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Review Article

Volumetric Overload Shocks (VOS) Resolving the Puzzle of the Transurethral Resection of the Prostate (TURP) Syndrome, Dilution Hyponatraemia (HN) and the Acute Respiratory Distress Syndrome (ARDS): The Minority Report!

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Abstract

Introduction and Objective: When the investigation of the TURP syndrome was started, it was generally thought to be "Rare, obscure and well known". However, the evidence indicated that it is bizarre illusive killer with multiple masks that was never incriminated for its killings. Here we report the volumetric overload shocks (VOS) resolving its puzzle as well as HN and ARDS.

Patients and Methods: Analytical literature review and data from our two clinical studies are used to resolve the puzzles. A reported case of permanent bilateral blindness is analyzed as an example of the illusive masks the TURP syndrome uses.

Results: Reported data indicate that VO was responsible for the dilution of serum solute contents and clinical picture. Volumetric overload was the only highly significant factor in relation to the severity of the TURP syndrome. The syndrome presented with myocardial, cerebral, respiratory, renal and hepatic failures masks or ARDS. We provide evidence that it is also responsible for the permanent bilateral blindness in the reported case. Mistaking the shock for haemorrhagic or septic shock caused death in 3 cases. Hypertonic sodium therapy has saved the lives of 20 patients.

Conclusion: Volumetric overload shocks are the patho-etiology of TURP, HN and ARDS. This has uncovered most masks behind which the TURP syndrome hides. Hypertonic sodium therapy is curable bringing patients back from dead. The minority report has proved correct.

Keywords: *Hyponatraemia; The TURP Syndrome; The Multiple Vital Organ Dysfunction/Failure Syndrome; ARDS; Shock; Capillary-Interstitial Transfer; Haemodynamic; Fluid Therapy; Volumetric Overload; Hypertonic Sodium Therapy*

Abbreviations

VOS: Volumetric Overload Shocks; VOS1: Volumetric Overload Shock, Type 1; VOS2: Volumetric Overload Shock, Type 2; TURP: The Transurethral Resection of the Prostate; ARDS: The Adult Respiratory Distress Syndrome; MVOD/F: The Multiple Vital Organ Dysfunction/Failure; HN: Hyponatraemia; HST: Hypertonic Sodium Therapy; G Tube: The Porous Orifice Tube; CVP: Central Venous Pressure; PBB: Permanent Bilateral Blindness; ivi: Intravenously Infused Fluids; SSC: Serum Sodium Concentration; EBM: Evidence Based Medicine

Introduction

Experience as senior house officer in urology with 3 patients witnessed being killed following the TURP surgery mistakenly treated as a known shock back in 1981-3 is unforgettable. I went to the mortuary and after attending their postmortem (PM) examination I looked

at their faces and whispered an apology being ignorant of what killed them. I made a pledge to find out what is wrong. The PM evidence clearly indicated both to the pathologist and I that they were internally drowned but nobody, no textbook and no article could explain how and why yet some showed me the way. I realized that the TURP syndrome killed them but was not incriminated. It took 33 years to find out exactly how and why as reported here.

Lately, the TURP syndrome presented with "Permanent Bilateral Blindness" (PBB) without even being incriminated. A highly accessed case report of "non-arteritic ischemic optic neuropathy" complicating the TUPP surgery was reported [1]. On reading the title, I immediately suspected the TURP syndrome and was sure as I finished the report. I was disappointed but not surprised as the TURP syndrome was not considered the diagnosis. The reason was clear from prepublication history particularly the impressive third reviewer's comments that brought the TURP syndrome into authors' attention for the first time during editorial consideration! This is indeed a devastating condition to endure after the TURP surgery that I find most provocative and diabolical.

After experiencing the wide spectrum of presentations of the TURP syndrome painfully, I still didn't anticipate "PBB" as one of its clinical features, even though I recognized the illusive pattern which has never been suspected. The case, however, is so unique and provoking in sense that, it has been some years since I read something novel that concerns the TURP syndrome as culprit.

Ironically the 70 year old story of the TURP syndrome [3] and hyponatraemia (HN) [4] started with a case report and may not end with one. It has repeated itself in illusive style changing identity from water intoxication [3] to HN [4]. This is important to identify as the irrigant used for TURP inducing it have already been replaced by normal saline [2]. Thus acute dilution HN characterizing and defining the TURP syndrome may never be seen again in urology. It will no longer be seen on the occurrence of fluid gain initiated by absorbed irrigant bolus or intravenously infused (ivi) (volumetric overload (VO)) into the peri-prostate, peripheral or central veins [5]. Hence I find this case "final ironic stint" that fits the elusive style of TURP syndrome at least before vanishing from urology discarding its own name and definition for ever. I shall do my best in order not to allow it get away without even being incriminated for such crimes. How the obvious can be so invisible?

The authors considered the TURP syndrome retrospectively on the 3rd reviewer's suggestion [1] but excluded it after looking up a recent review on the complications of the TURP surgery [2]. In their discussion [1], the authors based their opinion of excluding the TURP syndrome on one paragraph covering the "definition and disappearance of the TURP syndrome from urology" [2]. In my view, the recently published review article is excellent and comprehensive but unfortunately fails to enlighten about the diagnosis. One might argue that a physician armed with that review cannot recognize the TURP syndrome when he encounters one! In my experience the clinicians involved across specialties cannot agree on the diagnosis of this syndrome when faced with it. To further make it difficult we cannot exclude it retrospectively based on current investigations which I will explain later.

In my opinion, it is the TURP syndrome that is the real culprit for "PBB" in this case. The fact that it may totally lack HN that defines and characterizes it, took 25 years to investigate and unravel. The "nonarteritic ischaemia" is unlikely to be caused by local arterial insufficiency, but was secondary to optic disc oedema, which is part of an obscure systemic pathological mechanism with which the TURP syndrome and HN insult every cell and vital organ in the body.

Based on its known definition of acute dilution HN nadir of < 120 mmol/l, the TURP syndrome unfortunately becomes an invisible demon which attacks and kills patients in every clinical specialty without being incriminated, though it infamously originated in urology! There is nothing typical or diagnostic about it as it always has the most bizarre mixture of signs and illusive clinical presentation "masks" with which it continues to elude the medical profession. The only typicality about this syndrome is being atypical, bizarre and invisible.

Clinical manifestations of such cell oedema/ischemia damage show as features of the multiple vital organ dysfunction or failure (MVOD/F) syndrome [5]- also known as ARDS. Evidence for cardiac cell edema has also recently most elegantly demonstrated [15]. The usual culprits such as local arterial insufficiency, hypoxia, toxins, chemicals and sepsis of endogenous or exogenous origin have absent alibi while the syndrome occurs in absence of glycine amino acid [16-19]. Cardiac arrest [20], respiratory arrest [21] are also reported causes of death. However in clinical practice such conditions are considered primary causes of morbidity and mortality and treated as such while the culprit remains invisible and untreated. How to make the "invisible obvious" an "obviously visible"? This report aims to uncover the masks with which the TURP syndrome presented. It is the minority report.

Material and Methods

Literature review

This has been an ongoing in depth critical analysis of literature on the condition and related subjects in medicine, physiology and physics. Not only the stepping stones and relevant pieces identified but also errors and irrelevant pieces segregated and excluded while the missing pieces were invented.

Clinical prospective study on 100 patients and RCT on therapy of those fulfilling the definition criteria of the TURP syndrome was done. Data from this study accepted for MD thesis in 1988 [22] and reported at BJUI in 1990 [5] is presented here in novel manner to illustrate the issues. Another clinical study involved 23 case series among whom the 3 patients who died are reported.

The Case Report in which the TURP syndrome was not incriminated for PBB is freely accessed [1]. Reading this report may help readers identify how and where the culprit is hiding, while examining the evidence exposing and incriminating it.

Case scenario

The following case scenario is fair representation of most cases and contains most data needed to answer the quiz. The scenario replays the events in slow motion utilizing cool methodical analysis rather than that encountered in the hectic murky clinical setting.

The extreme HN with acute serum sodium concentration (SSC) nadir of < 100 mmol/l is invariably lethal during or immediately after surgery. The apparent cause of death is vascular collapse [7], cardiac [20] or respiratory arrest [21] behind which the TURP syndrome is offending but invisible. A nadir of < 120 mmol/l is the HN marker that defines and characterizes the TURP syndrome, only if measured and detected at the immediate postoperatively period after the bolus of sodium-free fluid VO or irrigant absorbed causing HN enters the patient vascular system diluting all his serum contents.

However, HN is in fact dynamic and may be erased in few minutes or hours! An "acute dilution HN" nadir of 120 mmol/l may either be self-corrected in hours, by intracellular shift of water, excretion of water, or in minutes by the intravenous infusion of sodium-based fluids given by the treating team for hypotension shock, assuming the kidney remains functional, there will only be mild mental confusion next day.

The same HN nadir of 120 mmol/l may be completely erased in minutes while the condition deteriorates despite the apparent correction of SSC. The acute dilution HN induced this clinical condition in the first place with sodium-free fluids VO bolus which is presenting as hypotension shock calling for further "volume expansion" using saline fluids! If blood sample was taken after resuscitating the patient with couple of bags of Hartmann's, Ringer's fluid, plasma and/or blood, HN may never be seen while the patient goes into coma. He may progress into vegetative state by the time he is seen by a physician or neurologist! The TURP syndrome is again lurking behind, invisible, now wearing the mask of encephalopathy coma and/or cerebro-vascular accident.

Please, read the above case scenario, consider the "orgy of evidence", in which only the "echo" crime is visible and admitted while the real killer is invisible and try answering the following questions.

Quiz

I. Please, look for how many clinical presentation "masks" that may kill the patient, mentioned and unmentioned, behind which the TURP syndrome is lurking invisible?

II. Please, identify and count how many biochemical and haematological serum solute contents are diluted yet may be "illusively" considered as nadirs of loss?

III. Please, look again more carefully, can you identify two major "paradoxes" of the TURP syndrome?

IV. Please, look again once more can you identify two major "missing" factors that play vital roles in the TURP syndrome pathogen esis and severity?

V. What is difference between cell and interstitial edema from clinical and pathological etiology point of view?

I have tried to present events as clearly as possible, but can you diagnose the TURP syndrome in the real murky clinical sitting? If you make a conference on the case, how many specialties should be involved, and what consensus on diagnosis is most likely to be agreed, particularly if serum sodium looked near normal after the resuscitation or if the name of the illusive culprit was not mentioned? Do you know of a therapy that is sure to save that patient's life, and may have spared his vision in the reported case?

Results

Most of the answers to the Quiz questions have been in print for 28 years [5], documented In Thesis for 30 years [22] and certainly obvious to me for 33 years yet remained invisible.

All the medical conditions mentioned above are "echoes" while the "real" crime and the offending culprit lurks invisible behind such presentation masks. Circulatory shock is a paradox of pathological VO [23] not due to any of the recognized shocks [7]. Also acute renal failure (ARF) is the second paradox of a pathological VO [5].

The data in table 1 shows the biochemical and haematological dilutional changes of serum solute contents. The means of postoperative changes in 100 patients show highly significant postoperative changes but do not tell that there are at least 10 (10%) cases of the TURP syndrome among them using more strict criteria for defining the TURP syndrome. Most of the serum solute contents of sodium, calcium and proteins as well as haemoglobin and hematocrit remain diluted (low) though SSC may appear near normal after resuscitation with saline based fluids and later after 24-48 hours (Table 1 and 2) (Figure 1).

In fact using the definition of HN of < 125 of the TURP syndrome, there were 16 cases! If you think this unreal, please look at the article reported side by side at the same BJUI issue [24] with TURP syndrome incidence of 83.3%!

- Professor Hahn's article was prospective study under epidural analgesia during which 2l of saline-based fluids were ivi into each patient.
- The study was done on 12 TURP patients of whom 10 developed the TURP syndrome. An incidence of (83.3%)!
- Glycine absorption ranged between 1 - 4.3l. I calculated total VO to be 3 - 6.3l after adding ivi fluids.
- They had HN nadir with SSC drop range of 6 - 22 mmol/L.
- ECG Bradycardia and depressed ST segment, chest pain and elevated cardiac enzymes plus transient increase in blood pressure and central venous pressure (CVP) was soon followed by hypotension shock described by Hahn as "Puzzling combination of hyper-hydration and hypotension"! Such data and the later reported data in 340 articles by Hahn and colleagues affirmed our data of minority report but the conclusions differ [5].
- I had realized this as "VO shock" that is inconsistent with currently received physiological and medical Knowledge!

Table 1 show all the dilution changes of serum contents as well as increases when a bolus of fluids dilutes plasma and body fluids. Figure 1 shows the graph of the main biochemical and haematological serum contents acutely diluted by "VO1" as shown on the peri-operative "Time" scale.

Plasma contents	A	B	C	D	Units	Significance
Osm measured	291	288	286	281	mmol/kg	p = 0.0001
Osm Calculated	290	288	281	283	mmol/kg	p = 0.0001
Osm Gap	1	0	5	-2	mmol/kg	p = 0.0001
Sodium	138	137	132	134	mmol/L	p = 0.0001
Potassium	4.4	4.5	4.7	4.2	mmol/L	p = 0.0001
Urea	7.1	7	7	7.9	mmol/L	p = <0.05
Glucose	6.5	6.2	11.2	8	mmol/L	p = 0.0001
Proteins	65	62	55	58	g/L	p = 0.0001
Albumin	40	38	34	35	g/L	p = 0.0001
Calcium	2.27	2.16	2.04	2.11	mmol/L	p = 0.0001
Co_2 [HCO_3]	28	26	26	27	mmol/L	NS
Bilirubin	9	9	9	12	µmol/l	p = 0.0001
AST	19	18	18	20	U/L	NS
Alk Phosphatase	100	100	91	90	µ/L	p = 0.0001
Hb	13.8	13.4	12.4	12.5	g/L	p = 0.0001
PCV	0.408	0.39	0.364	0.369		p = 0.0001
WCC	9.3	8.6	8.6	11.6		p = 0.0001
Glycine amino acid		293	3599	290	µmol/l	p = 0.0001
Serin amino acid		155.6	255	157.5		p = <0.05
Alanine amino acid		335	539	456.9		p = <0.05

Table 1: *Shows means of biochemical and haematological serum content concentration levels on admission (A), at post-anesthetic (B), postoperative (C) and next morning (D) as reported at the BJU [5]- reproduced with kind permission of late editor Professor GD Chisholm.*

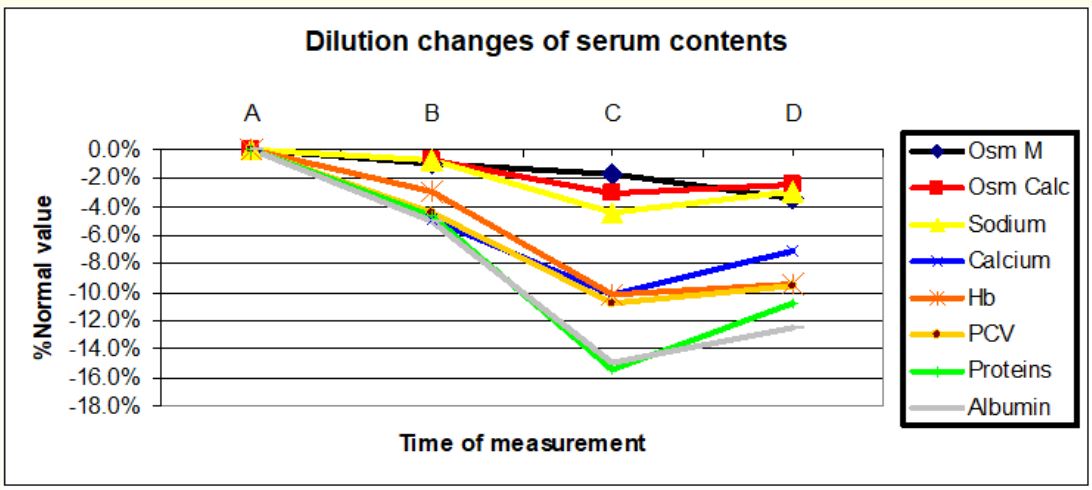

Figure 1: *Shows the changes of common serum biochemical and haematological contents. The most prominent dilution nadir is at postoperative C and despite correction tendency towards normal level dilution remained significantly low at D.*

The "VO and Time" are the two major "missing" factors from most reports that play vital roles in the pathogenesis of TURP syndrome and HN. The VO is directly while Time is inversely proportional to severity [22,23]. There is a difference between physiological and pathological VO that also differs from a type of fluid to another (sodium-free versus sodium-based fluids) and needs precise identification and quantification.

The data also show the increase in serum Glycine and Glucose that are solutes of the gained fluid bolus. Evidence of renal and hepatic dysfunction is shown but becomes obviously relevant and significant later. Evidence of early MVOD/F is shown by the 25% increase of leucocytes count, osmolarity gaps and acute renal and hepatic dysfunction plus the clinical evidence on respiratory, cardiac and cerebral (cell oedema) dysfunction and later failure. The fundamental difference between the TURP syndrome cases and asymptomatic patients is shown in table 2 that also lists absent alibi for the usual falsely incriminated suspects of haemorrhage and sepsis.

	Admission	Post-anaesth	Postop Recovery	Postop- 24h	p value
Time of measurement	A	B	C	D	
Plasma/ Serum Contents					
Osm Gap (M-C)	0.0%	-100.0%	400.0%	-300.0%	p = 0.0001
Osm M	0.0%	-1.0%	-1.7%	-3.4%	p = 0.0001
Osm Calc	0.0%	-0.7%	-3.1%	-2.4%	p = 0.0001
Sodium	0.0%	-0.7%	-4.3%	-2.9%	p = 0.0001
Calcium	0.0%	-4.8%	-10.1%	-7.0%	p = 0.0001
Hb	0.0%	-2.9%	-10.1%	-9.4%	p = 0.0001
PCV	0.0%	-4.4%	-10.8%	-9.6%	p = 0.0001
Proteins	0.0%	-4.6%	-15.4%	-10.8%	p = 0.0001
Albumin	0.0%	-5.0%	-15.0%	-12.5%	p = 0.0001
CO_2	0.0%	-7.1%	-7.1%	-3.6%	
Potassium	0.0%	2.3%	6.8%	-4.5%	p = 0.0001
Glucose	0.0%	-4.6%	72.3%	23.1%	p = 0.0001
Urea (RFT)	0.0%	-1.4%	-1.4%	11.3%	p < 0.05
WCC	0.0%	-7.5%	-7.5%	24.7%	p = 0.0001
Bilirubin (LFT)	0.0%	0.0%	0.0%	33.3%	p = 0.0001
AST (LFT)	0.0%	-5.3%	-5.3%	5.3%	p < 0.05
Alk Phosph (LFT)	0.0%	0.0%	-9.0%	-10.0%	p = 0.0001
Glycine amino acid		0.0%	1128.3%	-1.0%	p = 0.0001
Serine amino acid		0.0%	63.9%	1.2%	p < 0.05
Alanine amino acid		0.0%	60.9%	36.4%	p < 0.05

Table 2: *Shows % change of serum measurement of biochemical and haematological serum contents of normal on admission (A), at post-anesthetic (B), postoperative (C) and next morning (D). Note that the increases and dilution nadirs of contents are most pronounced at C and many remained significantly low at D despite tendency towards spontaneous correction. Increase in serum values at C and D occurred in Glycine, Glucose, K^+, renal and hepatic function tests and leucocytes count. Modified from table reported at the BJU [5] reproduced with kind permission of late editor of BJU Professor GD Chisholm.*

The clinical presentations of hypotension shock, cardiac bradycardia, dysrhythmia or arrest, respiratory distress or arrest, ARF and coma of cerebral edema are given. The introduction and discussion refuted false evidence and proposed the pathogenesis mechanism of cell edema ischemia occurring at the cell in HN and at capillary wall in cases of VO shock without HN or ARDS [5,22,23]. The physics evidence on the dynamic capillary-interstitial fluid exchange was appendix in Thesis [22] and was later reported at Medical Hypotheses in 2001 [25].

The 10 TURP syndrome patients entered RCT, 5 patients treated with 5%NaCl given promptly rapidly at onset that cured the sings and induced massive diuresis. The other 5 were conservatively treated with diuretics, saline and blood infusions that caused deterioration into coma, convulsion and paralysis of one patient thought to have suffered cerebro-vascular accident but was cured with HST later. The other 4 patients were totally confused. Figure 2 compares SSC changes in both groups. Diuretics up to 4 times the normal dose failed while belated 5%NaCl cured these patients and many others from the study and elsewhere.

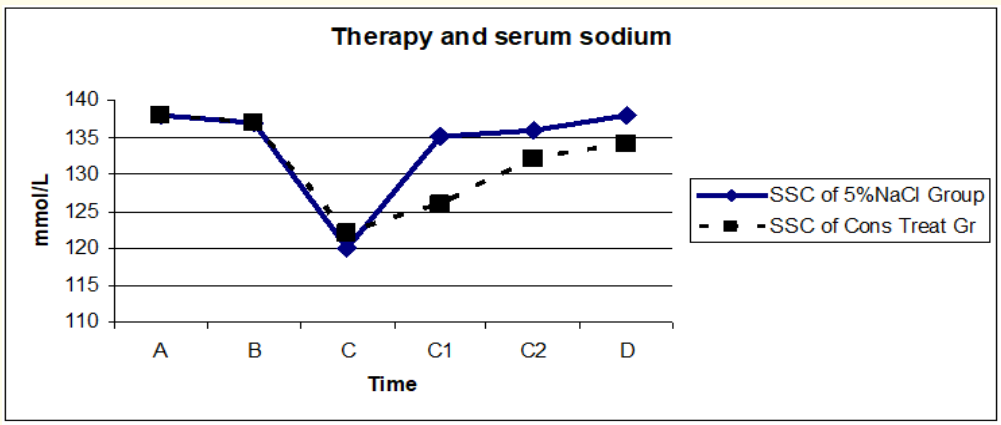

Figure 2: *Shows serum sodium concentration (SSC) level of 5% NaCl and conservative treated groups. The 5%NaCl infusion corrects SSC with prompt diuresis and recovery from coma. Infusion of saline-based fluid, blood transfusion and diuretics of conservative therapy though elevated SSC it caused clinical deterioration into coma of one and confusion of 4 patient at the 1st (D), 2nd-3rd postoperative days. Measurements at A, B, C, D as in table 1 and C1, C2 before and after therapy.*

The SSC rose to near normal of 137 and 134 mmol/L at the 1st-2nd postoperative days. Figure 3 shows the changes in measured serum osmolarity following both therapies, the terminal osmolarity gap seen in cases of MVOD/F affected the conservatively treated group only. The initial osmolarity gap was seen in all cases is shown in tables 1 and figure 3. Figure 4 shows the relation of VO and type of fluid in the TURP syndrome cases.

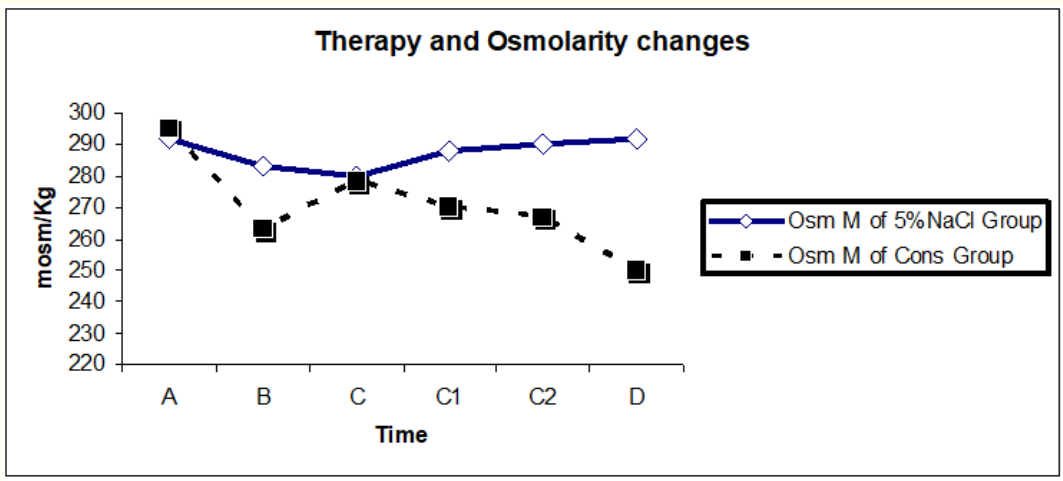

Figure 3: *Compares osmolality changes following 5% NaCl and conservative therapy the time scale includes the 2nd and 3rd postoperative day (points 5 and 6, respectively) where the osmolality gap at 6 is remarkable.*

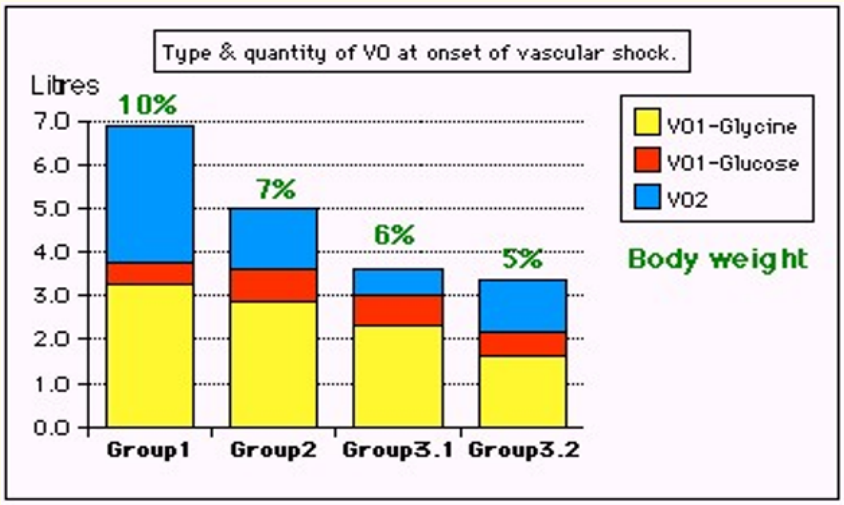

Figure 4: *Shows volumetric overload (VO) quantity (in litres and as percent of body weight) and types of fluids. Group 1 was the 3 patients who died in the case series as they were misdiagnosed as one of the previously known shocks and treated with further volume expansion. Group 2 were 10 patients 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 expansion using isotonic saline.*

Furthermore, Multiple linear regression analysis of all serum content changes and suspected causes in relation to clinical severity score showed significance of VO (p = 0007) and osmolarity (p = 0.0212) only. Serum solutes changes of sodium (p = 0.0597), albumin (p = 0.4809), Hb (p = 0.2587) and glycine (p = 0.4537) were insignificant [5]. If VO and osmolarity were removed from analysis the next two variables get promoted and gained significance! This is the 4th statistical error, identified here as the corrupt factor. It is commonly seen and gives inflated importance to a factor when the real relevant cause of disease is unknown thus unintentionally excluded from analysis. When deliberately excluded, by conflict of interest, it screws and corrupts the results.

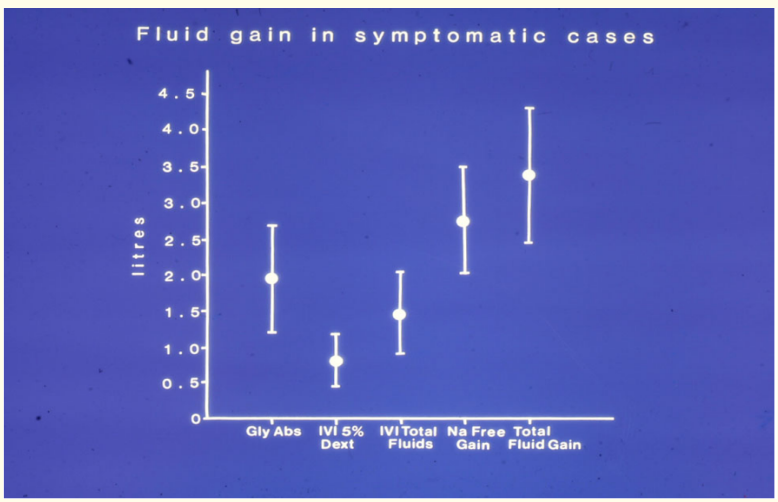

Figure 5: *Show the relation of fluid type and volumetric gain in the TURP syndrome cases from the prospective study.*

	TURP Synd.	Asympt.
Number of patients	10	90
P-value	* p = 0.0001	** p < 0.05
Volumetric Overload (VO) ml		
Glycine Irrigant Gained	1940	450
Intravenous iv Fluid Infused		
5% Dextrose	500	410
Saline	1100	500
Sodium-free Fluid	2440*	860
Sodium-based fluid and Blood	1100	500
VO Total	3540*	1360
Serum Glycine μmol/l	10499*	1508**
Serum Sodium Concentr'n Nadir	120.7*	132**
Serum Sodium Drop	17.4*	4.4**
Serum Osm D Drop	11.4*	0.7
Mean Measured Blood Loss	354	360
Maximum Blood Loss	< 0.410	< 1.31
Patients transfused	1	14
Urine culture +ve (UTI)	0	7
Blood Culture +ve	0	0
Hypothermia	0	0

Table 3: *Shows means of VO, osmolarity and serum sodium changes of the TURP syndrome and asymptomatic post TURP patients at C Time. Note the absent alibi of false suspects in hypotension shock such as blood loss, infection, bacteremia and hypothermia. When entered in Multiple linear Regression analysis only VO and Osmolarity were significant at (p = 0.0007) and (p = 0.0212), respectively. Serum sodium, Albumin, Haemoglobin and Glycine did not reach significance.*

Discussion

Some of the Quiz questions are very difficult to answer with current understanding of physiology and medicine. Don't feel bad about it as it has eluded authors who spent their career lives researching the TURP syndrome and HN but have not seen the obvious yet. If it makes you feel better, it took me 33 years to prove some answers given above and others below.

There is only one reported study that did precisely that. The above data in tables and figures and more in the original report are there [5] and all data and concepts have already been verified by others yet conclusions are fundamentally different! This was feasible because the author knew his hypothesis and what exactly was he looking for before conducting the prospective clinical study and RCT of therapy on TURP patients. This study may be considered the least expensive but most comprehensive and productive RCT ever!

Of relevance to the reported case: eye manifestations of the TURP syndrome are not new [26]. It has been documented that the TURP syndrome may cause sudden "Temporary Bilateral Blindness" preceded by diplopic blurred vision. Such eye manifestations have been attributed to glycine neuro-toxicity impeding nerve conduction. If you opt for "Toxic-Septic" hypothesis for the TURP syndrome, as the greatest researcher of the TURP syndrome of all times does, please remember before you incriminate the "glycine amino acid", that it is NOT mandatory for inducing the TURP syndrome at all as it occurs with glucose [11-14] and mannitol [16-19] and sorbitol. In fact if you think harder, one may find that neither glycine, nor TURP surgery, nor the syndrome name, nor definition and nor serum HN are mandatory either! Glycine may be just like alcohol an excellent marker for irrigating fluid absorption during TURP and may have similar toxicity at higher doses.

The "Toxic-Septic" hypotheses have been major conspiracy, (A discrepancy which distracted and eluded researchers for a long time), that mislead research and understanding. It has recently been confirmed, as known for decades, that 5% Glucose causes the TURP syndrome [11-14] as does Mannitol [16-19] and Sorbitol via the same cell "oedema ischaemia hypoxia" of the brain and heart in humans [11-14] and animals [10,15]. This occurs in the absence of arterial insufficiency, any toxin of chemical or sepsis origin as well as in the absence of arterial hypoxemia! It is impossible to incriminate arterial hypoxemia in theatre setting where a patient is rapidly correctly intubated, ventilated and well oxygenated. The eye is indeed the mirror image of the brain. The heart, lungs, kidneys and liver are similarly affected plus subtle haematological and gastro-intestinal abnormal findings [5].

The visual symptoms are only reported when the patient is conscious during a procedure performed under regional anesthesia. For obvious reasons the eye symptoms can neither be reported by patients under general anesthesia nor when he goes into coma due to cerebral edema. Eye examination at such time reveals the bilateral swollen optic discs. At this time visual loss is usually "temporary and recoverable", after couple days it is "permanent".

It is most interesting that the eyes not only show optic disc "oedema ischaemia hypoxia", but also its "vitreous body fluid" shows another unique finding of the TURP syndrome: severe HN matching that of the blood. Such HN of "vitreous body fluid" was reported by a group of pathologists on PM examination of patients killed by the TURP syndrome [27]. For mentioned reasons the SSC was normal and the syndrome was not considered a clinical diagnosis.

The authors of this unique letter suggested that estimation of sodium concentration of the "vitreous body fluid" at PM examination is diagnostic of the TURP syndrome even in the absence of serum HN. Even after the apparent correction of SSC level, vitreous body maintains HN for couple of days longer than serum HN nadir. This remains true even when erasure or apparent correction of SSC is induced by sodium-based fluid infusions given with the good intension of "resuscitation" but in fact cause deterioration, internal drowning and death.

A conflicting fact about the TURP syndrome is that it is not an acceptable cause of death in any mortality register of any country- yet hundreds or thousands of killed victims are reported in the literature! The cause of death is usually given the name of the echo crime of circulatory failure, cardiac or respiratory arrest or cerebral coma! This serial killer leaves no evidence, no trace, eludes witnesses and all its victims are either dead or in vegetative state of coma with no records.

Such illuminating PM evidence was reported in a letter [26] that remains the only unique evidence on the TURP syndrome at PM examinations! But, who cares to notice a letter in an era when prospective RCT that are enormous in size and expense are considered the only way for evidence-based medicine (EBM) irrespective whether it delivers solutions or not?! The evidence on such failure is demonstrable in both the TURP and the MOFD/F syndromes that also started as ARDS [28], changed to MVOD/F [5] and now called SIRS.

The prospective RCT with powerful computers and statistics, that I indeed use, are excellent and mandatory tools for verifying and providing the pieces of evidence, epidemiology research and comparing therapies but it has its limitations! It cannot, and will not, make discoveries neither in science nor in medicine when employed and interpreted with tunnel vision! How can a researcher prospectively use it for testing a hypothesis unknown to him, rejected or excluded as it does not conform to classic institution teaching?

Does the size and accuracy of data matter if interpretation is inaccurate as the interpreter is prejudiced with fixed idea, out of focus on what is important or unable of segregating the relevant from irrelevant? Many remember but can anyone imagine surgery and urology today, if the debate on laparoscopy went the wrong way and awaited verification by prospective RCT? I do not call for discarding prospective RCT here but indicate that other methods do provide equally valid evidence for EBM. Also statistical analysis is a wonderful powerful useful tool with known errors and lies but there is also the corrupt 4th error mentioned above.

The answers to most current medical dilemma do exist precisely in mind where the right question originated before it can be verified using any means and methods! This is when the invisible obvious becomes obviously visible that it may become so obvious that it becomes ludicrous trying to prove! In community, the mind can't see what the eye can't. In science, however, a creative mind sees before his own eyes can, followed by peers when enlightened and public when informed about whatever has been discovered or invented!

There is no substitute for experience. Observation and critical analysis among criteria that defines the creativity of human mind remain irreplaceable! There is still prominent and respectable place for letters, case reports, commentaries, literature analysis, case series, retrospective and observational studies and testimonials that prospective RCT may later verify but cannot replace.

Thus, I would agree with the authors and congratulate them on their case being the first I read as "PBB" to complicate the TURP surgery and for which the TURP syndrome was not incriminated [1]. I accept their reported findings including predisposing factors of hypotension shock though the apparently low haemoglobin and haematocrit may indicate dilution rather than anaemia of blood loss as shown in table 1 and figure 1. The reported intra-ocular signs may urge them to reconsider the TURP syndrome as a culprit in the light of this discussion. In fact the above case scenario, quiz and questions do apply to any TURP syndrome and acute dilution HN case whether reported or not- should data remain available even if the vital factors are missing.

It is worth noting that the advances in surgical and urological training as well as anesthesia techniques particularly on ICU in areas of cardiovascular, respiratory and renal support has not only reduced incidence but also actually modified the TURP syndrome presentation. This has allowed victims to survive longer with some "novel" masks or different morbidities such as PBB! Such incremental progress is one of the fundamental reasons among others that both the TURP and MVOD/F syndromes keep changing both their names and definitions.

The next statement is not aimed at confusing you further, and does not mean I withdraw anything I said above. It simply means forewarned is better armed! I only aim to show you a glimpse of the future that I saw clearly so long ago [5,22,23,25,29,30] as I do now and tomorrow [23,25] so that we may choose to do something to prevent it. It is our choice to determine our fate but only those who foresee the future may save it!

There are identical cases of blindness in which serum sodium may genuinely be normal, the authors referenced some, and we shall be seeing more in future. It shares most of what is mentioned above particularly cell edema of HN manifesting as MOVD/F and internal drowning with interstitial tissue of mainly trunk edema seen so commonly on ICU to complicate excessive sodium-based fluid infusions in cases of ARDS. Patients who improve must lose it before discharge and those who die go with it. However, the cell edema differs on two issues: HN is completely out of the picture and with which goes the definition and name of the TURP syndrome. The cell "oedema ishaemia hypoxia" mechanism remains, but its explanation exists elsewhere at the capillary wall as a result of failure of the optimum dynamic capillary-interstitial fluid circulation [25]. Here normal tissue/cell irrigation that is vital for viability of cell is replaced by flood drowning that kills viability of cells.

As 1.5% glycine has already been replaced by saline irrigation for the TURP surgery, HN will vanish into oblivion. The TURP syndrome will re-strike when it will not only be invisible but also without name or definition. It may vanish from urology not because it has finally decided to retire or repent, but in order to reappear with new mask under new name and definition. It will continue to get away with its crimes, if opportunity to solve its puzzle as it stands today is missed! The old story of the TUPP syndrome and HN ends here. The new conditions that I already know future names [23] may continue, but we now know how and where the culprit will be hiding.

Last but not least, I wish to affirm that both the TURP syndrome and acute dilution HN have a successful curative therapy of hypertonic sodium therapy (HST) of 5% NaCl [5,29] or 8.4% NaCo3 commonly available at resuscitation trolleys and equally effective. 29.2% NaCl is most effective but not recommended as it causes severe phlebitis and thrombosis. Such therapy guarantees complete recovery from shock, ARF and coma, when and if "accurately timely and promptly given" that prevents the patient deteriorating into the hopeless vegetative state physicians have to face as chronic HN when brain damage is irreversible [11-14,31-33]. Yet HST of 5% NaCl still worth a try as one can only be pleasantly surprised by seeing a Lazarus or two- curtsey of Dr MD Penney [29] who tried the therapy on his own patients and told me what the name means.

The therapy should be given promptly, rapidly without dithering or waiting for radiology to confirm the diagnosis. If the immediate postoperative biochemical and hematological evidence do not convince you nothing else will. I would recommend that after taking the blood sample for analysis to start therapy immediately without even waiting for the results. Just make sure you do not infuse any other fluids or blood. Please also refrain from replacing urine output when the patient passes 3 - 5 liters in response to HST therapy as he recover from coma and ask for a drink- both you and your patient deserve one.

The sprit of 3 killed patients refuses to let go of me, having tried long and hard enough to convince peers. A voice in head keep saying: "This is not good enough. No excuses. You must inform colleagues and authorities in order to make sure that the TURP syndrome does not kill, insult or blind other patients under whatever mask it disguises behind or name it uses". In despair, however, I recall the faces of those 20 patients I saved their lives just as they open their eyes awaken from coma asking for a drink. With their courteous smile encouraging me to keep exposing the offender while persuading colleagues.

The last 33 years of my career life were spent in investigating and reporting these articles [34-37]. The articles recognizes 2 new types of shocks and its treatment, proves that Starling's law for the capillary interstitial fluid transfer is wrong and provides an alternative mechanism; the hydrodynamics of a porous orifice (G) Tube. These discoveries resolve the puzzles of 2 clinical syndromes discovering its patho-etiology and new successful treatments; namely the TURP syndrome and ARDS.

Volumetric Overload Shock (VOS) is a clinical condition induced by large fluid infusions in a short time and is of two types; Type one (VOS1) and Type two (VOS2). VOS1 is induced by sodium-free fluid gain of 3.5 - 5 litres in one hour such as Glycine, Glucose, Mannitol and Sorbitol. It is seen in the TURP syndrome [5] or HN shock [4]. VOS2 is induced by massive infusion of sodium-based fluids such as normal saline, Ringer, Hartmann, plasma, plasma substitutes and blood transfusions that may complicate the therapy of VOS1. VOS2 also complicates fluid therapy in critically ill patients suffering from other known shocks such as hypovolaemic, haemorrhagic and septic shocks and presents with ARDS [28]. VOS2 is induced by the gain of > 12 litres of sodium-based fluids when reported in ARDS. The presence of massive interstitial tissue oedema with engorgement of vital organs, pleural and peritoneal effusions, in the presence of hypotension shock, casted doubt on Starling's law! These issues were investigated at the clinical and physiological/physical fronts [34-37].

Two clinical studies aiming to understand the TURP syndrome and recognizing VOS were done. A prospective clinical study on 100 consecutive TURP patients of whom the condition of TURP syndrome affected 10 patients with severe hypotension and bradycardia and severe acute dilution hyponatraemia of < 120 mmol/l [5]. Volumetric overload was the only significant factor in causing the condition. The second clinical study involved a case series of 23 cases of the TURP syndrome manifesting as VOS1 [37]. Volumetric overload quantity and type is shown in figure 4. The first 3 cases died as they were diagnosed and treated erroneously as one of the recognized shocks and treated with further volume expansion. The remaining 20 patients were correctly diagnosed as VOS1 and treated with HST of 5% Sodium Chloride or 8.4% Sodium Bicarbonate. Each patient passed 4 - 5 litres of urine followed by recovery from shock and coma. This treatment was successful in curing all patients bringing them back from dead [37].

Declaration of Interest

None declared by the authors.

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