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

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Clinical Case
Pituitary

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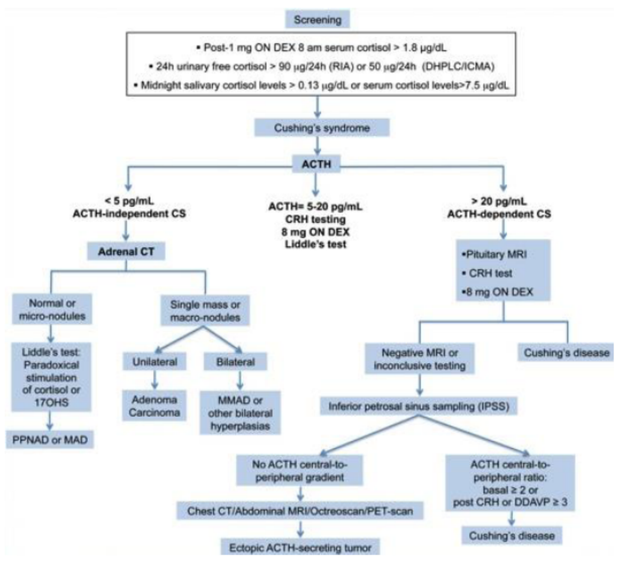
Introduction

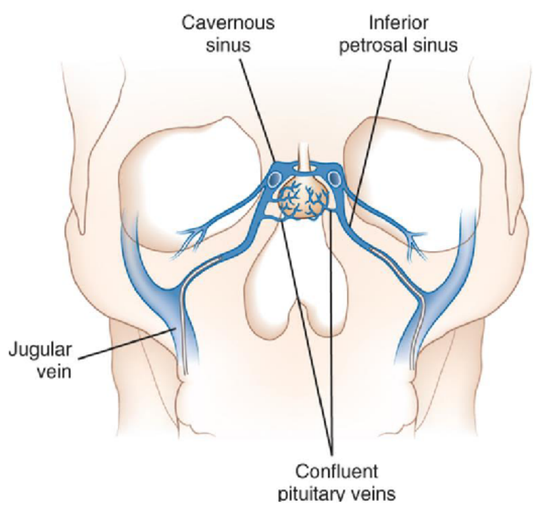
General anesthesia and surgical intervention in humans are known to affect the function of the hypothalamic pituitary adrenal axis (HPA)[1]. In the literature there are conflicting reports about the effect of propofol, a commonly used intravenous anesthetic agent, on HPA function.

While some studies demonstrate ACTH suppression[2,3] with profopol, some others report direct effect on the adrenal steroid production[4] or decreased functionality of ACTH receptor[5] with propofol use. Also, a few reports report normal or increased ACTH levels with propofol[6-9].

Evaluation of Cushing's Syndrome



Diagnostic Algorithm for Cushing's Syndrome



Procedure for IPSS

Case Report

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 corticotrophin 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.

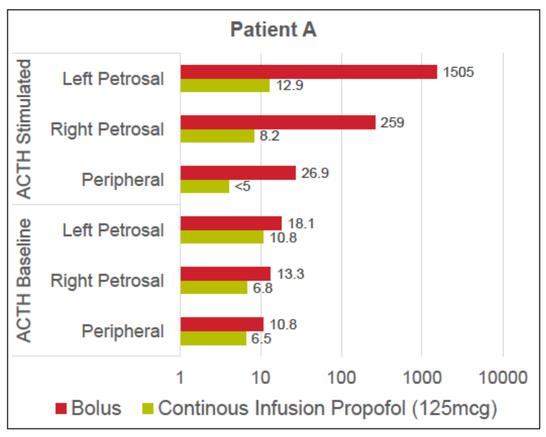
Subsequently, both patients underwent TSS for removal of corticotropinoma which was confirmed at histology; they remain in remission of hypercortisolemia to date.

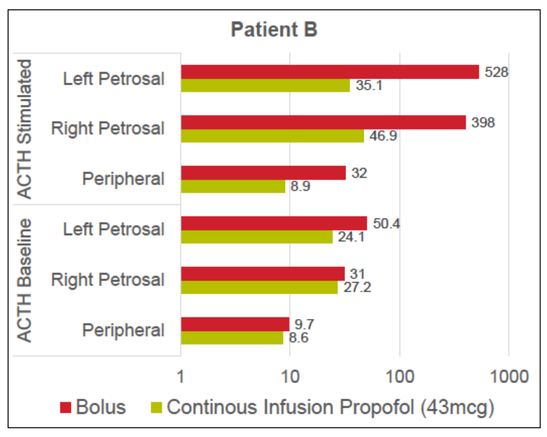
IPSS ACTH central-to-peripheral Ratio

	With Propofol Continous Infusion		With Propofol Bolus Infusion	
	Basal (≥2 - diagnostic)	Stimulated (≥3 - diagnostic)	Basal (≥2 - diagnostic)	Stimulated (≥3 - diagnostic)
Patient A	1.7	3.2	1.7	56
Patient B	3.2	5.3	5.2	16.5

ACTH Levels after IPSS

All levels are in pg/mL and are adjusted to axis of $\log_{10}$





Patient Characteristics

	A	B
Sex	M	M
Age	11yr	12yr
Weight (kg)	43.4	55
Height (cm)	135	148
Body Mass Index (BMI) kg/m^2	23.8	25.3
BSA (m^2)	1.25	1.48
Midnight Cortisol (mcg/dL) (>4.4 consistent with CS)	14.2	23.9
Morning ACTH (pg/mL) (>29 consistent with CD)	11.3	49.2
24hr urine free cortisol (mcg/24hr)	196.9	646
24hr urine 17OHS (mg/gram creatinine/24hr)	8.7	30
CRH stimulation test		
Peripheral / Baseline Cortisol (mcg/dL)	25.6	44.7
Peripheral / Baseline ACTH (pg/mL)	31.8	43
Post-CRH cortisol	52.6	18.8
Post-CRH ACTH	75	34
Δ cortisol % (>20% consistent with CD)	105	0
Δ ACTH % (>35% consistent with CD)	136	0
8mg dexamethasone test (Cortisol suppression >20% in CD)		
% Cortisol suppression	26.2 (DEX level was low)	95.5

Discussion and Conclusion

Historically, propofol has been shown to have direct antisteroidogenic effects on adrenal cells and to be a weak inhibitor of adrenal steroidogenesis[10]. Though less described, propofol has been shown to suppress ACTH by various mechanisms. It causes possible suppression of noxious stimuli that cause decrease CRH secretion, and thus promoting GABA mediated CRH[2].

It has also been linked to propofol mediated suppression of catecholamine release, decreases CRH[11].

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[12].

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.

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