Subject: Guidelines for management of patients with cranial diabetes insipidus at University Hospital Aintree and The Walton Centre for Neurology and Neurosurgery. Version 2.

Objective: To ensure safe practice and standardise the monitoring, investigations and treatment of patients who develop central diabetes insipidus post-operatively.

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Exclusion: This guideline should not delay the rapid assessment and treatment in the critical care units of severe cranial diabetes insipidus usually associated with severe brain injury.

1. Background: Cranial Diabetes Insipidus (CDI)

CDI is characterised by decreased secretion of ADH that results in polyuria and polydipsia by diminishing the patient’s ability to concentrate urine. It is a common, although usually transient, complication of neurosurgical procedures performed in the sellar and suprasellar region.

It may exhibit 1 of 3 patterns—transient, permanent, or triphasic. Transient cranial diabetes insipidus and the triphasic pattern are observed more often clinically.

- First, a polyuric phase occurs and lasts 4-5 days. Inhibition of ADH causes the polyuric phase. An immediate increase in urine volume and a concomitant fall in urine osmolality occur.
- Second, an antidiuretic phase of 5-6 days occurs, which results from release of stored hormone. The urine osmolality rises.
- The third phase can be permanent diabetes insipidus, when stores of ADH are exhausted and the cells that produce more ADH are absent or unable to produce.
- Polyuria, polydipsia, and nocturia (from 3-18 L) are the predominant symptoms.

Factors found to increase the risk of postoperative diabetes insipidus include young age, male sex, large intrasellar mass, cerebrospinal fluid leak and resection of certain types of lesions, including craniopharyngiomas, Rathke-cleft cysts and ACTH-secreting pituitary adenomas.
2. Diagnosis & Investigation

The diagnosis of diabetes insipidus (DI) is often made clinically, while the laboratory tests provide confirmation.

Patients should be monitored closely after surgery for the abrupt onset of hypotonic urine excretion and/or serum hyperosmolality. Ruling out secondary causes, such as diabetes mellitus, is also important. Beware that one of the most common causes of post-operative polyuria is excretion of excess fluid given during surgery and an osmotic diuresis as a result of treatment for cerebral oedema.

Close monitoring is vital:

- DAILY FLUID INTAKE
- DAILY URINE OUTPUT

Also measure:
- Serum electrolytes and glucose
- Urine specific gravity
- Urinary sodium
- Simultaneous serum and urine osmolality

A urine specific gravity of 1.005 or less and a urine osmolality less than 200 milliosmoles/kg is the hallmark of diabetes insipidus. Random plasma osmolality is generally greater than 287 milliosmoles/kg.

The water deprivation test is performed in ambiguous clinical circumstances, typically with more chronic forms of diabetes insipidus.

3. Management of postoperative diabetes insipidus

Treatment of postoperative diabetes insipidus should be individualised. Contact the Endocrine team at the University Hospital Aintree (Dr C Daousi or Professor IA MacFarlane or his Specialist Registrar on bleep 4128). Optimally, patients should be monitored for the development of polyuria or urine hypo-osmolality. Fluid intake and output should be carefully recorded, and patients questioned about their thirst. Once the diagnosis of cranial diabetes insipidus has been confirmed as described above, antidiuretic hormone therapy should be initiated.

Expectant monitoring

- Accurate recording of fluid intake and output
- Measurement of urine osmolality or specific gravity every 4–6 h, until resolution or stabilisation
- Measurement of serum sodium levels every 4–6 h, until resolution or stabilization

Maintenance of fluid balance

- Allow the patient to drink according to their thirst
- Supplement with hypotonic intravenous fluids—5% dextrose in water and half-normal saline—if the patient is unable to maintain normal plasma osmolality and serum sodium levels through drinking.
- Avoid hyperglycemia, volume overload, and a correction of hypernatremia that is too rapid. A good rule of thumb is to reduce serum sodium by 0.5 mmol/L/h.
Antidiuretic hormone therapy

- If the patient is not able to drink and keep up with the urinary losses then administration of desmopressin will become necessary. Desmopressin can be given intravenously or subcutaneously at an initial dose of 0.5–1 µg when urine output is > 200–250 ml/h for ≥ 2 h with urine specific gravity <1.005 or urine osmolality <200 milli-osmoles/kg H₂O. Repeat the desmopressin dose when urine output is again 200–250 ml/h for ≥ 2 h with urine specific gravity <1.005 or urine osmolality <200 milli-osmoles/kg H₂O.

Monitor for resolution of transient diabetes insipidus or triphasic response

- Positive daily fluid balance (ie >1.5-2 L) may suggest inappropriate antidiuresis.
- Antidiuretic hormone therapy should be suspended and fluids restricted to maintain serum sodium levels within the normal range.

4. Desmopressin

Desmopressin is the drug of choice for acute and chronic treatment of cranial diabetes insipidus. Treatment results in a prompt reduction of urine output and antidiuresis, which generally lasts 6–12 hours. It is important to monitor urine osmolality and volume and serum sodium level at frequent intervals to ensure that hypernatremia improves, and to determine when repeat dosing should occur. In order to avoid fluid retention and hyponatraemia, each dose of desmopressin should be given after the recurrence of polyuria, but before the patient actually becomes hyperosmolar. In general, urine excretion of 200–250 ml/h for at least two consecutive hours with urine osmolality <200 mOsm/kg H₂O or specific gravity <1.005 affirms the need for repeated treatment with desmopressin.

Patients with chronic cranial diabetes insipidus can be treated with intranasal desmopressin. The reliability of intranasal desmopressin spray can be diminished in patients with mucosal atrophy, congestion, scarring or nasal discharge, so it is advisable to wait several days postoperatively before starting intranasal desmopressin spray, especially in patients with nasal packing. Treatment should be designed to minimize polyuria and polydipsia, while avoiding hyponatremia due to overtreatment. Usual dose 10–40 micrograms daily (in 1–2 divided doses).

It is often useful to permit intermittent polyuric episodes every 1–2 weeks by delaying a dose of desmopressin, to verify the continued presence of diabetes insipidus and to allow excretion of any retained excess water.

Oral desmopressin has also been shown to be an effective treatment for CDI, and can be useful in patients with mucosal atrophy or scarring. Most patients require an oral desmopressin dose that is 20 times higher than the intranasal spray dose, because >99% of the oral desmopressin is destroyed by gastrointestinal peptidases. Most patients with CDI may require 200–600 micrograms of oral desmopressin divided in 2–3 doses per day to control polyuria. Please note the significant difference in the dose of oral desmopressin compared with intranasal desmopressin spray (oral dose x10-20 times higher than intranasal dose).
5. **Patient Education**

- Patients must be instructed in simple principles of water balance to avoid dehydration and water intoxication (if not carefully monitoring water intake).
- Patients with CDI also must take special precautions, such as when traveling, to be prepared to treat vomiting or diarrhea and to avoid dehydration with exertion or hot weather.
- All patients with CDI should be given a copy of the patient information sheet on cranial diabetes insipidus produced by the Pituitary Foundation (copies found on the neurosurgical wards and outpatient department at the Walton centre).

6. **Follow-up**

All patients with CDI after discharge from the ward should be reviewed within 2-3 weeks by the endocrine team in one of the joint pituitary clinics at the WCNN. The appointment should be arranged by the neurosurgical team in charge of the patient.

**References**


