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Hari Shanker Sharma
Uppsala University, Sweden

Pathophysiology of the Blood-brain barrier in CNS injury & Repairincluding High Altitude Brain Injury. New Roles of Nanomedicine

Recent advancement in nanomedicine suggests that nano drug delivery using nanoformulation enhances neurotherapeutic values of drugs or neurodiagnostic tools for superior effects than the conventional drugs or the parent compounds [1,2]. This indicates a bright future for nanomedicine in treating neurological diseases in clinics. However, effects of nanoparticles per se in inducing neurotoxicology, if any is still being largely ignored [3]. The main aim of nanomedicine is to enhance the drug availability within the central nervous system (CNS) for greater therapeutic successes. However, once the drug together with nanoparticles enters into the CNS compartments, the fate of nanomaterial within the brain microenvironment is largely remained unknown. Thus, to achieve greater success in nanomedicine our knowledge in expanding our understanding of nanoneurotoxicology in details is the need of the hour.

In addition, neurological diseases are often associated with several co-morbidity factors, e.g., stress, trauma, hypertension or diabetes. Recent observations show that brain injury occurring at high altitude (HA) could have adverse effects on the pathophysiological outcome. Thus, new research is needed to reduce HA induced exacerbation of brain pathology following trauma. These co-morbidity factors tremendously influence the neurotherapeutic potentials of conventional drugs. Thus, this is utmost necessary to develop nanomedicine keeping these factors in mind. Recent research in our laboratory demonstrated that engineered nanoparticles from metals used for nanodrug delivery significantly affected the CNS functions in healthy animals. These adverse reactions of nanoparticles are further potentiated in animals associated with heat stress, diabetes, trauma or hypertension at HA. These effects nanomaterials were dependent on their composition and the doses used. Thus, drugs delivered using TiO2 nanowired enhanced the neurotherapeutic potential of the parent compounds following CNS injuries in healthy animals. However, almost double doses of nanodrug delivery are needed to achieve comparable neuroprotection in animals associated with anyone of the above co-morbidity factors. Thus, cerebrolysin delivered either though TiO2-nased nanowires or PLGA-nanoparticles effectively reduced brain pathology in several diverse neurological diseases often complicated with various co-morbidity factors. Our observations showed that TiO2 cerebrolysin is also effective in brain injury performed at HA conditions in both cold & hot environment. These observations are the first to show that cerebrolysin could be useful in HA pathology in military personnel, pilots and injured soldiers airlifted for treatment. Taken together, it appears that while exploring new nanodrug formulations for neurotherapeutic purposes, co-morbidly factors and composition of nanoparticles require great attention. Furthermore, neurotoxicity caused by nanoparticles per se should be examined in greater details at normal altitude vs. HA before using them for nanodrug delivery in patients.

Biography

Hari Shanker Sharma, (Swedish Citizen), Director of Int. Expt. CNS Injury & Repair (IECNSIR); Professor of Neurobiology (MRC); Docent in Neuroanatomy (UU) is currently working in Uppsala University Hospital, Department of Surgical Sciences, Division of Anesthesiology & Intensive Care Medicine, Uppsala University, Sweden. Dr Sharma obtained his Ph D in Neuroscience in 1982 from Banaras Hindu University, Varanasi, India and Dr med Sci from Uppsala University in 1999. He has published over 300 peer reviewed research articles (ISI database h-index 36) related to Neuroprotection and Neuroregeneration in relation to the Blood-brain barrier in stress, trauma, and drugs of abuse in health and disease. His research on brain pathology and neuroprotection in different model is supported by Laerdal Foundation of Acute Medicine, Stavanger, Norway; role of nanoparticles in neurodegeneration and Neuroprotection for treatment strategies from European Aerospace Research & Development (EOARD), London, UK and US Air Force Research Laboratory, Wright Patterson Air Force Base, Dayton, Oh, USA; drug abuse research and neuroprotection from National Institute on Drug Abuse (NIDA); National Institute of Health (NIH).

sharma@surgsci.uu.se