LETTER TO THE EDITOR

Clinical trials for the treatment of spinal cord injury: cervical and lumbar enlargements versus thoracic area

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Sir, Mackay-Sim et al. (2008) evaluated the 3 year safety and efficacy of olfactory ensheathing cells (OEC) transplantation in three complete mid-thoracic spinal cord injured (SCI) patients and compared it with three control cases of SCI.

In this letter, we will discuss the safety, efficacy and availability of SCI improvement with regard to cell transplantation in human studies.

In terms of safety, the thoracic spinal cord is preferred level of study. The thoracic vertebrae are supported by the rib cage. Thus, motion and instability is less than the cervical and thoracolumbar junction and the stability of the thoracic spine provides less variability in the extent of spinal cord movement. The mid-thoracic area is the best level of study because if the procedure is complicated with say syrinx formation, there is a large distance from the cervical area and therefore cell transplantation leading to nearby damage is less likely. Any ascending damage to one or two spinal cord segments will be of less consequence in the mid-thoracic area than in the cervical region (Feron et al., 2005).

Regarding the ability to evaluate the efficacy of treatment, the mid-thoracic region is the most difficult to evaluate. In cases of small caudal improvement in the injured thoracic cord, motor evaluation is difficult and any sensory evaluation is subjective and less reliable than the motor examination. There is a large distance from the mid-thoracic to the cervical and lumbar enlargements making efficacy of small positive changes to motor system almost unrecognizable.

Regarding the availability of human cases, our evaluation found complete thoracic SCI in 12 out of 108 cases (11.1%). The cervical and thoracolumbar junction were more common sites of injury in general (Rahimi-Movaghar, 2005; Rahimi-Movaghar et al., 2006).

Thus, it is difficult to prepare enough samples for randomized controlled clinical trials in the thoracic area.

A brief review of the literature shows that the T8-T10 vertebrae is a common level of cell transplantation in animal SCI. The close proximity of the lower limbs to the lower thoracic cord in the small animal model such as rodents makes changes in lower extremity motor function more apparent (Rahimi-Movaghar et al., 2008).

In the past 6 years, three clinical trials of OEC transplantation have been published in human SCI in China, Portugal and Australia (Huang et al., 2003; Lima et al., 2006; Mackay-Sim et al., 2008).

The study of Mackay-Sim et al. demonstrated that cell transplantation had a 3-year safety window with no deleterious motor changes in the case or control groups. A single-blinded neurological assessment by a neurologist demonstrated a case of T4 sensory level in a cell transplant group whose light touch and pin prick sensitivity extended caudally from the T4 to the T10 level at 1 month. This sensory improvement remained constant over the next 35 months.

The observation of Guest et al. (2006), regarding the largest human cell transplantation study of SCI in China reported by Huang et al. (2003) described a patient with a complete C3 SCI who had a rapid caudal extension of sensory and motor improvement between 1 and 5 days. Elbow flexors and wrist extensor function improved objectively as the sensory examination improved (2006).

Six out of seven cases of complete SCI from C4 to T6 reported by Lima et al. (2005) had improvement of both sensory and motor function. Such a small number of patients prevents any useful statistical analysis, but ASIA score improvement was 6.3 and 3.9 in cervical and thoracic SCI, respectively.

Advance Access publication November 20, 2008
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In the Phase I study of Saberi et al. (2008), 33 patients were enrolled and evaluated (2008). The treatment regiment consisted of Schwann cell transplantation and a vigorous rehabilitation regime. We, as independent observers, evaluated patients at 3-month and 1-year follow-up. In four homogenous groups of chronic thoracic injury, there was a case of an incomplete (ASIA C) spinal cord injury at the T6–T7 level which had significant improvement in sensorimotor function of the lower limbs. It is unclear the contribution of any form of treatment to recovery in the setting of an incomplete SCI. Clinical trials in SCI patients often do not recommend including incomplete SCI patients due to their predictable recovery. One can not ascribe the above mentioned improvement solely to the administration of Schwann cell. One must be wary of the potential danger of cell transplantation as illustrated in the previous two described cases of incomplete SCI who had delayed neurologic worsening following treatment. (Saberi et al., 2008).

Following cell transplantation, the presence of caudal neural improvement in one or two segments in a complete SCI patient is difficult to perceive in the mid-thoracic level. An understanding of its mechanism of recovery is at this time unclear. Guest et al. (2006) suggests that the mechanism for caudal improvement may be due to improved functioning of normal fibres or strengthening of synaptic connections.

In the case of Mackay-Sim et al., I agree with Dietz that caudal extension from T4 to T10 is most probably related to spinal tract regeneration, but in other reported cases, especially in one or two segment improvement, peripheral nerve regeneration could have a role in caudal extension of sensory and motor fibres (Dietz, 2008).

Following cell transplantation, neurological examination should be performed daily for a week. It is possible that in the first case of transplantation of Mackay-Sim et al., if daily examinations were performed, caudal sensory progression may have been seen in first few days after transplantation and not at a month. The trial manager could report this sensory change and discuss 1-year efficacy in their first paper in 2005.

It may be that small subgroups of SCI patients with lesions between the cervical and lumbar enlargements may benefit more from cell therapy. In the future, the combination of neurotrophic factors and appropriate scaffolds are going to be added to cells in clinical trials to assist in SCI regeneration.

Acknowledgements

The author would like to thank Dr Alexander R. Vaccaro for editorial assistance.

References


Guest J, Herrera LP, Qian T. Rapid recovery of segmental neurological function in a tetraplegic patient following transplantation of fetal olfactory bulb-derived cells. Spinal Cord 2006; 44: 135–42.


