

Diabetes Insipidus in Neurosurgical Patients

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Abstract

Diabetes insipidus (DI) is an uncommon but important complication in the neurosurgical population. This retrospective study aimed to determine the incidence, profile and outcome of patients admitted to an 18-bedded neurosurgical intensive care unit who developed DI. The overall incidence was 3.7% (29/792 admissions). Aetiologies included subarachnoid haemorrhage (12/29), severe head injury (11/29), post-surgical excision of craniopharyngioma or pituitary adenoma (5/29) and acute haemorrhagic stroke (1/29). All patients were treated with a regime of fluid replacement, electrolyte correction, parenteral or intranasal desmopressin (DDAVP), or parenteral pitressin. Overall mortality was 72.4%. There were no deaths in the patients who underwent excision of tumours. Complications included acute pulmonary oedema, hypernatremia and hypokalaemia. The development of DI was found to be associated with impending brain death and mortality in the majority of patients with subarachnoid haemorrhage and severe head injury. However, careful diagnosis and management of DI after hypothalamo-neurohypophyseal surgery did not result in any permanent neurological sequelae.

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Key words: Head trauma, Hypernatremia, Hypothalamo-neurohypophyseal surgery, Intensive care unit, Vasopressin

Introduction

Diabetes insipidus (DI) is a syndrome characterised by the excretion of abnormally large volumes of dilute urine. It occurs uncommonly in neurosurgical patients, but is an important complication. The aim of this study was to study the incidence, profile and outcome of neurosurgical patients admitted to an 18-bedded neurologic intensive care unit (NICU), who developed DI.

Materials and Methods

A retrospective review of the records of all neurosurgical patients admitted to the NICU over a 14-month period who developed DI was undertaken. Patients who received antidiuretic hormone or analogues were captured on our records and their casenotes were critically reviewed to determine the diagnostic validity of diabetes insipidus. Only those who satisfied the diagnostic indicators of polyuria (24-hour urine volume more than 30 ml/kg body weight or >250 ml/h for two consecutive hours in adults), urine specific gravity <1.010 or urine osmolality <300 mOsm/kg with a simultaneously normal or high serum osmolality were included in the study.^{1,2} In equivocal cases, Notman and Moses' normogram, which compares simultaneous urine and plasma osmolality values in normal patients, under

varying conditions of hydration, was used.^{3,4} Demographic data, radiological and clinical diagnoses, initial Glasgow Coma Scale (GCS), surgery done, onset and duration of DI, fluid balance, drug therapy, complications of DI, therapy and outcome were noted. Onset time was defined as the time from the haemorrhage, head injury, or surgery for excision of tumours, to the onset of symptoms and signs of DI. Excluded were patients who had incomplete data or who were initially thought to have DI but did not satisfy diagnostic indicators.

Results

During the 14-month period, there were 792 neurosurgical admissions to the NICU. Using the diagnostic indices, 29 patients (3.7% of admissions) developed diabetes insipidus. All 29 (100%) had polyuria, 24 (82.76%) had urine specific gravity <1.010 and 24 (82.76%) had urine osmolality <300 mOsm/kg. Using the simultaneous comparison of urine osmolality and plasma osmolality, the results were all in zone C of Notman's normogram, denoting DI (Fig. 1).

The majority of patients who developed DI in the NICU were adults with subarachnoid haemorrhage (SAH) or severe head injury (HI). Other aetiologies included post-surgical excision of pituitary adenoma and craniopharyngioma, and acute haemorrhagic stroke.

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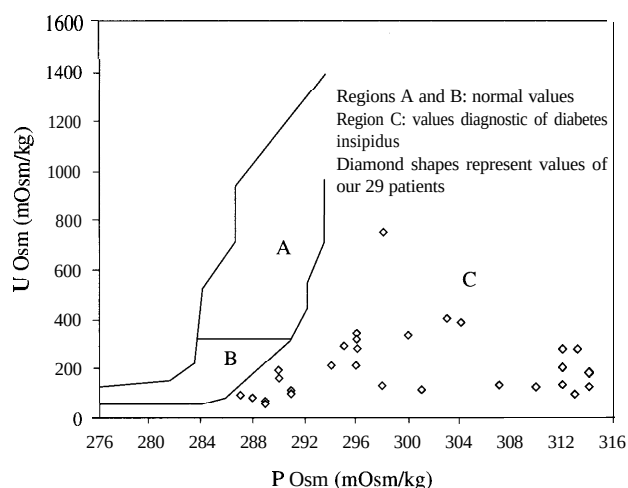


Fig. 1. Relationship of plasma to urinary osmolality under normal and polyuric conditions (Adapted with permission from Norman et al³).

There were 21 males and 8 females (Table I). There were equal numbers of male and female patients with subarachnoid haemorrhage and craniopharyngioma, but the head injured patients in this study were all males, which reflects the predominance of males involved in serious motor vehicle accidents and trauma. The patients with craniopharyngioma were both 5-year-olds.

Most of the patients with SAH and HI presented with poor post-resuscitation GCS of ≤ 8 (Table I), requiring mechanical ventilation and intensive monitoring. Twelve patients had subarachnoid haemorrhage; 7 with documented intracranial arterial aneurysms for which clipping was done for 5 patients and wrapping of a fusiform vertebral artery aneurysm for the sixth. The seventh patient was in a poor grade and no surgery was done. One patient had an arteriovenous malformation which was excised. Four patients with poor grade SAH did not undergo four-vessel angiography to confirm the diagnosis of ruptured aneurysms.

There were 11 patients with head injuries, 9 of whom were severely injured with an initial GCS ≤ 8 . Most of these had more than 1 type of injury. The majority had subdural haemorrhage (7/ 11) and/or cerebral oedema

with midline shift (7/11). Four out of the 11 had skull fractures (36%). Other injuries suffered were traumatic subarachnoid haemorrhage (3/ 11), intracerebral haemorrhage (2/11) and extradural haemorrhage (1 / 11). Nine patients underwent evacuation of the haematoma, with external ventricular drainage and intracranial pressure monitors inserted.

The onset time of DI ranged from less than 6 hours to 12 days (Table II).

Twenty of the 29 patients (69%) developed DI within the first 48 hours of injury. The onset in HI patients was often within the first 24 hours.

The overall mortality was 72.4% (21/29) (Table III). The mortality in the SAH group and HI group was high at 83% and 91%, respectively. There were no deaths in the post-tumour excision group. DI was transient in the 3 patients with transphenoidal pituitary surgery, and the SAH and HI survivors. It was permanent in the 2 children after craniopharyngioma excision. One of the children demonstrated the triphasic response, with an initial DI, a transient second phase of antidiuresis, followed by permanent DI.

Comparing the initial post-resuscitation GCS between survivors and non-survivors, it was found that in the SAH group, both the survivors had initial GCS > 8 , whereas the non-survivors were mainly in the severely injured group, with GCS ≤ 8 . In the HI group, the non-survivors were also mainly in the severely injured group. The mean duration of DI from onset to death was 2.2 days in the SAH group and 2.9 days in the HI group. There were no deaths in the tumour group.

In comparing the onset times of survivors versus non-survivors, it was found that the mean onset time of non-survivors was shorter compared to survivors, 48 ± 61 hours versus 70 ± 95 hrs. However, it was not statistically significant.

A complication associated with the treatment of DI was pulmonary oedema presenting in a 59-year-old man with insulin dependent diabetes mellitus and severe head injury after a motor vehicle accident, who underwent external ventricular drainage and evacua-

TABLE I: DEMOGRAPHIC DATA, AETIOLOGY AND INITIAL GLASGOW COMA SCALE (GCS) SCORES

Aetiology	Age (y)	Males	Females	Total	GCS ≤ 8
SAH	45 $\pm$ 19	6	6	12	8
HI	36 $\pm$ 16	11	0	11	9
Pit. Ad.	46 $\pm$ 11	3	0	3	0
Cranioph.	5 $\pm$ 0	1	1	2	0
Stroke	61	0	1	1	1

Cranioph.: craniopharyngioma; HI: head injury; Pit. Ad.: pituitary adenoma; SAH: subarachnoid haemorrhage; Stroke: acute haemorrhage stroke

Values are either number of patients or age in years $\pm$ standard deviation

TABLE II: ONSET TIME OF DIABETES INSIPIDUS DISTRIBUTED BY AETIOLOGY

Aetiology	Onset Time				
	<6 h	6 to <24 h	24 to <48 h	48 h to <1 week	>1 week
SAH	2	4	2	3	1
HI	2	5	0	3	1
Tumour	0	2	3	0	0
Stroke	0	0	0	0	1

SAH: subarachnoid haemorrhage; HI: head injury

Values represent number of patients

TABLE III: SEVERITY OF INJURY CORRELATED TO OUTCOME

	Post-resuscitation GCS		Mortality	Duration of DI Mean (range) in days	GOS
	≤8	>8			
1. SAH survivors	0	2	10 (83%)	2.5 (2 to 3)	4, 5
Non-survivors	9	1		2.2 (1 to 7)	1
2. HI survivors	1	0	10 (91%)	3	3
Non-survivors	8	2		2.9 (1 to 7)	1
3. Tumour survivors	0	5	1 (100%)	2 had permanent DI	4, 5
				9.3 (1 to 25)	5
4. Stroke	1	0		7	1

GCS: Glasgow Coma Scale; DI: diabetes insipidus; SAH: subarachnoid haemorrhage; HI: head injury;

GOS: Glasgow Outcome Score

1 = Death, 2 = Severely impaired, vegetative, 3 = Moderately impaired [Activities of Daily Living (ADL)-dependent],

4 = Favourable recovery (ADL-independent), 5 = Excellent recovery

tion of subdural and bifrontal haematoma. He developed DI 22 hours after the injury and received one dose of intranasal DDAVP 10 µg. Response to the treatment was good and urine output dropped. However he developed acute pulmonary oedema and required forced diuresis using intravenous frusemide.

There was a significantly higher incidence of hyponatremia (serum sodium levels >150 mEq/L) in non-survivors compared to survivors, 17/21 versus 1/8 ($P < 0.001$, Fisher's exact test). There was also a significantly higher incidence of hypokalaemia (serum potassium levels <3.0 mEq/L) in non-survivors compared to survivors, 14/21 versus 0/8 ($P < 0.0008$, Fisher's exact test).

Discussion

The neurosurgical population of patients who develops DI presents some special challenges. Inappropriate treatment may result in water retention with volume expansion, hyponatremia and natriuresis (the syndrome of inappropriate anti-diuretic hormone) with deleterious effects of cerebral oedema and intracranial hypertension. It is important to make an accurate and early diagnosis. These patients are often comatose and therefore unable to communicate thirst or alleviate it. Rapid dehydration may occur.⁵ They may already be haemodynamically unstable, and therefore unable to tolerate further fluid losses. Other causes for polyuria in this group of patients must be excluded e.g. solute diuresis from mannitol and uncontrolled diabetes mellitus, and free water diuresis from previous fluid resuscitation.²

Acquired causes of neurogenic DI include surgery in the hypothalamo-neurohypophyseal area, especially after surgery for posteriorly located pituitary adenomas or craniopharyngioma, and head trauma, where there may be shearing injury to the pituitary stalk.⁵ Generalised brain ischaemia, and pressure on the pituitary from a haematoma or aneurysm are some of the other possible causes.

The overall incidence of DI in the neurosurgical population varies according to the case mix. Balestrieri et al⁶ reported an incidence of 6.7% in a group of 135 post-craniotomy patients, most of whom had brain tumours and vascular anomalies. Others have reported incidences of 4% in aneurysm surgery and 2% in patients with severe head injury.^{7,8} In our series, the overall incidence was 3.7%. The onset ranges from several hours to weeks, but often occurs within the first 24 hours in severe head injury, as was in our study.⁵ Seckl et al⁹ found that very early onset is often associated with major hypothalamic damage and increased mortality. In this study, the mean onset times of non-survivors were also earlier than that of survivors. Verbalis et al⁵ found that the majority of head trauma patients who developed DI had significant injury, often associated with fractures. In our series, 82% of the head-injured patients had poor GCS of ≤8; 36% had skull fractures.

When the aetiology is surgery confined to the pituitary fossa, DI is usually transient, resolving over 2 to 5 days. However it may be permanent after suprasellar surgery, as in the 2 craniopharyngioma patients in this study. One of the children developed a triphasic response, described as an initial DI of a few days' duration, followed by a transient remission lasting 2 to 14 days, and eventually by a recurrence, which may be permanent. This may occur after complete pituitary stalk section. The second phase is believed to be due to the release of vasopressin stores from the damaged posterior pituitary tissues. This phase of anti-diuresis has to be recognised in order to avoid hyponatremia and fluid overload.⁵

The primary goals in the treatment of DI are to decrease urine output and restore normal plasma tonicity. Confirmation of the diagnosis is first sought by using the appropriate indicators; urine osmolality and specific gravity are measured, and blood samples are taken for plasma osmolality, electrolytes and blood sugar determination. Hourly monitoring of fluid intake and output, as well as vital signs, is instituted. If the patient is

haemodynamically unstable, central venous pressure or pulmonary artery wedge pressure is monitored to help optimise fluid replacement. Volume replacement for urine losses is instituted with isotonic solutions until the diagnosis is confirmed. Once confirmed, the appropriate volume and type of fluid replacement is started according to electrolytes and blood sugar levels. This remains an important cornerstone in the treatment for DI. However, in this population of patients where under- or over-hydration is equally hazardous, treatment with pitressin or DDAVP is recommended.

Parenteral 1-desamino 8-D-arginine vasopressin (DDAVP) is currently the drug of choice in the management of established neurogenic DI.¹⁰ This analogue has the advantages of greatly decreased pressor and uterotonetic effects and enhanced anti-diuretic properties. However, the longer half-life of 6 to 24 hours means it is less titratable to effect. The dose is 0.5 to 2 µg 12 to 24 hourly. Treatment is initiated with smaller doses, allowing breakthrough polyuria in between doses, so as to avoid overtreatment, with its attendant problems of hyponatremia and cerebral oedema, especially in patients who have a triphasic response or who have only transient DI. The latter group of patients may however be more safely managed with shorter acting vasopressin, either as an infusion of 1 to 2.5 units/h¹¹ or in small parenteral boluses of 5 units 3 to 4 hourly.

Replacement fluids used are hypotonic solutions e.g. Dextrose 5% or D3.75% /N.S.0.23% if the serum sodium is >145 mEq/L. Replacement is done with caution as overenthusiastic rapid correction with hypotonic fluids concomitant with DI therapy can lead to hyponatremia, cerebral oedema and seizures. Frequent monitoring of serum electrolytes and sugar, urine and plasma osmolality and urine specific gravity is instituted. Dextrose 5% may be avoided in favour of Dextrose 2.5% /saline 0.45% if hyperglycaemia is severe, as this will promote osmotic diuresis that masks the resolution of anti-diuretic hormone (ADH) deficiency, potentially resulting in overtreatment. Once the DI status is stabilised, the patients may be switched to intranasal DDAVP, 5 to 20 µg 8 to 12 hourly.¹²

In our study, the overall mortality was 72%. There were no deaths in the tumour group. The high mortality rates in the other groups correlated with the severity of the cerebral injury. In 19 of the 21 non-survivors, the development of DI was either immediately preceded or followed by clinical evidence of brain death, indicative of the underlying pathophysiological processes of posterior pituitary ischaemia, cessation of anterior artery blood flow, and/or followed by transtentorial hernia-

tion and brainstem death. In a separate study involving 25 severely head-injured patients managed in the same NICU, the overall mortality rate was 20%.¹³

The incidence of hyponatremia and hypokalaemia were found to be high in non-survivors. This is similar to the findings by Bingham,¹⁴ where in a group of unstratified but severely head-injured patients, serum Na >155 mEq/L and serum osmolality of >340 mOsm/kg was found to be associated with a high mortality. This reflects on the severity of the brain injuries suffered by this group of patients, the majority of whom presented with poor GCS scores.

Thus, the development of DI was associated with higher mortality in critically ill patients with severe head trauma and ruptured aneurysms. However, careful diagnosis and management of DI after tumour surgery did not result in any permanent neurological sequelae.

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