A PARADOX: TRAUMATIC BRAIN INJURY AND DRUG DELIVERY THROUGH BLOOD BRAIN BARRIER

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Abstract: The blood-brain barrier is considered as a paradox. On one hand it protects the brain being constant systemic pouring of noxious substances, but on other hand it prevents the delivery of most important drug or therapeutic agents to a patient with brain tumors. In spite of tremendous progress in field of neuroscience and general drug development, BBB is the main bottleneck in the field of neurotherapeutics for Alzheimer disease, Parkinson disease, multiple sclerosis, brain/spinal cord injury, brain cancer, HIV infection of brain etc. Not only the 100% of large molecules (Mol. wt. > 500 Dalton) do not crosses the blood brain barrier but also that 98% of small molecules do not cross it. To determine pharmacokinetic and pharmacodynamic performance of central nervous system target, it is desirable to know that whether a compound will penetrate and distribute within the CNS or not. Although, Traumatic brain injury (TBI) is common to the soldiers involved in Iraq and Afghanistan conflicts; It breaches the blood brain barrier and accelerate cytotoxic cascade by initiating transcriptional changes in the neurovascular network which ultimately leads to many neurological diseases like neuronal dysfunction, neuron degeneration, epilepsy, loss of coordination etc. But in mild traumatic brain injury the BBB membrane is readjusted within 15 min. So, the best strategy for drug delivery to the brain is the temporary physicochemical disruption of endothelial layer either by intracarotid infusions of membrane active agents for example bile salts, oleic acid, the cytostatic drugs etoposide, melphalan, cytochalasin B, Intracarotid low pH buffers or by drug distribution via convection flow under high flow microinfusion. Later progesterone can be used, which is now not only “female hormone” but limits the cytotoxic cascade events, initiated transcriptional changes in the neurovascular network. It reduces the major damage if delivered artificially immediately after blunt head injury.

Keywords: blood-brain barrier, Traumatic brain injury, neurotherapeutics, high flow microfusion, neuronal dysfunction, pharmacokinetic and pharmacodynamic performance