failure despite the increased dose, and had shorter recovery times for both motor and verbal functions. While language and memory findings were similar between the two groups in this study, additional research is necessary to clarify the effect of reduced anesthesia on interpretation of language and memory performance during the IAP.

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**Introduction:**
The Intracarotid Amobarbital Procedure (IAP) or Wada Test was developed for determining language laterality and postoperative memory deficits in patients for temporal lobectomy, with the identification of cerebral dominance for language critical in minimizing the effects of surgery on language function. The occurrence of aphasia, amnesia, or both after the injection of amobarbital suggest that the anesthesized hemisphere is critical for normal speech and memory function, and that the contralateral hemisphere alone is incapable of supporting these processes.\(^1\) A recent study reported that patients taking carbonic anhydrase inhibiting drugs have an increased rate of anesthesia failures during the IAP, and further suggested that such drugs be discontinued \(\geq 8\) weeks before an IAP is performed, as these medications possibly interfere with the anesthetic effects of amobarbital.\(^2\) Another report has described similar findings, that patients taking topiramate (TPM) and zonisamide (ZNS), both carbonic anhydrase inhibiting drugs, were at significant risk for reduced sensitivity to the effects of amobarbital.\(^3\) However, more studies are needed to confirm these observations. This present study aims to clarify the interaction between the carbonic anhydrase inhibiting drugs TPM and ZNS, and sodium amobarbital during the IAP in pediatric patients.

**Methods:**
- A retrospective chart review was performed on pediatric patients with intractable epilepsy who underwent the IAP between 2002 and the present at the Minnesota Epilepsy Group.
- Patients were excluded if they required an English translator during the procedure.
- A total of 35 patients were identified and grouped according to the type of AED received at the time of the procedure.
  - 15 patients were taking TPM or ZNS
  - 20 patients were on other AEDs
- Independent samples t-tests were conducted to determine significant differences in amobarbital dose, time to first motor function return, and time to first verbalization between the 2 groups
- Language lateralization and hemispheric memory capacity findings were also evaluated by group.

**Results**

**Patient Demographics**
- The 2 groups did not differ with respect to mean age in years (12.53 years for TPM/ZNS and 12.15 years for other AEDs), mean IQ (82.40 for TPM/ZNS and 87.8 for other AEDs), or mean number of AEDs (2.5 for TPM/ZNS and 2.1 for other AEDs).
Results (Cont.)

Antiepileptic Drug Effects on Anesthesia

- Patients taking TPM or ZNS were 5 times more likely to require an additional bolus of amobarbital to achieve sufficient motor loss and required a statistically significantly higher total dose of amobarbital to achieve complete anesthetization for both left (p<0.05) and right (p<0.05) injections than patients taking other AEDs.
- 12 patients (80%) in the TPM/ZNS group required an additional bolus of amobarbital due to insufficient motor loss; of these, 5 patients (33%) did not achieve complete motor loss despite the additional anesthetic.
- For the other AED group, only 3 patients (15%) required an additional bolus of amobarbital to achieve complete motor loss, with one patient (5%) experiencing anesthesia failure.
- 10 patients (67%) in the TPM/ZNS group and 4 patients (25%) in the other AED group demonstrated a clinically significant obtundation following at least one injection of anesthetic.
- Patients taking TPM or ZNS experienced a clinically significantly shorter recovery time for both motor (86.29 sec. vs. 142.20 sec) and verbal (89.21 sec. vs. 142.15 sec) functions following left injection, although these differences did not reach statistical significance. For the right injection, the differences on these variables were not clinically or statistically significant.

Language and Memory

- Language lateralization and hemispheric memory capacity findings were similar between the two groups.

Conclusions:

- These results are consistent with previous studies and suggest reduced anesthesia effect of sodium amobarbital during the IAP in pediatric patients taking TPM or ZNS
- Pediatric patients taking these drugs were more likely to require an additional bolus of amobarbital, received a greater total dose of amobarbital, were more likely to experience anesthesia failure despite the increased dose, and had shorter recovery times for both motor and verbal functions
- While language and memory findings were similar between the two groups in this study, additional research is necessary to clarify the effect of reduced anesthesia on interpretation of language and memory performance during the IAP

References:

### Table 1

**Patient Demographics (N=35)**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>TPM/ZNS</th>
<th>Other AEDs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient, n</strong></td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (range)</td>
<td>12.53 (6-17)</td>
<td>12.15 (6-17)</td>
</tr>
<tr>
<td><strong>Sex, N (male)</strong></td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (range)</td>
<td>54.3</td>
<td>52.0</td>
</tr>
<tr>
<td><strong>IQ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (range)</td>
<td>82.40 (42-121)</td>
<td>87.85 (74-126)</td>
</tr>
<tr>
<td><strong>Number of AEDs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (range)</td>
<td>2.53 (1-4)</td>
<td>2.05 (1-4)</td>
</tr>
</tbody>
</table>

### Table 2

**TPM/ZNS Effects on Anesthesia**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>TPM/ZNS</th>
<th>Other AEDs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean total sodium amobarbital dose administered, mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left injection (p&lt;0.05)</td>
<td>123.21*</td>
<td>93.75</td>
</tr>
<tr>
<td>Right injection(p&lt;0.05)</td>
<td>128.46†</td>
<td>93.06‡</td>
</tr>
<tr>
<td><strong>Mean time to first coherent Verbalization, sec.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left injection</td>
<td>86.29*</td>
<td>142.40</td>
</tr>
<tr>
<td>Right injection</td>
<td>74.38†</td>
<td>49.39‡</td>
</tr>
<tr>
<td><strong>Mean time to first return of motor function, sec.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left injection (p=0.07)</td>
<td>89.21*</td>
<td>142.15</td>
</tr>
<tr>
<td>Right injection</td>
<td>118.62†</td>
<td>124.61‡</td>
</tr>
</tbody>
</table>

*One patient belonging to the TPM/ZNS group did not receive injection in the left hemisphere.  
†Two Patients belonging to the TPM/ZNS group did not receive injection in the right hemisphere.  
‡Two patients belonging to the other AEDs group did not receive injection in the right hemisphere.
Figure 1

Language Lateralization by AED Group

- TPM/ZNS
- Other AEDs

Brain Hemisphere:
- Left
- Right
- Bilateral
- Could not be determined

Figure 2

Memory Performance by AED Group

- TPM/ZNS
- Other AEDs

Hemisphere Injected:
- Left
- Right