

# TURP Syndrome – A Quick Review and Update

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## ABSTRACT

Transurethral resection of prostate syndrome (TURP-S) is one of the commonest and dreaded complications of urological endoscopic surgery. It is characterized by cardiocirculatory and neurological changes consequent to acute changes in intravascular volume and plasma solute concentrations occurring as a result of excess absorption of irrigating fluid. Even in best of hands, incidence of TURP-S is up to 20% and carries a significant mortality rate - 0.5-5% die perioperatively. It may occur at any time perioperatively and has been observed as early as few minutes after surgery has started and as late as several hours after surgery have been completed. Symptoms and signs are varied and unpredictable, and result from fluid overload and disturbed electrolyte balance and hyponatremia. Treatment is largely supportive and relies on removal of the underlying cause, and organ and physiological support. Preoperative prevention strategies are extremely important.

**Keywords:** TURP syndrome, constant vigilance, prevention, early diagnosis, treatment

**T**ransurethral resection of the prostate syndrome (TURP-S), first described by Creevy in 1947 is defined as a clinical condition characterized by cardiocirculatory and neurological changes consequent to acute changes in intravascular volume and plasma solute concentrations occurring as a result of excess absorption of irrigating fluid. It is one of the commonest and dreaded complications of urological endoscopic surgery. Even in best of hands, incidence of TURP-S is up to 20% and carries a significant mortality rate - 0.5-5% die perioperatively. It may occur at any time perioperatively and has been observed as early as few minutes after surgery has started and as late as several hours after surgery has been completed. TURP-S like syndrome may occur during endoscopic procedures such as ureterorenoscopy (URS), hysteroscopic submucosal fibroid resection, transcervical resection of endometrium (TCRE), percutaneous nephrolithotomy (PCNL), etc.

## PATHOPHYSIOLOGY

TURP-S affects many systems and the pathophysiology can be summarized under the following heads:

- Hypervolemia
  - Increased fluid absorption
  - Antidiuretic response to stress

- Alteration in concentration of plasma solutes
  - Hyponatremia (dilutional)
  - Hypo-osmolality
  - Hyperglycinemia
  - Hyperammonemia
  - Hypocalcemia
  - Hypoproteinemia (Hypoalbuminemia)
  - Decreased hematocrit
- Role of anesthesia and drugs
- Hemolysis
- Role of bacterial endotoxins

## IMPORTANT CONSIDERATIONS

### Hemolysis

When hypotonic irrigant such as distilled water is used, there is acute hypo-osmolality with massive hemolysis. Bleeding and red cell destruction are additional sources of volume and oxygen carrying capacity losses. The hemoglobinemia and hemoglobinuria coupled with hypotension can cause acute renal failure and death. Again, hyperkalemia occurring due to cell breakdown may cause cardiac arrest.

### Hyponatremia

Dilutional hyponatremia (serum Na<sup>+</sup> <130 mmol/L) is the hallmark of TURP-S syndrome. Hyponatremia causes lowering of cell membrane potential. Thus,

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there is disturbance of nerve conduction and muscle contraction. Also, hyponatremia leads to a reduction in plasma osmolality. Hence, water enters the intracellular space causing cell edema, hemolysis, pulmonary edema, kidney failure and in severe cases cerebral edema.

### Hypo-osmolality

The real cause of neuronal disturbance is the rapidly established hypo-osmolality and not hyponatremia. The effective pore size of blood brain barrier is such that it makes the barriers essentially impermeable to sodium but freely permeable to water. Physiologically, the neurons react to serum hypo-osmolality with a mechanism called 'idiogenic osmoles'. When there is acute change of serum osmolality (within minutes to hours), this compensatory mechanism may not be triggered fast enough to prevent neuronal expansion, cerebral edema and increased intracranial pressure, which in turn cause bradycardia and hypertension by Cushing's reflex. A volume of more than 2 liters, gained in 1 hour can lead to TURP-S; >3.5 liters precipitates shock and multiple system dysfunction.

### Hyperglycinemia

Although glycine is accepted as the most likely cause of 'visual disturbance' following TURP, it may also result in 'glycine-induced encephalopathy and seizure' and 'toxic renal effects'. The glycine absorbed with the irrigating fluid is metabolized at the hepatic and kidney level with the synthesis of ammonia, glyoxylic acid, glycolic acid, serine and elastase, which are accumulated both in blood and cerebrospinal fluid (CSF). Glycine is the major inhibitory neurotransmitter at the levels of retina, whereas glyoxylic acid and glycolic acid are neurotoxic.

Its link with the receptor of  $\gamma$ -aminobutyric acid (GABA) opens channels for the chloride located at the neuron surface with consequent hyperpolarization of ganglion cells (retina) thus inhibiting the neuronal impulses. Normal plasma glycine levels are 13-17 mg/L whereas levels as high as 1,029 mg/L (up to 65 times normal) can be reached leading to transient blindness.

Glycine may also lead to encephalopathy and seizure via "NDMA (N-methyl-D-aspartate), an excitatory neurotransmitter. Renal toxic effects of glycine may occasionally occur from hyperoxaluria (glycine metabolites-oxalate and glycolate).

### Hyperammonemia

Ammonia is a major by-product of glycine metabolism. High ammonia concentration suppresses

norepinephrine and dopamine release in the brain. This causes the encephalopathy of TURP-S. Fortunately ammonia toxicity is rare in man. Characteristically, the toxicity occurs within 1 hour after surgery. The patient develops nausea and vomiting and then lapses into coma. Blood ammonia rises above 500  $\mu\text{mol/L}$  (normal value is 11-35  $\mu\text{mol/L}$ ). Hyperammonemia lasts for over 10 hours postoperatively, probably because glycine continues to be absorbed from the periprostatic space.

It is not clear why hyperammonemia does not develop in all TURP patients. Hyperammonemia implies that the body cannot fully metabolize glycine through the glycine cleavage system, citric acid cycle and conversion to glycolic acid and glyoxylic acid. Another possible explanation is arginine deficiency. Ammonia is normally converted to urea in the liver via the ornithine cycle. Arginine is one of the intermediary products necessary for this cycle. When a patient has arginine deficiency, ornithine cycle is not fuelled and thus ammonia accumulates.

### SIGNS OF SYMPTOMS OF TURP-S

The first sign of significant fluid absorption is a gradual or sudden rise of blood pressure (BP) (generally between 20 and 60 mmHg) accompanied by a bradycardia (10-25 beats/min). Retrosternal chest pain is another early symptom.

#### Cardiopulmonary

|                      |             |
|----------------------|-------------|
| Hypertension         | Hypotension |
| Tachycardia          | Bradycardia |
| Dysrhythmia          | Cyanosis    |
| Respiratory distress | Shock-death |

#### Hemolytic and Renal

- Hyponatremia
- Hemolysis/Anemia
- Hyperglycinemia
- Acute renal failure-death

#### Central Nervous System

- Nausea and vomiting
- Visual disturbance- Temporary total blindness
- Confusion, restlessness
- Twitches - seizures
- Lethargy - Paralysis
- Dilated, nonreactive pupils
- Coma - death

## PREVENTION OF TURP-S

This has two aspects: Surgical and anesthetic, but no method ensures that TURP-S will be avoided. Surgical preventive aspects are all designed to limit the absorption of excess irrigant during TURP.

### Surgical Aspects of Prevention

- Avoidance of early capsular perforation and opening of various sinuses during TURP.
- Limiting the intravesical pressure by:
  - Adjusting the height of the irrigation bag.
  - Use of continuous flow systems or suprapubic trocar.
- Limiting the resection time to 1 hour and proper selection of gland size.
- Selection of proper irrigation fluid.
- Use of bipolar saline TURP (using sodium chloride irrigation).
- Selecting alternative intervention in high-risk cases.
- Novel and experimental approaches:
  - Intraoperative intra-prostatic vasopressin.
  - Use of 5 $\alpha$ -reductase inhibitors.

Although TURP is still considered the gold standard, there are other attractive techniques such as Ho:YAG and potassium-titanyl-phosphate lasers, microwave ablation and cryosurgery. Their main advantages over conventional TURP include minimal blood loss, low morbidity and minimal fluid absorption.

### Anesthetic Aspects of Prevention

- Preoperative screening
  - Recognizing high-risk patients for TURP-S.
  - Assigning proper ASA grade.
  - Optimization of cardiopulmonary system.
- Intra- and postoperative aspects
  - Proper choice of anesthetic technique
  - Intense monitoring of vitals:
    - SpO<sub>2</sub>
    - ECG
    - Noninvasive BP
    - Heart rate/Pulse rate
    - End tidal CO<sub>2</sub> (EtCO<sub>2</sub>)
    - Respiration
  - Prevention of hypothermia:
    - Adjusting OT temperature

- Use of warm blankets, mattresses
- Intravenous (IV) fluids and irrigating fluids pre-warming to 37°C.
- Blood sample measurements:
  - Osmolality
  - Plasma sodium
  - Plasma glycine concentration.

(The above blood samples should be monitored just before surgery, every 15 minutes during surgery and 30 minutes after termination of operation)

- Other relevant measurements are:
  - Breath ethanol content
  - Plasma magnesium level (indicates susceptibility to seizures)
  - Serum acid phosphates
  - Arterial blood gases (may herald metabolic acidosis)
  - Plasma concentration of fluorescein
  - Plasma concentration of potassium
  - Use of load cell transducers.

### Ethanol Monitoring

Highly specific and inexpensive method. This simple and safe method clearly requires a 1% ethanol marker in the irrigating fluids. It is measured by instrument called Alcomed. Cut-off level is 0.2 mg/L.

## TREATMENT

- In the early phase:
  - Intraoperatively, as soon as the signs and symptoms of TURP-S appear, the following measures should be taken:
    - Alert the operating surgeon.
    - Try to minimize fluid absorption (adjusting reservoir height or putting a suprapubic trocar) and sometimes it is advisable to terminate surgery as soon as possible after proper hemostasis.
    - IV furosemide (40-100 mg) to induce diuresis.
    - Draw arterial blood sample for ABG and serum electrolytes.
- In the late intraoperative or early postoperative phase:
  - Mannitol is useful in promoting diuresis and eliminating intravascular volume overload.

- Ascertain normal gaseous exchange between lungs and blood.
- Packed RBC
- O<sub>2</sub> by mask
- Calcium and magnesium ions to give positive inotropic effects, when needed.
- If required, support respiration by endotracheal intubation and intermittent positive pressure ventilation.
- Correct hyponatremia by using hypertonic saline (3%).
- When there is hypotension, peripheral vasoconstrictors are useful.
- In case of convulsion, short-acting anti-convulsants diazepam or midazolam IV and in resistant cases, phenytoin or barbiturates can be given.
- Packed RBC rather than whole blood is indicated in case of significant blood loss.
- Restricted and cautious administration of IV fluid is necessary as these patients are very prone to pulmonary edema.
- For temporary total blindness, reassurance that unimpaired vision is expected to return within 24 hours is the best treatment as half-life of glycine is only 85 minutes.

### CLINICAL RELEVANCE

Circulatory overload occurs when weight of prostate is >45 g. Ideal height of irrigating fluid is 60 cm, so that approximately 300 mL of fluid is obtained per minute for good vision. Symptoms of water intoxication appear when serum sodium level falls 15-20 mEq/L below normal levels. Clonus and positive Babinski responses are seen. Papilloedema with dilated, sluggishly reacting pupils and low voltage EEG can occur. When serum sodium level is below 120 mEq/L, there is hypotension due to reduced myocardial contractility. Below 115 mEq/L, bradycardia, widening of QRS complexes, ventricular ectopics and T-wave inversion are seen. At levels below 100 mEq/L generalized seizures coma, respiratory arrest, ventricular tachycardia, ventricular fibrillation and finally cardiac arrest occurs. Sodium deficit = Normal serum sodium - estimated serum sodium × volume of body water (body water is usually 60% of body weight).

The most feared complication of correcting hyponatremia is central pontine myelinolysis (CPM),

also referred to as 'osmotic demyelination syndrome' as demyelination can occur in extrapontine areas. Also CPM is most commonly seen in women, probably due to sex differences in cellular ion pump capacity. It has been reported after rapid as well as slow correction of serum sodium concentration in TURP patients. About 1.5-2 mmol/L/hr correction in the serum sodium levels has been suggested to be safe. Visual disturbances: Transient blindness, foggy vision and patients see halos around objects. Pupils may be dilated and unresponsive. Optic disc appears normal. Perception to light and blink responses are preserved but pupillary responses to light and accommodation are lost in TURP blindness.

### SUMMARY

TURP is a procedure carried out on predominantly elderly population with a higher incidence of co-existing disease. Consequently anesthetizing for the procedure may present a challenge. Early detection and prompt treatment of the syndrome are vital for a favorable outcome. Newer techniques of TURP promise a reduced risk of TURP-S.

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