

Postoperative Dilution Hyponatraemia and the TURP Syndrome: Critical Analytical Review of Literature on Patho-Etiology and Therapy

Ahmed N Ghanem*

Consultant Urological Surgeon, Mansoura, Egypt

***Corresponding Author:** Ahmed N Ghanem, Consultant Urological Surgeon, Mansoura, Egypt.

Received: May 30, 2019; **Published:** July 05, 2019

Abstract

Introduction and Objective: To present a critical analytical review on hyponatraemia (HN) and its diagnosis and therapy. The concept of volumetric overload shock (VOS) as the real patho-aetiology is affirmed. The correct therapy is hypertonic sodium therapy (HST) of 5% NaCl or Sodium bicarbonate of 8.4% NaCO₃.

Materials and Methods: The critical analytical review of literature on HN is presented. Results of my own research on the condition are summarized.

Result: Literature analytical review on HN demonstrates that it has been proved most illusive gigantic puzzle that eluded researchers over the last 7 decades. HN of < 120 mmol/l can be serious or fatal. It presents as circulatory shock to surgeons and anesthetists during or immediately after the surgery and as coma to physicians later. Its real patho-etiology is VOS and the correct therapy is HST.

Conclusion: The puzzle of acute dilution HN has been resolved by introducing the concept of VOS and the successful life saving treatment of HST of 5% NaCl or 8.4% NaCO₃.

Keywords: *Hyponatraemia; TURP Syndrome; NaCO₃*

Background

The following critical analysis is intended to be neither ordinary nor comprehensive literature review. It quotes original authors for their clinical observations and factual data but may agree or disagree on their interpretation and conclusions.

Critical analysis of literature

A recent MEDLINE search returned about 3/4 million reports on HN and over 3 thousands on the transurethral of the prostate (TURP) syndrome. The main bulk of evidence pieces were contributed by hundreds of authors over the past 7 decades. A Swedish Team headed by Professor Hahn contributed >340 articles during the last 2 decade [1], affirming known data and adding new pieces fitting the puzzle but it has remained scrambled. Like most previous authors dilutional and toxic hypotheses explaining pathophysiology of the TURP syndrome were advanced. This has always led to a dead end due to a fault at basic physiology.

Previous prospective studies highlight the controversies on the on HN and TURP syndrome [1-11]. Although all studies are correct and similar, the insult of "VO versus T" causing the dynamic HN nadirs and illusive clinical masks was invisible, allowing different data interpretations and conclusions to be drawn. It remains unknown why HN is none symptomatic at times [2-4] and severe or lethal at another [2,8,9]. Something serious is amiss making HN so illusive. When HN presents with shock and anuria to surgeons [9] it is attributed to multiple dilutional and toxic hypotheses or to recognized shock and accordingly treated with further volume expansion with disastrous results [7]. When it presents with coma to physicians, among other features of the multiple vital organ dysfunction/ failure

(MVOD/F) syndrome, it is attributed to recognized coma with huge differential diagnosis [2-7]. The main objective of investigations was to understand this condition and identify a single insult for explaining the generalized cell disorder and its bizarre MVOD/F features manifesting as severe to lethal HN and the TURP syndrome [9].

Of historical interest, in 1948, Creevy [11] coined the name TURP reaction induced by the absorption of distilled water irrigant that caused red cell haemolysis. In 1913, Rowantree [12], first reported acute water intoxication. Since the introduction of osmotic electrolyte-free irrigants, haemolysis is no longer seen in current clinical practice [2]. Irrigant absorption induces the current TURP syndrome characterized by acute dilutional HN [13]. Literature analysis demonstrates that all postoperative HN was also induced by electrolyte-free fluid of 5% Glucose but rarely reported. Professor Arieff reported this fact in a unique article [14].

In 1946, Danowski, Winkler and Elkington [15], first reported HN shock and introduced its hyper tonic sodium therapy (HST) of 5% NaCl. In 1956, Harrison, *et al.* [13], reported the TURP syndrome as 'dilutional hyponatraemic shock' and the first clinical use of HST of 5% NaCl as successful treatment.

Basic issues

HN is the obvious prominent marker among many dilutional serum solute changes [1-7]. However, it was noted that HN was unconvincing for explaining pathophysiology of the TURP syndrome [16,17], as its nadir has not consistently matched clinical severity. Hence, other 20 dilutional and toxic hypotheses plus multiple recognized clinical conditions have been used interchangeably and in combinations for explanation of its patho-etiology [7-9]. Some authors thought that hypo-osmolality [1,18,19] was more potent pathological mechanism than HN [1]. Though correct, hypo-osmolality has proved more illusive and rapidly transient than HN.

As mentioned, fluids in common clinical uses are of two main types: Sodium-free fluid volumetric over load Type 1 (VO1) of 5% Dextrose and 3% Mannitol are isotonic to plasma. Irrigant fluids of 1.5% Glycine (hypotonic of 200 mosm/l), 3% Mannitol and 1% Sorbitol (isotonic) gained importance as absorption is common after TURP surgery [8-14]. Sodium- based fluid volumetric overload Type 2 (VO2) include 0.9% Normal Saline, Ringer Lactate, Hartmann's, plasma substitutes such as 'Dextran', plasma and blood. The value of ivi fluids in saving millions of lives is undoubted. Like any good therapy, however, it has side effects and complication. An excess quantity of fluid gaining access into the vascular system is referred to here as VO, which though iatrogenic is inadvertent.

Predisposing factors

Local factors that relate to the TURP procedure are well known to affect the absorbed irrigant [2,10] but quantity, type and T have been overlooked. Local factors of TURP surgery mainly testify to urologist's experience with such highly technical single-handed procedure, and of relevance to the prevention of fluid absorption [2]. Predisposing factors remain, however, of limited value to pathophysiology and management of both HN and the TURP syndrome, induced by the absorbed sodium-free fluid irrigant or VO1. This fact is overlooked in surgical setting when the syndrome presents with vascular hypotension shock [20,21], it is unduly attributed to haemorrhage [20] or sepsis [19]. Ghanem has proved that it is a new type of shock called volumetric overload type 1 shock of sodium-free fluid type 1 (VOS1) [10,21-24].

Patho-physiological aetiology

In most studies on the TURP syndrome, as indeed in hospital-induced postoperative HN, the quantity of VO1 fluids responsible for the dilutional HN and other serum contents is not reported. This has repeated errors on analysis of data, interpretation and conclusions. The only prospective study that quantified the precise per-operative fluid balance was ours [24,25], affirmed later by other studies [10,22,23]. The input fluids of absorbed 1.5% Glycine irrigant and ivi fluids during surgery as well as the output fluids of blood loss and urine were measured in a prospective study [24]. Sepsis was excluded by the negative urine analysis and blood and urine cultures of symptomatic cases.

Precise quantity of VO, its type and T during which it occurred (“VO versus T”) identified the dynamic insult that remains invisible. Although data of most prospective studies is correct and similar [2,5,16,25], the interpretation and conclusion was split and full implications require clarification. A rare report estimated VO1 of > 7L of 5% Dextrose in patients suffering from critical or lethal HN, in which Professor Arief correctly proposed a hypothesis of generalized cell anoxia causing the encephalopathy coma [14].

The stepping-stones

The words ‘Shock, HST and anoxia’ [13,14,15] are the most important advances provided by the last half a century of research on postoperative HN and the TURP syndrome. Ironically, the value of “shock concept” has been overlooked until recently [22,23]. When shock was considered, it was incorrectly attributed to bleeding [20] or sepsis [19]. Because HN has really never been a convincing cause of shock, other dilutional and toxic hypotheses were introduced [8,16,26,27]. The words were the main stepping-stones that led across the difficulties to new understanding since 1984. It encouraged one to persist with ardor, diligence and sanctity on exploring the un-trodden road away from the main stream of research on HN, TURP syndrome and MVOD/F syndrome.

Over-Under emphasized issues

The route of fluid infusion, whether through a prostate or peripheral vein, or the peritoneum, is of minor relevance but overlooking the precise gained VO caused split conclusions when shock or MVOD/F occurred. The hypothesis was that: all the bizarre presentations of severe HN and the TURP syndrome must have the same aetiology despite the multiple clinical masks of shock [22,23] and MVOD/F, occurring either individually such as coma [14] or in combinations [22,23]. It makes little difference whether VO induced electrolyte disturbance after fluid therapy for resuscitation of trauma and major surgery, the absorption of irrigant fluid during TURP procedure, gynaecological, renal stone, Laser surgery [34] or gained during dialysis or parenteral nutrition on ICU. What makes the real difference is: how and why VO quantity and type, and T culminate into the culprit insult causing shock and MVOD/F that is most illusive to surgeons and physicians.

Overlooked key issues

The dynamic effect of “VO versus T” on grades, nadirs and clinical severity masks of HN and TURP syndrome was overlooked or at best assumed. Multiple dilutional and toxic hypotheses confused the issue and made the “VO versus T” insult invisible and HN illusive. Having worked it all out, communicated the concepts as it progressed [28-38] and reported some studies [21,22,24] while other reports followed later [23] the scientific challenge took many years of observations, work and analysis to unravel.

New concept

The bottom line for understanding the patho-physiological aetiology of postoperative HN in general and the TURP syndrome in particular concerns: how much volume, of what type and during what time a fluid gained access into the vascular system, and what is its immediate haemodynamic effects and delayed clinical masks? The concept of shock affirmed not to be due to any of the unduly incriminated recognized shocks. Both vascular shock and acute renal failure (ARF) with oliguria or anuria [21,22] were observed paradoxical effects of VO and the analogy with MVOD/F was reported. Other authors [7] affirmed our data on incidence and quantity of absorbed irrigant and blood loss in the absence of sepsis. However, the concept of “VO versus T” has remained invisible so has the debate-resolving advances on the subjects [21-24].

It seems unbelievable that 7 decades of research on postoperative HN and the TURP syndrome neither addressed these issues nor provided precise answers! This may perhaps be explained by the fact that although the concept is simple, the clinical reality of HN is extremely complex and some received concepts on fluid therapy do not allow acceptance of the observed paradoxes of shock and anuria.

“VO versus T” induces HN and shock that determines its dynamic grades, nadirs, biochemical severity and clinical masks that are necessary for making the correct diagnosis, differential diagnosis and management. Although most cases of HN are none symptomatic and self-correcting, identifying the dynamic insult may improve understanding and management of severe to lethal cases [14] with wide biochemical range and clinical severity of HN in between.

A unique example

The TURP syndrome is generally thought ‘well known, rare, obscure and limited to urology’ but it was foreseen as unique model for resolving its own puzzle and that of postoperative HN. It is agreed that the TURP syndrome is induced by irrigant absorption and characterized by dilution HN. It has been reported clinically with all osmotic irrigant fluids including glycine, mannitol, sorbitol, ethanol, urea and glucose. This makes toxic and dilutional hypotheses and sepsis unduly incriminated, particularly as it has been induced experimentally in animals, big and small by ivi fluids, under clean conditions [15].

The TURP syndrome is a unique model of postoperative HN in that: the time of the TURP procedure of about one hour is exactly the time during which VO occurs and induces VOS [21,22]. Both irrigant absorption and ivi fluids contribute to VO but only VO1 is responsible for the dilutional HN, while VO2 though has no such dilution effect it adds to illusion. HN nadir is the lowest drop of SSC induced by a specific VO1 quantity. HN nadir is so dynamic and its main insult of “VO versus T” is so obvious that it has remained invisible and elusive.

Prospective studies

Investigations to resolve the puzzle of postoperative HN and the TURP syndrome have continued at basic physics/physiology roots [38,39] and clinical front [21-24]. Every argument was dully studied, verified, comprehended and concluded before communicated [28-37] and later reported [22-24]. Editors and Peers of respected Journals repeatedly rejected many articles that remain vague or immature such as a report on 23 case series of severe to lethal postoperative HN and TUPP syndrome, studied over a period of years from the time of onset [10]. The hardest aspect of this scientific challenge, however, was the lengthy difficult analysis of hundreds prospective studies data in order to identify correct, reject false and discover missing pieces that resolve the gigantic jigsaw puzzle.

Mild to severe features

Our prospective study [21,24] quantified the precise VO1 causing the lowest dilutional drop of SSC at the immediate postoperative (Secondary HN nadir) and at 24h later (Tertiary HN nadir) in relation to the clinical picture of the TURP syndrome, taking time T into account. Appropriate statistics demonstrated that VO of 3.5L is the real insult and most significant factor ($p = 0.0001$) causing the severe signs of HN and TURP syndrome. Such data made it feasible to determine whether the patient was in a state of hyper or hypovolaemia when shock occurred. It also allowed the determination of the “Missing VO” that shifted out of intra-vascular fluid (IVF) and extra-cellular fluid (ECF) compartment into the intracellular fluid that was not reflect by the tertiary HN nadir and made clinical features most illusive.

The clinical features of mild to moderate VO1 included blurred or temporary loss of vision, confusion, tingling sensation, muscle twitches, lung wheezes and crepitation, hyper- then hypotension, bradycardia and dysrhythmia on ECG tracing [21]. A single case may pass through the stages from prodromal to moderate to severe to critical to lethal within a variable length of time during surgery or post-operative period. When spinal or epidural anaesthesia is used, medications are excluded as possible causes of the respiratory and cardiac dysfunction signs while cerebral signs may predominate.

Causation of mild to severe features

Most previous prospective studies documented prodromal to severe cerebral, cardiac and respiratory features, but were usually attributed to drugs, anesthesia, changes of serum electrolytes, toxicity of the solute of gained irrigant and lately hypothermia by one study. This signifies that all dilutional, toxic, sepsis and hypothermia hypotheses were incorrect and VO1 was overlooked as the insult.

The relation of VO to the haemodynamic disturbance of shock with respect to dilutional HN as its main serum marker, in the absence of recognized shock, required careful analysis for reaching the correct conclusion on the pathophysiology of HN and the TURP syndrome. Precise quantification of VO1 and incidence of HN and the TURP syndrome, differentiating none symptomatic and symptomatic cases at the secondary and tertiary HN nadirs while correlating clinical signs to VO and HN has paved the way for resolving this dilemma.

Definition of the TURP syndrome

The definition of a severe TUR syndrome has both biochemical and clinical components. The biochemical definition is an acute drop of SSC of > 20 mmol/l, or dilutional HN nadir of < 120 mmol/l. The clinical component is the occurrence of myriad of vascular, cardiac, respiratory and cerebral signs. The concept of haemodynamic vascular shock was affirmed not to be due to bleeding or sepsis, irrespective whether named dilutional hyponatraemic, hypo-osmotic or VO1 shock [9]. The bizarre severe signs of vital organ disorders were aggregated into MVOD/F to signify a common pathological insult to be differentiated from the recognized causes of shock and any pathology of individual MVOD/F.

Based on this definition, most prospective studies concluded that post TURP HN is common with wide range of incidence between 10 and 42% [2] of which severe TURP syndrome morbidity affects 10% and mortality is rare (0.5 - 1.5%). This more or less matches the incidence of critical postoperative HN that has a mortality of over 60% [14]. A study that attempted grading of clinical symptoms stopped short of encountering critical to lethal cases, as a limitation of all prospective clinical studies.

Linking the biochemical with clinical definition by identifying the lesser degree of HN due to minor irrigant absorption or VO1 with its prodromal symptoms is important. Identifying circulatory disturbance and MVOD/F of massive VO1 is also vital for making correct diagnosis and differential diagnosis. Establishing these issues, it would be easy to identify symptomatic and non-symptomatic HN patients and conclude whether the TUR syndrome occurred or not- irrespective of the presence or absence of the illusive HN marker.

Retrospective studies and severe to lethal features

Severe to lethal HN and TURP syndrome cases were all reported retrospectively with shock, sudden cardiac arrest and death during surgery or immediate postoperative period. Critical presentations included respiratory distress and pulmonary oedema, ARF with dysfunction or anuria, coma and other combined signs of MVOD/F [10] occur. Features of cerebral and cardiac infarctions combined with vascular circulatory failure have also been reported. Hepatic dysfunction and coagulopathies may occur.

These bizarre presentations of HN and TURP syndrome have been incorrectly attributed to recognized shocks [19,20], primary vascular occlusive cardiac and cerebral insult [26-32], hypoxaemia, hypothermia and/or the multiple dilutional and toxic hypotheses [2]. The patho-physiological mechanism of VO insult causing shock and generalized cellular anoxia of MVOD/F is different. It gets more illusive and confusing as some authors may never encounter the TURP syndrome or deny its entire existence while intermediate symptoms have enormous differential diagnosis. Both the biochemical and clinical definitions of acute HN and the TURP syndrome require further qualification based on the identification of the real insult, dynamic HN nadirs, severity grades and masks.

Experimental evidence

Severe to lethal features of HN and TURP syndrome have been induced in animals by ivi of VO1 fluids under controlled conditions, in which neither haemorrhage nor sepsis shock play a role. The difference between hypo and iso-osmotic HN and its effect on brain cells is documented [40]. Fluid dynamics, cardiovascular haemodynamic effects [27,42], hormonal response and renal function of VO1 fluids on animals, big and small, are also documented [26,41]. The histo-pathological effect of VO1 on brain and cardiac cells [26] has been reported which though it mimics anoxic cell ischaemia, it is nether induced by sepsis, chemical toxicity, hypoxaemia nor arterial obstruction! It is unfortunate that authors have attributed the changes to Glycine or ammonia toxicity [8,9]. Animal studies affirm that shock and ARF are paradoxical effects of massive VO1 that are identical to that of clinical HN and TURP syndrome.

Conclusion

Hyponatremia is an iatrogenic complication of fluid therapy in clinical practice. It has eluded researchers over the last 7 decades. It can be serious or lethal if acutely induced to below 120 mmol/l. It presents with acute vascular shock to surgeons and anesthetists during or immediately after surgery and with coma to physicians later. Other features of MVOD/F syndrome appear later if the patient survived for a few days. Its real patho-etiology is VOS1. The correct life saving therapy is HST of 5% NaCl or 8.4% NaCO₃.

Bibliography

1. Hahn RG. "Total fluid balance during transurethral resection of the prostate". *International Urology and Nephrology* 28.5 (1996): 665-671
2. Rao PN. "Fluid absorption during urological surgery". *BJU International* 60 (1987): 93-99.
3. Gale D and Nottley RG. "TURP without TURP syndrome". *BJU International* 57.6 (1985): 708-710.
4. Goel CM., et al. "Transurethral syndrome. A prospective study". *European Urology* 21.1 (1992): 15-17.
5. Hahn RG and Ekergreen JC. "Pattern of irrigating fluid absorption during transurethral resection of the prostate as indicated by ethanol". *Journal of Urology* 149.3 (1993): 502-506.
6. Ekengreen J and Hahn R. "Blood loss during transurethral resection of the prostate as measured by the Hemocue photometer". *Scandinavian Journal of Urology and Nephrology* 27.4 (1993): 501-507.
7. Hahn RG., et al. "Double blind randomized study of symptoms associated with absorption of glycine 1.5% or mannitol 3% during transurethral resection of the prostate". *Journal of Urology* 160.2 (1998): 397-401.
8. Hoekstra Pt., et al. "Transurethral prostatic resection syndrome- a new perspective: Encephalopathy with associated hyperammonaemia". *Journal of Urology* 130 (1983): 704-707.
9. Roesch RP., et al. "Ammonia toxicity resulting from glycine absorption during TURP". *Anesthesiology* 58.6 (1983): 577-579.
10. Ghanem KA and Ghanem AN. "Volumetric overload shocks in the patho-etiology of the transurethral resection prostatectomy syndrome and acute dilution hyponatraemia: The clinical evidence based on 23 case series". *Basic Research Journal of Medicine and Clinical Sciences* 6.4 (2017).
11. Creevy CD. "A fatal haemolytic reaction during transurethral prostatic resection". *Surgery* 21.1 (1947): 56-66.
12. Rowntree LO. "Water Intoxication". *JAMA Internal Medicine* 32.2 (1923): 157-174.
13. Harrison III RH., et al. "Dilutional hyponatraemic shock: another concept of the transurethral prostatic reaction". *Journal of Urology* 75.1 (1956): 95-110.
14. Arief AI. "Hyponatraemia convulsion, respiratory arrest and permanent brain damage after elective surgery in healthy women". *The New England Journal of Medicine* 314.24 (1986): 1529-1535.
15. Danowski TS., et al. "The treatment of shock due to salt depression comparison of isotonic, of hypertonic saline and of isotonic glucose solutions". *Journal of Clinical Investigation* 25.1 (1946): 130.

16. Hahn RG., *et al.* "Factors influencing the osmolality and the concentration of blood haemoglobin and electrolytes during transurethral resection of the prostate". *Acta Anaesthesiologica Scandinavica* 31(1987): 601-607.
17. Zhang W and Hahn RG. "Double toxicity of glycine solution in the mouse". *BJU International* 77 (1996): 203-206.
18. Sellevold O., *et al.* "Changes in oncotic pressure, osmolality and electrolytes following transurethral resection of the prostate using glycine as irrigant". *Scandinavian Journal of Urology and Nephrology* 17 (1983): 31-36.
19. Bertrand J., *et al.* "Le syndrome de resection de la prostate (TURP) syndrome, mythe ou realite?" *Jour d' Urologie* 87 (1981): 1-4.
20. Spencer Hoyt H., *et al.* "Types of shock reaction during transurethral resection and relation to acute renal failure". *Journal of Urology* 79 (1958): 500-507.
21. Ghanem SA., *et al.* "Volumetric Overload Shocks in the Patho-Etiology of the Transurethral Resection of the Prostate (TURP) Syndrome and Acute Dilution Hyponatraemia: The Clinical Evidence Based on Prospective Clinical Study of 100 Consecutive TURP Patients". *Surgical Medicine Open Access Journal* 1.1 (2017).
22. Ghanem AN and Ghanem S A. "Volumetric Overload Shocks: Why Is Starling's Law for Capillary Interstitial Fluid Transfer Wrong? The Hydrodynamics of a Porous Orifice Tube as Alternative. *Surgical Science*, 2016 7: 245-249. Webster NR. Monitoring the critically ill patient". *Journal of the Royal College of Surgeons of Edinburgh* 44.6 (1999): 386-393.
23. Ghanem AN. "The Transurethral Prostatectomy (TURP) Syndrome: An Investigation of the Osmotic and Metabolic Sequelae of Volumetric Overload". MD Thesis. The Institute of Urology and Nephrology, Mansoura University, Egypt (1988).
24. Ghanem AN and Ward JP. "Osmotic and metabolic sequelae of volumetric overload in relation to the TURP syndrome". *BJU International* 66 (1990): 71-78.
25. Hahn RG., *et al.* "Renal function during intravenous infusion of urological irrigating fluids in the sheep". *Acta Veterinaria Scandinavica* 40.6 (1996): 671-683.
26. Hahn RG., *et al.* "Morphological and X-ray Micro-analytical Changes in Mammalian Tissue after Overhydration with Irrigating Fluids". *European Urology* 29.3 (1996): 355-361.
27. Hahn GH., *et al.* "Pathology of the heart after overhydration with glycine solution in the mouse". *APMIS* 104.12 (1996): 915-920.
28. Ghanem AN. "Hyponatraemia and hypo-osmolality". *Lancet* (1988): 572.
29. Ghanem AN. "Hypoalbuminaemic hyponatraemia: a new syndrome?". *British Medical Bulletin* 291 (1985): 1502-1503
30. Ghanem AN. "Serum osmolality gap". *Lancet* (1987): 223-224
31. Ghanem AN., *et al.* "Dangers in treating hyponatraemia". *British Medical Journal* 294 (1987): 837.
32. Ghanem AN and Ward JP. "Fluid absorption during urological surgery". *BJU International* 61 (1988): 168-169.
33. Ghanem AN. "Frequency and causes of fluid absorption: a comparison of the three techniques for resection of the prostate under continuous pressure monitoring". *BJU International* 84.7 (1999): 891.
34. Ghanem AN. "Monitoring the critically ill patient". *Journal of the Royal College of Surgeons of Edinburgh* 45.2 (2000): 138-139.

35. Ghanem AN. "Something old, something new and something frivolous about hyponatraemia". *British Medical Journal* (2000).
36. Ghanem AN. "Preventing renal failure in the critically ill: identifying the problem and finding solution: The magic bullet is "back to basic" physics and physiology and 'to the future' on capillary hydrodynamics as a 'porous orifice (G) tube". *British Medical Journal* 322.7300 (2001): 1437-1439.
37. Ghanem AN. "Hyponatraemia: nadirs and paradox of the 'missing' volumetric overload in acute hyponatraemia". *British Medical Journal* (2001).
38. Ghanem AN. "Magnetic field-like fluid circulation of a porous orifice tube and its relevance to the capillary-interstitial fluid circulation: preliminary report". *Medical Hypotheses* 56.3 (2001): 325-334.
39. Ghanem KA and Ghanem AN. "The proof and reasons that Starling's law for the capillary-interstitial fluid transfer is wrong, advancing the hydrodynamics of a porous orifice (G) tube as the real mechanism". *Blood, Heart and Circulatory Physiology* 1.1 (2017): 1-7.
40. Melton JE and Nattie EE. "Brain and CSF water and ions during dilutional and iso-osmotic hyponatraemia in the rat". *American Physiological Society* 244.5 (1983): 724-732.
41. Zhang W and Hahn RG. "Water and solute excretion after intravenous infusion of new irrigating fluids in the rabbit". *Scandinavian Journal of Urology and Nephrology* 29.3 (1995): 241-247.
42. Stalberg HP, *et al.* "Haemodynamics and fluid balance after intravenous infusion of 1.5% Glycine in sheep". *Acta Anaesthesiologica Scandinavica* 37.3 (1993): 281-287.

Volume 3 Issue 8 August 2019

©All rights reserved by Ahmed N Ghanem.