

Transurethral Resection of the Prostate Syndrome: Almost Gone but Not Forgotten

Amr Hawary, M.Sc. (Urol), MRCS,¹ Karim Mukhtar, M.Sc. (Anesth), FRCA,²
Andrew Sinclair, FRCS (Urol),¹ and Ian Pearce, FRCS (Urol)¹

Abstract

Transurethral resection of the prostate (TURP) syndrome is a rare but potentially fatal syndrome with multifactorial pathophysiology that is now better understood. Unfortunately, despite this improved understanding, it is not yet obsolete and still remains a risk. Many reviews of TURP syndrome have been presented from an anesthetic perspective; this review reflects more the urologic perspective with emphasis on the importance of multidisciplinary management of this complex syndrome. We present a review of TURP syndrome that specifically assesses advances in the understanding of risk factors, pathophysiology, and techniques used to prevent this syndrome. The databases Medline, Embase, Cochrane Controlled Trial Register, and Database of Abstracts of Reviews of Effects were systematically reviewed from inception to April 2009 for the keywords TUR (P), TUR (P) syndrome, and transurethral resection of prostate. There was no language restriction for our search. Randomized controlled trials, review articles and case series were included in our search. Our review showed a declining trend in the incidence of TURP syndrome despite TURP remaining the gold standard for the management of benign prostatic obstruction. Technologic advances using an array of laser techniques, the use of bipolar circuitry, together with advances in training techniques have helped minimize the risk of development of this syndrome.

This review demonstrates the complexity of TURP syndrome. Even with a greater understanding of the pathophysiology, it highlights the unpredictability of the syndrome from presenting symptoms, preventative measures, and management. TURP syndrome cannot be protocol driven and the need for vigilance, a high index of suspicion, intensive monitoring, and a multidisciplinary approach is vital.

Introduction

WATER INTOXICATION was first reported by Wier and associates¹ in 1922 as excess water intake that results in consciousness disorders and convulsions; however, its management has evolved over the years, as our understanding of the underlying pathophysiology has increased.

Transurethral resection (TUR) syndrome is an iatrogenic form of water intoxication, a combination of fluid overload and hyponatremia that is seen in a variety of endoscopic surgical procedures, although classically after transurethral resection of the prostate (TURP). It occurs when irrigating fluid is absorbed in sufficient quantity to produce systemic manifestations.

Although most commonly seen during or after TURP, TUR syndrome has also been reported after transurethral resection of bladder tumors,² diagnostic cystoscopy,³ percutaneous ne-

phrolithotomy,⁴ arthroscopy,⁵ and various endoscopic gynecologic procedures that use irrigation.^{6,7}

Several studies in the last 20 years have shown the incidence of mild to moderate TUR syndrome to be between 0.5% and 8%^{8–10} with a reported mortality rate in the region of 0.2% to 0.8%.^{11,12} Recent larger studies have demonstrated lower incidence rates of between 0.78% and 1.4%.^{13,14}

Severe TURP syndrome is rare; however, its mortality rate, unlike that of milder forms, has been quoted as high as 25%.¹⁵ TURP syndrome may be seen from as early as 15 minutes after resection starts¹⁶ to up to 24 hours postoperatively.¹⁷ This long period reflects the need for the different teams that are involved in the patients perioperative and postoperative care to be aware of the early signs and symptoms of TURP syndrome to ensure that the right diagnosis is reached without delay and for the appropriate management to be instituted.

¹Manchester Royal Infirmary, Central Manchester University Hospitals, Manchester, United Kingdom.

²Royal Liverpool and Broadgreen University Hospitals, Liverpool, United Kingdom.

Presentation

TURP syndrome is multifactorial, initiated by the absorption of irrigation fluid that leads to cardiovascular, central nervous system (CNS), and metabolic changes. The clinical picture varies according to its severity and is influenced by the type of irrigant used as well as patient and surgical factors. These multiple influencing factors help to explain the lack of a classical presentation for TURP syndrome. Signs and symptoms (Table 1) are often vague, variable, and nonspecific, making it a challenging diagnosis for the unknowing or the unexpected.

One of the earliest signs reported is transient prickling and burning sensations in the face and the neck together with lethargy and apprehension; the patient may become restless and complain of a headache. The most consistent signs are bradycardia and arterial hypotension, which may be detected in the perioperative period by the anesthesia team. A general nonspecific sense of being unwell is slightly more common than perioperative nausea or vomiting, which is reported in about 10% of patients.¹⁸ Abdominal distention secondary to absorption of the irrigating fluid through perforations in the prostatic capsule may also occur.¹⁹

In the later postoperative period, nausea and vomiting, visual disturbances, twitches, and focal or generalized seizures and altered states of consciousness ranging from mild confusion to stupor and coma have also been reported.^{20–22} The cause of these CNS disturbances has been attributed to hyponatremia, hyperglycinemia, and/or hyperammonemia. Hyponatremia may occur when any type of irrigating fluid is used, but hyperglycinemia and hyperammonemia occur exclusively with the use of glycine.²³

There are several reports in the literature documenting visual disturbances as a complication of TURP syndrome, but this only appears to occur when glycine is used in combination with severe hyponatremia. The visual symptoms range from “dim vision” to temporary blindness lasting for several hours.^{24,25}

Pathophysiology

The pathophysiology of TURP syndrome is complex and often fails to follow a set pattern of events. This makes the understanding of the pathophysiology and the different possible symptoms and signs together with identifying the high-risk patients of utmost importance.

TABLE 1. SIGNS AND SYMPTOMS OF TRANSURETHRAL RESECTION OF THE PROSTATE SYNDROME

<i>Central nervous system</i>	<i>Cardiovascular and respiratory</i>	<i>Metabolic and renal</i>
Restlessness	Hypertension	Hyponatremia
Headache	Tachycardia	Hyperglycinemia
Confusion	Tachypnea	Intravascular hemolysis
Convulsions	Hypoxia	Acute renal failure
Coma	Frank pulmonary edema	
Visual disturbances	Hypotension	
Nausea and vomiting	Bradycardia	

Fluid overload

The absorption of small volumes of irrigating fluid via the prostatic sinuses occurs in almost every TURP.²⁶ The uptake of 1 L of irrigant into the circulation within 1 hour corresponds to an acute decrease in the serum sodium concentration of 5 to 8 mmol/L and heralds a statistically increased risk of absorption-related symptoms.^{27,28}

Both hypertension and hypotension may occur with TURP syndrome; hypertension and reflex tachycardia are explained by the rapid volume expansion that can reach up to 200 mL/min. Patients with poor left ventricular function may, in addition, have pulmonary edema from acute circulatory overload.²⁹

Transient hypertension, which may be absent if bleeding is profuse, can be followed by a more prolonged period of hypotension,^{30,31} for which there are several theories. Hyponatremia coupled with hypertension may lead to net water flux along osmotic and hydrostatic pressure gradients out of the intravascular space and into the pulmonary interstitium, triggering pulmonary edema and hypovolemic shock.³² The release of endotoxins into the circulation and the associated metabolic acidosis may also contribute to the hypotension.^{10,33}

Hyponatremia

The symptoms of hyponatremia are related to both the severity and the speed by which the plasma sodium concentration falls. Only rapid high-volume absorption can produce the very low serum sodium concentrations typical of severe TURP syndrome.³⁴ A drop in serum sodium concentration to <120 mmol/L liter⁻¹ defines severe TURP syndrome.²⁰ This decrease in sodium concentration creates an osmotic gradient between intracellular and extracellular fluid within the brain, which results in a fluid shift away from the intravascular space leading to brain edema, raised intracranial pressure, and neurologic symptoms.³⁵ Severe and rapidly evolving hyponatremia may manifest with seizures, coma, permanent brain damage, respiratory arrest, brain stem herniation, and ultimately death.³⁶

Hypo-osmolality

The main physiologic determinant of CNS deterioration is not hyponatremia itself, but acute hypo-osmolality. This is to be expected, because the blood-brain barrier is virtually impermeable to sodium but freely permeable to water.³⁷ The brain reacts to hypo-osmotic stress with intracellular decreases in sodium, potassium, and chloride.

The decrease in intracellular sodium, potassium, and chloride helps to reduce intracellular osmolality and prevent swelling.³⁸ Brain edema is a serious issue, and development of cerebral herniation a few hours postoperatively is a major cause of death from fluid absorption.³⁷

Hyperammonemia

Glycine gains entry into the intravascular space and is metabolized in the portal bed and kidneys via oxidative deamination.³⁹ The brain also contains a glycine cleavage enzyme system that splits glycine into carbon dioxide and ammonia.⁴⁰ The increase in serum ammonia levels

during endoscopy is secondary to glycine absorption illustrated by the fact that hyperammonemia does not develop in patients undergoing retropubic resections without glycine.³⁵

Hyperammonemic encephalopathy may develop as a result of the formation of glyoxylic acid and ammonia.⁴¹ Blood ammonia concentrations $>100 \mu\text{mol/L litre}^{-1}$ (normal range 10–35) are associated with neurologic signs and symptoms.²⁶

Irrigation Fluids

An ideal irrigating fluid should be isotonic, nonhemolytic, electrically inert, nontoxic, transparent, easy to sterilize, and inexpensive.⁴² Unfortunately such a solution does not exist, and each irrigating fluid comes with its own potential complications. Several irrigation fluids have been used and abandoned over the years. Glycine, Cytal, and physiologic saline are still commonly used by a large number of urologic surgeons worldwide.

Glycine

Glycine is a nonessential amino acid with a plasma concentration of 0.3 mmol/L in humans and is metabolized in the liver into ammonia. 1.5% glycine is almost universally used as an irrigation solution in traditional therapeutic endoscopic urologic procedures. It is nonconductive, nonhemolytic, and has a neutral visual density; however, it is hypotonic with an osmolality of about 220 mmol/L compared with plasma osmolality of approximately 290 mosm/L.

Glycine has been shown to reduce the vitality and survival of isolated cardiomyocytes⁴³ and has been associated with subacute effects on the myocardium, manifested as T-wave depression or inversion on electrocardiography for up to 24 hours after surgery.⁴⁴ Absorption exceeding 500 mL has been shown to double the long-term risk of acute myocardial infarction.⁴⁵

Glycine is also an inhibitory neurotransmitter in the retina; hence, absorption of large amounts leads to slowing down of the transmission of impulses from the retina to the cerebral cortex. Prolongation of visual-evoked potentials and deterioration of vision occur after the absorption of as little as a few hundred mL of 1.5% glycine irrigation.⁴⁶ TURP blindness is caused by retinal dysfunction from glycine toxicity.¹⁵

Glycine may also exert toxic effects on the kidneys.⁴⁷ Hyperoxaluria from metabolism of glycine into oxalate and glycolate has been proposed as a route whereby glycine may induce renal failure in susceptible patients.⁴⁸

Cytal solution

Cytal solution is a combination of 2.7% sorbitol and 0.54% mannitol and has gained popularity in the United States as an irrigating fluid. It is nonelectrolytic hypo-osmolar with an osmolality of 178 and is rapidly cleared from the plasma. It is, however, expensive, and sorbitol is metabolized to fructose, which may itself cause reactions in patients with fructose hypersensitivity. Fructose may also induce coma in patients with liver disease.⁴⁹

Physiologic saline

Physiologic saline cannot be used as an irrigating fluid during standard prostatic resection, because its ionic content

dissipates the current, preventing both cutting and coagulation. It is mainly used for irrigation with the bipolar resectoscope, but can cause hyperchloremic acidosis because of excessive chloride content.⁴⁰

Management of TURP Syndrome

A high index of suspicion for the development of TURP syndrome must be present in the minds of both the urologic surgeon and the anesthetist as its management burden is their shared responsibility along with other medical teams.

Most patients who are undergoing TURP, transcervical resection of the endometrium, or TUR of bladder tumors are elderly. The functional capacity of organs reduces with age, resulting in a reduced reserve and less ability to endure stress. Coexisting diseases further depress organ function and reserve, exacerbating risk.⁵⁰

The ability of the kidneys to balance sodium and water is impaired in elderly patients as a result of low plasma renin activity, urinary and blood aldosterone levels, and a decreased response to antidiuretic hormone. Fluid replacement should be controlled within normal maintenance levels.⁵¹

Therefore, in the presence of cardiac or renal disease, intravenous fluids should be cautiously administered in elderly patients who are undergoing endoscopic surgery to reduce the risk of and prevent exacerbation of TUR syndrome.⁵⁰

Monitoring

Estimating the amount of irrigation fluid that is absorbed during an endoscopic procedure is the key to assessing the potential risk of development of TURP syndrome. In simplistic terms, the difference between the amount of irrigating fluid used and the volume recovered can be used as a guide to fluid absorption (volumetric fluid balance), but factors such as blood loss, irrigant spillage, urinary excretion, and hemodilution make this a very inaccurate measure.⁵²

Ethanol monitoring method. Measurements of the 1% ethanol concentration in exhaled breath can be easily made during surgery. Ethanol may be added to the irrigating fluid and its level can be measured in exhaled breath, which reflects the amount of irrigating fluid absorbed. This method is sensitive enough to detect approximately 75 mL of fluid absorption per 10 minutes of surgery. Ethanol monitoring can be used whether the patient receives a spinal or general anaesthetic and can be used irrespective of pulmonary function and in the presence of chronic obstructive pulmonary disease, which is common in elderly patients who are undergoing TURP.^{53,54}

Central venous pressure monitoring. The absorption of irrigating fluid into the circulation is mirrored by an instant rise in central venous pressure (CVP). Approximately 500 mL of fluid must be absorbed within 10 minutes to increase the CVP by 2 mm Hg.⁵⁵ The CVP, however, is also affected by the volume of blood loss and intravenous fluid administration and, hence, is not an absolutely accurate means of assessing fluid absorption and the risk of TURP syndrome.¹⁰

Gravimetry method. This requires that the patient undergo surgery on a bed-scale and relies on the assumption that any increase in body weight is caused by fluid absorption. The

method must take blood loss and all intravenous infusions into account, and recordings must be made when the bladder is empty.⁵⁶

Prevention

Different measures have been proposed to minimize the incidence of TURP syndrome; unfortunately none of these measures can completely and reliably prevent its occurrence.

Patient position on the operating table

Decreasing both the hydrostatic pressure within the bladder and the prostatic venous pressure leads to a reduction in the volume of irrigating fluid that is absorbed into the circulation. In the Trendelenburg position (20 degrees), the intravesical pressure needed to initiate absorption is 0.25 kPa (approximately equal to 2.5 cm H₂O) increasing to 1.25 kPa in the horizontal position. Thus, the risk of TUR syndrome increases with the Trendelenburg position; hence, the importance of patient positioning on the operating table, especially in high-risk patients.⁵⁷

Operative time

Although massive fluid absorption has been documented to occur within 15 minutes of the start of surgery,³⁰ it is recommended that the operative time be limited to less than 60 minutes. Mebust and colleagues⁵⁸ retrospectively reviewed 3885 patients who underwent TURP and found that with a resection time more than 90 minutes, the incidence of intraoperative bleeding was significantly higher (7.3%) with an incidence of development of TURP syndrome of 2% compared with the group with a resection time of less than 90 minutes in which the incidence of intraoperative bleeding was only 0.9%, with a TURP syndrome incidence of 0.7%.

Prostate gland size

Mebust and coworkers⁵⁸ also reported that patients with gland sizes larger than 45 g were at a greater risk of TURP syndrome development (1.5% compared with 0.8%), perhaps explained by the fact that larger glands need longer resection time and are usually subject to greater blood loss with higher levels of irrigant absorption.

Fluid bag height

The optimum and safe height of the irrigating fluid during TURP remains a controversial issue in urology with a variety of contradicting reports and recommendations. Madsen and Naber⁵⁹ demonstrated that both the pressure in the prostatic fossa and the amount of the irrigation fluid absorbed depend on the height of the irrigating fluid above the patient and suggested that the optimum height should be 60 cm above the patient. They demonstrated a twofold increase in fluid absorption when the irrigant height was increased by 10 cm. This was challenged by Hahn and Ekengren,⁶⁰ who studied 550 patients who were undergoing TURP and randomly changed the irrigating fluid height between 60 and 100 cm above the patient with no reported difference in the volume of irrigant fluid absorbed at different bag heights.

In 1997, van Renen and Reymann⁶¹ studied the effect of fluid height during TURP on serum sodium and osmolality.

They randomized 40 patients in two groups with half of them undergoing TURP with an irrigating fluid height of 70 cm while in the other group, the irrigating fluid height was 150 cm. They failed to find any statistically significant change in serum sodium or osmolality during the 24-hour study period. The issue, therefore, remains unresolved.

Operative experience

A general consensus exists among urologic surgeons that greater surgical experience equates to a shorter operative time, the use of less irrigation, fewer prostatic capsule perforations, and the opening up of a smaller number of prostatic venous sinuses, thus leading to a lower incidence of fluid absorption and TURP syndrome. This theory has been recently challenged by Cury and associates,⁶² who prospectively randomized 76 patients who were undergoing TURP into three groups operated on by three groups of surgeons with differing levels of experience. TURP syndrome developed in four (6%) patients without a significant difference between the groups; interestingly, the volume of irrigating fluid used, the mean irrigating fluid absorbed, and the proportion of patients absorbing more than 1000 mL of irrigating fluid were not statistically different between the three groups. The operative time was significantly longer and the mean serum sodium levels were lower during TURP in patients who were operated on by the inexperienced urologic surgeons. The lowest mean sodium levels during TURP were higher than 129 mEq/L (mild hyponatremia). The incidence of TURP syndrome, however, was similar among the three groups. Senior urologic surgeons were able to resect four times more tissue per unit time than those with less experience, which may be important in minimizing the risk of secondary TURP because of adenomas that were incompletely resected. The authors suggested that more experienced resectionists operate with greater speed and aggression, leading to earlier capsule breach and greater fluid absorption in a shorter time.

Intraprostatic vasopressin injection

Sharma and Harvey⁶³ studied the effect of transrectal intraprostatic vasopressin (IPVP) injection in 36 consecutive patients who were undergoing TURP. TURP syndrome did not develop in any of the patients, and there was a reduction in blood loss during the resection, which limited the amount of irrigant that entered the systemic circulation. Hemoglobin levels were stable in all patients with the exception of four (9%) in whom the decrease in hemoglobin level was thought to be secondary to hemodilution. Sodium levels showed insignificant changes in all patients with the exception of one in whom a capsular damage was noticed early. A beneficial side effect of the reduction in bleeding is, of course, improved vision, which would enable the surgeon to discover any capsular perforations earlier in the procedure. IPVP seems, therefore, to be of help during TURP by decreasing bleeding and restricting the volume of irrigant that enters the vasoconstricted vessels, thus reducing the risk of development of TURP syndrome.

Low pressure irrigation

Performing TURP under low pressure prevents absorption of large volumes of irrigation fluid via opened prostatic sinuses. Several approaches have been used to lower the in-

travesical pressure during TURP, including perioperative suprapubic catheterization, intermittent evacuation of irrigating fluid, or the use of an Iglesias resectoscope, which offers continuous flow resection. In a meta-analysis of irrigant fluid absorption during resection using those different approaches to lower intravesical pressure, it was found that 2 kPa was the level at which the intravesical pressure significantly increased.⁶⁴

Bipolar TURP

Bipolar TURP is performed using physiologic saline as the irrigant fluid, which addresses a fundamental concern of conventional monopolar TURP (ie, the use of hypo-osmolar irrigation). As a result, the risks of dilutional hyponatremia and TUR syndrome are eliminated, allowing for longer and safer resection.⁶⁵ In a recent review of the published literature, Mamoulakis and colleagues⁶⁶ concluded that bipolar TURP eliminated the risk of development of TURP syndrome.

Laser prostatectomy and TURP syndrome

Laser prostatectomy is the latest modality for the management of benign prostatic obstruction (BPO). Different types of lasers have been used to surgically manage benign prostatic enlargement. Photoselective vaporization of the prostate (green light laser) allows effective superficial tissue coagulation, which minimizes intravascular absorption of fluid, rendering the development of TURP syndrome unlikely. Pfizenmaier and coworkers⁶⁷ prospectively evaluated 173 patients who were treated with green light laser; TURP syndrome did not develop in any patient. Nevertheless, reports of TURP syndrome development secondary to intravascular absorption of sterile water are starting to be seen in the literature, although the true incidence is unknown at present.⁶⁸

Holmium laser enucleation of the prostate (HoLEP) is another popular method of surgical management of benign prostatic hyperplasia using holmium/yttrium-aluminum-garnet laser together with mechanical morcellation. Shah and coworkers⁶⁹ prospectively evaluated 53 patients who underwent HoLEP, assessing fluid absorption via the ethanol breath technique, and concluded that there was no significant change in serum electrolytes and no risk of TURP syndrome in this group of patients. The same results were reached by Seki and colleagues⁷⁰ when they retrospectively reviewed 97 patients who had HoLEP and reported that TURP syndrome developed in none of their patients. Laser surgery for BPO is comparatively still in its infancy, and increased exposure and experience will determine its true impact on the incidence of TURP syndrome.

Treatment

Although prevention of TURP syndrome is of the utmost importance, cases still occur, and early identification of symptoms is essential to avoid the onset of severe manifestations in patients who are undergoing endoscopic surgery. If TURP syndrome is detected intraoperatively, bleeding points should be coagulated, and the surgery terminated as soon as realistically and effectively possible. Supporting respiration with supplemental oxygen is necessary, and intubation and ventilation may also be needed along with intravenous anti-convulsants.⁷¹

Mildly symptomatic patients who are exhibiting nausea, vomiting, and agitation with stable hemodynamic parameters should be monitored in a high dependency setting until symptoms resolve. Supportive therapy, including antiemetics, is usually necessary.

Bradycardia and hypotension can be managed with atropine, adrenergic drugs, and calcium.⁷² Conversely, plasma volume expansion may be necessary, because hypotension and low cardiac output may develop when irrigation is discontinued.⁷³

Severe hyponatremia (serum sodium <120 mmol/L liter⁻¹) can be treated, after careful consideration, with hypertonic saline 3% (about 1000 mL/12 hrs). This combats cerebral edema, expands the plasma volume, reduces cellular swelling, and increases urinary excretion without increasing total solute excretion.⁷⁴

Patients who do not receive hypertonic saline or experience a delay in its administration, more frequently have residual neurologic damage or die.⁹ It is vital to remember that serum sodium concentrations of 100 mmol/L liter⁻¹ can be fatal.⁷⁵

The most feared complication of rapid correction of hyponatremia is central pontine myelinolysis, which has been reported after both rapid and slow correction of serum sodium concentration in TURP patients.⁷⁶ However, raising the serum sodium concentration by 1 mmol/L liter⁻¹/h is considered safe.⁷⁷

Hyperglycinemia may be the cause of TURP encephalopathy through its positive action on N-methyl-D-aspartic acid (NMDA) receptors and, hence, seizures could theoretically be managed by NMDA receptor antagonists⁷⁸ or glycine antagonists.⁷⁹ Seizures may also be caused by low serum magnesium from dilution or loop diuretics.⁸⁰ Magnesium exerts a negative effect on NMDA receptors⁸¹; hence, a trial of magnesium therapy may also control seizure activity.

Diuretic therapy

Both furosemide and mannitol have been used; furosemide induces a greater sodium diuresis in cases of life-threatening acute pulmonary edema compared with the relatively sodium sparing diuretic mannitol.⁸² Furosemide is not recommended in a hemodynamically unstable patient, because it may worsen any hyponatremia and hypotension.

The half life of glycine is 85 minutes,⁸³ and as one would expect, visual disturbances usually resolve spontaneously within 24 hours and do not need intervention.⁸⁴

Anesthesia and TUR Syndrome

General and regional anesthesia have been shown to result in comparable short- and long-term cardiac morbidity and mortality after TURP.⁸⁵ Spinal anaesthesia is widely considered to be the anesthetic technique of choice for TURP. Under general anesthesia, the diagnosis of TUR syndrome may be more problematic, because patients are unable to complain of the wide range of early symptoms, and clinicians must therefore rely on the later changes in blood pressure and pulse together with electrocardiographic changes.

Spinal anesthesia is reported to reduce the risk of pulmonary edema; it decreases blood loss and permits early detection of mental status.⁸⁶ Spinal anesthesia, however, reduces CVP, potentially resulting in greater absorption of irrigating fluid than with general anesthesia.⁸⁷ It is important to limit the

distribution of spinal block to reduce adverse hemodynamic and pulmonary effects. Intrathecal opioids enhance analgesia from subtherapeutic doses of local anesthetic drugs and make it possible to achieve successful spinal anesthesia.⁸⁸

Fluid loading can be used cautiously to reduce spinal anesthetic induced hypotension, although it has not always been effective, because the reduced physiologic reserve of the elderly makes them less able to increase their cardiac output in response to fluid loading.^{89,90}

Conclusions

This review highlights the progress that has been made in the physiologic understanding, diagnosis, and management of TURP syndrome. It also highlights the fact, however, that even with this understanding, the condition is difficult to eliminate, predict, diagnose, and manage. In particular, the diagnosis and treatment rely on clinical acumen and a multidisciplinary team approach.

This is not a condition that can be protocol driven because of its variable presentations. Successive patients may present with almost completely opposite clinical pictures so that one patient may need treatment for hypertension and fluid overload while another may need support for hypotension. The same patient may need support for both fluid overload and subsequently hypotension in different phases of TURP syndrome. Although this article deliberately does not try to provide a treatment algorithm for TURP syndrome, the detailed explanation of all its aspects and the assessment of new evolving minimally invasive procedures in the current era will hopefully provide the knowledge and confidence to manage this increasingly rare yet dangerous and potentially fatal condition.

Disclosure Statement

No competing financial interests exist.

References

- Weir JF, Larson EE, Rowntree LG. Studies in diabetes insipidus water balance. *Arch Intern Med* 1922;29:306.
- Hahn RG. Transurethral resection syndrome after transurethral resection of bladder tumours. *Can J Anaesth* 1995;42:69–72.
- Siddiqui MA, Berns JS, Baime MJ. Glycine irrigant absorption syndrome following cystoscopy. *Clin Nephrol* 1996;45:365–366.
- Gehring H, Nahm W, Zimmermann K, et al. Irrigating fluid absorption during percutaneous nephrolithotripsy. *Acta Anaesthesiol Scand* 1999;43:316–321.
- Ichai C, Ciais JF, Roussel LJ, et al. Intravascular absorption of glycine irrigating solution during shoulder arthroscopy: A case report and follow-up study. *Anesthesiology* 1996;85:1481–1485.
- Istre O, Bjoennes J, Naess R, et al. Postoperative cerebral oedema after transcervical endometrial resection and uterine irrigation with 1.5% glycine. *Lancet* 1994;344:1187–1189.
- Baggish MS, Brill AIO, Rosenweig B, et al. Fatal acute glycine and sorbitol toxicity during operative hysteroscopy. *J Gynecol Surg* 1993;9:137–143.
- Neal DE. The National Prostatectomy Audit. *Br J Urol* 1997;79(suppl 2):69–75.
- Ghanem AN, Ward JP. Osmotic and metabolic sequelae of volumetric overload in relation to the TUR syndrome. *Br J Urol* 1990;66:71–78.
- Sohn MH, Vogt C, Heinen G, et al. Fluid absorption and circulating endotoxins during transurethral resection of the prostate. *Br J Urol* 1993;72:605–610.
- Chilton CP, Morgan RJ, England HR, et al. A critical evaluation of the results of transurethral resection of the prostate. *Br J Urol* 1978;50:542–546.
- Estey EP, Mador DR, McPhee MS. A review of 1486 transurethral resections of the prostate in a teaching hospital. *Can J Surg* 1993;36:37–40.
- Zepnick H, Steinbach F, Schuster F. [Value of transurethral resection of the prostate (TURP) for treatment of symptomatic benign prostatic obstruction (BPO): An analysis of efficiency and complications in 1015 cases.] (Ger) *Aktuelle Urol* 2008;39:369–372.
- Reich O, Gratzke C, Bachmann A, et al. Morbidity, mortality and early outcome of transurethral resection of the prostate: A prospective multicenter evaluation of 10,654 patients. *J Urol* 2008;180:246–249.
- Hahn RG. Irrigating fluids in endoscopic surgery. *Br J Urol* 1997;79:669–680.
- Hurlbert BJ, Wingard DW. Water intoxication after 15 minutes of transurethral resection of the prostate. *Anesthesiology* 1979;50:355–356.
- Swaminathan R, Tormey WP. Fluid absorption during transurethral prostatectomy [letter]. *Br J Urol* 1981;282:317.
- Hahn RG. Fluid absorption in endoscopic surgery. *Br J Anaesth* 2006;96:8–20.
- Olsson J, Nilsson A, Hahn RG. Symptoms of the transurethral resection syndrome using glycine as the irrigant. *J Urol* 1995;154:123–128.
- Hatch PD. Surgical and anaesthetic considerations in transurethral resection of the prostate. *Anaesth Intensive Care* 1987;15:203–211.
- Marx GF, Orkin LR. Complications associated with transurethral surgery. *Anesthesiology* 1962;23:802–813.
- Henderson DJ, Middleton RG. Coma from hyponatraemia following transurethral resection of the prostate. *Urology* 1980;15:267–271.
- Jensen V. The TURP syndrome. *Can J Anaesth* 1991;38:90–96.
- Kay MC, Kay J, Began F, et al. Vision loss following transurethral resection of the prostate. *J Clin Neuro Ophthalmol* 1985;5: 273–276.
- Creel DJ, Wang JM, Wong KC. Transient blindness associated with transurethral resection of the prostate. *Arch Ophthalmol* 1987;105:1537–1539.
- Hoekstra PT, Kahnoski R, McCamish MA, et al. Transurethral prostatic resection syndrome—a new perspective: Encephalopathy with associated hyperammonemia. *J Urol* 1983;130:704–707.
- Olsson J, Nilsson A, Hahn RG. Symptoms of the transurethral resection syndrome using glycine as the irrigant. *J Urol* 1995;154:123–128.
- Hahn RG, Ekengren JC. Patterns of irrigating fluid absorption during transurethral resection of the prostate as indicated by ethanol. *J Urol* 1993;149:502–506.
- Desmond J. Serum osmolality and plasma electrolytes in patients who develop dilutional hyponatremia during transurethral resection. *Can J Surg* 1970;13:116–121.
- Harrison RH III, Boren JS, Robison JR. Dilutional hyponatremic shock: Another concept of the transurethral prostatic resection reaction. *J Urol* 1956;75:95–110.

31. Hahn RG. Acid phosphatase levels in serum during transurethral prostatectomy. *Br J Urol* 1989;64:500–503.
32. Ceccarelli FE, Mantell LK. Studies on fluid and electrolyte alterations during transurethral prostatectomy. *J Urol* 1961;85:75–82.
33. Hahn RG. Acid-base status following glycine absorption in transurethral surgery. *Eur J Anaesthesiol* 1992;9:1–5.
34. Hamilton Stewart PA, Barlow IM. Metabolic effects of prostatectomy. *J R Soc Med* 1989;82:725–728.
35. Reynolds RM, Padfield PL, Seckl JR. Disorders of sodium balance. *BMJ* 2006;332:702–705.
36. Ellis SJ. Severe hyponatraemia: Complications and treatment. *QJM* 1995;88:905–909.
37. Fenstermacher JD, Johnson JA. Filtration and reflection coefficients of the rabbit blood-brain barrier. *Am J Physiol* 1966;211:341–346.
38. Andrew RD. Seizure and acute osmotic change: Clinical and neurophysiological aspects. *J Neurol Sci* 1991;101:7–18.
39. Desmond J. Complications of transurethral prostatic surgery. *Can Anaesth Soc J* 1970;17:25–36.
40. Wilkes NJ, Woolf R, Mutch M, et al. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid–base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. *Anesth Analg* 2001;93:811–816.
41. Zucker JR, Bull AP. Independent plasma levels of sodium and glycine during transurethral resection of the prostate. *Can Anaesth Soc J* 1984;31:307–313.
42. Madsen PO, Madsen RE. Clinical and experimental evaluation of different irrigating fluids for transurethral surgery. *Invest Urol* 1965;3:122–129.
43. Zhang W, Andersson BS, Hahn RG. Effect of irrigating fluids and prostatic tissue extracts on isolated cardiomyocytes. *Urology* 1995;46:821–824.
44. Hahn RG, Essén P. ECG and cardiac enzymes after glycine absorption in transurethral prostatic resection. *Acta Anaesthesiol Scand* 1994;38:550–556.
45. Hahn RG, Nilsson A, Farahmand BY, et al. Operative factors and long-term risk of acute myocardial infarction after transurethral resection of the prostate. *Epidemiology* 1996;7:93–95.
46. Hahn RG, Andersson T, Sikk M. Eye symptoms, visual evoked potentials and EEG during intravenous infusion of glycine. *Acta Anaesthesiol Scand* 1995;39:214–219.
47. Perry TL, Urquhart N, MacLean J, et al. Nonketotic hyperglycinemia: Glycine accumulation due to absence of glycine cleavage in brain. *N Engl J Med* 1975;292:1269–1273.
48. Maatman TJ, Musselman P, Kwak YS, Resnick MI. Effect of glycine on retroperitoneal and intraperitoneal organs in the rat model. *Prostate* 1991;19:323–328.
49. Woods HF, Albert KG. Dangers of intravenous fructose. *Lancet* 1972;2:1354–1357.
50. Jin F, Chung F. Minimizing perioperative adverse events in the elderly. *Br J Anaesth* 2001;87:608–624.
51. Smith HS, Lumb PD. Perioperative management of fluid and blood replacement In: McLeskey CH, ed. *Geriatric Anesthesiology*. Baltimore: Williams & Wilkins, 1997, pp. 311–324.
52. Olsson J, Rentzhog L, Hjertberg H, Hahn RG. Reliability of clinical assessment of fluid absorption in transurethral prostatic resection. *Eur Urol* 1993;24:262–266.
53. Hahn RG. Ethanol monitoring of irrigating fluid absorption. *Eur J Anaesthesiol* 1996;13:102–115.
54. Hahn RG. The use of ethanol to monitor fluid absorption in transurethral resection of the prostate. *Scand J Urol Nephrol* 1999;33:277–283.
55. Hahn R, Berlin T, Lewenhaupt A. Irrigating fluid absorption and blood loss during transurethral resection of the prostate studied by a regular interval monitoring (RIM) method. *Scand J Urol Nephrol* 1988;22:23–30.
56. Shipstone DP, Inman RD, Beacock CJ, Coppinger SW. Validation of the ethanol breath test and on-table weighing to measure irrigating fluid absorption during transurethral prostatectomy. *BJU Int* 2002;90:872–875.
57. Hultén J. Prevention of irrigating fluid absorption during transurethral resection of the prostate. *Scand J Urol Nephrol* 1984;82(suppl):1–80.
58. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: Immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3885 patients. *J Urol* 1989;141:243–247.
59. Madsen PO, Naber KG. The importance of the pressure in the prostatic fossa and absorption of irrigating fluid during transurethral resection of the prostate. *J Urol* 1973;109:446–452.
60. Hahn RG, Ekengren J. Absorption of irrigating fluid and height of fluid bag during transurethral resection of the prostate. *Br J Urol* 1993;72:80–83.
61. van Renen RG, Reymann U. Comparison of the effect of two heights of glycine irrigation solution on serum sodium and osmolality during transurethral resection of the prostate. *Aust N Z J Surg* 1997;67:874–877.
62. Cury J, Coelho RF, Bruschini H, Srougi M. Is the ability to perform transurethral resection of the prostate influenced by the surgeon's previous experience? *Clinics (Sao Paulo)* 2008;63:315–320.
63. Sharma DP, Harvey AB. Does intraprostatic vasopressin prevent the transurethral resection syndrome? *BJU Int* 2000;86:223–226.
64. Hahn RG. Intravesical pressure during irrigating fluid absorption in transurethral resection of the prostate. *Scand J Urol Nephrol* 2000;34:102–108.
65. Issa MM. Technological advances in transurethral resection of the prostate: Bipolar versus monopolar TURP. *J Endourol* 2008;22:1587–1595.
66. Mamoulakis C, Trompetter M, de la Rosette J. Bipolar transurethral resection of the prostate: The 'golden standard' reclaims its leading position. *Curr Opin Urol* 2009;19:26–32.
67. Pfitzenmaier J, Gilfrich C, Pritsch M. Vaporization of prostates of > or = 80 mL using a potassium-titanyl-phosphate laser: Midterm-results and comparison with prostates of <80 mL. *BJU Int* 2008;102:322–327.
68. Dilger JA, Walsh MT, Warner ME, et al. Urethral injury during potassium-titanyl-phosphate laser prostatectomy complicated by transurethral resection syndrome. *Anesth Analg* 2008;107:1438–1440.
69. Shah HN, Kausik V, Hegde S, et al. Evaluation of fluid absorption during holmium laser enucleation of prostate by breath ethanol technique. *J Urol* 2006;175:537–540.
70. Seki N, Tatsugami K, Naito S. Holmium laser enucleation of the prostate: Comparison of outcomes according to prostate size in 97 Japanese patients. *J Endourol* 2007;21:192–196.
71. Munn J. TURP syndrome. In: Allman K, Wilson I, ed. *Oxford Handbook of Anaesthesia*. 2nd ed. Oxford, UK: Oxford University Press, 2006, pp. 570–571.
72. Singer M, Patel M, Webb AR, Bullen C. Management of the transurethral prostate resection syndrome: Time for reappraisal? *Crit Care Med* 1990;18:1479–1480.
73. Tauzin-Fin P, Krol-Houdek MC, Saumtally S, et al. [Glycine poisoning after percutaneous kidney surgery.] (Fre) *Can J Anaesth* 1993;40:866–869.

74. Wang C, Chakrabarti MK, Whitwam JG. Specific enhancement by fentanyl of the effects of intrathecal bupivacaine on nociceptive afferent but not on sympathetic efferent pathways in dogs. *Anesthesiology* 1993;79:766–773.
75. Norris HT, Aasheim GM, Sherrard DJ, Tremann JA. Symptomatology, pathophysiology and treatment of the transurethral resection of the prostate syndrome. *Br J Urol* 1973;45:420–427.
76. Brunner JE, Redmond JM, Haggard AM, et al. Central pontine myelinolysis and pontine lesions after rapid correction of hyponatremia: A prospective magnetic resonance imaging study. *Ann Neurol* 1990;27:61–66.
77. Ayus JC, Arieff AI. Glycine-induced hypo-osmolar hyponatremia. *Arch Intern Med* 1997;157:223–226.
78. Fitzpatrick JM, Kasidas GP, Rose GA. Hyperoxaluria following glycine irrigation for transurethral prostatectomy. *Br J Urol* 1981;53:250–252.
79. Kish SJ, Dixon LM, Burnham WM, et al. Brain neurotransmitters in glycine encephalopathy. *Ann Neurol* 1988;24:458–461.
80. Schwarcz R, Meldrum B. Excitatory amino acid antagonists provide a therapeutic approach to neurological disorders. *Lancet* 1985;2:140–143.
81. Malone PR, Davies JH, Stanfield NJ, et al. Metabolic consequences of forced diuresis following prostatectomy. *Br J Urol* 1986;58:406–411.
82. Weinberg MS, Donohoe JF. Hyponatremia in the syndrome of inappropriate secretion of antidiuretic hormone: Rapid correction with osmotic agents. *South Med J* 1985;78:348–351.
83. Norlén H, Allgén LG, Vinnars E, Bedrelidou-Classon G. Glycine solution as an irrigating agent during transurethral prostatic resection. Glycine Concentrations in blood plasma. *Scand J Urol Nephrol* 1986;20:19–26.
84. Mantha S, Rao SM, Singh AK, et al. Visual evoked potentials and visual acuity after transurethral resection of the prostate. *Anaesthesia* 1991;46:491–493.
85. Edwards ND, Callaghan LC, White T, Reilly CS. Perioperative myocardial ischaemia in patients undergoing transurethral surgery: A pilot study comparing general with spinal anaesthesia. *Br J Anaesth* 1995;74:368–372.
86. Azar I. Transurethral prostatectomy syndrome and other complications of urological procedures. In: McLeskey CH, ed. *Geriatric Anaesthesiology*. Baltimore: Williams & Wilkins, 1997, pp. 595–607.
87. Gehring H, Nahm W, Baerwald J, et al. Irrigation fluid absorption during transurethral resection of the prostate: Spinal vs. general anaesthesia. *Acta Anaesthesiol Scand* 1999;43:458–463.
88. Kuusniemi KS, Pihlajamäki KK, Pitkänen MT, et al. The use of bupivacaine and fentanyl for spinal anesthesia for urologic surgery. *Anesth Analg* 2000;91:1452–1456.
89. Coe AJ, Revanäs B. Is crystalloid preloading useful in spinal anaesthesia in the elderly? *Anaesthesia* 1990;45:241–243.
90. Critchley LA, Short TG, Gin T. Hypotension during subarachnoid anaesthesia: Haemodynamic analysis of three treatments. *Br J Anaesth* 1994;72:151–155.

Address correspondence to:
 Amr Hawary, M.Sc. (Urol), MRCS
 Department of Urology
 Manchester Royal Infirmary
 Oxford Road
 Manchester M13 9WL
 United Kingdom
 E-mail: amrhawary@hotmail.com

Abbreviations Used

BPO = benign prostatic obstruction
 CNS = central nervous system
 CVP = central venous pressure
 HoLEP = holmium laser enucleation of the prostate
 NMDA = N-methyl-D-aspartic acid
 TUR = transurethral resection
 TURP = transurethral resection of the prostate