Water and Sodium Disorders in Children Undergoing Surgical Treatment of Brain Tumors†

PARAVEE HIRANRAT, MD, MSc*,
VICHIT SUPORNSILCHAI, MD*,
SUMARLEE SRIVUTHANA, MD*
PISUT KATAVETIN, MD**,
SUTTIPONG WACHARASINDHU, MRCP (UK)*,

Abstract

Background : Many children with brain tumors have abnormalities in water and sodium homeostasis, such as diabetes insipidus (DI), the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting syndrome (CSW), either pre-operatively or post-operatively. But little data have been published on the incidence, time of onset and clinical course of water and sodium disorders in children with brain tumors.

Objectives : To characterize the water and sodium disorders in children undergoing surgical treatment for brain tumors

Patients and Method : The medical records of children with brain tumors admitted for surgery at King Chulalongkorn Memorial Hospital from January 1997 to December 2002 were retrospectively reviewed.

Results : There were 79 patients, 46 males and 33 females included in this study. Water and sodium disorders occurred in 36 patients (45.57%), 23 patients had DI, 12 patients had SIADH and 1 patient had cerebral salt wasting syndrome (CSW). Nine of the 36 patients had pre-operative onset of water and sodium disorders (8 DI and 1 SIADH). The development of DI and SIADH was associated with the location of the brain tumors. Patients with sellar and suprasellar tumors had the highest incidence of DI (75.86%). Patients with tumors of the cerebral hemispheres had the highest incidence of SIADH (44.44%). Onset of post-operative DI ranged from 2 to 19 hours (mean 9.68 hours) and most patients developed SIADH within 24 hours post-operatively.

Conclusions : DI and SIADH are common problems in children with brain tumors, especially after surgical treatment and the onset usually occurs within 24 hours after surgery. Patients with sellar and suprasellar tumors are more likely to have DI, patients with tumors of cerebral hemispheres and posterior fossa tumors are more likely to have SIADH.

Key word : Diabetes Insipidus, Inappropriate Antidiuretic Homone Secretion, Cerebral Salt Wasting, Brain Tumor

HIRANRAT P, KATAVETIN P,
SUPORNSILCHAI V, WACHARASINDHU S, SRIVUTHANA S
J Med Assoc Thai 2003; 86 (Suppl 2): S152-S159

* Endocrine unit, Department of Pediatrics,
** Nephrology unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
† Portions of the data included in this paper were presented in abstract form at the 55th Thai Congress of Pediatrics held in Chiang Mai on December 4th-6th, 2002.

Children with brain tumors often have abnormalities in water and sodium homeostasis, such as diabetes insipidus (DI), the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or cerebral salt wasting syndrome, especially those undergoing surgical treatment. These complications may occur either pre-operatively or post-operatively. Prompt diagnosis and appropriate management are critical to prevent morbidity from fluid and electrolyte imbalance. Some studies have described water and sodium disorders but in only specific subtypes and locations of brain tumors[1-4]. Little data have been published on the overall incidence, time of onset and clinical course of water and sodium disorders in children with brain tumors. Therefore, the authors performed this retrospective study to determine the incidence, time of onset and duration of water and sodium disorders in children undergoing surgical treatment of brain tumors. The authors also analyzed the data to identify factors associated with the development of water and sodium disorders in these patients.

PATIENTS AND METHOD

The databases of King Chulalongkorn Memorial Hospital were searched to identify children who had a diagnosis of brain tumors and had been treated with surgical resection between January 1997 and December 2002. The medical records of the patients were retrospectively reviewed to extract information about type and location of the brain tumor, fluid intake and output, serum electrolyte, serum osmolarity, urine electrolyte, urine osmolarity or specific gravity, body weight, vital signs and central venous pressure.

In the present study, the authors defined diabetes insipidus (DI) on the basis of polyuria (urine > 4 ml/kg/h) with diluted urine (urine sp.gr. < 1.010 or urine osmolarity < 300 mOsm/L) in association with high serum osmolarity (serum osmolarity > 300 mOsm/L) and hypernatremia (serum Na > 145 mmol/L) that responds to treatment with desmopressin (DDAVP) [5]. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) was defined as low serum osmolarity (serum osmolarity < 280 mOsm/L) and hyponatremia (serum Na < 135 mmol/L) with relatively concentrated urine (urine osmolarity > 100 mOsm/L) and high urine sodium (urine Na > 20 mmol/L) in the absence of dehydration, renal failure, hypothyroidism, adrenal insufficiency and effect of DDAVP treatment[6]. Cerebral salt wasting syndrome (CSW) was defined as low serum osmolarity (serum osmolarity < 280 mOsm/L) and hyponatremia (serum Na < 135 mmol/L) with relatively concentrated urine (urine

osmolarity > 100 mOsm/L) and high urine sodium (urine Na > 20 mmol/L) in the presence of volume depletion without other causes of natriuresis (e.g. diuretic administraion)[6].

Statistical analysis for the association of various factors and the development of water and sodium disorders was performed using the Chi-square test. Multivariate analysis of these factors was performed using binary logistic regression.

RESULTS

There were 79 patients, 46 males and 33 females. The age at the time of surgery ranged from 1 month to 15 years (mean 8.37 years).

According to the location of the brain tumors [7], 9 patients had tumors of the cerebral hemispheres, 29 patients had sellar and suprasellar region tumors, 5 patients had thalamic tumors, 7 patients had pineal region tumors and 29 patients had posterior fossa tumors.

According to the pathological diagnosis[8], 25 patients had astrocytomas, 15 patients had medulloblastomas, 15 patients had germinomas, 6 patients had craniopharyngiomas, 6 patients had ependymomas, 4 patients had pituitary adenomas, 4 patients had gliomas, 2 patients had teratomas, 1 patient had a neuroblastoma and 1 patient had an epidermoid cyst.

Incidence of water and sodium disorders

Water and sodium disorders occurred in 36 patients (45.57%, 95% CI 34.59-56.55), 23 patients had diabetes insipidus (8 pre-operative and 15 post-operative), 12 patients had SIADH (1 pre-operative and 11 post-operative) and only 1 patient had post-operative cerebral salt wasting syndrome (Table 1).

Factors associated with the development of water and sodium disorders

Age and sex

The authors divided all patients into 3 age groups: 0-5 years (n = 27), 5-10 years (n = 22) and 10-15 years (n = 30). The incidence of SIADH in various age groups was significantly different ($p < 0.05$), with the highest incidence in the age group 0-5 years. The incidence of diabetes insipidus and cerebral salt wasting syndrome were similar among the different age groups ($p > 0.05$) (Table 2). Male and female patients had a similar incidence of water and sodium disorders ($p > 0.05$) (Table 3).

Location of brain tumors

The incidence of diabetes insipidus and SIADH in various locations of brain tumors were significantly different ($p < 0.001$ and $p < 0.05$ respectively) (Table 4).

Table 1. Incidence of water and sodium disorders.

Result	Number of patients			Incidence (%) (n = 79)	95% CI
	Pre-operative	Post-operative	Total		
DI	8	15	23	29.11	19.10-39.13
SIADH	1	11	12	15.19	7.28-23.10
CSW	0	1	1	1.27	-1.20-3.73
Total	9	27	36	45.57	34.59-56.55

Table 2. Incidence of water and sodium disorders in different age groups.

Age (yr)	Incidence of water and sodium disorders					
	DI [a]		SIADH [b]		CSW [c]	
	%	95% CI	%	95% CI	%	95% CI
0-5	18.52	3.87-33.17	29.63	12.41-46.85	3.70	0-10.82
5-10	31.82	12.36-51.28	9.09	0-21.1	0	
10-15	36.67	19.43-53.91	6.67	0-15.6	0	

a. Chi-square test, $p > 0.05$
b. Chi-square test, $p < 0.05$
c. Chi-square test, $p > 0.05$

Table 3. Incidence of water and sodium disorders according to sex.

Sex	Incidence of water and sodium disorders					
	DI [a]		SIADH [b]		CSW [c]	
	%	95% CI	%	95% CI	%	95% CI
Male	21.74	9.82-33.66	15.22	4.84-25.6	0	
Female	39.39	22.72-56.06	15.15	2.92-27.38	3.03	0-8.88

a. Chi-square test, $p > 0.05$
b. Chi-square test, $p > 0.05$
c. Chi-square test, $p > 0.05$

Table 4. Incidence of water and sodium disorders according to location of brain tumors.

Location of brain tumors	Incidence of water and sodium disorders					
	DI [a]		SIADH [b]		CSW [c]	
	%	95% CI	%	95% CI	%	95% CI
Cerebral hemispheres	0		44.44	11.98-76.91	0	
Sellar/suprasellar region	75.86	60.29-91.44	3.45	0-10.09	0	
Thalamus	20	0-55.06	0		0	
Pineal region	0		0		0	
Posterior fossa	0		24.14	8.56-39.71	1.27	0-3.73

a. Chi-square test, $p < 0.001$
b. Chi-square test, $p < 0.05$
c. Chi-square test, $p > 0.05$

Diabetes insipidus only occurred in patients with sellar and suprasellar region tumors (22 patients) and thalamic tumor (1 patient). Patients with tumors of cerebral hemispheres and posterior fossa tumors had a high incidence of SIADH (44.44% with tumors of the cerebral hemispheres and 24.14% with posterior fossa tumors). Cerebral salt wasting syndrome occurred in only 1 patient who had a posterior fossa tumor. In the present study, no patients with pineal region tumors had water and sodium disorders.

Pathological diagnosis

The incidence of diabetes insipidus and SIADH in various pathological diagnosis of brain tumors were significantly different ($p < 0.001$ and $p < 0.01$ respectively) (Table 5).

Among the patients with sellar and suprasellar tumors (Table 6), the authors observed that patients who developed pre-operative diabetes insipidus were more likely to have a pathological diagnosis of germinoma (6 of 8 patients) and teratoma (2 of 2 patients). It was also found that patients with a craniopharyngioma were more likely to have post-operative diabetes insipidus (6 of 6 patients).

Multivariate analysis

In univariate analysis, the development of diabetes insipidus was significantly associated with location and pathological diagnosis of brain tumors, the development of SIADH was significantly associated with age group, location and pathological diagnosis of brain tumors. But multivariate analysis of these factors showed that only the location of the brain tumors was significantly associated with the development of diabetes insipidus and SIADH (Table 7).

Clinical courses of post-operative water and sodium disorders

In 15 patients who developed post-operative diabetes insipidus, the onset of diabetes insipidus ranged from 2-19 hours (mean 9.68 hours). The duration of diabetes insipidus following surgical treatment of brain tumors was 2 days in 1 patient, 5 days in 1 patient and permanent in the other 13 patients. SIADH occurred in 11 patients post-operatively, the onset ranged from 2-72 hours (mean 26.23 hours). SIADH in the majority of these cases (8 of 11 patients) occurred within 24 hours after the surgery. The duration of post-operative SIADH ranged from 2-16 days

Table 5. Incidence of water and sodium disorders according to pathological diagnosis.

Pathological diagnosis	Incidence of water and sodium disorders					
	DI [a]		SIADH [b]		CSW [c]	
	%	95% CI	%	95% CI	%	95% CI
Astrocytoma	16	1.63-30.37	16	1.63-30.37	4	0-11.68
Medulloblastoma	0		20	0-40.24	0	
Germinoma	53.33	28.08-78.58	0		0	
Craniopharyngioma	100		0		0	
Ependymoma	0		66.67	28.95-100	0	
Pituitary adenoma	75	32.56-100	0		0	
Glioma	0		0		0	
Teratoma	100		0		0	
Neuroblastoma	0		100		0	
Epidermoid cyst	0		0		0	

a. Chi-square test, $p < 0.001$
b. Chi-square test, $p < 0.01$
c. Chi-square test, $p > 0.05$

Table 6. Water and sodium disorders in sellar and suprasellar region tumors according to pathological diagnosis.

Pathological diagnosis	Number of patients				Total
	DI		SIADH	No disorder	
	Pre-operative	Post-operative			
Astrocytoma	0	3	1	5	9
Germinoma	6	2	0	0	8
Craniopharyngioma	0	6	0	0	6
Pituitary adenoma	0	3	0	1	4
Teratoma	2	0	0	0	2
Total	8	14	1	6	29

Chi-square test, $p < 0.01$

(mean 6 days). In 1 patient who had post-operative cerebral salt wasting syndrome, the onset and duration were 13 hours and 6 days respectively.

DISCUSSION

The overall incidence of water and sodium disorders in the present study was higher than the previous report by Blumberg et al[9] (45.57% *vs* 12% respectively).

From the pathophysiological point of view, water and sodium disorders that occur pre-operatively are likely to be associated with location and nature of the tumor itself. However, post-operative water and sodium disorders are more likely to be associated with site and extent of brain injury from the surgical procedures which was also determined by the location of the brain tumor. This may explain the relationship between location of brain tumors and the development of water and sodium disorders in the present study.

Patients with sellar and suprasellar region tumors had very high incidence of diabetes insipidus (75.86%), especially after surgery because tumor of this region or surgery to it may cause injury to the hypothalamus or the proximal pituitary stalk[10].

Although the triphasic pattern, DI-SIADH-DI, is well characterized in patients with sellar and suprasellar tumors during the post-operative period [11,12], the authors could not identify this pattern in the present study, but it cannot be ruled out. Because the SIADH phase, if it exists, probably could not be differentiated from the effect of DDAVP given to patients with diabetes insipidus.

Patients with tumors of the cerebral hemispheres and posterior fossa tumors had a high incidence of SIADH (44.44% and 24.14% respectively).

Table 7. Factors associated with the development of water and sodium disorders.

Conditions	Associated Factors	Univariate Analysis	Multivariate Analysis
DI	Location	$p < 0.001$	$p < 0.001$
	Pathological diagnosis	$p < 0.001$	ns*
SIADH	Age group	$p < 0.05$	ns*
	Location	$p < 0.05$	$p < 0.05$
	Pathological diagnosis	$p < 0.05$	ns*

* ns = not significant, $p > 0.05$

Pathophysiology of SIADH in these patients is still unclear. It may be associated with loss of regulatory signals from the brainstem and cerebral cortex.

Cerebral salt wasting syndrome occurred in only one patient (1.27%). This finding suggests a low incidence of cerebral salt wasting syndrome in children with brain tumors undergoing surgery. Singh et al (13) suggest that cerebral salt wasting syndrome is probably much less common than the literature indicates and increasing case reports of cerebral salt wasting syndrome in recent years may be due to the fallacy of diagnostic criteria. However, the differentiation between SIADH and cerebral salt wasting syndrome which share the features of hyponatremia and natriuresis are very important because therapies for these two conditions are different and inappropriate management may result in unnecessary morbidity.

The onset of post-operative diabetes insipidus and cerebral salt wasting syndrome were within 24 hours after surgery in all patients. Post-operative SIADH occurred within 24 hours in most cases, but it may be delayed until 3 days after surgery in a few cases. Therefore, meticulous fluid management and close monitoring of volume status, urine output, urine specific gravity, serum and urine electrolyte (also serum and urine osmolarity, if necessary) are recommended in children with brain tumors, especially during the first three days of the post-operative period.

In conclusion, water and sodium disorders are common problems in children with brain tumors, especially those undergoing surgical treatment. The onset of water and sodium disorders usually occurs within 24 hours after surgery. Patients with sellar and suprasellar tumors are more likely to have diabetes insipidus. On the other hand, patients with tumors of the cerebral hemispheres and posterior fossa tumors are more likely to have SIADH.

(Received for publication on April 6, 2003)

REFERENCES

1. Lehrnbecher T, Muller-Scholden J, Danhauser-Leistner I, Sorensen N, von Stockhausen HB. Perioperative fluid and electrolyte management in children undergoing surgery for craniopharyngioma. Child's Nerv Syst 1998; 14: 276-9.
2. Daaboul J, Steinbok P. Abnormalities of water metabolism after surgery for optic/chiasmatic astrocytomas in children. Pediatr Neurosurg 1998; 28: 181-5.
3. Honegger J, Buchfelder M, Fahlbusch R. Surgical treatment of craniopharyngiomas: Endocrinological results. J Neurosurg 1999; 90: 251-7.
4. Bin-Abbas B, Mawlawi H, Sakati N, Khafaja Y, Chaudhary MA, Al-Ashwal A. Endocrine sequelae of childhood craniopharyngioma. J Pediatr Endocrinol Metab 2001; 14: 869-74.
5. Hyperosmolal states-hypernatremia. In: Rose BD, Post TW, Editors. Clinical physiology of acid-base and electrolyte disorders. 5th edition. Boston: Mcgraw-Hill; 2001: 746-93.
6. Hypoosmolal states-hyponatremia. In: Rose BD, Post TW, Editors. Clinical physiology of acid-base and electrolyte disorders. 5th edition. Boston: McGraw-Hill; 2001: 696-745.
7. Intracranial tumours-classification according to site. In: Lindsay KW, Bone I, editors. Neurology and neurosurgery illustrated. 3rd edition. Edinburgh: Churchill Livingstone; 1997: 297.
8. Intracranial tumours-pathological classification. In: Lindsay KW, Bone I, editors. Neurology and neurosurgery illustrated. 3rd edition. Edinburgh: Churchill livingstone; 1997: 294-6.
9. Blumberg DL, Sklar CA, Wisoff J, David R. Abnormalities of water metabolism in children and adolescents following craniotomy for a brain tumor. Childs Nerv Syst 1994; 10: 505-8.
10. Baylis PH. Posterior pituitary. In: Besser GM, Thorner MO, editors. Comprehensive clinical endocrinology. 3rd edition. Edinburgh: Mosby; 2002: 85-101.
11. Shucart WA, Jackson I. Management of diabetes insipidus in neurosurgical patients. J Neurosurg 1976; 44: 65-71.
12 Seckl J, Dunger D. Post-operative diabetes insipidus. BMJ 1989; 298: 2-3.
13 Singh S, Bohn D, Carlotti APCP, Cusimano M, Rutka JT, Halperin ML. Cerebral salt wasting: Truths, fallacies, theories, and challenges. Crit Care Med 2002; 30: 2575-9.

ความผิดปกติของสมดุลย์น้ำและเกลือแร่ในผู้ป่วยเด็กที่ได้รับการผ่าตัดเนื้องอกในสมอง†

ภารวี หิรัญรัตน์, พบ, วทม, พิสุทธิ์ กตเวทิน, พบ**,*
วิชิต สุพรศิลป์ชัย, พบ, สุทธิพงศ์ วัชรสินธุ, MRCP (UK)*, สุมาลี ศรีวัฒนา, พบ**

ที่มา : ผู้ป่วยเด็กที่ได้รับการผ่าตัดเนื้องอกในสมอง จะพบมีความผิดปกติของสมดุลย์น้ำและเกลือแร่ได้ทั้งก่อนและหลังผ่าตัด โดยความผิดปกติที่พบได้บ่อย คือ ภาวะเบาจืด และกลุ่มอาการที่เกิดจากการหลั่ง antidiuretic hormone อย่างไม่เหมาะสม (SIADH)

วัตถุประสงค์ : เพื่อศึกษาเกี่ยวกับความผิดปกติของสมดุลย์น้ำและเกลือแร่ในผู้ป่วยเด็กที่ได้รับการผ่าตัดเนื้องอกในสมอง

วิธีดำเนินการศึกษา : ได้ศึกษาข้อมูลย้อนหลังของผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่าเป็นเนื้องอกในสมองและรับไว้รักษาในโรงพยาบาลจุฬาลงกรณ์เพื่อทำการผ่าตัด ตั้งแต่ปี พ.ศ. 2540–2545 รวมระยะเวลา 6 ปี

ผลการศึกษา : ในจำนวนผู้ป่วยทั้งหมด 79 ราย ซึ่งเป็นเพศชาย 46 ราย เพศหญิง 33 ราย พบความผิดปกติของสมดุลย์น้ำและเกลือแร่ 36 ราย คิดเป็นร้อยละ 45.57 แบ่งเป็นภาวะเบาจืด 23 ราย SIADH 12 ราย และ cerebral salt wasting syndrome (CSW) 1 ราย มีผู้ป่วย 9 รายจาก 36 รายที่มีความผิดปกติของสมดุลย์น้ำและเกลือแร่ตั้งแต่ก่อนการผ่าตัด ในจำนวนนี้ 8 รายเป็นเบาจืด ส่วนอีก 1 รายเป็น SIADH พบว่าตำแหน่งของเนื้องอกในสมองเป็นปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะเบาจืดและ SIADH ผู้ป่วยที่มีเนื้องอกบริเวณ sellar และ suprasellar จะมีภาวะเบาจืดได้บ่อยที่สุด คิดเป็นร้อยละ 75.86 ส่วนผู้ป่วยที่มีเนื้องอกบริเวณ cerebral hemispheres จะมีภาวะ SIADH ได้บ่อยที่สุด คิดเป็นร้อยละ 44.44 ระยะเวลาในการเกิดภาวะเบาจืดมีตั้งแต่ 2 ชั่วโมง จนถึง 19 ชั่วโมง ส่วนภาวะ SIADH มักจะเกิดภายใน 24 ชั่วโมงหลังการผ่าตัด

สรุปผล : ผู้ป่วยเด็กที่ได้รับการผ่าตัดเนื้องอกในสมอง จะมีภาวะเบาจืดและ SIADH ได้บ่อย และมักจะเกิดภายใน 24 ชั่วโมง หลังการผ่าตัด โดยผู้ป่วยที่มีเนื้องอกบริเวณ sellar และ suprasellar มักจะมีภาวะเบาจืด ส่วนผู้ป่วยที่มีเนื้องอกบริเวณ cerebral hemispheres และ posterior fossa มักจะมีภาวะ SIADH

คำสำคัญ : ภาวะเบาจืด, กลุ่มอาการที่เกิดจากการหลั่ง antidiuretic hormone อย่างไม่เหมาะสม, กลุ่มอาการ cerebral salt wasting, เนื้องอกในสมอง

ภารวี หิรัญรัตน์, พิสุทธิ์ กตเวทิน,
วิชิต สุพรศิลป์ชัย, สุทธิพงศ์ วัชรสินธุ, สุมาลี ศรีวัฒนา
จดหมายเหตุทางแพทย์ ฯ 2546; 86 (ฉบับพิเศษ 2): S152–S159

* หน่วยต่อมไร้ท่อและเมตาบอลิซึม, ภาควิชากุมารเวชศาสตร์,
** หน่วยโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330

† ข้อมูลส่วนหนึ่งในการศึกษานี้ได้ผ่านการนำเสนอในรูปบทคัดย่อในการประชุมวิชาการประจำปีของราชวิทยาลัยกุมารแพทย์ ครั้งที่ 55 ที่จังหวัดเชียงใหม่ ระหว่างวันที่ 4–6 ธันวาคม พ.ศ.2545