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Editorial

Endothelial Glycocalyx and Fluid Haemodynamics

Uma Hariharan, MBBS, DNB, PGDHM[1*]; Vinodh Natarajan, MBBS, MD[2]; Rakesh Garg, MD, DNB, FICA, PGCCHM, MNAMS, CCEPC, FIMSA[3]

[1]Department of Anaesthesiology and Intensive Care, Dr. Ram Manohar Lohia Hospital (Dr. RMLH) & Post-Graduate Institute of Medical Education and Research (PGIMER), Central Health Services, New Delhi, India
[2]Department of Anaesthesiology Dr. Ram Manohar Lohia Hospital (Dr. RMLH) & Post-Graduate Institute of Medical Education and Research (PGIMER), Central Health Services, New Delhi, India
[3]Fellowship in Palliative Medicine, Associate Professor of Anaesthesiology, Intensive Care, Pain and Palliative Medicine; Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi 110029, India

Corresponding author
Uma Hariharan, MBBS, DNB, PGDHM
Fellowship Onco-anesthesia, Advanced Regional Anesthesia and Palliative Care; Assistant Professor, Department of Anaesthesiology and Intensive Care, Dr. Ram Manohar Lohia Hospital (Dr. RMLH) & Post-Graduate Institute of Medical Education and Research (PGIMER), Central Health Services, New Delhi, India
Tel. +91-9811271093; E-mail: uma1708@gmail.com

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Intravenous fluid therapy is one of the most fascinating and dynamic aspects of patient management, both in the peri-operative period and in critical care. The molecular mechanisms of fluid haemodynamics involve the complex interactions of the electron microscopic structure called 'endothelial glycocalyx'. The presence of co-existing pathologies and physiological changes in a particular patient population also compounds the fate of the fluids administered. This article presents a brief outline of the role of endothelial glycocalyx and its review of literature pertaining to fluid therapy.

ENDOTHELIAL GLYCOCALYX AND ITS REVIEW OF LITERATURE

Danielli in 1940, proposed the existence of a delicate layer between vascular endothelial cells and flowing blood.[1] Forty years later, Copley et al studied the structure and properties of this delicate layer with the advent of the electron microscope and named as "endothelial glycocalyx".[2] The glycocalyx (GCX) is a complex gel between flowing blood and endothelial cell wall and it reduces the access of cellular and macromolecular components of blood to the surface of endothelium. The glycocalyx itself is not inactive and transmits force to the underlying cell. Glycoproteins and proteoglycans form the bulk of glycocalyx. Proteoglycans (PG) have a protein core to which are attached negatively charged glycosaminoglycans (GAG) side chains. These PGs vary in the size of their core proteins, the number of GAG side chains, and their binding to the cell membrane. The most common GAG (50-90%) in the vascular system is heparan sulphate (HS). HS is found on several core proteins including *perlecan, glypican, and syndecans*. The *syndecan* family consists of transmembrane proteoglycans found in the GCX. They shed in a soluble form when the GCX becomes disordered and their levels in serum correlate with the extent of endothelial glycocalyx damage.[3]

The glycocalyx forms a luminal mesh that provides the endothelial cells with a framework to bind plasma proteins and soluble GAGs. The composition and dimensions of the glycocalyx fluctuate as it continuously replaces the material sheared by flowing plasma. The glycocalyx is itself inactive, but once plasma constituents (mainly albumin) are bound, it forms a physiologically active endothelial surface layer (ESL) with a functional thickness of over 1 μm, quantitatively fixing around 700-1000 ml of plasma at the endothelial surface under normal conditions. The plasma molecules of this non-circulating part are in continuous dynamic equilibrium with those of circulating part, representing the distribution space of the circulating blood cells. The physiological role of glycocalyx is impressive and it acts as an intravascular fringe, completely repels red and white cells and allows molecules of size <70 kDa (kilo-daltons). The hydrostatically forced plasma constituents are retained in this layer and used for building up ESL. Athereosclerosis-related damage to the glycocalyx also needs to be considered in the resulting pathophysiological changes. Finally, a smaller ultra-filtrate volume only reaches interstitial space and thus it provides a pivotal role in vascular permeability. Beyond its significance for the vascular barrier, the ESL participates in various physiological processes such as preventing firm adhesion of leukocytes and blood platelets to the vessel wall, transmission of shear stress, and in a modulation of inflammatory and haemostatic processes.[4] The knowledge about the two required components of a properly working vascular barrier, an intact endothelial gly-

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cocalyx, and a sufficient minimal concentration of suitable plasma proteins building up to the ESL is important for the clinician, as it gives a good estimation of what might happen if this skeleton structure is altered. Pathophysiological sequelae of glycocalyx failure or perturbation include generation of tissue oedema, systemic inflammatory response syndrome, diabetic angiopathy, and, possibly, atherogenesis. Situations in which damage to the glycocalyx has been reported include ischemia/reperfusion injury, sepsis, volume overload, diabetes, and trauma. Concerning fluid and volume handling, especially the aspect of intravascular hypervolemia, most likely threatening the integrity of the endothelial glycocalyx via the release of natriuretic peptides from the atria activating various metalloproteinases, deserves attention.[5] Chappell D et al in their study stated that volume loading has a detrimental effect on vascular competence and may impair patient outcome. The underlying cause for the detrimental action of volume loading is presumably to be found in a volume-sensitive regulatory system. The heart releases atrial natriuretic peptide (ANP) into the circulation in the face of mechanical wall stress and, thus, also in hypervolemia. This hormone is known to induce rapid shifts of intravascular fluid into the interstitial space, and it also has a parallel effect on the endothelial glycocalyx. Elevated levels of ANP and glycocalyx degradation products (*hyaluron, syndecans, and heparin sulphates*) are evident from their serum concentrations depicting the damage to ESL layer.[6]

It is always essential to protect this delicate layer of endothelial glycocalyx to have a good result in fluid therapy. Several glycocalyx saving strategies like use of hydrocortisone are attempted in perioperative setting to minimise noxious surgical stimuli damaging vascular endothelium.[7] The role of fresh frozen plasma (FFP) in providing required plasma constituents to build up ESL is controversial, but the newer studies demonstrated the decrease in glycocalyx degradation products whenever FFP was transfused.[8] But the easiest way of protecting the endothelial glycocalyx is just the avoidance of fluid overloading and transfusing only the appropriate amount of fluids. In recent times, individualized goal-directed therapy has become popular and more effective in the perioperative fluid management. The concept of goal-directed therapy (GDT) was first described by Shoemaker in 1988 and it means that achieving supra-normal circulating functions (the target values for cardiac index, oxygen delivery, and oxygen consumption) is by appropriate use of fluids and inotropes in the peri-operative period.[9] Peri-operative GDT describes fluid administration, with the aim of optimising a patient's cardiac function and ultimately oxygen delivery. Several clinical reviews support the use of GDT in the perioperative settings. The use of GDT should be encouraged by increasing the availability of appropriate monitoring equipment and imparting the knowledge about that concept among the practising anaesthesiologists.[10]

CONCLUSION

The concept of fluid management is dynamic and fascinating. It is our responsibility to understand the role of the endothelial glycocalyx before starting any fluid therapy in patients during the peri-operative period and critical care. Hypervolemia and overzealous fluid therapy must be avoided at all costs. Individualised goal directed fluid therapy should be followed, guided by appropriate hemodynamic monitoring. The right amount of fluid, for the right patient, at the right time is the best policy.

CONFLICTS OF INTEREST

All the authors hereby declare that there are no conflicts of interests.

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