Serum sodium changes during and after transurethral prostatectomy

Sir,

I read with interest this timely article,[1] on which authors and editors are commended. It demonstrates that postoperative hyponatremia (HN) is common, (41%) but the transurethral resection of prostate (TURP) syndrome may not be encountered. It is humbly gratifying that the authors do not only affirm the accuracy of our study data[2] but also support conclusions and concepts inviting clarification. As mentioned, HN is a common postoperative complication but a segment causes serious morbidity and mortality among men,[1,2] women[3] and children[4,5] that affects about 1% or 250,000 cases among roughly 25,000,000 inpatient operations performed each year in the United States of America.[6] It remains unknown when and why HN may cause such serious morbidity and mortality or how best it should be treated.[3-6] Its illusive presentations to surgeons and physicians highlight its great interest to both and the international concern and anxiety it causes. Hyponatremia and the TURP syndrome are elusive because they lack clear precise definition. Pathophysiology and etiology are unknown. Diagnosis and differential diagnosis are difficult and management is hotly debated. Serious and lethal cases were reported retrospectively[3-6] and prospective studies[7] have repeatedly added little but fueling debates.

Hyponatremia is a multidimensional clinical and biochemical jigsaw puzzle. Resolving it required precise quantification of the insult and identification of factors affecting HN nadirs, severity grades and clinical masks. This scientific challenge, undertaken since 1984,[8] was unraveled at basic physics and physiology,[9] and the clinical front.[2] It required more than the analysis of thousands and doing some prospective studies. Observation, vision and analysis over 17 years of hard work allowed a forthcoming final solution. Although most of the puzzle pieces were added by hundreds of authors, the vital stepping-stones[10,11] that led through the difficulties to a new understanding have been overlooked or ignored until a decade ago.[2] "Shock and hypertonic sodium therapy" were reported half a century ago.[10,11] The received 21 dilutional and toxic hypotheses[1,2,7] used interchangeably and in combinations with recognized clinical conditions for explanation testify that the puzzle of HN and TURP syndrome has remained unresolved. The main insult is rarely reported. It is so obvious that it is invisible. Also, dynamic range and nadirs of HN allowed many false interpretations and conclusions of the same data. The TURP syndrome is thought 'well known rare obscure entity limited to urology'. It is induced by irrigant absorption and characterized by acute dilutional HN.[11] Though most cases are self-correcting, understanding the pathophysiology may improve management of serious HN cases presenting postoperatively with sudden death, shock or vital organ dysfunction/failure (OD/F) of encephalopathy that leaves the patient in a vegetative state.[3-6] The TURP syndrome was foreseen as a unique example for resolving the puzzle of such severe or lethal postoperative HN.

The TURP syndrome is unique in that: The time of surgery, usually <1 hour, is exactly the time during which the absorbed irrigant responsible for most of the dilution of serum solute contents occurs. The bottom line for understanding the pathophysiology of postoperative HN and the TURP syndrome concerns: How much volume, of what type and during what time a fluid gained access to the vascular system, and what is its immediate hemodynamic and late clinical effects? Volumetric overload (VO) is the main insult, reported over a decade ago.[2] It is the only significant factor in a multiple regression analysis ($p=0.0001$). Osmolality and HN were also significantly important but transient, lasting hours and days. Volumetric overload has not been fully appreciated, particularly when its type of sodium-free (VO1) and sodium-based (VO2) fluid, and time (T) are taken into account in relation to HN nadirs and its clinical presentation masks. Unbelievably, half a century of prospective research on HN and TURP syndrome neither addressed these issues nor provided answers! Precise relation of VO to severity grade, nadirs and presentation masks of HN is necessary for making the correct diagnosis, differential diagnosis and management. Precise VO was at best assumed and there remain other factors and paradoxes to be recognized that cause errors and misconceptions to be corrected.

Local factors that relate to the TURP procedure are well known to affect the quantity of absorbed irrigant.[1,2,7] They mainly testify to the urologist's experience with such highly technical procedure, and are relevant to the prevention of fluid absorption but of limited value to the pathophysiology and management of both the TURP syndrome and dilutional HN. Our study quantified fluid balance during and after TURP and determined its effect on serum osmolality, sodium and other solute contents, correlating this with the clinical picture while taking T into account.[2] The total VO of absorbed irrigant and intravenously infused (IVI) fluids of 3.5L induced severe HN and TURP syndrome. Other authors affirmed our data[1,7] but not many could accept new concepts because it contradicts received

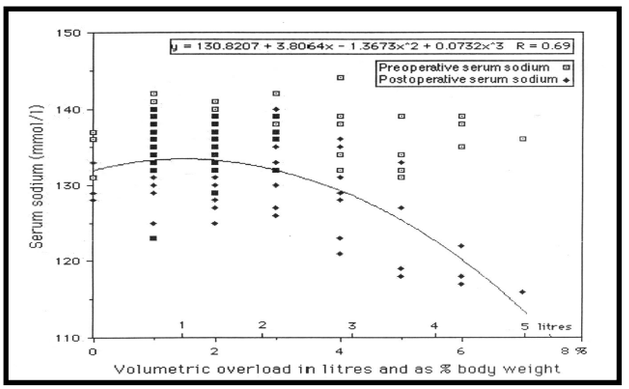

Figure 1 - A scatter graph of pre and post-operative serum sodium concentrations of 100 transurethral resection of prostate patients with a curve fit of the latter demonstrating the direct proportional relationship between volumetric overload (VO) and drop of postoperative serum sodium level. Volumetric overload includes both absorbed 1.5% glycine irrigant and the intravenously infused fluids. The 10 cases that suffered from the transurethral syndrome are segregated on the right lower part of the graph. Their mean VO was 3.5L (5% body weight).

wisdom on fluid therapy. Full implications of "VO versus T" require clarification. The route of fluid gain, whether through prostate, peripheral vein or peritoneum, is of minor relevance.

The biochemical definition of a severe TURP syndrome is an acute drop of serum sodium of >15 or to a level below 120 mmol/l.[2,7] Hyponatremia of lesser magnitude is usually self-correcting. Based on this definition, most prospective studies conclude that they have not encountered the syndrome. Linking biochemical with clinical definition by identifying prodromal symptoms of minor irrigant absorption[2,7] and the gross systemic disturbance of massive VO, it would be easy to identify and detect symptomatic and non-symptomatic HN patients, and conclude whether the TURP syndrome occurred or not. Reporting data[2,7] has not resolved the puzzle, why? Most authors quoted the well-known fact that HN of the TUR syndrome is induced by the absorbed electrolyte-free irrigant such as glycine, mannitol, sorbitol and glucose. Yet, most studies on the TURP syndrome and postoperative HN did not report the quantity of VO1 fluids responsible for the dilutional changes of all serum solutes. Furthermore, the drop of serum contents such as sodium, calcium, protein and hemoglobin (Hb) is thought due to "loss" rather than VO1 dilution, causing repeated errors on data analysis, interpretation and conclusions. In particular, the relation of VO to vascular hemodynamic shock, with respect to dilutional HN as marker in the absence of any sepsis or hemorrhage shock, require careful analysis for reaching the correct conclusion. Other illusive aspects are: The role of T in inducing the dynamic HN nadirs and the presentation with OD/F masked as cerebral[3-6] or cardiac infarction, respiratory, renal and/or hepatic failure.[1,2] **Figure 1** demonstrates the relation of VO1 of combined absorbed irrigant and IVI fluids to the postoperative serum sodium level, with direct proportional relationship between VO1 and HN. **Figure 2** shows the changes of serum solute concentrations at the immediate postoperative period as a percentage of preoperative normal values, comparing non-symptomatic and symptomatic patients, and at 24 hours for the latter group. All these diluted serum contents gave rise to dilutional, and most raised solutes gave rise to toxic hypothesis, to which glycine, ammonia[9] and sepsis toxicity are unduly added. Serum glycine was raised to 10499 and returned to normal level of (293) μmol/l at 24 hours later, without specific therapy. The graphs are data of prospective study on 100 TURP patients[2] and reproduced from Medical Dictorate Thesis accepted

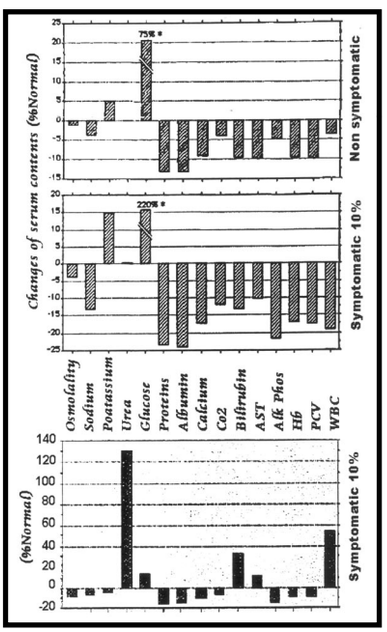

Figure 2 - Demonstrates the immediate postoperative changes of serum solutes as percent of its normal preoperative level. The top 2 graphs represent none symptomatic majority and 10% symptomatic cases that suffered from the transurethral prostatectomy (TURP) syndrome. All low serum solutes have all been incriminated in hypotheses for the TUR syndrome. The real culprit of sodium-free fluids volumetric overload type one (VO1) is invisible as it contradicts preconceived concepts on fluid therapy. The bottom graph demonstrates raised renal and hepatic function tests and white cell count. Elevation of solute levels may be physiological recovery after diuresis or illusive pathological due to osmotic water shift into cells. CO2 - carbon dioxide, AST - aspartate transaminase, Alk Phos - alkaline phosphatase, Hb - hemoglobulin, PCV - packed cell volume, WBC - white blood count.

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The objective here is to introduce new concepts of relevance to the aetiology of TUR syndrome in particular, postoperative HN in general and conditions induced by massive VO at large. Namely to identify the role of "VO versus T" in pathogenesis of the paradoxical "VO shock", affirming that "hypotension is not synonymous with hypovolaemia" in the management of shock. Making the analogy of OD/F to severe presentations of HN and TURP syndrome serves the aim of unveiling illusive masks. This may help resolving the complex clinical puzzles by suggesting that brain and heart infarction or OD/F my be masks of HN rather than primary vascular occlusive anoxic etiology.[3] My research has revealed common errors and misconceptions with roots that extend deeper into the basic physics and physiology.[9] This is particularly important when HN is erased by massive VO2 fluids infusion in the belief that haemorhage, hypovolaemia or sepsis is at operation. The concept of "aggressive volume expansion" for shock therapy requires reconsideration in view of the observation that VO paradoxically causes shock and anuria,[2] and the recently reported discovery.[9] The bizarre features of the TURP syndrome and wide range of severity, paint the illusive masks of clinical presentations, making the differential diagnosis enormous and extremely hard. Prodromal symptoms may be attributed to anaesthetia or drugs while severe cases may be mistaken for recognized medical conditions of shock, cardiac or brain infarction. The cause of death may be missed, even at postmortem examination.[12] The fact that one or 2 litres of normal saline are better tolerated than a hypotonic 1.5% Glycine or isotonic 5% Dextrose solution, does not mean a direct proportional relationship between VO2 quantity and safety. Though VO2 fluid may correct low serum sodium, it makes HN illusive, confuse diagnosis and aggravate VO causing internal drowning. The osmotic shift of water into the intracellular compartment causes apparent improvement of tertiary HN that masks "Missing VO1",[13] giving false sense of security while cellular dysfunction of OD/F occurs. Cellular, unlike interstitial venous and cardiac, oedema is not pitting. It manifests with the bizarre features of OD/F. Elevated renal and hepatic function tests and white cell count occur as a result of the "VO versus T" insult **(Figure 2).** The presentation of dilutional hyponatraemic shock[10,11] induced by large VO1 and manifesting with acute vascular hypotension is paradoxical.[2] It misleadingly calls for further 'volume expansion' with VO2 fluids for combating the hypotension shock. Treating such shock with further 'vascular expansion' causes irreversible shock and establishes OD/F.[9] Acute massive hypervolaemia, like hypovolaemia of severe hemorrhage, causes profound haemodynamic disturbance of shock as well as internal drowning. Such concept can only be understood when the newly reported phenomenon discovered in the porous orifice (G) tube,[9] which mimics a capillary, is applied to the capillary-interstitial fluid and circulatory dynamics. The G tube phenomenon challenges the physiological law dictating the rules on fluid therapy and underling the current received concepts on managing the acutely ill patients.[13]

The real value of understanding the exact pathophysiology of the 'well known rare obscure TURP syndrome' lies not only in resolving its own puzzle but also that of its common identical twins[8] presenting with HN encephalopathy.[3-6] This may pave the way for identifying new type of vascular shock and optimizing fluid therapy in shock management that may resolve the puzzle of OD/F syndrome.[9,13]

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