Neurosurgical Forum

LETTERS TO THE EDITOR

Postoperative hyponatremia

TO THE EDITOR: We read with great interest the article by Williams et al.¹ on postoperative hyponatremia (Williams CN, Riva-Cambrin J, Bratton SL: Etiology of postoperative hyponatremia following pediatric intracranial tumor surgery. *J Neurosurg Pediatr* 17:303–309, March 2016).

We congratulate the authors, as they present the largest cohort to date of pediatric patients with hyponatremia after surgical treatment of brain tumors.

We agree with the authors that the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting (CSW) have been reported among patients with pediatric intracranial tumors and other lesions. However, these studies have not completely evaluated the patient characteristics associated with SIADH versus CSW in children following neurosurgery.

This is an issue of great interest because hyponatremia is known to develop—sometimes surprisingly—in children after neurosurgical procedures of relatively low complexity, such as shunt placement or endoscopic ventriculostomy. Moreover, the development of postoperative hyponatremia is not limited to specific tumor locations or histological types. We would like to suggest that the number of patients affected might be higher than suspected. The authors report a rate of 12%, but in our opinion, this complication can be more frequent.

The authors assessed, as potential causes of hyponatremia, intravenous fluid type and amount, medications, dilutional hyponatremia, hyperosmolar hyponatremia, hypovolemic hyponatremia from vomiting or diarrhea, adrenal insufficiency, hypothyroidism, CSW, and SIADH. Tumor locations, presence of metastases, histological findings, hydrocephalus, and existence of stroke were reviewed. Infectious complications, such as pneumonia, bacteremia, meningitis, and urinary tract infections, were also included for analysis.

However, the authors were not able to identify differ-

ences with respect to tumor locations and histology. They argue that perhaps the low number of patients may be the cause for the lack of statistically significant results. When reviewing our own series, the conclusions are similar.

Currently, our group is working on a different approach to the problem of hyponatremia in the pediatric neurosurgical patient. We think that this approach can complement the investigation of the causes of development and type of hyponatremia described by the authors in their paper.

Specifically, we are evaluating at this time whether mechanical or anatomical displacement of the hypothalamus may be, together with the above-described potential causes, considered as a major cause in the development of hyponatremia in these patients, as well as a factor affecting its type and duration.

Large supratentorial lesions displacing the hypothalamus and tumors of the third ventricle and hydrocephalus with extreme dilation of the third ventricle are more common in children. In fact, these lesions tend to be seen in very young children. Moreover, posterior fossa lesions and tumors remote from the hypothalamus are frequently accompanied by enlargement of ventricles, including the third ventricle.

We hypothesized that the mechanical displacement of the hypothalamus—rather than lesion histology or location—would be a cause to consider. In young children these displacements may be substantial, even by centimeters. The severity and type of hyponatremia may also be related to the anatomical recovery.

We are now reviewing our own cases with a view to this hypothesis, and as shown in Fig. 1, the correlation with hyponatremia is very clear. To date, we have identified diverse patterns of response to displacement recovery that are summarized in the figure. In essence, severe hypothalamic displacement implies severe and prolonged changes in electrolyte balance. The correction is very complex, and hyponatremia can alternate with hypernatremia. When displacement is not severe, as in the treatment of lesions of the third ventricle, the sodium anomalies are typically not severe or long-lasting.

FIG. 1. Examples of changes in plasma sodium level (mEq/L) and their relation with hypothalamic displacement. Preoperative and postoperative Gd-enhanced T1-weighted MR images obtained at the hypothalamic level in 6 different patients are shown along with graphs of changes in the patients' plasma sodium levels. **A and B:** Postoperative (*left*) and preoperative (*right*) coronal MR images showing severe displacement in a patient with a low-grade third-ventricle glioma (A) and a patient with a third-ventricle craniopharyngioma (B). **C:** Postoperative (*left*) and preoperative (*right*) coronal MR images showing moderate displacement in a patient with severe hydrocephalus due to shunt malfunction after craniopharyngioma surgery. **D:** Postoperative (*left*) and preoperative coronal (*center*) and sagittal (*right*) MR images showing mild displacement in a patient with a posterior third-ventricle lesion (atypical teratoid rhabdoid tumor). **E:** Postoperative (*left*) and preoperative coronal (*center*) and sagittal (*right*) MR images showing minimal displacement in a patient with a posterior fossa medulloblastoma. Figure is available in color online only.

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References

1. Williams CN, Riva-Cambrin J, Bratton SL: Etiology of postoperative hyponatremia following pediatric intracranial tumor surgery. *J Neurosurg Pediatr* 17:303–309, 2016

Disclosures

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Response

No response was received from the authors of the original article.

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Early seizure prophylaxis in pediatric severe traumatic brain injury: still a long way to go

TO THE EDITOR: It was with great interest that I read the article by Ostahowski et al.⁵ (Ostahowski PJ, Kannan N, Wainwright MS, et al: Variation in seizure prophylaxis in severe pediatric traumatic brain injury. *J Neurosurg Pediatr* 18:499–506, October 2016). The authors wanted to demonstrate the variation in seizure prophylaxis in a retrospective cohort study of 5 pediatric trauma centers. Overall, 79% of 236 patients received seizure prophylaxis (mostly with fosphenytoin), and in only 63% of these patients was this prophylaxis introduced in the first 24 hours after trauma.

Posttraumatic seizures (PTSs) are defined as those occurring early, within 7 days of injury, or late, beyond 8 days of recovery.⁷ It is estimated that early PTSs occur in about 10% of children after a traumatic brain injury (TBI). Risk factors associated with the occurrence of PTS have been examined in previous studies and include location of the lesion (mainly nonfrontal traumas), cerebral contusions, retained bone and metal fragments, depressed skull fracture, focal neurological deficits, loss of consciousness, Glasgow Coma Scale (GCS) score < 10 at admission, duration of posttraumatic amnesia, subdural or epidural hematoma, and penetrating injury.³

It is already known that PTS increases the risk of childhood-onset epilepsy, although this association remains unclear. A recent study published by Camfield and Camfield¹ consisted of a survey of 472 adults who had developed epilepsy in childhood, and 11% reported a serious injury

before the onset of epilepsy. In that paper, most injuries occurred years after the initial diagnosis of seizure (range 1.5–30 years), and the authors concluded that early seizure prophylaxis could be useful to reduce the incidence of PTS.

Although PTS remains a significant concern among pediatricians, neurologists, and neurosurgeons, there is little evidence that antiepileptic drugs really reduce the incidence of these seizures in a TBI setting. In the last set of guidelines for the management of severe TBI in children and adolescents, published by Kochanek et al. in 2012,³ only 1 study conducted by Lewis et al.⁴ was included in the analysis of the possible benefits of seizure prophylaxis. In that retrospective cohort study, 194 children with TBI were analyzed. For children with a GCS score of 3–8, treatment with prophylactic phenytoin was associated with a reduced rate of seizures (15%) compared with the rate among patients not treated with prophylactic medication ($p = 0.04$). In the guidelines' conclusions,³ Kochanek and colleagues state that there are only Level III (weak) recommendations that prophylactic treatment with phenytoin can be considered to reduce the incidence of early PTS in pediatric patients with severe TBI.

Another point of interest is which anticonvulsant drug should be used. Some recent studies have included levetiracetam as a drug of choice to prevent PTS. In a prospective observational study by Chung and O'Brien,² 34 patients with moderate to severe TBI received either levetiracetam or phenytoin. The authors concluded that early clinical PTS occurred frequently in children with moderate to severe TBI despite seizure prophylaxis with levetiracetam and that younger children and those with abusive head trauma were at an increased risk for seizures. Tanaka and Litofsky⁶ also pointed out that levetiracetam may not be a better choice for PTS prophylaxis if compared to phenytoin or fosphenytoin.

Given this, the article by Ostahowski et al.⁵ brings useful and important information about how PTS prophylaxis is conducted in trauma centers among all those uncertain conclusions about when to start it or which drug to use. Some interesting points to be elucidated include the efficacy and safety of drugs required for the prevention of early PTS, the mechanisms of epileptogenesis after TBI, and improvements in the classification of PTS, including the use of electroencephalography in the emergency department to detect and classify PTS. Although one would think that PTS prophylaxis is almost universal in the initial prescriptions for children with moderate to severe TBI, the paper by Ostahowski and colleagues showed that this practice is variable and that the outcomes are unclear. It is clear that larger studies with proper allocation and randomization should be performed to find the real place for PTS prophylaxis in this scenario.

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References

1. Camfield C, Camfield P: Injuries from seizures are a serious, persistent problem in childhood onset epilepsy: a population-based study. *Seizure* 27:80–83, 2015

2. Chung MG, O'Brien NF: Prevalence of early posttraumatic seizures in children with moderate to severe traumatic brain injury despite levetiracetam prophylaxis. **Pediatr Crit Care Med** 17:150–156, 2016
3. Kochanek PM, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S, et al: Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. **Pediatr Crit Care Med** 13 (Suppl 1):S1–S82, 2012 (Erratum in **Pediatr Crit Care Med** 13:252, 2012)
4. Lewis RJ, Yee L, Inkelis SH, Gilmore D: Clinical predictors of post-traumatic seizures in children with head trauma. **Ann Emerg Med** 22:1114–1118, 1993
5. Ostahowski PJ, Kannan N, Wainwright MS, Qiu Q, Mink RB, Groner JI, et al: Variation in seizure prophylaxis in severe pediatric traumatic brain injury. **J Neurosurg Pediatr** 18:499–506, 2016
6. Tanaka T, Litofsky NS: Anti-epileptic drugs in pediatric traumatic brain injury. **Expert Rev Neurother** 16:1229–1234, 2016
7. Yablon SA: Posttraumatic seizures. **Arch Phys Med Rehabil** 74:983–1001, 1993

Disclosures

The author reports no conflict of interest.

Response

We thank Dr. Filho for a thorough discussion of the evidence leading to recommendations regarding antiepileptic drug use in pediatric TBI. We also thank him for taking an interest in our paper. One goal of our study was to examine practices between and within centers, and a second goal was to try to understand whether this variability is a reason why previously published studies regarding antiepileptic use were negative. In fact, the Brain Trauma Foundation Guidelines, which have outlined evidence-based treatment for children with TBI, have very few studies from which to glean information regarding PTS prophylaxis.¹ While we expected between-center variability in antiepileptic drug use, we were surprised by the within-center use. This finding suggests that we must first come to consensus on medication choices and include their use in different treatment locations in all analyses. Although our research outlines the general use of antiseizure medication as prophylaxis in this pediatric population, we agree that more research is needed to provide higher-level evidence for the use of seizure prophylaxis in TBI. Higher-level studies are needed to determine best practices, including the specific medication to use for seizure prophylaxis, the efficacy of seizure prophylaxis in preventing seizures, and methods to identify PTS earlier after TBI.

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References

1. Kochanek P, Carney N, Adelson P, Ashwal S, Bell M, Bratton S, et al: Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. **Pediatr Crit Care Med** 13 (Suppl 1):S1–S82, 2012 (Erratum in **Pediatr Crit Care Med** 13:252, 2012)

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Cranial vault remodeling

TO THE EDITOR: We read with interest the article by Utria et al.⁵ (Utria AF, Lopez J, Cho RS, et al: Timing of cranial vault remodeling in nonsyndromic craniosynostosis: a single-institution 30-year experience. *J Neurosurg Pediatr* 18:629–634, November 2016), and we would like to make the following observations on the basis of the literature and our personal experience.

The authors present groundbreaking results or at least call into question one of the most established paradigms in the treatment of craniosynostosis. To date, a young age is regarded as an added value to surgery; that is, the earlier the intervention the better the results,³ whereas delayed surgery is associated with higher complication rates.¹ Pediatric neurosurgeons believe that there should be a balance between early intervention and surgical risk in deciding the optimal moment for surgery.

The authors list several reasons to justify their results, some of which we share. We understand that a historical series covering 30 years involves the participation of several neurosurgeons with varying degrees of experience in this type of intervention. For the same reason, throughout the study period craniosynostosis techniques have been modified, as have the systems for fixing bone flaps, for example, passing steel wires and mini-plates of titanium or resorbables.

We agree with the authors that the use of the Whitaker categories is a subjective assessment open to bias and lacking surgical outcomes or measurements such as radiological or anthropometric data permitting objective preoperative and postoperative cephalometric evaluation.⁶

Strikingly, the authors fail to comment on endoscopic surgery, which should be performed earlier. In most series it is recommended before 3–4 months of age to ensure better outcomes and fewer complications.^{2,4}

Finally, we agree with the authors that future studies should aim to incorporate objective surgical outcome measurements.

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References

1. Iyengar RJ, Klinge PM, Chen WS, Boxerman JL, Sullivan SR, Taylor HO: Management of craniosynostosis at an advanced age: controversies, clinical findings, and surgical treatment. **J Craniofac Surg** 27:e435–e441, 2016
2. Jimenez DF, Barone CM: Early treatment of coronal synostosis with endoscopy-assisted craniectomy and postoperative cranial orthosis therapy: 16-year experience. **J Neurosurg Pediatr** 12:207–219, 2013
3. Raimondi AJ: **Pediatric Neurosurgery. Theoretical Principles—Art of Surgical Techniques**. Berlin: Springer, 1998
4. Rivero-Garvía M, Márquez-Rivas J, Giménez-Pando J: Craniosynostosis. **J Neurosurg Pediatr** 7:218–219, 2011 (Letter)
5. Utria AF, Lopez J, Cho RS, Mundinguer GS, Jallo GI, Ahn ES, et al: Timing of cranial vault remodeling in nonsyndromic craniosynostosis: a single-institution 30-year experience. **J Neurosurg Pediatr** 18:629–634, 2016
6. Whitaker LA, Bartlett SP, Schut L, Bruce D: Craniosynostosis: an analysis of the timing, treatment, and complications in 164 consecutive patients. **Plast Reconstr Surg** 80:195–212, 1987

Disclosures

The authors report no conflict of interest.

Response

We thank Dr. Gelabert-González and colleagues for their thoughtful comments regarding our article. There are several key issues that remain unanswered regarding the surgical management of craniosynostosis. Our study aimed to shed some light on the optimal timing for surgery, which remains an important unanswered question. There is a fine balance between the advantages of early intervention 1) to release synostotic sutures to prevent restrictive brain growth and 2) to have the regenerative bone capabilities of a younger child, and the advantages of later intervention 1) to minimize calvarial vault remodeling relapse rates and 2) to have more surgical and anesthetic reserve in an older child. Currently, management is largely dictated by surgeon preference and the timing of patient presentation.^{1,5} Using 30-year data at a single large academic institution, we sought to examine what the most optimal time of surgery would be in terms of revision rates, as defined by Whitaker categories. Further, we aimed to determine through subanalysis if the type of suture involvement, type of surgical procedure, and surgeon would impact revision rates. While we were able to conclude that, overall, performing early surgery is associated with higher revision rates, we were not able to demonstrate statistical significance for any other factors. Future studies with even greater patient numbers are needed to assess whether this association is found in particular subtypes of craniosyn-

stosis. Our hypothesis, given our experience, is that it may indeed be suture dependent.

Gelabert-González et al. astutely pointed out that endoscopic surgery is normally performed earlier, typically before 3 months of age. This is also the case at our institution. Although we included in our analysis 101 patients (Table 2 in the original article) who underwent multiple strip craniectomies in the younger-than-6-months cohort, we examined patients who predated the widespread use of endoscopic craniectomies at our hospital. Consistent with the literature, which has shown that outcomes are similar between open and endoscopic craniosynostosis repair,^{2,3,4} we too have anecdotally found no difference in the relapse rates between these groups. Perhaps postoperative helmeting techniques are contributing to decreased revision rates in this particular subgroup? We hope to further explore this question more robustly in a subsequent study.

Our study provides evidence that an association exists between early surgical intervention and higher revision rates (as indicated by Whitaker scores). Although the drivers behind this strong association are unclear, future efforts should focus on exploring whether this association can be replicated 1) in all or only certain types of craniosynostosis and 2) with open cranial vault and endoscopic repair.

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References

1. Foster KA, Frim DM, McKinnon M: Recurrence of synostosis following surgical repair of craniosynostosis. **Plast Reconstr Surg** 121:70e–76e, 2008
2. Han RH, Nguyen DC, Bruck BS, Skolnick GB, Yarbrough CK, Naidoo SD, et al: Characterization of complications associated with open and endoscopic craniosynostosis surgery at a single institution. **J Neurosurg Pediatr** 17:361–370, 2016
3. Kung TA, Vercler CJ, Muraszko KM, Buchman SR: Endoscopic strip craniectomy for craniosynostosis: do we really understand the indications, outcomes, and risks? **J Craniofac Surg** 27:293–298, 2016
4. Rottgers SA, Lohani S, Proctor MR: Outcomes of endoscopic suturectomy with postoperative helmet therapy in bilateral coronal craniosynostosis. **J Neurosurg Pediatr** 18:281–286, 2016
5. Whitaker LA, Bartlett SP, Schut L, Bruce D: Craniosynostosis: an analysis of the timing, treatment, and complications in 164 consecutive patients. **Plast Reconstr Surg** 80:195–212, 1987

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