Delayed symptomatic hyponatremia case series

Patel et al., retrospectively reviewed a series of over 300 consecutive patients undergoing endoscopic transsphenoidal surgery and identified patients with delayed symptomatic hyponatremia as well as patient, tumor, and surgical characteristics. In addition, they recorded inpatient post-operative sodium and specific gravity values as well as treatment upond discharge. Univariate and multivariate analyses were carried out to identify predictors of delayed hyponatremia and stratify patients into risk groups.

They found that 15% of patients developed delayed hyponatremia and that this occurred most commonly on post-operative day 7. This accounted for more than half of re-admissions after this type of surgery. Female patients and patients needing fluid restriction or fludrocortisone upon discharge were more likely to develop delayed hyponatremia. Patients with post-operative diabetes insipidus were less likely to develop delayed hyponatremia. Using ROC analysis they developed a score which reliably could stratify patients at risk for delayed hyponatremia.

They confirm the risk of delayed hyponatremia after transphenoidal surgery and identify factors that are revealed before discharge to identify patients at higher risk of delayed hyponatremia. These data may help identify patients who require treatment upon discharge and short interval follow up to avoid significant costs of re-admission ¹⁾.

2017

Data from before and after delayed hyponatremia (DH) care pathway implementation were retrospectively reviewed. Patient demographics and clinical characteristics were compared. Readmission causes, clinical pathway failures, sodium trends, and symptoms were evaluated.

Before the DH care pathway implementation, 229 (55%) patients were treated (group 1); afterward, 188 (45%) were treated (group 2). Baseline characteristics were equivalent between groups, except for glucocorticoid supplementation, which was higher in group 2. The incidence of detected DH was significantly lower in group 1 (16/229, 7%) than group 2 (29/188, 15%) (P = .006) likely due to the impact of routine screening in group 2. Ten group 1 patients (4%) were readmitted for hyponatremia and 6 (3%) were managed as outpatients. Eleven group 2 patients (6%) were readmitted and 17 (9%) were managed as outpatients. Readmission rates between groups were similar (P = .49). Patients readmitted with severe hyponatremia experienced symptoms \geq 24 h before presentation. The protocol failed to prevent readmission because outpatient management for mild or moderate DH (n = 4) failed, sodium levels precipitously declined after normal screening (n = 3), and severe hyponatremia developed after scheduled screenings were missed (n = 3).

Although more DH patients were identified after care pathway implementation, readmission rates were not reduced and clinical outcomes were not changed. Because DH onset timing varies, some patients have highly acute presentation, and most readmitted patients develop symptoms before reaching their sodium nadir, close symptom monitoring may be a reasonable alternative to routine screening².

Of 303 patients who had transsphenoidal surgery, 27 (8.9%) were readmitted within 30 days. Most of the 27 (15 [55.6%]) had delayed hyponatremia. Other causes were diabetes insipidus (4 [14.8%]), adrenal insufficiency (2 [7.4%]), and cerebrospinal fluid leak, epistaxis, cardiac arrhythmia, pneumonia, urinary tract infection, and hypoglycemia (1 each [3.7%]). Outpatient sodium screening was performed as needed. In cases of hyponatremia, the mean postoperative day of readmission was day 8 (range, 6-12 days) and the mean serum sodium was 119 mmol/L (range, 111-129 mmol/L). Numerous patient and surgical factors were examined, and no specific predictors of readmission were identified. We developed an outpatient care pathway for managing hyponatremia with the goal of improving readmission rates.

This study establishes a quality benchmark for readmission rates after transsphenoidal surgery for pituitary lesions and identifies delayed hyponatremia as the primary cause. Implementation of an outpatient care pathway for managing hyponatremia may improve readmission rates ³.

2013

A retrospective analysis of a single-institution prospective database was conducted; all patients undergoing TSS for lesions involving the pituitary gland were followed up in a multidisciplinary neuroendocrine clinic, and demographic, imaging, and clinical data were prospectively collected. Patients were examined preoperatively and followed up postoperatively in a standardized fashion, and their postoperative sodium levels were measured at Weeks 1 and 2 postoperatively. Levels of hyponatremia were rated as mild (serum sodium concentration 130-134 mEq/L), moderate (125-129 mEq/L), or severe (< 125 mEq/L). Routine clinical questionnaires were administered at all postoperative office visits. Postoperative hyponatremia was analyzed for correlations with demographic and clinical features and with immediate postoperative physiological characteristics. RESULTS: Over a 4-year interval, 373 procedures were performed in 339 patients who underwent TSS for sellar and parasellar lesions involving the pituitary gland. The mean $(\pm SD)$ age of patients was 48 \pm 18 years; 61.3% of the patients were female and 46.1% were obese (defined as a body mass index $[BMI] \ge 30$). The overall prevalence of DPH within the first 30 days postoperatively was 15.0%; 7.2% of the patients had mild, 3.8% moderate, and 3.8% severe hyponatremia. The incidence of symptomatic hyponatremia requiring hospitalization was 6.4%. The Fisher exact test detected a statistically significant association of DPH with female sex (p = 0.027) and a low BMI (p = 0.001). Spearman rank correlation detected a statistically significant association between BMI and nadir serum sodium concentration (r = 0.158, p = 0.002) and an inverse association for age (r = -0.113, p = 0.031). Multivariate analyses revealed a positive correlation between postoperative hyponatremia and a low BMI and a trend toward association with age; there were no associations between other preoperative demographic or perioperative risk factors, including immediate postoperative alterations in serum sodium concentration. Patients were treated with standardized protocols for hyponatremia, and DPH was not associated with permanent morbidity or mortality. CONCLUSIONS: Delayed postoperative hyponatremia was a common result of TSS; a low BMI was the only clear predictor of which patients will develop DPH. Alterations in immediate postoperative sodium levels did not predict DPH. Therefore, an appropriate index of suspicion and close postoperative monitoring of serum sodium concentration should be maintained for these patients, and an appropriate treatment should be undertaken when hyponatremia is identified ⁴⁾.

2011

Kinoshita et al. evaluated (i) the incidence of post-operative hyponatremia (serum Na levels \leq 135 mEq/L) and the emergence of hyponatremic symptoms, and assessed (ii) the risk factors under a uniform protocol of i.v. infusion with steroid and electrolyte fluid. We examined 88 consecutive operated patients (female: 60; male: 28) with pituitary neuroendocrine tumor. Apart from reconfirming the effects of the purported risk factors, we focused on the degree of serum Na decline on post-operative hyponatremia. Although remained stable during early post-operative period (4 days after surgery), the serum Na levels subsequently decreased after post-operative day 4 in 81 of 88 cases (92.0%). Of 88 patients, 27 (30.7%) and 9 (10.2%) cases suffered from hyponatremia, and developed hyponatremic symptoms. Interestingly, the degree of serum Na levels decline (from preoperative levels) indicated a useful independent risk factor for monitoring hyponatremic symptoms (p = 0.006) and the degree of decline tended to be greater in elder patients (> 60 years) (p = 0.0346). Serum Na levels should be monitored from, at least, post-operative day 7 to detect early development of hyponatremia. Special attention and recovery effort should be given to elder patients with marked serum Na level decline after surgery ⁵.

2008

The incidence and risk factors of symptomatic and asymptomatic hyponatremia were investigated in 94 patients who underwent transsphenoidal surgery and serum sodium level monitoring between January 2002 and December 2006. The records were retrospectively reviewed to determine the incidence and risk factors (age and sex, tumor size, endocrinologic findings) of hyponatremia. Postoperatively, the serum sodium levels of the patients were measured at least once within 2 or 3 days. Hyponatremia was found in 17 of the 94 patients, of whom 7 became symptomatic. The mean sodium level of symptomatic patients with hyponatremia at diagnosis was 123.5 mEg/l, compared with 129.8 mEq/l of asymptomatic patients. The serum sodium levels began to fall on mean postoperative day 7 and reached nadir on mean day 8. All 17 patients with hyponatremia were treated with mild fluid restriction. Four symptomatic patients with severe hyponatremia were treated with 3% hypertonic saline infusion in addition to fluid restriction. One symptomatic patient with severe hyponatremia was treated with fluid restriction only. All patients recovered within 5 days of management. Sex, tumor type, and tumor size did not correlate with development of delayed hyponatremia, but patients aged >/=50 years were more likely to develop hyponatremia. Postoperative hyponatremia after transsphenoidal surgery is more common than previously reported and may lead to fatal complications. Therefore, all patients should undergo serum electrolyte level monitoring regularly for at least 1 or 2 weeks after transsphenoidal surgery ^{b)}.

2007

Patients who underwent transsphenoidal surgery at the University of Southern California University Hospital between 1997 and 2004 had serum sodium levels drawn on an outpatient basis on postoperative Day 7. Patient records were retrospectively reviewed to determine the incidence of, and risk factors for, symptomatic and asymptomatic hyponatremia. Two hundred forty-one patients had routine serum sodium levels drawn as outpatients on postoperative Day 7. Twenty-three percent of these patients were found to be hyponatremic (Na < or =135 mEq/L). The overall incidence rate of symptomatic hyponatremia in the 241 patients was 5%. The majority of hyponatremic patients (80%) remained asymptomatic, whereas 20% became symptomatic. In patients with symptomatic hyponatremia, the mean sodium level at diagnosis was 120.5 mEq/L, compared with 128.4 mEq/L in asymptomatic, hyponatremic patients (p < 0.0001). Female patients were more likely to develop hyponatremia than male patients (33% compared with 22%, p < 0.03). Fifty-two percent of patients who had transient diabetes insipidus (DI) early in their postoperative course subsequently developed hyponatremia, compared with 21% of those who did not have DI (p < 0.001). Patient age, tumor type, and tumor size did not correlate with development of delayed hyponatremia. Outpatients with moderately and severely low sodium levels were 5 and 12.5 times more likely, respectively, to be symptomatic than were patients with mild hyponatremia.

Delayed hyponatremia occurs more frequently than was previously suspected in patients who have undergone transsphenoidal surgery, especially in female patients and those who have previously had transient DI. The majority of hyponatremic patients remain asymptomatic. Obtaining a serum sodium value on an outpatient basis 1 week after pituitary surgery is helpful in recognition, risk stratification, and subsequent intervention, and may prevent potentially serious complications ⁷⁾.

1999

1571 patients with pituitary neuroendocrine tumors (238 Cushing's disease, 405 acromegaly, 534 hormonally inactive adenomas, 358 prolactinoma, 23 Nelson's syndrome, and 13 thyrotropinoma) were daily examined within a 10-day postoperative inpatient observation period. Prevalence of patterns of polyuria (> 2500 ml) and oliguria/hyponatraemia (< 132 mmol/l) were surveyed as well as predictors of postoperative morbidity. RESULTS: 487 patients (31%) developed immediate postoperative hypotonic polyuria, 161 patients (10%) showed prolonged polyuria and 37 patients (2.4%) delayed hyponatraemia. A biphasic (polyuria-hyponatraemia) and triphasic (polyuria-hyponatraemia-polyuria) pattern was seen in 53 (3.4%) and 18 (1.1%) patients, respectively. Forty-one patients (2.6%) displayed immediate postoperative (day 1) hyponatraemia. Altogether, 8.4% of patients developed hyponatraemia at some time up to the 10th day postoperative, with symptomatic hyponatraemia in 32 patients (2.1%). Risk analysis showed that patients with Cushing's disease had a fourfold higher risk of polyuria than patients with acromegaly and a 2.8-fold higher risk for postoperative hypotonic polyuria, but this was not considered clinically relevant.

The analysis illustrates that disturbances in osmoregulation resulting in polyuria and pertubations of serum sodium concentration are of very high prevalence and need observation even after selective transsphenoidal surgery for pituitary neuroendocrine tumors, especially in patients with Cushing's disease⁸⁾.

1995

To clarify the frequency, presentation, and outcome of this poorly understood complication, Taylor et al. reviewed the database of 2297 patients who underwent transsphenoidal pituitary surgery between February 1971 and June 1993. Of 53 patients (2.3%) treated for symptomatic hyponatremia, 11 were excluded (2 received arginine vasopressin within 24 hours, 1 had untreated hypothyroidism, 4 had untreated adrenal insufficiency, and 4 had incomplete records). The remaining 42 patients (1.8%), 11 men and 31 women aged 21 to 79 years, presented 4 to 13 days (mean, 8 d) postoperatively with nausea and vomiting (20 patients), headache (18 patients), malaise (12 patients), dizziness (4 patients), anorexia (2 patients), and seizures (1 patient). Hyponatremia was unrelated to sex, age,

adenoma type, tumor size, or glucocorticoid tapering. Although the clinical picture in our patients is consistent with SIADH, this was not supported by the antidiuretic hormone levels, which were normal or low-normal in the two patients in whom they were measured, suggesting the possibility that low serum sodium may not reflect SIADH. In all patients, hyponatremia resolved within 6 days (mean, 2 d); treatment consisted of salt replacement and mild fluid restriction in 37 patients and fluid restriction only in 4 (treatment unknown in 1). Delayed hyponatremia after transsphenoidal resection of pituitary neuroendocrine tumor is not as rare as previously thought, nor is it necessarily associated with SIADH or with hypoadrenalism during glucocorticoid tapering ⁹.

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