Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 3 Issue 5 May 2020

Editorial

Hepatic and Gastro-Intestinal Manifestations of Volumetric Overload Shocks (VOS) Causing ARDS

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Received: March 22, 2020

Published: April 01, 2020

Substantial physics and physiological evidence with clinical relevance and significance currently exists that affirms Starling's law is wrong (Figure 1) [1-3]. Evidence that volumetric overload shocks (VOS) [4-7] cause the acute respiratory distress syndrome (ARDS) is also available [8]. These VOS are complications of fluid therapy in surgical patients due to many errors and misconceptions on fluid therapy [8] that mislead physicians into giving too much fluids during the resuscitation of shock and prolonged major surgery [9]. The clinical manifestations of VOS causing ARDS is shown in table 1, among the multiple system and vital organ dysfunctions are the hepatic and gastro-intestinal (GIT) manifestations [10-14]. These include hepatic dysfunction with elevated bilirubin, alkaline phosphates and liver enzymes of SGOT [10,11] and delayed recovery of intestinal function or paralytic ileus with nausea and vomiting [12,13].

Indeed, both hepatic and GIT manifestations have been reported in ARDS [10-14]. These are, however, attributed to sepsis and septic shock or the underlying presenting condition, anaesthesia and/or the major surgery exactly as is the situation with ARDS. Volumetric overload (VO) over time, or the retained VO at the time of ARDS onset of morbidity and mortality has never been incriminated by previous authors. Although, recent reports of multicenter prospective studies such as PRISM [15] and ProCESS/ARISE/ProMISe [16] have documented VO or retained fluid of 3 - 10 liters (L) in the result section associated with morbidity of ARDS but not incriminated as its patho-aetiology.

Furthermore, these hugely expensive multicenter prospective studies did not mention the VO associated with and causing the mortality. All the self-references mentioned here affirm VO/Time as the pathological insult that induces VOS causing ARDS and acute kidney injury (AKI) as parts of MODS and is highly significant ($p = 0.0001$) (Figure 2 and Table 2). This concept of VO/Time was first reported in MD Thesis in 1988 [17], in an original article in 1990 [18], another in 2001 [19] and extensively between 2016 and 2020 [1-9]. For VOS 1 the mortality occurred with 7L or 10% Body weight (BW) (Figure 3). For VOS 2 mortality is associated with 12 - 14L as first reported by Ashbough., *et al.* [20], but again not incriminated as the patho-aetiology of ARDS.

Hahn [21] wrote: "Adverse effects of crystalloid fluids are related to their preferential distribution to the interstitium of the subcutis, the gut, and the lungs. The gastrointestinal recovery time is prolonged by 2 days when more than 2 litres is administered.

Cerebral	Cardiovascular	Respiratory	Renal	Hepatic and GIT
Numbness	Hypotension	Cyanosis.	Oliguria	Dysfunction:
Tingling	Bradycardia	FAM[4]	Annuria[8]	Bilirubin ↑
SBB[1]	Dysrhythmia	APO)[5]	Renal failure or	Enzymes ↑
COC[2]	CV Shock*	RA[6]	AKI[9]	Alkaline Phos↑
Convulsions	Cardiac Arrest	Arrest	Urea ↑	GIT symptoms.
Coma	Sudden Death	CPA[7]	Creatinine ↑	DGR[10]
PMBCI [3]		Shock lung		Nausia and Vomiting.
		ARDS[$]		

Table 1: Shows the manifestations of VOS 1 of the TURP syndrome for comparison with ARDS manifestations induced by VOS2.

Abbreviations

SBB[1]: Sudden Bilateral Blindness; COC[2]: Clouding of Consciousness; PMBCI[3]: Paralysis mimicking bizarre cerebral infarctions, but is recoverable on instant use of HST of 5%NaCl and/or $NaCO_3$, and so is coma and AKI; FAM[4]: Frothing Around the Mouth; APO[5]: Acute Pulmonary Oedema; RA[6]: Respiratory Arrest; CPA[7]: Cardiopulmonary Arrest; ARDS[$]: Occurs later on ICU; AKI[9]: Acute Kidney Injury; DGR[10]: Delayed Gut Recovery; CV Shock*: Cardiovascular shock of VOS reported here as VOS 1 and VOS2; Annuria[8]: That is unresponsive to diuretics but responds to HST of 5%Ncl and/or 8.4%$NaCO_3$; AKI[8]: Acute Kidney Injury. Also occurs the excessive bleeding at the surgical site and leukocytosis occurred in the absence of sepsis and septic shock.

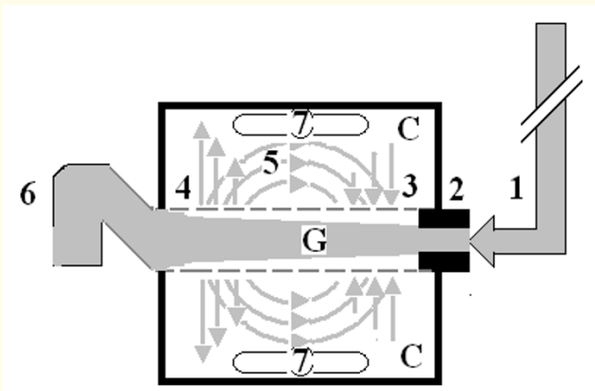

Figure 1: Shows a diagrammatic representation of the hydrodynamic of G tube and surrounding chamber C. The G tube is a plastic porous tube and the chamber around it is another bigger plastic tube to form the G-C apparatus- akin to capillary-interstitial fluid circulation unit. The diagram numbers should read as follows:

1. The inflow pressure pushes fluid through the orifice.
2. Creating fluid jet in the lumen of the G tube**.
3. The fluid jet creates negative side pressure gradient causing suction maximal over the proximal part of the G tube near the inlet that sucks fluid into lumen.
4. The side pressure gradient turns positive pushing fluid out of lumen maximum over the distal part near the outlet.
5. Thus, the fluid around G tube inside C moves in magnetic field-like circulation (5) taking an opposite direction to lumen flow of G. tube.
6. The inflow pressure 1 and orifice 2 induce the negative side pressure energy creating the dynamic G-C circulation phenomenon that is rapid, autonomous and efficient in moving fluid out from the G tube lumen at 4, irrigating C at 5, then sucking it back again at 3.
7. Maintaining net negative energy pressure inside chamber C.

**Note the shape of the fluid jet inside the G tube (Cone shaped), having a diameter of the inlet on right hand side and the diameter of the exit at left hand side (G tube diameter). I lost the photo on which the fluid jet was drawn, using tea leaves of fine and coarse sizes that runs in the center of G tube leaving the outer zone near the wall of G tube clear. This may explain the finding in real capillary of the protein-free (and erythrocyte-free) sub-endothelial zone in the Glycocalyx paradigm (Woodcock and Woodcock 2012) [37].

Infusion of 6 - 7 litres during open abdominal surgery results in poor wound healing, pulmonary oedema, and pneumonia. There is also a risk of fatal postoperative pulmonary oedema that might develop several days after the surgery. Even larger amounts cause organ dysfunction by breaking up the interstitial matrix and allowing the formation of lacunae of fluid in the skin and central organs, such as the heart." Other authors recently reported that infusion of > 5L of crystalloids is associated with high morbidity of ARDS, and increased mortality [22].

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 cohort prospective study on transurethral resection of the prostate. The gained fluids were 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 Litres. A mean of 3.5 (p = 0.0001) litres VO occurred in symptomatic patients presenting with hypotensive shock, recognized as VOS 1 (see text).

Parameter	Value	Std. Err	Std. Value	T Value	P
Intercept			0.773		
Fluid Gain (l)	0.847	0.228	1.044	3.721	0.0001
Osmolality	0.033	00.014	-0.375	2.42	0.0212
Na^+ (C_B)	0.095	0.049	0.616	1.95	0.0597
Alb (C_B)	0.062	0.087	0.239	0.713	0.4809
Hb (C_B)	-0.282	0.246	-0.368	1.149	0.2587
Glycine (C_B)	-4.973E-5	5.975E-5	-0.242	0.832	0.4112

Table 2: 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 hypoosmolality are the only significant factors. The table was produced on an Apple® Mackintosh® using Stat View® statistical package 35 years ago (Reproduced with the permission of authors and editor of BJU Int. from reference 4).

For the interested reader to appreciate the concept of VO/Time inducing VOS [4-7], he needs to understand and feel comfortable with the hydrodynamic of the G tube [1]. The errors and misconceptions caused by the faulty rules on fluid therapy dictated by the wrong Starling's law should be recognized [8]. These errors mislead physicians into giving too much fluid causing VO [9] presenting with cardiovascular shock in theatre or during the resuscitation of another well-known shock. These VOS cause ARDS, AKI, hepatic dysfunction as and GIT manifestations as parts of MODS, are new discoveries in medicine and physiology originated in urology [23].

Figure 3: 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 based on the conservative approach. They had the clinical picture of VOS 2 and ARDS. Group 2 were 10 patients from the series who were correctly diagnosed as volumetric overload shock (VOS 1) and treated with hypertonic sodium therapy (HST). Group 3 were 10 patients who were seen in the prospective study and subdivided into 2 subgroups; 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 crystalloids/plasma/blood of the standard conservative approach but much less volume- being "Guarded". One patient from the conservatively treated group 3.2 developed ARDS with coma, convulsions and bizarre paralysis on the second postoperative day. He was seen by a Neurologist and diagnosed as cerebrovascular accident. He fully and immediately recovered from ARDS, coma and paralysis after belated treatment with HST using 5% NaCl and 8.4% NaCO3. After HST the patient recovered fully from AKI, ARDS, Coma and paralysis. Recovery from AKI that was unresponsive to loop diuretics occurred with the infusion of HST after passing 4.5L of urine. Groups 2 and 3.1 responded similarly to HST (Reproduced with the permission of author from open access journal).

Starling [24] based his hypothesis on Poiseuille's work on strait uniform diameter tube [25] in which the hydrostatic pressure causes filtration, and the oncotic pressure force of plasma albumin causes re-absorption [26]. Recent evidence demonstrates Starling's law is wrong on both oncotic and hydrostatic pressure forces and provides the correct replacement of hydrodynamic of the porous orifice G tube (Figure 1) [1].

The capillary has a pre-capillary sphincter [27] and wide pores [28] that allow the passage of molecules larger than plasma proteins. This makes the capillary a porous orifice (G) tube with different hydrodynamic from Poiseuille's tube [1]. The side pressure of G tube causes suction not filtration. The wide capillary pores nullify the oncotic force *in vivo* based on biochemical [29] and clinical research using albumin [30-32] and hydroxyethyl starch [33] versus saline for fluid resuscitation. The osmotic chemical composition of various body fluids is identical to plasma proteins [29]. The interstitial fluid (ISF) space has a negative pressure of -7 cm water [34], so is lymph [35]. Clinical evidence on plasma albumin versus Saline shows no significant difference [30-32]. This evidence affirms that the oncotic force does not exist in vivo that partly prove Starling's law wrong. Inadequacy in explaining the capillary–ISF transfer, has previously called for reconsideration of Starling's hypothesis [36].

New physics [1,2] and physiological [3] research demonstrate that side pressure does not cause filtration across the wall of G tube, it causes suction. In G tube the negative side pressure gradient on its wall causing suction maximum near the inlet and turns positive maximum near the exit causing filtration. This creates a circulation between fluid in the lumen of G tube and surrounding fluid chamber (C) that runs in the opposite direction creating autonomous, dynamic rapid magnetic field like circulation (Figure 1) [1]. Physiological study [3] completed the evidence that Starling's law is wrong as the capillary works as G tube not Poiseuille's tube. Oedema occurred with both albumin and saline when the fluid is run through the vein but not the artery. Both absorption and filtration are autonomous functions of G tube thus fit to replace Starling's law.

The clinical significance is that Starling's law dictates the faulty rules on fluid therapy causing many errors and misconceptions [8] that mislead physicians into giving too much fluid infusions of albumin and crystalloids for the resuscitation of shock [9] which both cause edema of ISF space and vital organs as well as hypervolaemia with hypotension [1,4-7]. This shock is mistaken for septic or hemorrhagic shock and is wrongly treated with further huge volume expansion, occurring with both liberal and conservative approach of fluid therapy [37]. Woodcock and Woodcock [37] also revised Starling equation and the glycocalyx model of trans-vascular fluid exchange for an improved paradigm for prescribing intravenous fluid therapy.

Volumetric overload inducing VOS is of 2 types; VOS 1 causes the transurethral resection of the prostate [TURP] syndrome [18], now being linked to ARDS or MODS [1,38,39] and AKI [40,41]. Volumetric overload is induced by persistence to elevate central venous pressure (CVP) to high level of 18 - 22 cm H_2O [42] as based on the faulty Starling's law. A book has been published [43] and new article is now under consideration that demonstrates VOS Cause ARDS: The plenary evidence on patho-aetiology and therapy, Constructing the BRIDGE between physics, physiology, biochemistry and clinical medicine [44].

Conflict of Interest

None declared by the author.

Funding Source

None declared by the author.

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