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What Exactly is the TUR Syndrome and How Should it be Treated?

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Review Article

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Abstract

The introduction of this article reports a mini review of the subject. The TUR syndrome is precisely defined. The patho-aetiology, clinical picture and effective therapy are reported. The TUR syndrome is defined as severe cardiovascular reaction shock induced by massive gain of the sodium-free irrigating fluid such as 1.5% Glycine into the cardiovascular system and is characterized by severe hyponatremia. The main presentation is severe cardiovascular shock and post-operative coma and convulsions, but other manifestations of the multiple organ dysfunction syndrome occur. The correct lifesaving therapy for the TUR syndrome, hyponatremia and ARDS is hypertonic sodium of 5%NaCl and 8.4% $NaCo_3$.

Keywords: The TUR Syndrome; Hyponatraemia; ARDS; Volumetric Overload; Shock

Abbreviations: SBB: Sudden Bilateral Blindness; COC: Clouding of Consciousness; MBCI: Paralysis mimicking bizarre cerebral infarctions; FAM: Frothing Around the Mouth; APO: Acute Pulmonary Oedema; RA: Respiratory Arrest; CPA: Cardiopulmonary Arrest; AKI: Acute Kidney Injury; DGR: Delayed Gut Recovery.

Introduction

The transurethral resection of the prostate (TURP) procedure has long been recognised as the safest method of prostatectomy [1] and is currently the operation of choice for prostatic enlargement. However, like any other operation, it has its complications both general and specific. Specific complications may be immediate such as severe bleeding and the TUR syndrome or delayed such as urethral stricture formation.

The TUR syndrome is one of its acute complications with an average postoperative mortality of 1.59% [2]. Other authors have calculated that it accounts for a morbidity of 17-24% and a mortality of 1-2% [3,4]. Based on a prospective study an incidence of 7% with a mortality of 1% was reported [5]. Since 10% of males above the age of 40 years will, sooner or later, become candidate for prostatectomy [6], the total number of patients at risk from this complication is considerable [4].

Creevy first described the TUR syndrome as acute water intoxication that led to intravascular haemolysis, jaundice and acute tubular necrosis and death from renal failure at the time when water was used as the irrigating solution during the TURP procedure [7-11]. Creevy credited both Foley and Mclaughlin for similar and independent observations. Foley observed red urine, due to intravascular haemolysis, spurting from the ureteric orifices during the TURP procedure [7].

Non-haemolytic irrigating solutions were then introduced. Creevy used glucose and Nespit experimented with glycine. Nesbit outlined the criteria for a suitable irrigant as non-haemolytic, non-toxic, transparent, and cheap [12]. Saline was excluded because it disseminates electric current. Glycine was preferred to glucose because of the hyperglycaemia that may complicate the use of glucose

solutions [12]. Urea, Mannitol and Cytal (mainly composed of sorbitol and mannitol) and other irrigating fluids were introduced later [13].

The introduction of non-haemolytic and non-electrolytes solutions was considered the most important advance of transurethral surgery [14]. Such solutions are non-haemolytic to red blood cells but may be either hypo- or iso-osmotic to the plasma. Plasma osmolality measures 280-300 mosm/l while that of 1.5% glycine is reported to be 220 but measures 195 mosm/l by freezing point depression.

Non-haemolytic solutions have reduced the morbidity and mortality of the TUR syndrome, as compared to water intoxication, by half from 50% and 4% respectively [9,11]. Red cell haemolysis and its consequences such as hemoglobinemia, tubular necrosis, renal failure and jaundice have become no longer features of the TUR syndrome [15], but a complex clinical syndrome has continued to occur [16].

Although the cause of the TURP syndrome remains controversial and even its existence may be doubted [17], it has become clear that it is associated with the systemic absorption of a large volume of the sodium-free irrigating fluid [18]. Fluid absorption may occur through the peri-prostatic venous plexus of veins directly injected by the resectoscope flow into the circulation after breaching the prostatic capsule [19,20], or through the peritoneal membrane in cases of intra-peritoneal perforations [21,13].

In 1956 Harrison III et al recognized the concept of hyponatraemic shock as the patho-aetiology of the TUR syndrome and introduced 5% NaCl as its successful treatment. This successful treatment was overlooked because it was considered by the medical authorities on hyponatraemia that hypertonic sodium therapy (HST) was contraindicated. In 1990 (Ghanem and Ward) introduced the concept of Volumetric overload shocks as the patho-aetiology of the TUR syndrome and rejuvenated HST in its successful treatment. It has been demonstrated that HST restores serum sodium and osmolality with a matching immediate improvement in clinical picture (Figure 1).

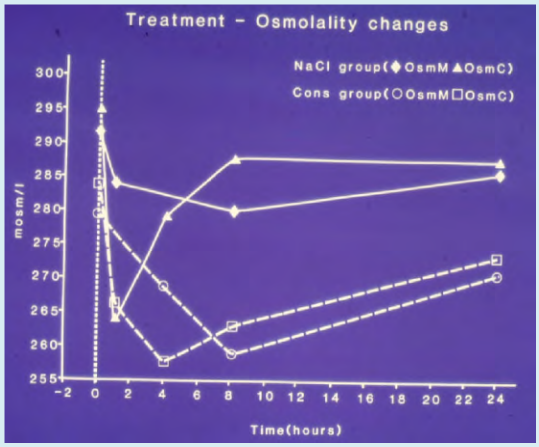

Figure 1: Shows mean changes in measured serum osmolality (OsmM) and calculated osmolality (OsmC)a and serum sodium concentration in patients with the TURP syndrome comparing those infused with 5% hypertonic sodium (solid lines) and those treated conservatively (slashed lines). OsmC was calculated from the formula 2xNa+urea+glucose in mmol/l of serum concentration48 thus reflecting changes in serum sodium concentration. The vertical dotted line represents the start of operation (Time B) followed by C, C1, C2 (end of treatment) and D, respectively.

The latest shift to using normal saline as the irrigating solution may eradicate the TUR syndrome with its characteristic hyponatraemia from urological practice but it will be reincarnated into ARDS as predicted by Ghanem [22-25] based on the concept of VO induced by saline based fluids [22].

Definition

The TUR syndrome is defined as severe cardiovascular reaction shock induced by massive gain of the sodium-free irrigating fluid such as 1.5% Glycine into the cardiovascular system and is characterized by severe hyponatraemia of <120 mmol/l.

Patho-Aetiology

The toxic hypothesis of glycine and hypernatremia. These have traditionally been used as the patho-etiological explanation for the TUR syndrome with little impact on its correct management and understanding of the condition [26,27]. Hahn, et al. Remains a firm believer of the toxic

hypothesis [28,29]. However, neither hyponatraemia nor the high serum Glycine reached statistical significance in multiple regression analysis Table 1 but volumetric overload was the most highly significant factor (p=0.0007) in a prospective study on the TUR syndrome [22].

P	T Value	Std. Value	Std. Err	Value	Parameter
		0.773			Intercept
0.0007	3.721	1.044	0.228	0.847	Fluid Gain (l)
0.0212	2.42	-0.375	0.014	0.033	Osmolality
0.0597	1.95	0.616	0.049	0.095	Na+ (C_B)
0.4809	0.713	0.239	0.087	0.062	Alb (C_B)
0.2587	1.149	-0.368	0.246	-0.282	Hb (C_B)
0.4112	0.832	-0.242	5.98E-05	-4.97E-05	Glycine (C_B)

Table 1: Shows the multiple regression analysis of total per-operative fluid gain, drop in measured serum osmolality (OsmM), sodium, albumin, Hb and increase in serum glycine occurring immediately post-operatively in relation to signs of the TURP syndrome. Volumetric gain and hypo-osmolality are the only significant factors.

Volumetric Overload Shocks (VOS)

This concept is relatively new and has proved most successful in saving the lives of the TUR syndrome cases [22-24]. Most of the volumetric overload (VO) in the TUR syndrome is type one induced by sodium-free fluids such as Glycine, Mannitol, Glucose and Sorbitol. Also any fluid that is intravenously infused during the procedure contributes to the pathogenesis. Table 1 demonstrates that VO is the most highly significant factor in causing the TUR syndrome. The magnitude of the VO is demonstrated in Figures 2 & 3. The concept also allows recognizing VO shocks (VOS) that is of two types: Type 1 induced by sodium-free fluids and type 2 induced by sodium-based fluids which clearly indicate that VOS should not be treated with further volume expansion which is lethal. The correct treatment is HST of 5%NaCl and 8.4%Na Co_3. Though this good therapy remains contraindicated in the management of Hyponatraemia [26,27,30]. These authorities on hyponatraemia changes their views and approved HST as a good successful treatment.

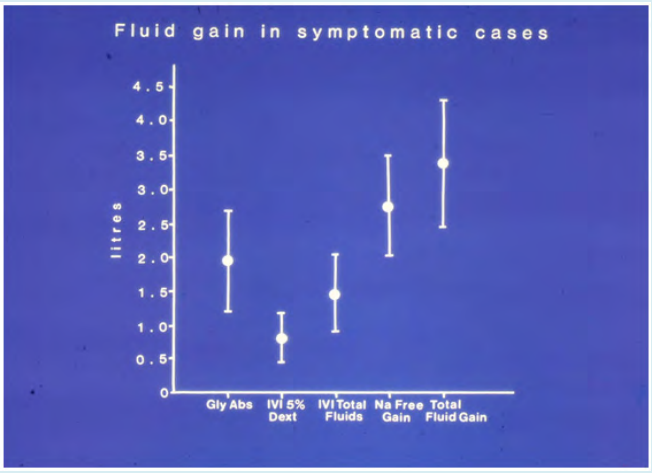

Figure 2: shows the means and standard deviations of volumetric overload in 10 symptomatic patients presenting with shock and hyponatraemia among 100 consecutive patients during a prospective study on transurethral resection of the prostate. The fluids were of Glycine absorbed (Gly abs), intravenously infused 5% Dextrose (IVI Dext) Total IVI fluids, Total Sodium-free fluid gained (Na Free Gain) and total fluid gain in liters.

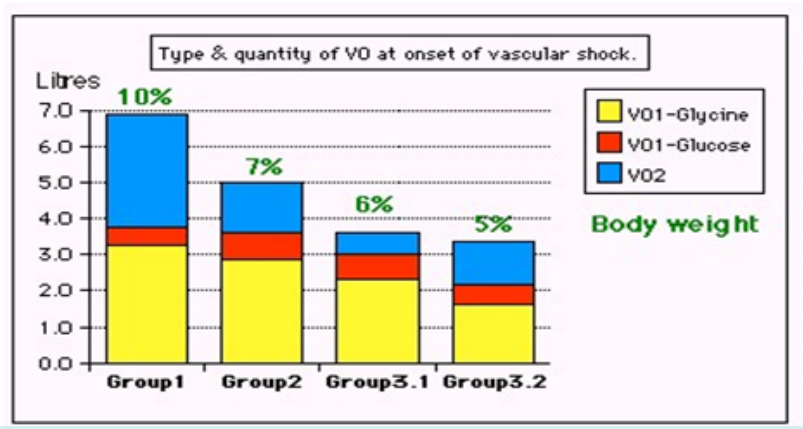

Figure 3: shows volumetric overload (VO) quantity (in liters and as percent of body weight) and types of fluids. Group 1 was the 3 patients who died in the case series as they were misdiagnosed as one of the previously known shocks and treated with further volume expansion. Group 2 were 10 patients from the series who were correctly diagnosed as volumetric overload shock and treated with hypertonic sodium therapy (HST). Group 3 were 10 patients who were seen in the prospective study and subdivided into 2 groups; Group 3.1 of 5 patients treated with HST and Group 3.2 of 5 patients who were treated with guarded volume.

Clinical Picture

The clinical picture of the TUR syndrome is predominated by the cerebral symptoms of coma, convulsions, and bizarre paralysis [31,32]. However, the cardiovascular shock of VOS precedes this presentation. Other manifestations of the multiple organ dysfunction syndrome (MODS) appear later in the surviving cases that present with features of the acute respiratory distress syndrome (ARDS) (Table 2). Table 3 shows the mean summary of data on biochemical abnormalities, postoperative serum solute changes, therapy and outcome comparing the 3 groups of 23 case series patients whose VO is shown in Figure 2.

Cerebral	Cardiovascular	Respiratory	Renal	Hepatic & GIT
Numbness	Hypotension	Cyanosis.	Oliguria	Dysfunction:
Tingling	Bradycardia	FAM	Annuria	Bilirubin ↑
SBB	Dysrhythmia	APO)	Renal failure or	SGOT ↑
COC	CV Shock*	RA	AKI[9]	Alkaline Phosph.
Convulsions	Cardiac Arrest	Arrest	Urea ↑	GIT symptoms.
Coma	Sudden Death	CPA	Creatinine ↑	DGR
PMBCI		Shock lung		Paralytic ileus
		ARDS		Nausea & Vomiting.

Table 2: Shows the manifestations of VOS 1 of the TURP syndrome for comparison with ARDS manifestations induced by VOS2. The manifestations are the same but one vital organ-system may predominate.

1	Gr1		Gr2	Gr3	Gr3.1	Gr3.2	Normal Units	
2	Number of patients 3		10	10	5	5	mean	
3	Age 71		70	75	72	78	72 Years	
4	Body weight (BW) 69		70	68	71	65	69 Kg	
5	Postoperative serum solute concentration						Preoperative	
6	Osmolality	**271**	**234**	**276**	282	271	292	Mosm/1

7	Na+	**110**	**108**	**120**	119	121	139	Mmol/1
8	Ca++	**1.69**	**1.79**	**1.85**	1.84	1.86	2.22	"
9	K+ (P<.05)	5.6	4.8	5	4.9	5	4.46	"
10	Co_2 (P=.002)	23	23	25.5	24	26.4	27.3	"
11	Glucose	**13.2**	**17.3**	**16.4**	**15.9**	**16.9**	6.2	"
12	Urea (P=.0726)	**26.5**	**9**	6.6	6.8	6.4	6.7	"
13	Bilirubin (P<.05)	**19**	**16**	8	6	9	7	"
14	AST	124	32	20	18	21	20	"
15	Protein	**43**	**52**	48	44	52	62	g/l
16	Albumin	**23**	**30**	30	28	32	39	"
17	Hb (P=.0018)	119.3	127.9	114.5	105.2	123.8	123.8	"
18	WCC (P<.005)	**18.9**	**16.2**	7.5	7.8	7.2	8	per HPF
19	Glycine			10499			293	µmol/1
20	Therapy	CT	HST	Randomized:	HST	CT©		
21	Outcome	Death	Full Recovery		Full Recovery	Morbidity		

Table 3: Shows the mean summary of data on biochemical abnormalities, therapy and outcome comparing the 3 groups of 23 case series patients whose VO is shown in (Figure 3). Groip-1 was the 3 patients who died and had post-mortem examination, Group-2 were a series of severe TURP syndrome cases successfully treated with hypertonic sodium therapy (HST), and Group-3 were 10 patients encountered in the prospective study who were randomized between HST (3.1) and conservative treatment (CT) (3.2). The significant changes of serum solute contents are shown in bald font with the corresponding p- value. Most of the patients showed manifestation of ARDS of which the cerebral manifestation predominated, being on initial presentation (Regional Anaesthesia) and representation of VOS 1 (General Anaesthesia). However, most patients were given large volume of saline that elevated serum sodium to near normal while clinical picture became worse. They suffered VOS2 that caused ARDS.

Therapy of VOS causing the TUR syndrome, hyponatraemia, and ARDS

Prevention: Being iatrogenic complications of fluid therapy, both VOS causing the TUR syndrome and ARDS are preventable. To prevent VOS and ARDS a limit to the maximum amount of fluid used during shock resuscitation or major surgery must be agreed upon (New guidelines are required). Surgical care providers must exercise judicious use of crystalloid fluid administration in the trauma bay, ICU, and floor.

Replace the loss in haemorrhagic hypovolaemic shock but do not overdo it. If hypotension develops despite volume replacement later during ICU stay, inotropic drugs, hydrocortisone 200 mg and hypertonic sodium therapy (HST) should be used-see later. The latter restores the pre-capillary sphincter tone (peripheral resistance) so that the capillary works as normal G tube again, but NO isotonic crystalloids or colloids over-infusions is required. This corrects shock and arrythmia and elevates blood pressure.

To learn the new correct science, one must unlearn the old incorrect habits.

The following practices should be abandoned:

Bolus Fluid Therapy in Surgical Patients

Abandon the aggressive current liberal regimen of Early Goal-Directed Therapy (EGDT) in treating shocked and septic patients. Multiple huge multicentre trials have proved it to be the wrong practice. Please refrain from persisting to elevate CVP to levels above 12 and up to 18-22 cm using isotonic saline-based fluids in shock management. This is a major cause for inducing VOS and ARDS during shock resuscitation, particularly septic shock.

Therapeutic

Hypertonic sodium therapy (HST) of 5%NaCl and/or 8.4%NaCo3 has truly proved lifesaving therapy for the TUR syndrome and acute dilution HN as well as Secondary VOS 2 that complicates fluid therapy of VOS 1 causing ARDS [32,22,23]. It works by inducing massive diuresis being a potent suppressor of antidiuretic hormone. It may also work on the capillary pre-sphincter restoring its tone [33].

My experience in using it for treating established ARDS with sepsis and primary VOS 2 that causes ARDS is limited.

However, evidence on HST suggests it will prove successful if given early, promptly, and adequately to ARDS patients while refraining from any further isotonic crystalloid or colloid fluid infusions using saline, HES and/or plasma therapy- just give the normal daily fluid requirement and no more. After giving HST over one hour using the CVP catheter already inserted, the patient recovers from AKI and produces through a urinary catheter massive amount of urine of 4-5 litres as you watch. This urine output should not be replaced. Just observe the patient recovering from his AKI, coma and ARDS and asks for a drink. This is done in addition to the cardiovascular, respiratory, and renal support on ICU. Patients with AKI on dialysis, the treating nephrologist should aim at and set the machine for inducing negative fluid balance.

The HST of 5%NaCl and/or 8.4%$NaCo_3$ is given in 200 ml doses over 10 minutes and repeated. I did not have to use more than 1000 ml during the successful treatment of 16 ARDS patients. Any other hypertonic sodium concentration is not recommended. A dose of intravenous diuretic may be given but it does not work in a double or triple the normal dose. A dose of 200 mg of hydrocortisone is most useful. Antibiotic prophylactic therapy is given in appropriate and adequate doses to prevent sepsis and septic shock. No further fluid infusions of any kind crystalloids, colloids and blood are given. The urinary loss should not be replaced as this defeat the objective of treatment.

Conflict of Interest

None

Funds Received

None

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