

# Postoperative Diabetes Insipidus and Hyponatremia in Children after Transsphenoidal Surgery for Adrenocorticotropin Hormone and Growth Hormone Secreting Adenomas

Carolina Saldarriaga, MD<sup>1</sup>, Charlampos Lyssikatos, MD<sup>1</sup>, Elena Belyavskaya, MD<sup>1</sup>, Margaret Keil, PhD, CRNP<sup>1</sup>, Prashant Chittiboina, MD<sup>2</sup>, Ninet Sinaii, PhD, MPH<sup>3</sup>, Constantine A. Stratakis, MD, DMSci<sup>1</sup>, and Maya Lodish, MD, MHSc<sup>1</sup>

**Objectives** To define the incidence and risk factors of postoperative sodium alterations in pediatric patients undergoing transsphenoidal surgery (TSS) for adrenocorticotrophic hormone and growth hormone secreting pituitary adenomas.

**Study design** We retrospectively reviewed 160 patients  $\leq 18$  years of age who had TSS for pituitary adenomas at our institution from 1999 to 2017. Variables included daily serum sodium through postoperative day 10, urine specific gravity, and medications administered. We examined associations between sex, repeat surgery, manipulation of the posterior pituitary (PP), tumor invasion into the PP, tumor type and size, cerebrospinal fluid (CSF) leak, lumbar drain insertion, body mass index, puberty, and development of diabetes insipidus (DI) or syndrome of inappropriate antidiuretic hormone secretion (SIADH).

**Results** Mean age was  $12.9 \pm 3.4$  years (female = 81). Patients had adrenocorticotrophic hormone (150/160) and growth hormone (10/160) producing adenomas. Forty-two (26%) patients developed DI. Among the 37 of 160 who required desmopressin acutely, 13 of 37 required it long term. Risk of long-term need for desmopressin was significantly higher in patients who had CSF leak 9 of 48 ( $P = .003$ ), lumbar drain 6 of 30 ( $P = .019$ ), manipulation 11 of 50 ( $P < .001$ ), or invasion 4 of 15 ( $P = .022$ ) of the PP. Sixty patients developed hyponatremia, 19 because of SIADH, 39 to hypotonic fluids and 2 to cerebral salt wasting syndrome. Patients with SIADH were placed on fluid restriction; 1 received salt tablets.

**Conclusions** Among 160 children who underwent TSS for pituitary adenomas, the incidence of DI and SIADH after TSS was 26% and 14%, respectively. Combined risk factors for DI and/or SIADH include female sex, manipulation of and/or tumor invasion into the PP, and CSF leak or lumbar drain. (*J Pediatr* 2017;■■:■■-■■).

**Trial registration** ClinicalTrials.gov: NCT00001595 and NCT00060541.

Sodium alterations are common after transsphenoidal surgery (TSS) of the pituitary gland. Diabetes insipidus (DI), presenting as polyuria and hyperosmotic state, occurs early after pituitary surgery. The incidence of postoperative DI in adults is variable, ranging from 10% to 20% in tumors localized to the sella and even higher in larger tumors that extend to the hypothalamus.<sup>1</sup> Hyponatremia has also been reported after TSS and usually occurs 4-7 days postoperative, is transient, and has been associated with postoperative morbidity. The incidence of hyponatremia ranges from 16% to 40% in adults<sup>2-5</sup> and may be due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) that develops from the uncontrolled release of antidiuretic hormone (ADH) by degenerating pituitary nerve terminals containing neurosecretory granules.<sup>6,7</sup>

The predictors and incidence of sodium alterations following TSS have been addressed in various studies in adults, however, limited data exist in children. Previous studies have found variable risk factors for the development of DI or SIADH, including smaller tumor size, extensive surgical manipulation of the posterior pituitary (PP), adrenocorticotropin hormone (ACTH) producing adenoma, presence of cerebrospinal fluid (CSF) leak, low body mass index (BMI), or high estrogen levels.<sup>3,4,6-9</sup> However, results have been inconsistent and

ACTH	Adrenocorticotropin hormone
ADH	Antidiuretic hormone
BMI	Body mass index
CSF	Cerebrospinal fluid
CSW	Cerebral salt wasting syndrome
DI	Diabetes insipidus
GH	Growth hormone
NIH	National Institutes of Health
PP	Posterior pituitary
RR	Relative risk
SIADH	Syndrome of Inappropriate Antidiuretic Hormone Secretion
TSS	Transsphenoidal surgery

From the <sup>1</sup>Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institutes of Health; <sup>2</sup>National Institute of Neurological Disorders and Stroke; and <sup>3</sup>Biostatistics and Clinical Epidemiology Service (BCES), National Institutes of Health, Bethesda, MD

Funded by the intramural programs of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (Z01 HD008920), and the National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland. The authors declare no conflicts of interest.

Portions of this study were presented at the 10th Annual Meeting of the Pediatric Endocrine Society, September 14-17, 2017, Washington, D.C.

0022-3476/\$ - see front matter. Published by Elsevier Inc.  
<https://doi.org/10.1016/j.jpeds.2017.11.042>

have not been studied in a large cohort children. Thus, the goal of this study was to determine the incidence and risk factors for sodium alterations in children during the first 10 days following TSS. We analyzed ACTH and growth hormone (GH)-producing adenomas, as they are the most common functional adenomas in children where surgery is the first-line treatment.<sup>10</sup> The data provides guidance for patients who may be at risk and need increased surveillance.

## Methods

To assess risk factors associated with the development of sodium alterations, we retrospectively reviewed clinical notes, surgical and pathology reports, medications, and laboratory results of 161 children (ages 3–18 years) who underwent sublabial open TSS at the National Institutes of Health (NIH) Clinical Center from 1999 to 2017.

All patients underwent surgery (161 total, 81 female), 1 patient was excluded because of previous permanent DI; 150 patients had ACTH-producing and 10 had GH-producing adenomas. All parents gave written informed consent, and children gave assent to participate in the clinical trial protocol (NIH 97-CH-0076; [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00001595): NCT00001595) that was approved by the Institutional Review Board. Patients undergoing TSS were enrolled in a separate clinical trial (NIH 03-N-0164; [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00060541): NCT00060541) approved by the Combined Neurosciences Institutional Review Board of the NIH. Patients were admitted before surgery, and baseline measurements included sodium, osmolality, and kidney function tests. All patients had normal renal function before surgery.

Following TSS, sodium values, fluid intake, and urinary output were measured daily for 10 days. Urine specific gravity as well as serum and urine osmolality were ordered if sodium values were <135 or >145, or if there was evidence of polyuria (>4 cc/kg/hour or >300 cc/hour in patients weighing >75 kg).

Among patients with Cushing disease, empiric glucocorticoid replacement was withheld during the first 5 days to evidence disease remission. However, if the patient developed symptoms of steroid insufficiency, dexamethasone was administered per os at a dose of 0.5 mg/day (adjusted for weight for patients <50 kg). A maintenance dose of hydrocortisone at 12–15 mg/m<sup>2</sup>/day was prescribed for discharge in patients who had biochemical remission. In addition, during the first 12 years of the study (1999–2011), 0.5 mg of IV dexamethasone were given every 6 hours starting on the day of surgery and ending at 11 PM on postoperative day 1 as part of a neurosurgical clinical study that investigated the usefulness of this practice in reducing perioperative inflammation.

DI was defined as polyuria and urine specific gravity <1.003 (or rapidly decreasing in the context of rising serum osmolality). The use of desmopressin was recorded in the medication administration records. We defined “long-term need for desmopressin” as need for desmopressin after discharge.

Hyponatremia was defined as sodium <135 mmol/L. Patients were considered to have SIADH if they had euvoletic hyponatremia (with increased urine osmolality), unex-

plained by the administration of hypotonic fluids. Treatment for SIADH included fluid restriction to <1 L/day when sodium levels ranged between 130 and 135 mmol/L and 600–800 cc/day when sodium levels were <130 mmol/L; salt tablets were considered in patients nonresponsive to fluid restriction. Cerebral salt wasting was diagnosed in patients who developed hyponatremia, per protocol were fluid restricted and despite fluid restriction continued to have polyuria, high urine osmolality, worsening hyponatremia, and hypovolemia. They were treated with normal saline boluses to replete their volume loss and subsequently their sodium levels normalized without need for further interventions.

Surgical and pathology reports were reviewed to determine the size of the tumor, manipulation or invasion of the PP, and presence of CSF leak and/or spinal drain. Tumors <1 cm were classified as microadenomas, and ≥1 cm as macroadenomas. We defined manipulation of the PP present when incision or removal of PP for biopsy was reported during the surgical procedure. Pathology and intraoperative reports were reviewed to determine tumor invasion of the PP. We classified patients as having “repeat surgery” if they underwent more than one TSS (ie, second or third).

Sodium values were measured by ion-selective determination of analytes in mmol/L (Roche, Basel, Switzerland). Serum cortisol was collected at midnight and 8 AM, and measured in solid-phase using competitive chemiluminescence enzyme immunoassay (2005–2017 Siemens, Munich; <2005 Nichols Advantage, San Juan Capistrano, California). ACTH was measured by chemiluminescence immunoassay (Siemens, Munich, Germany).

## Statistical Analyses

Data are reported as frequencies and percentages, or as mean ± SD and median (IQR), as appropriate. Associations between risk factors and disease outcomes of DI, SIADH, or either DI and/or SIADH were assessed using  $\chi^2$  or Fisher exact tests, as appropriate, or Cochran-Armitage Trend test for ordered categorical variables. T tests or Wilcoxon rank-sum tests compared continuous data between disease groups. Relative risks were computed for all risk factors, and ORs were computed for continuous variables using logistic regression models. A *P* value of less than .05 or a 95% CI excluding 1.0 were considered statistically significant. Data were analyzed using SAS v 9.4 (SAS Institute Inc, Cary, North Carolina).

## Results

A total of 161 patients underwent TSS. One patient was excluded due to DI after a previous pituitary surgery. Demographics are summarized in [Table 1](#). Mean age at the time of surgery was 12.9 ± 3.4 years. Of the 81 female patients and 79 male patients, 94% (n = 150) had ACTH, whereas 6% (n = 10) had GH-producing adenoma. A total of 127 patients underwent first TSS, 31 patients had a second TSS, and 2 required a third TSS for residual/recurrent tumor. Median time to the subsequent surgery was 0.9 months (IQR: 15 days–1 year; range: 6 days–9 years). Mean BMI z score was 2.01 ± 0.75.

Download English Version:

<https://daneshyari.com/en/article/8812405>

Download Persian Version:

<https://daneshyari.com/article/8812405>

[Daneshyari.com](https://daneshyari.com)