Anesthesia during petrosal sinus sampling and possible interference with corticotropin (ACTH) levels

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Clinical Case Pituitary

Eunice Kennedy Shriver National Institute of Child Health and Human Development

Introduction

General anesthesia and surgical intervention in humans are known to affect the function of the hypothalamic pituitary adrenal axis (HPA)¹. In the literature there are conflicting reports about the effect of propofol, a commonly used intravenous anesthetic agent, on HPA function. While some studies demonstrate ACTH suppression²,³ with propofol, others report direct effect on the adrenal steroid production⁴ or decreased functionality of ACTH receptor⁵ with propofol use. Also, a few reports report normal or increased ACTH levels with propofol⁶⁻⁹.

Evaluation of Cushing's Syndrome

We report two males (11 & 12yr) with ACTH-dependent Cushing syndrome (CS) who underwent inferior petrosal sinus sampling (IPSS) with general anesthesia. ACTH was measured from bilateral petrosal and peripheral sites at baseline and after administration of corticotropin releasing hormone (CRH). Anesthetic agents used included: propofol infusion (patient A: 7.8mg/kg; patient B: 29mg/kg), fentanyl, and midazolam. ACTH results from IPSS were atypical for both patients (i.e. no stimulation of ACTH (peripherally) and overall low values of ACTH). Since the ACTH results precluded scheduling of transsphenoidal surgery, the IPSS procedures were repeated. Results of the 2nd IPSS showed appropriate stimulation of peripheral and central ACTH levels and peripheral to central ratios consistent with Cushing disease (CD) in both patients. Anesthetic agents used included single dose propofol at induction (approximately 50 minutes prior to sampling) (patient A: 1.8mg/kg; patient B: 1.4mg/kg), fentanyl, and midazolam. Subsequently, both patients underwent TSS for removal of corticotopina which was confirmed at histology; they remain in remission of hypercortisolemia to date.

Case Report

The study was approved by the institutional review board of the National Institute of Health. Consent was obtained from all patients prior to participation. Clinical data were collected retrospectively from patient medical records and were summarized in tables and figures.

Discussion and Conclusion

Historically, propofol has been shown to have direct antisteroiogenic effects on adrenal cells and to be a weak inhibitor of adrenal steroidogenesis. Though less described, propofol has been shown to suppress ACTH by various mechanisms. It causes possible suppression of noxious stimuli that decrease CRH secretion, and thus promoting GABA mediated CRH release. It has also been linked to propofol mediated suppression of catecholamine release, decreases CRH.

Also propofol causes inhibition of the ERK ½ phosphorylation and thus IL-1β up regulation by lipopolysaccharide in glial cells and BV-2 microglial cell lines, thus decreasing ACTH release. These 2 cases presented provide a novel insight about a possible short-term inhibition of ACTH secretion by propofol in vivo and highlight the importance of future research. A better understanding of the interaction of propofol with ACTH may be of vital importance in the intra- and post-operative care of patients as well as in diagnostic endocrine testing that involves anesthesia.

References


IPSS ACTH central-to-peripheral Ratio

<table>
<thead>
<tr>
<th>Patient</th>
<th>With Propofol Continuous Infusion</th>
<th>With Propofol Bolus Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>(22 - diagnostic)</td>
<td>STIMULATED (23 - diagnostic)</td>
</tr>
<tr>
<td>Patient A</td>
<td>1.7</td>
<td>56</td>
</tr>
<tr>
<td>Patient B</td>
<td>3.2</td>
<td>52</td>
</tr>
</tbody>
</table>

CRH stimulation test

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Patient A</th>
<th>Patient B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral/Basal Cortisol (mg/L)</td>
<td>25.6</td>
<td>44.7</td>
</tr>
<tr>
<td>Periphera/Basal ACTH (pg/mL)</td>
<td>31.4</td>
<td>48.3</td>
</tr>
<tr>
<td>Post-CRH cortisol</td>
<td>52.6</td>
<td>18.8</td>
</tr>
<tr>
<td>Post-CRH ACTH</td>
<td>75</td>
<td>34</td>
</tr>
<tr>
<td>Δ cortisol (%&lt;20% consistent with CD)</td>
<td>105</td>
<td>0</td>
</tr>
<tr>
<td>Δ ACTH (%&lt;35% consistent with CD)</td>
<td>136</td>
<td>0</td>
</tr>
</tbody>
</table>

8mg dexamethasone test (Cortisol suppression >25% in CD)

| Δ Cortisol suppression % | 26.2 | 95.5 |

IPSS ACTH levels at IPSS (levels in pg/mL) and are adjusted to 100 pg/mL

Clinical Cases: Pituitary/Adrenal

Poster presented at:

ECE 2015

Clinical Cases: Pituitary/Adrenal

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