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Cisternostomy – Introducing the concept of "CSF shift edema"

Cisternotomia para tratamento cirúrgico do edema cerebral, por acumulação de LCR

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Abstract

Brain edema after severe head injury plays an important role in the outcome, and overall survival of injured patients, and it is one of the main targets in the therapeutic approach in the clinical practice. The physiopathology of traumatic brain swelling is complex and not yet totally understood, but until now it is supposed to be mainly vasogenic and cytotoxic, in origin. However, based on new understandings of the hemodynamic of cerebrospinal fluid (CSF), an additional mechanism of brain swelling is proposed in this paper. In our opinion, an increase of pressure in the subarachnoid space, secondary to traumatic subarachnoid hemorrhage, would result in a shift of CSF from the cisterns into the brain parenchyma, through the para-vascular spaces, following a pressure gradient, and resulting in an increase of the water content of the brain. This mechanism of brain swelling has been described for the first time in this paper and would be termed as "CSF Shift edema". This "CSF-shift", driven by pressure gradient, would lead in addition, to an increase of pressure inside the para-vascular spaces and in the interstitium of the brain, disturbing the functions of the para-vascular system with implications in the development of secondary brain injury. Cisternostomy, an innovative technique in the handling of traumatic brain injury, would directly reverse the direction of the "CSF Shift", what would explain the fast decrease of brain swelling right after the procedure. In addition, this technique would reduce the pressure in the para-vascular spaces and interstitium leading to a recovery of the functionality of the para-vascular system, which would result in a decrease of secondary brain damage. The proposed mechanism would explain the advantage of this technique in terms of morbidity and mortality, compared to decompressive hemicraniectomy.

Keywords: head trauma, decompressive hemicraniectomy, cisternostomy, brain edema, CSF shift edema, paravascular pathway

Resumo

O edema cerebral após traumatismo craniano grave desempenha um papel importante no resultado final e sobrevivência global dos pacientes afetados, e é um dos principais alvos na abordagem terapêutica na prática clínica. A fisiopatologia do edema cerebral traumático é complexa e ainda não totalmente compreendida, mas até agora supõe-se ser principalmente vasogénico e citotóxico, na sua origem. No entanto, com base nos novos entendimentos da hemodinâmica do líquido cefalorraquidiano (LCR), é proposto neste trabalho um mecanismo adicional de edema cerebral. Na nossa opinião, um aumento de pressão no espaço subaracnóide, secundária a hemorragia subaracnóide traumática, resultaria numa mudança do LCR a partir das cisternas para o parênquima cerebral, através dos espaços para-vasculares, na sequência de um gradiente de pressão, resultando num aumento do conteúdo de água do cérebro. Este mecanismo de edema cerebral foi descrito pela primeira vez neste trabalho e poderia ser denominado como "LCR-shift". Este "LCR-shift", impulsionado por um gradiente de pressão, conduzido pelo gradiente de pressão, levaria a um aumento de pressão no interior dos espaços perivasculares e no interstício do cérebro, perturbando as funções do sistema para-vascular com implicações no desenvolvimento de lesão cerebral secundária. A cisternotomia, uma técnica inovadora no tratamento da lesão cerebral traumática, iria reverter directamente a direcção do "LCR-shift", o que poderia explicar a diminuição rápida do edema cerebral logo após o procedimento. Além disso, esta técnica iria reduzir a pressão nos espaços paravascular e interstício que conduziria a uma recuperação da funcionalidade do sistema para-vascular, o que iria resultar numa diminuição dos danos cerebrais secundário. O mecanismo proposto poderia explicar a vantagem desta técnica em termos de morbidade e mortalidade, em comparação com a hemicraniectomia descompressiva.

Palavras-Chave: traumatismo craniano, hemicraniectomia descompressiva, cisternostomia, edema cerebral, edema LCR-shift, via paravascular

Introduction

Traumatic brain injury (TBI) is a life threatening condition in which the development of secondary cerebral edema is one of the most critical factors in patient's morbidity and mortality.

Excessive accumulation of interstitial fluid is detrimental to brain function in a "bilateral direction" because this excessive accumulation of fluid increases the diffusion distance for oxygen and other nutrients from the vessels, compromising cellular metabolism, and this would also limit the diffusional removal of potentially toxic byproducts (Scallan et al., 2010).

Occurring within the closed confines of the skull and meninges, overall brain swelling leads to raised intracranial pressure, decrease of brain's compliance and cessation of the brain blood supply. Therefore, the degree and extent of edema determines the clinical outcome of the patient (Marmarou et al., 2007). Both, vasogenic and cytotoxic edema have been implicated in the pathophysiology of brain swelling after severe head injury, secondary to disruption of the blood–brain barrier (BB), and cellular swelling due to a leakage of intracellular osmolytes into the extracellular space, respectively (Unterberg et al., 2004), (Stephens et al., 2015). However, in our opinion, an additional source of brain swelling may be implicated in the pathophysiology of post-traumatic edema, as discussed above.

Discussion

To understand the mechanisms that underlie postraumatic brain edema and how cisternostomy may help, we would first need to review some new concepts about the dynamics of fluid in the central nervous system (CNS).

Ventricular, subarachnoid, perivascular, and interstitial compartments constitute a continuum, or a fluid functional unit (Brodbelt et al. 2003), (Bulat & Klarica 2011). The cerebro spinal

fluid (CSF) in the subarachnoid space and the interstitial fluid (ISF) are particularly connected through the para-vascular spaces (Figure 1. Schema of pathophysiology).

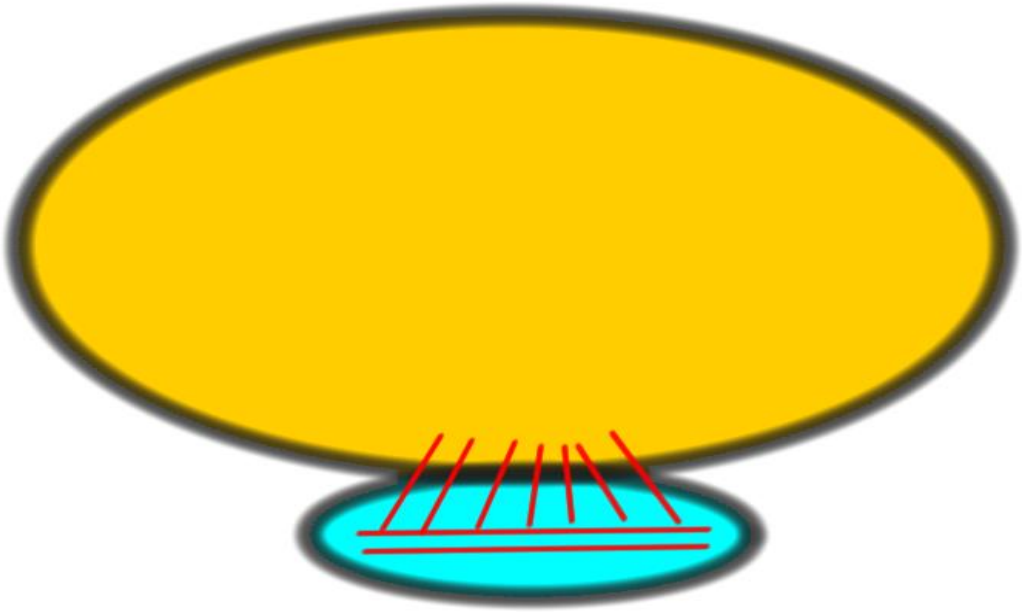

Figure 1 – This schematic diagram shows the connection between brain interstitial fluid (in yellow) and the cistern (in blue) through the para vascular spaces around the perforating arteries (in red).

These are the spaces between the end feet of the perivascular astrocytes and the vessel wall (Thrane et al. 2013), extending all the way along penetrating arterioles to capillaries and along veins (Iliff et al. 2012). These para-vascular spaces have recently been described as a system to clear interstitial waste from the brain interstitium and called "glympathic system"(Iliff et al. 2012, 2013), (Xie et al. 2014),(Yang et al. 2013).

According to the authors, fluid exchange, mediated by aquaporin 4 (AQP4), the main water channel in the brain (Iliff et al. 2012), (Papadopoulos & Verkman 2013) (Nakada 2014) takes place between ISF and para-vascular spaces clearing solutes with outflow of

solutes mainly in the para-venular side (Iliff et al. 2012). Arterial pulsation seems to play an important role in the flux of fluid along this para-vascular pathway (Iliff et al. 2013).

Reabsorption of CSF is no longer believed to occur through Pacchionnian granulations. Nowadays, it is believed that in physiological conditions, reabsorption of CSF and ISF occurs mainly across the vessels of the brain, particularly across the walls of venous capillaries and postcapillary venules (Bulat et al., 2008; Bulat & Klarica, 2011) depending on hydrostatic pressure and osmotic forces (Orešković & Klarica, 2010), (Maraković et al., 2010), (Chikly & Quaghebeur, 2013), also controlled by (AQP4) (Papadopoulos & Verkman, 2007), in the perivascular astrocytic endfeet (Mathiisen et al., 2010).

To sum up, both reabsorption of excess water and waste from the ISF depends on the patency of para-vascular spaces and depends on the hydrostatic and osmotic pressures between ISF, the para-vascular channels and the vascular system. The exchanges of fluid and waste take place through AQP4, which allows very fast bidirectional flow in response to pressure and osmotic gradients, (Agre 2006).

In the setting of severe head trauma, subarachnoid hemorrhage (SAH) is almost always associated (Cherian et al., 2016). In our opinion, this arterial bleeding into the cisterns would lead to a rise of the pressure in the subarachnoid compartment. In the case of an aneurysm rupture, this bleeding stops immediately as the intracranial pressure soon becomes equal to that of the MAP. However, the capillary bleeding in trauma occurs at a relatively lower pressure and may continue on for a longer time, as long as the ICP is not equal to the mean arterial pressure. This would provoke a shift of CSF from the cisterns into the para-vascular spaces and from there to the ISF, driven by pressure gradient and perhaps mediated by AQP4.

We propose this as an additional mechanism of posttraumatic edema and would call it “CSF-shift edema”, (Figure 2).

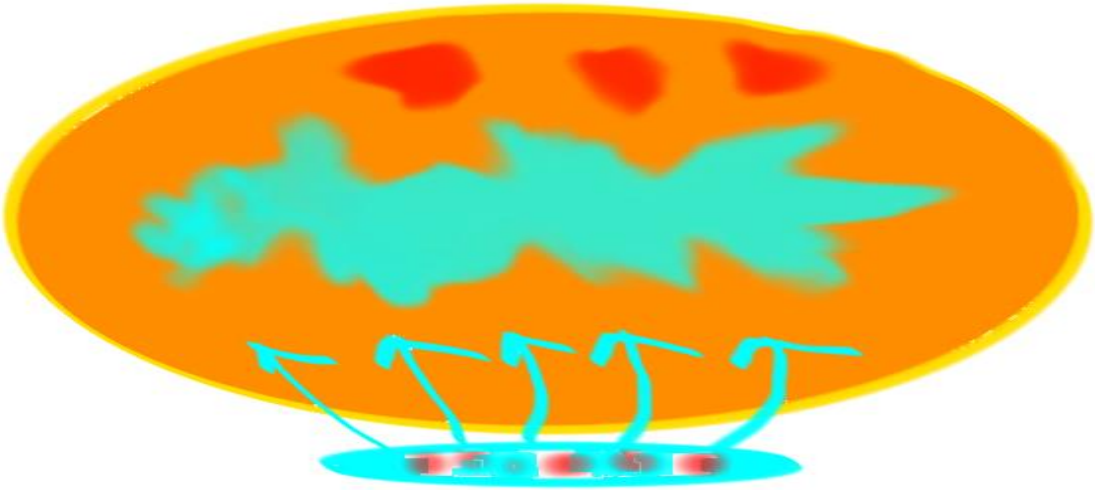

Figure 2. “CSF shift Edema” – The subarachnoid hemorrhage in trauma raises the pressure in the cisterns, however the intracerebral pressure remains lower than the cisternal compartment. This results in a shift of CSF driven by the pressure gradient, through the Virchow Robin spaces into the brain. This mechanism of edema has been termed as “***CSF shift edema***”.

The increase in pressure originated in the subarachnoid space would be transmitted to the rest of the fluid unit: para-vascular spaces and interstitial fluid. As a consequence of the increase of pressure in the interstitial fluid a functional blockage of the para-vascular system (glympathic system) may take place because the transmural pressure gradient between capillaries and interstitial fluid is reduced and capillaries and veins are physically compressed (Unterberg et al., 2004). The blockage of function of the paravascular spaces would lead to a decrease in the absorption of fluid from the ISF by the capillaries and to a decrease of clearance of mediators that are released from the injured cells, following traumatic brain injury, including excitotoxic neurotrasminers (glutamate), lactate or free oxygen radicals (Unterberg et al., 2004). Those mediators enhance vasogenic and/or

cytotoxic brain edema perpetuating the accumulation of fluid in the brain, as well as excitotoxic cell damage and inflammation that may lead to microglia activation, apoptotic and necrotic cell death (Werner & Engelhard, 2007), (Unterberg et al., 2004), therefore increasing secondary brain damage.

In addition, the patency of para-vascular system may also have an important role in local control of brain temperature which appears to increase after head injuries (Soukup et al., 2002).

Decompressive craniectomy decreases the intracranial pressure and therefore the pressure in the interstitium by increasing the volume, resulting in an expansion of the brain through the craniectomy site. However, as the origin of the high pressure in the fluid unit would be in the subarachnoid compartment, particularly in the basal cisterns, the pressure in the interstitial fluid cannot be less than the pressure in the subarachnoid compartment [(around 60mmHg which is the pressure in the small arteries in the subarachnoid space (Shulman, 1965), source of the subarachnoid bleeding)]. It means that even if the intracranial pressure is released by decompressive craniectomy, the functional blockage of the para-vascular system would persist to a significant level and therefore the underlying mechanism for cytotoxic edema persists as well as the impairment of absorption of interstitial fluid by the capillaries and probably the lack of buffering of temperature by CSF. It is possible that as a part of the entire expansion of the intracranial volume all these pressures do come down, but this procedure does not address the root of the problem, which is the increase in subarachnoid pressure and consequent intracerebral pressure.

Cisternostomy, is a surgical procedure combining the principles of microvascular and skull base surgery, to open the basal cisterns of the subarachnoid space to atmospheric pressure (Cherian &

Munakomi, 2013). This technique applied in selected cases of severe traumatic brain injuries has proved to dramatically decrease the mortality and morbidity of patients compared with decompressive hemicraniectomy (Cherian et al., 2013, 2016).

We hypothesize that interstitial fluid (ISF), accumulated in the postraumatic brain, exits along the para-vascular pathway, following a pressure gradient, after cisternostomy; moving fast from the high pressure of the edematous brain towards the lower atmospheric pressure of the opened basal cisterns (Figure 3).

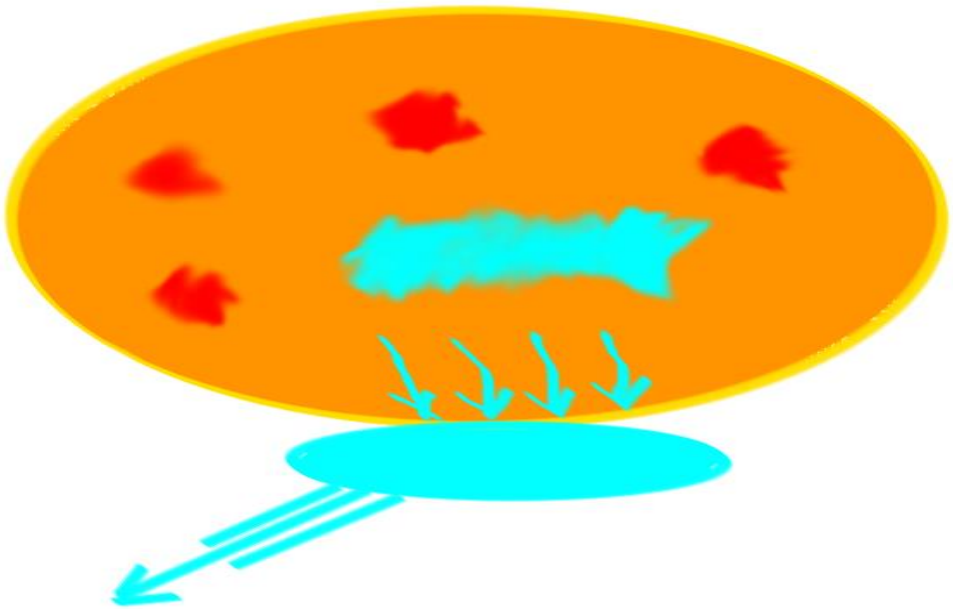

Figure 3. The surgical procedure of Cisternostomy utilizes skullbase technique to access and open the cisterns. This results in reversal of the pressure gradient of the "CSF shift edema" and the fluid shifts back into the cisterns. This also brings down the intracerebral pressure.

This mechanism would explain the fact that immediately after the opening of the cisterns a decrease of the tension of the brain, an increase of the brain compliance and increase of cerebral pulsation are observed (see the video below).

Neurosurgeons are familiar with this phenomenon in aneurysm and tumor surgery where opening the brain provides an improvement in the compliance of the brain. However, this had never been applied in trauma patients, as opening the cisterns in those cases is challenging and commonly are in hands of juniors, residents or consultants. Furthermore, the movement of fluid from the injured brain towards the cisterns, achieved by cisternostomy, would wash out mediators that are released from the injured cells, following trauma and thus reduce secondary traumatic brain damage of the brain.

The decrease of pressure in the opened cisterns would be transmitted through the fluid unit to para-vascular spaces and interstitial level allowing a recovery of the paravascular flow so increasing the reabsorbing of ISF fluid by capillaries, allowing to removal of neurotoxic substances in the interstitium and locally reducing brain heat, that would help in the decrease of secondary damage of post-traumatic brain.

The proposed pathophysiology would explain the improvement of the evolution and clinical outcome in the short and long term of the patients treated with cisternostomy compared with those treated with decompressive craniectomy (Cherian et al., 2013, 2016). In our opinion, cisternostomy address one of the possible roots of traumatic brain edema by reversing the edematous mechanism of “csf-shif edema”, allowing to a removal of neurotoxic substances in the interstitium and recovering the functionality of the para-vascular system.

Conclusion

The shift of CSF from the cisterns to the brain following a pressure gradient or “CSF-shift edema”, could play an

essential role in the pathophysiology of brain swelling and in the development of secondary brain damage of the brain.

By cisternostomy, the direction of the “CSF-shift” is reversed resulting in a immediate reduction of the brain swelling and probable alleviation of the underlying mechanism leading to secondary brain damage.

Video Cisternostomy

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