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Current Scenario on Neural tissue engineering

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Abstract

Worldwide millions of people suffer from nerve tissue injury- SCI (Spinal Cord Injury) that will result paralysis and experience of life-threatening problems. Till date there are different methods have been described to be effective in the treatment of SCI but there is no remedy available for full functional recovery of SCI**.** Stem cells and tissue specific growth factors entrapped matrixes along with the tissue engineering principle are the used for the treatments and for repairing SCI. Although these techniques overcome the limitation of traditional clinical methods but still they cannot restore the bio-functionality of the regenerated tissue after the injury. Therefore, the major challenge that is faced by the biomedical experts is to repair and regenerated a structural bio-functional damaged nerve tissue**.**

Key words: soya bean , Chunks , Water absorption capacity, moisture level, Protein test

1. Introduction

Spinal nerve cord is a complex tissue system of mixed nerve that carries motor, sensory, autonomic signals from between the brain and the other body parts (Afifi 1998). There are 31 pairs of spinal nerves one on each side of the vertebral column. These nerves are grouped into corresponding regions of spine and make the peripheral nervous system. Spinal nerves are classified into 4 subtypes: Cervical nerves - 8 pairs; thoracic nerves- 12 pairs and 5 pairs of lumbar, sacral. coccygeal nerves are 1 pair in number. Spinal nerve formed form a combination of nerve fibre from its dorsal and ventral roots. All the spinal nerve except the C1 emerges from the spinal column through an opening (intervertebral foramen) between adjacent vertebrae. The Spinal cord has different function: signal receiving and passing, sensation, muscle contraction, co-ordination and movement of body parts. Therefore, the injury of Spinal cord tissue results severe health care issues such as are stop signalling pathway to and from the Central nervous system, sever pain, loss of sensation, uncontrolled or imbalanced body movements and coordination and most of the people get paralyzed, and experience life-threatening problems. According to the WHO survey, annually more than 50000 people suffer/annually from SCI (Spinal Cord Injury) at global level (Muheremu et al., 2016**).** There many causes of SCI such as road-accident, trauma, improper physical activities, infections, cancers etc and most of the victims of SCI are young persons (Tator, 1995). SCI patients tolerate not only the physical illness but also the psychological and economic problems. Therefore, its major issue both the prevention and the cure SCI patients at worldwide level in effective manner (Kwon et al., 2010).

2. Conventional Treatments

SCI is a complicated spine injury and commonly irreparable due to the lack of regeneration capability of nerve cells. In case non-surgical injuries such as cervical spine, traction is done to take the spine into correct position along with the nerve relaxant medication to relief the pain. In case of traumatic injury such as disc rupture or tumours, surgery should be required for the blood clot, lesion removal etc.

Hence, till date there is different clinical methods are used for the treatment of SCI but no one is best. There is no remedy available for full functional recovery of SCI**.** However, none of those methods were efficient enough to gain any functional recovery after the injury and finding a solution for the repairing of SCI is a major challenge in the current world (Kwon et al., 2010)**.** Stem cells and neural

growth factors are the only treatments available presently for repairing SCI, though it cannot restore functional recovery completely. Researcher found that the major challenge is axonal regeneration and and rewiring of the damges spinal cord (David and Aguayo, 1981). But many scientists found that axon of the central nervous system have capability to re-grow into the peripheral nerve grafts. Therefore, many experts agree that the greatest hope for treatment of spinal cord injuries will involve a combinatorial approach that integrates biomaterial scaffolds, cell transplantation and molecule delivery, and work with this theme is in progress but not any good achievement till date **(**Muheremu et al., 2016**)**.

3. Tissue engineering approaches

For the regeneration of tissue or organ tissue engineering triads play an important role- cells, scaffold and growth factors. Currently, stem cell-based therapies are the most promising treatment for the damaged neural; tissue regeneration (Straley et al., 2010). There are different kind of stem cells e.g. embryonic stem cells (ESCs), Bone marrow derived mesenchymal stem cells (MSCs), Neural stem cells (NSCs), induced Pluripotent stem cells(iPSCs) and Adipose derived stem cells (ADSCs), clinically used for the repairing the nerve injuries (McDonald et al., 1999; Keirstead et al., 2005; Sasaki et al., 2001; Osaka et al., 2010; Geffner et al., 2008; Attar et al., 2011; Li et al., 2007; Lee et al., 2009; Abematsu et al., 2010 & Karimi-Abdolrezaee et al., 2010; Tsuji et al., 2010; Kobayashi et al., 2012; Kingham et al., 2014; Widgerow et al., 2014; Lenka et al., 2009; Goel et al., 2009 & Raheja et al., 2012). However, the selection a specific cell line, their number or dosage and application is still a big question for researchers (Petrova, 2015). Currently researchers focused on the ADSCs as the most promising cell lines, due to their large avaibility, cost-effective and easy collection as waste product surgical procedures. They have also better stem cell fraction, proliferation, differentiation rate with low morbidity as compare to the other cell types. (Strem et al., 2005).

In case of neural tissue cells need to proliferate in proper alignment for proper conduction and signalling. Thus, we need a proper matrix having aligned matrix fibers as similar to the native Spinal cord tissue and for this biomaterials are must. Both polymeric and natural polymers are used as biomaterial for the attachment and proliferation of cells, and fill the damaged nerve gap. They provide a controlled microenvironment and create a biomimetic environment for the cell growth, signalling and conduction.

The combinatorial approaches of tissue engineering i.e., cells with the scaffold is a significant method for full functional regenerated tissue as well as for the biomolecules delivery at the damaged site. **(**Muheremu et al., 2016**)**. Biomaterials used for scaffold fabrication are very complex in nature providing the concomitant delivery of cells, neurotrophic factors or other bioactive substances to the targeted site (Zeng et al., 2011; Shrestha et al., 2014().)**.**

In last decades many biomaterials either natural or synthetic as well as both degradable and nondegradable has been used to design the scaffolds for SCI repair, but finding an ideal biomaterial for repairing SCI is still a scientific challenge (Perale et al., 2011& Haggerty et al., 2013).

Nautral polymers - Collagen, gelatin, agarose, alginate, chitosan, fibrin, methylcellulose and some extracellular matrix (ECM) derived proteins are the most widely studied and potential used natural materials for tissue engineering of damaged tissue (Cholas et al., 2012; Zeng et al., 2011; Lai et al., 2016; Stokols et al., 2006; Gros et al., 2010; Wang et al., 2010; Chen et al., 2011; Francis et al., 2013; Fuhrmann et al., 2016; Wang et al., 2011).

Besides that all natural polymer, Silk is most explored and utilized biomaterial for tissue regeneration due to its good mechanical strength, biocompatibility, non-toxicity, and *in vivo* biodergardble nature. Many researchers also focused in silk as biomaterial for the fabrication of nerve tissue grafts (Subia et al., 2015**).** They designed nanocomposite of silk and gold and used this blend to fabricated aligned electrospun fibrous matix and reproted that regeneration of as a nerve conduit (NC) under in vivo condition in rat model for the treatment of sciatic nerve injury (Das et al., 2015).

Although many researchers have been focusing the new biomaterials- biological and physiological properties like flexibility and conductivity for the proper and better SCI repairing (Huang et al., 2006; Wu et al., 2016**).** Therefore, some synthetic polymers include poly(lactic acid) (PLA), poly(2-

hydroxyethyl methacrylate) (PHEMA), poly(glycolic acid) (PGA), poly(lactic-co- glycolic acid) (PLGA) poly-ε-caprolactone (PCL), self-assembling peptides (SAPs), PANI and PLA-b- PHEMA copolymer) having good mechanical stability, conductivity and biocompatibility are also focused for the nerve tissue regeneration (Patist et al., 2004; Hurtado et al., 2011; Pritchard et al., 2010; Kang et al., 2012; Zamani et al., 2015; Silva et al., 2010; Hwang et al., 2011; Tsai et al.,2004; Kubinova et al.,2013; Pertici et al., 2014; Gelain et al., 2011; Zhou et al., 2013).
Commercially, FDA approved synthetic polymer based scaffold (e.g. *Neurolac, Neurotube and Salu Tunnel Nerve Protector)* are clinically used for peripheral nerve injuries (Kehoe et al., 2012; Das et al., 2015)**.**
Other than them several researchers has also been focused on the nanomaterials for the better tissue rergnation. Carbon nanotube is one of the most focused materials that has been studied by the scientist in the field of biomedical engineering. Mitra & co-workers studied the *in vitro* neural cells growth and regeneration the on carbon nanoparticle matrix and reported that proper aligned growth of neuroblastoma and schwann cells on the scaffold (Mitra et al., 2013). In another research, aligned carbon nanotube (CNT) and chitosan composite scaffold is used to study the nerve cell growth on the fabricated multiwalled CNT-chitosan nanocomposite. This study showed that the matrix helos in the controlled the cell migration in aligned direction by sending electoral cues under *in vitro* condition (Gupta et al., 2016).

In the last few years, it was reported that ECM (extracellular matrix) based scaffold e.g., collagen matrix, powder, hydrogel are the potential biomaterial for nerve tissue regeneration. FDA also approved many acellular allogenic and xenogenic products- *NeuraGen, Neuroflex, NeuroMatrix, AxoGuard Nerve Connector* for the clinical application and commercially used for repairing peripheral nerve injury (Kehoe et al., 2010)). They provides 3D natural biomimetic house with growth factor rich signalling molecule for proper cell adherence and proliferation. The acellular spinal cord ECM bio-molecules give signals to the stem cells and differentiate them into nerve cells (Vaccari et al., 2009; Zhang et al., 2010. Thus, this acellular ECM scaffold with nerve cells shows synergistic effect and might be a best option for the treatment of SCI and their biofunctional regeneration. For the fabrication of acellular ECM nerve grafts xenogenic porcine optic nerve, spinal cord and brain tissue was studied by the researchers and their cytocompatibility was studied by using PC 12 cell culture (Medberry et al., 2012). In another study, injectable ECM hydrogel of porcine spinal cord or urinary bladder along with hMSCs was used to treat the spinal lesion cavity (Tukmachev et al., 2015). This hydrogel matrix showed the faster degradation that results poor *in vivo* tissue regeneration.

4. **Conclusion:**

Many researchers have been working on neural tissue injury, but the success rates are significant as compare to the other tissue regeneration. However, there are lot of products are commercially available for PNI but there is no best treatment of the SCI. For this area selection of a specific cell line, growth factor and choice of materials are not only the single factor, but their proper combinatorial approaches in a controlled manner will result in fully functional nerve tissue regeneration. Thus, we have to focus on new technologies and engineering principle for repairing SCI.

Conflict of interest:

Authors declare that they have no conflict of interest.

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