Management of Diabetes Insipidus following Surgery for Pituitary and Suprasellar Tumors

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Abstract

Central diabetes insipidus (CDI) is a common complication of pituitary surgery. However, it is most frequently transient. It is defined by the excretion of an abnormally large volume of dilute urine with increasing serum osmolality. The reported incidence of CDI after pituitary surgery is variable, ranging from 0-90%. Large tumor size, gross total resection, and intraoperative cerebrospinal fluid (CSF) leak usually have an increased risk of CDI as also seen with craniopharyngioma and Rathke’s cleft cysts. It can be associated with high morbidities and mortality if not promptly recognized and treated on time. It is essential to rule out other causes of postoperative polyuria to avoid unnecessary pharmacotherapy and iatrogenic hyponatremia. Once the diagnosis of CDI is established, close monitoring is required to evaluate the response to
treatment and to determine whether the CDI is transient or permanent. This review outlines the evaluation and management of patients with CDI after pituitary and suprasellar tumors surgery to help recognize the diagnosis, consider the differential diagnosis, initiate therapeutic interventions, guide monitoring, and long-term management.

**Keywords:** Central diabetes insipidus (CDI), polydipsia, polyuria, pituitary adenoma, preoperative risk factor, and pituitary surgery, arginine vasopressin, desmopressin, and treatment.

**Introduction**

Pituitary adenomas are the third most common intracranial neoplasm which account for 10-15% of all diagnosed intracranial tumors and are frequently treated with transsphenoidal surgery (TSS), except prolactinomas.¹ Neurosurgical operations for pituitary and suprasellar tumors may result in postoperative complications due to the crucial anatomical location of these tumors. The resulting postoperative complications can manifest as anterior or posterior pituitary dysfunction, particularly sodium disturbances due to the changes in antidiuretic hormone (ADH) secretion, which remains one of the most frequent postoperative reasons for hospital readmission.² The patterns of water and electrolyte disorders after transsphenoidal surgery (TSS) can be divided into either polyuria or oliguria/hyponatremia, depending on the presence of either low or high levels of ADH respectively.² Some disturbance of water and electrolytes may not reach the level of clinically defined CDI or syndrome of inappropriate antidiuretic hormone (SIADH). However, they may still require acute or chronic management and are generally divided into six profiles of polyuria or hyponatremia by some authors as follows: transient or sustained polyuria, immediate or delayed hyponatremia, and biphasic or triphasic diabetes insipidus (DI).²³ CDI manifests as excretion of large amounts of dilute urine that frequently occurs in the acute phase following surgery for pituitary adenomas, subarachnoid hemorrhage, or traumatic brain injury. Nonetheless, it occurs rarely in association with large pituitary adenomas before surgical interventions, and its occurrence in this setting should question this diagnosis and point towards other diagnoses such as craniopharyngioma or granulomatous diseases.⁴

Serum sodium and osmolality levels are generally maintained within a very narrow range (within 1–2 %) despite marked variations in water and salt intake, and this is controlled by two
mechanisms, namely the AVP and thirst. The development of CDI after TSS for pituitary adenoma is common nonetheless, it is usually transient. Most patients who have free access to fluids and have intact thirst mechanisms can maintain normal serum sodium and normal fluid balance as well as avoid dehydration and hypernatremia that usually result from the development of a significant water deficit. Hence, it is exceptionally vital to frequently monitor the urine output, serum sodium, as well as the daily fluid balance in all neurosurgical patients following TSS. When patients have impaired levels of consciousness due to different factors such as sedation or if the thirst mechanism is impaired, such as in the rare subtype of adipsic DI, patients can develop significant water deficit and severe hypernatremia.5,6

The measurement of copeptin as a surrogate marker for AVP in the diagnostic workup of the three main causes of polyuria, i.e. CDI, nephrogenic diabetes insipidus (NDI) and primary polydipsia has revolutionized the management approach of the patients with these suspected conditions, given its stable assays, high diagnostic accuracy, and high specificity.7-10 Due to a scarcity of studies comparing different treatment and monitoring strategies for acute CDI following transphenoidal pituitary surgery, there is a general lack of clear guidelines based on grades of evidence for acute DI post TSS management, which hasn’t changed much in the past decade. Nonetheless, there has been increasing adverse events, including death, which has been highlighted in recent years for the patients with established CDI, mainly due to poor knowledge or a total lack of knowledge of health professionals dealing with this condition.11 Hence, there is a need to update the knowledge highlighting all the pitfalls that can lead to adverse patient outcomes.

The rationale for this review article is to present updated information regarding the frequency, predictors of occurrence, clinical presentation, diagnostic workup, including the role of measurement of copeptin, which fills an important gap that exists regarding the limitation of water deprivation test in differentiating between CDI and primary polydipsia. We will also review the therapeutic interventions for CDI, including those used for treating the rare and serious subtype of adipsic DI, as well as the prognosis of CDI after TSS.

Epidemiology
CDI is a significant complication after pituitary surgery, and it has been reported in the medical literature. Transient diabetes insipidus (TDI) has been reported in 1.6–45.6% of the patients after pituitary surgery with a transnasal microsurgical approach and in 2.5–26% in those who had surgery with the transnasal endoscopic approach. Permanent diabetes insipidus (PDI) is less common and has been reported in 0–10% in patients following the microsurgical approach and in 0–12.5% in patients following the endoscopic approach. The evidence is inconsistent regarding whether endoscopic TSS is associated with a lower incidence of diabetes insipidus in comparison to microscopic TSS, with some studies showing a lower incidence while some do not. One study investigated the DI after transcranial pituitary surgery and found the incidence of TDI and PDI to be 21.1% and 12.2%, respectively. CDI is more common after craniopharyngioma surgery and has been reported in up to 90% of the patients. Additionally, DI occurs in the acute phase of traumatic brain injury (TBI) in 20% of cases and 15% of the cases of subarachnoid hemorrhage (SAH). CDI in the vast majority of cases of TBI and SAH is transient. Persistent CDI in the setting of TBI and SAH is usually a late manifestation of severely raised intracranial pressure (ICP) and in this context has a very grave prognosis.

**Predictors**

Early detection of CDI can be meaningful to patients’ care and outcomes after pituitary surgery. Diabetes insipidus after pituitary surgery is reported to be associated with 3.9-fold increase in patients’ mortality. Therefore, risk factors for CDI after pituitary surgery have been explored in several studies. The factors that may predict both transient and permanent DI include craniopharyngioma, Rathke’s cleft cysts, larger tumor size, low postoperative copeptin levels, and intraoperative cerebrospinal fluid (CSF) leak. Other factors that have been shown to predict TDI only include ACTH-producing adenoma, visual abnormalities on presentation, suprasellar tumor extension, gross total resection, postoperative CSF leak, and first postoperative serum sodium of > 145 mmol/L. In contrast, predictors of PDI only include younger age, reoperation, the former likely due to large tumor mass, while the latter due to the possible injury to the neurohypophysis and/or stalk traction. After the transcranial pituitary surgery, the degree of deformation of the third ventricle and hypothalamus as assessed by preoperative magnetic resonance imaging and postoperative hemorrhage was associated with both transient and permanent DI.
**Presentation and Diagnosis**

**Clinical presentation**

CDI should be considered when a patient excretes large volumes of diluted urine after surgery, typically ranging from 3.5–16.8 L per day,\(^{27}\) in the presence of high or normal serum sodium and osmolality. The onset of polyuria is usually abrupt and occurs within the first 12–24 h after surgery.\(^{28}\) However, later presentation (2 weeks to 3 months post-surgery) has been reported in patients with Rathke’s cleft cyst.\(^{29}\) The pathophysiology of this is not well understood but was suggested to result from the release of cyst contents, causing inflammation to the infundibulum.\(^{30}\)

Polyuria is the hallmark of CDI. However, not all patients with polyuria after pituitary surgery have CDI as polyuria could result from the reactive postoperative diuresis in patients who received excess amounts of intravenous fluids during surgery. It is also essential to rule out other common causes of polyuria such as hyperglycemia and diuretics use before labeling a patient with CDI. The classic triphasic water dysregulation is rare and occurs in approximately 1.1-3.4 % of the postoperative patients where transient DI, a polyuric phase occurring due to the abrupt cessation of AVP release as a result of the temporary hypothalamic dysfunction, is followed by the second phase that resembles the syndrome of inappropriate antidiuretic hormone secretion (SIADH), which is caused by the sudden release of AVP from the degenerating pituitary. Finally, depletion of AVP stores leads to permanent CDI.\(^{31,32}\) The onset of polyuria is usually abrupt and occurs within the first 12–24 h after surgery. The initial transient phase of DI happens within 1 and 3 days after surgery and typically lasts for 5 to 7 days. The second phase will ensue 7 to 8 days postoperatively and can last for 2 to 14 days if there is no recovery of ADH-secreting neurons. The third phase occurs when DI reappears as result of depletion of ADH stores.\(^{33-36}\)

Patients with DI will typically complain of persistent excessive thirst and will drink to compensate for the water loss to maintain serum sodium within the normal range. However, patients with limited access to water, impaired consciousness level or impaired thirst sensation may rapidly develop signs of dehydration on physical examination in addition to hypernatremia (serum sodium >145 mmol/L) if free water loss is not replaced.\(^{37,38}\)
**The diagnostic workup**

The diagnosis of CDI postoperatively starts with the risk assessment using pre- and intraoperative predictive factors before the patient is transferred from the operation room.

Excessive thirst and polyuria are the clinical features that typically trigger an evaluation for CDI.\(^{39}\) Hence, careful documentation of hourly fluid intake and urine output is essential for the early identification of CDI. It is crucial to keep in mind that polyuria may not always be due to DI; it can also be due to a sharp drop of GH level post acromegaly surgery, and the use of certain medications like furosemide or SGLT2 inhibitors\(^ {40}\) as seen in cases of mobilization of intraoperative fluids and hyperglycemia. Therefore, documentation of hypotonic polyuria is essential in establishing the diagnosis of DI. Seckel and Dunger criteria to diagnose CDI relies on the presence of hypotonic polyuria (urine osmolality <300 mOmol/kg and urine output more than 2 mL/kg/hr) in addition to increased serum osmolality (>300 mOsmol/kg) after excluding other causes of polyuria, such as glucosuria.\(^ {41}\) In adult patients, in particular, urine output of more than 250 mL per hour for two consecutive hours when supplemented with the presence of normal or high serum sodium, normal or high serum osmolality with a urine osmolality of less than 300 mOsmol/kg is highly suggestive of DI.\(^ {42}\) Urine specific gravity is quickly done at the bedside and could provide a quicker evaluation of urine tonicity with a value of less than 1.005 suggests low urine osmolality.\(^ {43}\)

However, despite the availability of all these tools, the diagnosis of post-pituitary surgery CDI could be a challenge due to several factors. First, there is a lack of universal diagnostic criteria for DI, and there is enormous variability in monitoring patient’s post-pituitary surgery. Moreover, the current diagnostic criteria may not apply to patients who are able to consume water and self-manage CDI, especially if the DI is partial. Furthermore, thin adults could have DI, but their urine output is <200 mL/hour, which may delay the diagnosis. For such patients, using weight-based criteria to define polyuria (urine output of >2 mL/kg/hour or >50 mL/kg/day) would be more accurate. Additionally, the frequency of monitoring electrolytes is highly variable among physicians.\(^ {44}\) Therefore, the frequent assessment of electrolytes and osmolality in patients with a decreased level of consciousness or impaired thirst sensation is necessary for early detection of CDI.
The difficulty in diagnosing CDI, particularly in the immediate postoperative period, has led to the exploration of other ways to diagnose CDI. Plasma AVP measurement has been explored, however, it could be challenging as its half-life is short (16 minutes), and the AVP is usually unstable in collected plasma samples and is affected by many factors leading to inaccurate AVP level. Moreover, AVP measurement with ELISA is not usually feasible due to the small size of AVP. Also, AVP measurement, usually by RAI and requiring relatively large sample volume, is not available timely to diagnose DI as it relatively requires a long time and specialized labs to process it. For these reasons, AVP measurement is rarely useful in the diagnosis of postoperative DI.

Copeptin is the C-terminal peptide of pro-vasopressin, co-secreted with AVP in an iso-osmolar manner, and reflects AVP level accurately. Unlike AVP, copeptin measurement is less cumbersome as it remains stable in collected plasma samples for days and its measurement is associated with less preanalytical errors. Copeptin is highly accurate in identifying the etiology of polyuria in the non-acute setting. However, its utility in the post-pituitary surgery setting has been evaluated in a few studies only. A multicenter study of 50 out of 205 patients who developed CDI revealed that a copeptin level of <2.5 pmol/h is accurate in establishing the diagnosis of CDI with a specificity of 97% and positive predictive value (PPV) of 81% when measured within 24 hours of surgery. In contrast, a value of >30 pmol/l almost excluded the diagnosis with a negative predictive value (NPV) of 95%. The performance of the test was better when performed <12 hours post-surgery with lower accuracy beyond 24 hours. Similarly, the test was superior in predicting persistent rather than transient DI (68% vs. 32%). Another study of 8 out of 58 patients with CDI with a standardized copeptin testing time showed that a peak copeptin level of < 12.8 pmol/l at 60 minutes post-extubation predicted CDI, while permanent CDI was excluded with 100% NPV in those with a level of >4.2 pmol/l.

Interestingly, there was no significant difference in the copeptin level between the two groups in the subsequent assessments at 6–48 hours post-extubation. Copeptin is a promising marker that will likely be a routine diagnostic test in the evaluation of CDI in the future. For the time being, the limited number of studies about copeptin use, the uncertainty about the optimal time of its measurement post-surgery, and the limited availability of the assay are factors limiting its
widespread use. Table 1 summarizes the various parameters that are frequently needed to be evaluated in post-pituitary surgery patients and the expected changes in these parameters in patients with post-operative DI. We propose a risk-based algorithm on the frequency of laboratory investigation to identify DI in the postoperative period (Figure 1).

**Treatment**

Although ADH secretion impairment and disturbance of fluid balance often begin during the intraoperative period, CDI usually presents within a few hours after surgery. It is imperative to rule out intraoperative fluid overload and glycosuria as potential causes of polyuria. It is also important to note that patients with acromegaly may experience increased urinary output following the resection of their pituitary mass due to diuresis of excess fluid within the soft tissues.55,56 Furthermore, about 50% and 80% of patients with transient DI recover within 7 and 90 days of surgery respectively.57 As such, patients are advised to monitor for the cessation of thirst sensation and resolution of polyuria as potential signs of DI recovery. Also, periodic monitoring of electrolytes can be useful to confirm DI recovery, as water deprivation tests are not routinely recommended in this situation.58 Additional advice is to delay DDAVP dose for few hours to see if increased thirst and polyuria persists.58

Patients require continuous monitoring of fluid intake, urine output, and frequent assessment of electrolyte. Desmopressin should be used cautiously as required, especially during the first two weeks postoperatively to avoid hyponatremia due to over replacement.32 Treatment of postoperative CDI is multifaceted and can be divided into acute or chronic phases, depending upon the stage of the disease to restore osmotic equilibrium. Although specific guidelines related to the management of post-operative DI are unavailable, in recent past a disease state review followed by guidelines on hypopituitarism was published giving some guidance to the clinical management.43,59 The general strategies of management of CDI are given in Table. 2. The acute phase management covers the first two phases of the triphasic water dysregulation phenomenon.
Acute Management of Central DI

Free water access

The management is straightforward, provided there is an intact thirst mechanism; the patient is not receiving fluids for any reason and can drink water at will. Water balance can be achieved under such a situation as long as the patient can consume enough fluids. In patients with a decreased level of consciousness, impaired thirst mechanisms or those on intravenous (IV) fluids will require continuous adjustment of IV fluids and pharmacotherapy to maintain adequate hydration and sodium equilibrium. The appearance of hypernatremia and polyuria along with dehydration heralds the onset of CDI. It should be aggressively sought out during the immediate post-operative period as hypernatremia can cause brain shrinkage leading to vascular rupture and intracranial bleeding along with other complications.

The serum sodium level can be normalized safely at a correction rate of 1 mEq/l/hr without any untoward complications. Hypotonic fluids should be used when intravenous fluids are mandated. Least amount of fluid possible should be used and rapid overcorrection must be avoided as it can lead to cerebral edema.

Vasopressin

Vasopressin is available as an aqueous solution. Due to its short half-life of around 20 min, it should be given through IV infusion when acute control of antidiuresis is needed. Infusion is usually started at a rate of 0.25 to 1.0 micro unit/kg/hour and titrated every half hour after that to maintain urine output rate around 100 mL/hour and/or urine specific gravity around 1.010 to 1.020.

Desmopressin

Desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP) is a synthetic analogue of vasopressin, having a prolonged action profile with minimal vasopressor activity. It can be given orally, intranasally, subcutaneously, or intravenously. Studies have shown a definite relationship between the magnitude and duration of its therapeutic effect and its IV dosage. In patients with CDI, one microgram IV "push" infusion can increase urine osmolality to a maximum of 700–800 mOsmol/kg. Further increase in dose from 1 to 8 micrograms only led
to prolongation of the duration of action from around 26 hours to 46 hours. The magnitude and
duration of its therapeutic effects showed large interindividual variability attributed to
individual differences in renal concentration abilities as it persisted even when the dose was
increased to more than two micrograms. Further studies have shown that the antidiuretic efficacy depends on the total dose as well as the
rate of increase in plasma DDAVP level. The human kidney loses concentrating capacity in the
absence of vasopressin. Therefore, once treatment is initiated, it requires at least 8 hours of
continued therapy for full recovery. Based on several studies, the parenteral DDAVP can be
administered safely to acutely ill patients of CDI. However, the needed dose depends on the
individual response, intactness of thirst mechanism, and other factors determining fluid intake. In
patients with intact thirst mechanisms, a starting dose of 0.25 to 0.50 micrograms twice daily as
an IV infusion over 2 hours is usually administered, which is adjusted further to normalize urine
output and maintain sodium equilibrium. A smaller dose of 0.06 to 0.125 micrograms is usually
preferred with further titration to the desired effects for patients who are unable to drink at will
or are on IV fluids. Although hyponatremia can be a manifestation of excessive DDAVP
administration, the second phase of the triphasic water dysregulation phenomenon also presents
with hyponatremia. Both of these have the same underlying mechanism and management
principles that require withholding DDAVP along with careful electrolytes and fluid balance
monitoring.

**Chronic Management of Central DI**

Since CDI rarely remits once established, it requires continuous, complete, around-the-clock
management of the polyuria and maintenance of sodium and water equilibrium. Hypernatremia
rarely goes unnoticed as it is always associated with polyuria and dehydration. Management
principles of hypernatremia are same as mentioned above, however in case the duration of
hypernatremia cannot be ascertained correctly, the serum sodium level should be corrected at a
rate of 0.5 mEq/L/hr, with no more than an 8 to 10 mEq/L decrease over 24 hours while
keeping the target sodium level to be 145 mEq/L.
Minimizing the risk of hyponatremia due to excessive water retention is another critical challenge as it can be symptomatic occasionally and, rarely, life threatening. Excessive fluid consumption suppresses vasopressin secretion in normal subjects by non-osmotic mechanisms,\textsuperscript{75,76} leading to diuresis and thus preventing over-hydration. This ‘escape’ mechanism is not possible in patients with CDI as they are on exogenous long-acting desmopressin. Consequently, dilutional hyponatremia occurs. Longer-acting form of antidiuretic therapy and limiting fluid intake to the amounts required to satisfy thirst are the possible ways to achieve this goal. Titration of antidiuretic dose to keep 24 hours urine output above the normal range (15 to 30 mL/kg/d) is equally important.\textsuperscript{77}

**Desmopressin – DDAVP nasal spray**

Intranasal DDAVP has an absorption ratio of around 10–20% when compared to IV preparation in patients with CDI.\textsuperscript{78} Also, it has interindividual and intraindividual variability in the magnitude and duration of its antidiuretic effect. The variability is irrespective of age, the severity of polyuria, or bodyweight\textsuperscript{79,80} leading to the duration of action ranging from 4–18 hours to 8–24 hours seen with 5–10 and 20 micrograms respectively.\textsuperscript{70,81,82} The intranasal preparation is useful as it allows individualization of treatment and dose titration by metered-dose spray (2.5–10 microgram per spray). It is important to note that the absorption of nasal DDAVP may be decreased in the setting of nasal inflammation and rhinorrhea, such as in upper respiratory tract infections, and therefore patients might need to use extra doses or shift to other routes if polyuria and dehydration are present.

**Desmopressin oral tablets**

Due to their large molecular size and susceptibility to enzymatic degradation coupled with short plasma half-life, vasopressin and DDAVP were considered initially to be unsuitable for oral use. However, despite low oral bioavailability of around 16\textsuperscript{83} a stable antidiuretic effect with a clear dose-response relationship has been observed in clinical trials,\textsuperscript{84} and preparation strengths (0.1, 0.2, and 0.4 mg) are available for oral use. DDAVP oral doses required for equivalent antidiuretic efficacy are around 10–20 times of the intranasal doses; however, the ease of administration makes oral formulations the preferred route of treatment for most patients. Although individualization of therapy and titration of the dose is needed, 0.1 to 0.2 mg every
eight hourly is the usual maintenance dose,\textsuperscript{81} while less frequent dosing, such as once or twice daily, is generally sufficient for infants and children.\textsuperscript{85}

**Desmopressin oral formulations—oral melt**
Since 2005, DDAVP has been available as a sublingual lyophilizate (MELT) formulation containing 60, 120, and 240 micrograms having bioavailability around 25%.\textsuperscript{86} In a recent study, DDAVP Melt has shown a similar level of antidiuretic control and was found to be as efficacious as intranasal DDAVP in both children and adults.\textsuperscript{87}

**Cdi in Special Populations**

**Neonatal/infants/children**
The treatment of CDI in this group requires consideration of their diets which contains a proportionally larger amount of water. Therefore, to prevent hyponatremia, urine volume must not be reduced too much and it needs careful dose titration with close input/output and plasma sodium monitoring. Continuous intravenous infusion of low dose DDAVP (0.1–0.2 microgram s.c./i.m)\textsuperscript{88} or arginine ADH (0.25–3 mU/kg/h) under intensive monitoring\textsuperscript{89} is often used in the first 24–48 h post-operatively. Once CDI is stable and permanent, regular DDAVP can be prescribed. Diluted rhinyl preparation of nasal spray in the amount containing 1 to 5 micrograms of DDAVP once or twice daily usually provides good control of CDI in infants.\textsuperscript{90} DDAVP can be given subcutaneously in doses ranging from 0.02 to 0.08 micrograms once or twice daily.\textsuperscript{91} Children and their parents need to be educated about the features of water intoxication and the hazards of excessive fluid intake.

**Pregnancy and lactation**
DDAVP being resistant to placental leucine aminopeptidase can be administered safely to pregnant women, both for gestational DI as well as patients with pre-existing CDI getting pregnant.\textsuperscript{92,93} Compared to non-pregnant women, the doses needed are usually the same or slightly higher. Placental leucine aminopeptidase usually disappears in 4–6 weeks postpartum when DDAVP can be discontinued in patients with gestational DI. It should be borne in mind during the monitoring of therapeutic effects that serum sodium level during pregnancy decreases
typically by approximately 5 mmol/L compared to the nongravid state. As DDAVP appears in a very tiny amount in breast milk, it can be continued during lactation.\textsuperscript{94}

**Elderly**

As mentioned above, CDI requires lifelong management, and even if the underlying cause is eliminated, CDI once established rarely remits. The treatment of CDI in the elderly does not differ much from that in young adults, though they face a higher risk of developing hyponatremia, primarily when intranasal DDAVP is used.\textsuperscript{79} The etiology is not clear at present. Abnormalities of osmoregulation of thirst and fluid intake along with increased renal sensitivity to DDAVP may be the possible explanation as this population is known to be affected by these factors.\textsuperscript{95}

**Hypodipsia/Adipsia with CDI**

Anterior hypothalamus injury leading to osmoreceptor damage culminates in the absence or deficiency of thirst and results in the rare entity of adipsic DI. As a result, these patients have neither of the homeostatic mechanisms required for water balance regulation. Consequently, their management becomes difficult, and they suffer from wide fluctuation in serum sodium levels.\textsuperscript{96} In addition, during acute illnesses, patients can develop life-threatening hypernatremia, resulting in somnolence, seizures, hemiplegia, coma, and acute renal failure and can be associated with thrombotic episodes. Furthermore, other complications such as obesity, sleep apnea, which is largely attributed to hypothalamic abnormalities may be seen in association with adipsic DI, and these conditions contribute to the excess morbidity and mortality found in a patient with adipsic DI.\textsuperscript{97} It becomes necessary to prescribe fluid intake on a sliding scale based on daily weight and serum sodium level\textsuperscript{98} DDAVP alone or in combination with hydrochlorothiazide are useful agents.

An alternative and more practical approach is to set a target weight (kg) at which the patient is known to be euvolemic and normonatremic and maintain fixed urine output at 1.5–2L with a fixed amount of DDAVP. Furthermore, daily fluid intake can be titrated as obligate load (1.5L in temperate climates) + (target weight – daily weight) to maintain volume status, sodium, and osmolality within the defined range.\textsuperscript{99} Successful treatment can be achieved through daily
measurement of body weight and probably weekly serum sodium measurement along with careful monitoring and patient and family education. Additionally, due to the high rates of venous thrombosis and thromboembolism in patients with adipsic DI, it is recommended to give low molecular weight heparin during periods of hypernatremia dehydration. Also, screening for sleep abnormalities is indicated. The principles of management of adipsic DI are given in Table 3.

Conclusions
CDI is a frequent complication that occurs in patients who undergo surgery for pituitary and suprasellar tumors and is the commonest leading cause for hospital readmission of these patients. Therefore, clinicians dealing with these patients need to perform a thorough preoperative risk assessment in order to identify known predictive factors for CDI, such as patients with craniopharyngioma and those with larger tumors, in order to have clear strategies in place for early diagnosis and management. Moreover, post-operative evaluation should be done in the early and late postoperative periods in order to reduce the risk of complications and unnecessary readmissions to the hospital. While the management of CDI that complicates surgery for pituitary and suprasellar tumors is a commonly encountered topic, nonetheless, it remains a challenging area for clinicians and requires high standards of medical knowledge together with very good clinical experience and skills, especially regarding the decision about when to start desmopressin therapy and for how long as well as planning the long term follow up for those who develop permanent CDI.

Conflict of interest
None

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Table 1: Biochemical parameters in patients with postoperative DI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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<tbody>
<tr>
<td>Fluid balance</td>
<td>Variable, usually negative (more output than input)</td>
</tr>
<tr>
<td>Urine output</td>
<td>At least &gt;250 cc/hour for 2 consecutive hours in addition to other parameters</td>
</tr>
<tr>
<td>Serum osmolality</td>
<td>Normal (if the patient has free access to water) or high &gt; 300mOsmol/kg (if the patient has limited access to water)</td>
</tr>
<tr>
<td>Serum Sodium</td>
<td>Normal (if the patient has free access to water) or high &gt;145 mmol/l (if the patient has limited access to water)</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>Persistently &lt;300mOsmol/L</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>Persistently &lt;1.005</td>
</tr>
<tr>
<td>Copeptin</td>
<td>&lt;2.5pmol/l</td>
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Table 2: General management strategies for a patient with CDI

**Immediate postoperative period:**
- Assessment of volume and hydration status; and measurement of serum sodium
- Close monitoring of serum sodium and urine output
- Optimizing fluid replacement
- Consideration of desmopressin therapy in a patient with excessive, inappropriately dilute urine output
- Titration of desmopressin dose to keep 24 hours urine output above the normal range (15 to 30 mL/kg/d)

**After hospital discharge:**
- Limiting fluid intake to the amounts required to satisfy thirst
- Performing electrolyte panel checks in any unwell patient after hospital discharge. Close postoperative follow-up
- Patient should be monitored for water intoxication and hyponatremia.
- Delay a dose of desmopressin once or twice per week to allow an aquarexis to occur
- Regular patient and their family counseling about the principle of the treatment regime
Table 3: Management of hypodipsia/adipsia with CDI [100]

<table>
<thead>
<tr>
<th>Step</th>
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<tr>
<td>Set a target weight (kg) at the weight the patient is known to be euvolemic and normonatremic</td>
</tr>
<tr>
<td>Fix 24 hours urine output at 1.5-2 L</td>
</tr>
<tr>
<td>Determine the obligate fluid intake (Approximately 1.5L)</td>
</tr>
<tr>
<td>Measure weight daily</td>
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<tr>
<td>Daily water intake = obligate volume + (target weight - daily weight)</td>
</tr>
<tr>
<td>Check plasma sodium weekly</td>
</tr>
<tr>
<td>Educate patients and their family about the principle of the treatment regime</td>
</tr>
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Fig.1 Post pituitary surgery evaluation (Risk-based assessment)
U=urine, S=serum, LOC=level of consciousness, PRN=as needed