PRESS INFORMATION

CLINICAL BRIDGING OF SPINAL CORD REGENERATION

Background Information

Spinal Cord Injury is a devastating condition with millions around the world afflicted. The present approaches to treat Spinal Cord Injury have met with only little success. Cell Based therapies offer great promise to this condition and there are several clinical trials using different Cell sources to treat spinal Cord Injury. Adult stem Cells derived from bone marrow are of particular interest due to their multipotent nature and proven potential in the repair, regeneration, rejuvenation and restoration of damaged organs including liver, heart etc. In recent years, there are many proven studies on the efficacy of Bone Marrow derived Stem Cells in the repair and regeneration of nerve tissue, especially in Spinal Cord Injury (1,2,3). This study of ours has proven the efficacy of transplantation of Bone Marrow derived stem cells in a novel polymer scaffold, by promoting recovery of functions in a dog with spinal Cord Injury which was followed up for two years**.**

Thermo reversible gelation polymer (TGP) as a scaffold:

The scaffold used in the study is Thermoreversible gelation polymer (TGP) which is a hydrogel with unique properties making it highly suitable for growing cells in it and is biocompatible to be implanted inside the body. Some of its properties include

Chemical properties:

It is a copolymer composed of thermoresponsive polymer blocks [poly(N-isopropylacrylamide-co-n-butyl methacrylate) poly(NIPAAm-co-BMA)] and hydrophilic polymer blocks (polyethylene glycol [PEG])(4). It is highly lipophilic with a network structure at the molecular level, enabling sustained release of a variety of growth factors which has been proven by earlier studies(5) .

Physical properties:

It has dynamic temperature dependant visco-elastic properties. It is hydrophilic at temperatures below the sol-gel transition temperature and is hydrophobic at temperatures above the sol-gel transition temperature. Thus in cell culture and implantation, cells can be embedded in the liquid Gel solution at lower than 20 deg C and cultured three dimensionally or transplanted *in vivo* in a hydrogel state at 37 deg C (6). Further TGP also helps cells to grow in an undifferentiated manner for a longer period of time compared to conventional scaffolds (5)

Biological Characteristics:

The TGP is biologically inert (7) and since it is completely synthetic, it can overcome the issues of Biological contamination which is major issue with other scaffolds derived from animal sources. TGP has been used for the culture of a variety of cells including continuous cell lines (8), embryonic stem cells , induced pluripotent stem cells (9), corneal limbal stem cells (6), chondrocytes (5) etc with proven success. All these studies have proven that TGP does not have any toxicity on the cells cultured in it.

Implantation of Cells in Scaffold in Small Animal Models:

In vivo implantation of Stem Cells embedded in TGP has been proven to be safe and efficacious in animal studies earlier. In central nervous system injury, the study by Osanai et al (10) is the fore-runner to the present study. In that study, Bone marrow stromal cells (BMSC) were embedded in TGP and implantation of this BMSC-TGP construct in the mice subjected to cerebral infarct was compared with two other study groups, BMSC without TGP group and PBS group. The results proved that the TGP hydrogel completely disappeared and provoked no inflammation in the brain of the mice. Further the transplanted cells were widely engrafted around the cerebral infarct in the BMSC-TGP construct treated mice and the number was larger than the BMSC without TGP group (10). **This study established that use of a scaffold along with cells is more advantageous *in vivo* than injection of cells alone and this formed the basis of our study in a large animal with spinal Cord Injury.**

Our Study:

The dog included in our study was a six month old, congenitally deaf boxer breed dog which was admitted to the TANUVAS with Grade IV paraplegia with total loss of motor and sensory functions of the hind limbs including loss of bladder and bowel function due to a road traffic

accident. Under general anaesthesia following myelography, autologous bone marrow aspirate was collected from femur of the dog with compressed fracture of Thoracic vertebra 12 (T12) and dislocation between T11 and T12 and the aspirate was transferred to the Cell processing unit of Nichi-in Center for Regenerative Medicine (NCRM), Chennai. The aspirate was subjected to Cell processing using established protocols and Bone Marrow Mononuclear cells (BMMNCs) were isolated. A portion of the BMMNCs were embedded in TGP and was engrafted intra lesionally. After 19 days, a portion of the isolated BMMNCs which was separately stored was also administered intravenously to potentiate the cell transplantation and the animal was followed up with a regular follow-up for a period of two years.

The recovery of motor and sensory functions was noticed on the 53rd day. The animal attempted to stand on the 79th day and ambulation was possible on the 98th day. The animal was able to walk satisfactorily on the 133rd day and thereafter the animal returned to its normal life and the status has been maintained constant for the past two years.

The above clinical protocol for spinal cord regeneration evolved by TANUVAS – NCRM was published in a peer reviewed journal – Stem Cell Research & Therapy with the comment *"the finding is encouraging since spinal cord injuries are common conditions in humans and lack effective therapies".* This study is one of its kinds in the world and will serve to bridge the gap between veterinary and human sciences with the hope of treating millions inflicted with spinal cord injury

This technology will be discussed by experts from the Field of Stem cell Research, Human and veterinary sciences and they will be illuminating us with their views and opinion on this study which is going to be a hallmark in the translation of cell based therapies from the benchside to the bedside.

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***The full publication is available online at:**

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