March-April 2016 Volume 5: Issue 2

Four Leg Rehab News

Stems Cells & Neurologic Lesions

The future is now! Regenerative Medicine has the potential to change healthcare forever!

This edition of Four Leg News is all about stem cells and the neurologic system… spinal cord injuries in particular. I have to say that I was not only impressed, but also additionally optimistic for the future of stem cells with the spinal cord injured patient. The research looked at acute lesion, chronic lesion, intravenously administered cells, & locally administered cells! It's a very exciting time and the future looks bright!

I hope you enjoy this read as much as I enjoyed finding these articles for you!

Cheers! Laurie

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CANINE REHAB EDUCATIONAL RESOURCES

You really have to be some kind of a creep for a dog to reject you. —Joe Garagiola

A Systematic Review of the Safety and Efficacy of Mesenchymal Stem Cells for Disc Degeneration: Insights and Future Directions for Regenerative Therapeutics

Rita Lok-Hay Yim, Juliana Tsz-Yan Lee, Cora H. Bow, Bjorn Meij, Victor Leung, Kenneth M.C. Cheung, Patrick Vavken, and Dino Samartzis
Stem Cells and Development, Volume 23, Number 21, 2014, pages 2553 to 2567.

Intervertebral disc is a shock absorber of the spine.

Disc components = a central gelatinous-based nucleus pulposus (NP) and the peripheral annulus fibrosus (AF).

Disc degeneration is the progressive process of the loss of structural and functional integrity of the disc and is characterized by chemical changes in water and proteoglycan content. Degenerative changes may lead to altered spinal motion, potential disc herniation and compression of the nerve roots, and adjacent disc degeneration that may in time become symptomatic.

Cell-based therapies for treating disc degeneration have gathered considerable attention over the past decade. This modality allows the injection of cells into the disc to repair lost cells and matrix, and to increase proteoglycan content.

The review found that the use of MSCs for treatment of disc degeneration was safe & effective with a 2.7% complication rate occurring exclusively in rabbits.

MSCs isolated from bone marrow were found to be the best studied source compared with MSCs isolated from adipose and synovial tissue. Emerging evidence supports that MSCs replicate and differentiate toward NP cells when injected into a degenerated site and they stimulate endogenous NP cells to proliferate and hence repopulate the intervertebral disc. There is a lack of collective evidence to support that injected BM-MSCs only differentiate into NP cells. Other mechanisms of action may also play a role.

This is the first study to address, in a systematic fashion, the safety and efficacy of MSCs for the treatment of disc degeneration in animal models. MSC's are effective in halting the progression of disc degeneration or increasing disc height.

I think dogs are the most amazing creatures; they give unconditional love. For me, they are the role model for being alive.

—Gilda Radner

A Meta-Analysis of the Motion Function through the Therapy of Spinal Cord Injury with Intravenous Transplantation of Bone Marrow Mesenchymal Stem Cells in Rats

Duo Zhang, Xijing He
PLOS One, April 2014, Volume 9, Issue 4, e93487

To evaluate the locomotor recovery with animal models of spinal cord injury (SCI) the BBB scale, which is a sensitive and reliable measure of locomotor rating scale and set up by Basso, Beattie and Bresnahan, is widely used. The BBB scale is estimated by observing the movements of lower limbs and joints of rats. A full score of 21 / 21 on the BBB rating scale means normal function. Lower scores equate with compromised function. This systematic review and Meta-analysis of BBB score in SCI rats through the comparison between the intravenous bone marrow mesenchymal stem cells (BMSCs) transplantation group and the control group is expected to offer academic support for cure of SCI.

Overall, the BBB score of BMSCs group was significantly higher than control group at 1 week, 3 weeks and over 5 weeks after transplantation. This result shows clearly that intravenous transplantation with BMSCs promotes the motor function of spinal cord injured rats.

The Meta-analysis indicated that intravenous transplantation with BMSCs is an effective therapy for SCI in rats. Motor function was increased after intravenous transplantation with BMSCs. Even at 7 days after SCI, this therapy can still work and yield positive effects. This result is a report from 9 studies.

This field [stem cells research] isn't growing, it's EXPLODING.
-Barth Green

Why you care…

Firstly, I think it is important to point out and remind you that this is a meta-analysis, not just one study. The studies they looked at were on rats. I'm amazed quite frankly! How relatively simple! If I were paralyzed or my dog, I'd be willing to try intravenous stem cells!

"There it is. You forgot to convert to dog years."

Antioxidant and anti-inflammatory effects of intravenously injected adipose derived mesenchymal stem cells in dogs with acute spinal cord injury

Duo Zhang, Xijing He
PLOS One, April 2014, Volume 9, Issue 4, e93487

Much of the current research on spinal cord injury (SCI) is focused on developing treatment methods that limit or prevent secondary injury. Minimizing secondary injury is generally achieved by ensuring adequate perfusion and oxygenation and by ancillary administration of neuroprotective agents for improving clinical signs.

Transplantation of mesenchymal stem cells (MSCs) has been shown to provide neuroprotection, increase neuronal regeneration, and ameliorate the clinical signs of SCI. Transplanted MSCs have been shown to not only improve the inflammatory environment and enhance the survival of endogenous nerve cells, but also reduce fibrosis formation. Additionally, the MSCs were able to partially differentiate into neural cells.

Based on our hypothesis, administration of adipose derived-MSCs should ultimately result in less scar tissue formation, aid in growth of neural progenitor cells, and improve limb function.

The purpose of the study was to reduce the usage and risk of high doses of glucocorticoid steroids, and to determine whether AD-MSCs could be used as an early alternative treatment modality for acute SCI.

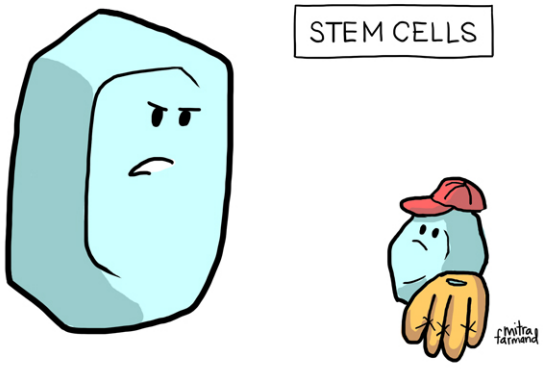
Methods: 16 adult beagles with SCI were assigned to one of 4 different groups: IV adipose-derived stem cell, steroid, both steroid & stem cell & a control. AD-MSCs (1 x 10^7 cells) were injected intravenously once a day for 3 days beginning at 6 hours post-SCI. The steroid (methylprednisolone sodium succinate) was also injected intravenously according to the standard protocol for acute SCI.

Results: Subjects in the stem cell group had significantly enhanced motor function compared with those in the control group at 7 days post treatment. In addition, gastro-intestinal hemorrhage was not observed in the control or the AD-MSCs groups but was observed in both steroid groups. Hemorrhages were less commonly observed in the stem cell group and a lower inflammatory response was observed in the stem cell and stem cell & steroid groups.

Administration of AD-MSCs improved hind-limb functions and reduced the occurrence of adverse effects that are associated with high doses of glucocorticoid steroids.

Why you should care…

This is a dog study, and it uses adipose derived stem cells! Good to know and good to recommend by all accounts thus far!



Transplantation of autologous bone marrow mesenchymal stem cells in the treatment of complete and chronic cervical spinal cord injury

Guanghui Dai, Xuebin Liu, Zan Zhang, Zhijun Yang, Yiwu Dai, Ruxiang Xu
Brain Research 1533, 2013, pages 73 to 79

Spinal cord injury (SCI) often occurs due to high-energy trauma. Although complete transection of the spinal cord rarely occurs, during the early period of the injury, the 'spine fracture squeeze' as well as inflammatory edema often causes total loss of nerve functions. As a result, neuronal cells die in the span of first 12 h to a few weeks.

The transplantation of stem cell (SC) from various sources has shown promise in nerve regeneration after SCI. The current research on the mechanism of stem cell transplantation suggest that transplanted bone marrow mesenchymal stem cells (BMMSCs) are capable of surviving in the region of injury and differentiate into nerve cells (neurons, astrocytes and oligodendrocytes). Additionally, they are involved in axon regeneration and remyelination, neurotrophic effect, neovascularization, directed migration of endogenous neural stem cells (NSCs) and regulation of local inflammation.

Methods: 40 patients (humans!) with chronic and complete cervical SCI were selected for BMMSCs transplantation and were followed for 6 months to assess the feasibility and clinical efficacy. The treatment group received BMMSCs transplantation to the area surrounding injury.

Results: Ten patients (50%) showed clinical improvement. Among these, one patient had improvement in motor function alone, two had both motor and sensory improvement, one had improvement in sensory and urinary function and six patients had improvement in both motor, sensory and bladder functions. In the control group, none of the cases showed improvement in any of motor, sensory, or urinary functions.

In the treatment group, no signs of adverse events such as wound infection, incision leakage of cerebrospinal fluid, intracranial infection, or any deteriorating complications occurred. No sign of tumor was evident at the transplant site 6 months after BMMSC transplantation.

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Weird Research!

Did you know, that Chinese researchers were able to make mouse sperm using stem cells? They then used it to fertilize female mouse eggs, which resulted in mouse babies, which were able to reproduce later on in adulthood! They think the research could be a stepping-stone to help with male infertility.

Did you know that the soft tooth pulp in the centre contains nerve stem cells? There is even a company called Store-A-Tooth that will store a baby tooth & harvest the material to create stem cells should you need them for some reason in the future!

Did you know that there is a company (Memphis Meats) that is growing meat in a petri dish? They're a Californian company that is taking regenerative stem cells from animals, sticking them in a petri dish with oxygen, sugar & minerals and in only 3 weeks... "Voila! Meat"!

(Continued from page 5)

Conclusion: Based on the results of this clinical study, we consider that BMMSCs transplantation has a clear role in promoting neurological rehabilitation for the complete and chronic cervical spinal cord injury. The improvements were not only presented as enhanced motor, sensory and urinary functions, but also objectively evaluated with neuronal electrophysiological examination and measurement of residual urine volume.

Why this matters…

I know that we are here to discuss CANINE rehab, but a couple of things jump out at me; 1) this is a HUMAN study! Oh my! And 2) these patients were chronic!!! Double wow! Okay, so only 50% improved, but if it were me (or my dog), I'd be pretty pumped! Now, I have to admit that I'm not100% sure how the stem cells were administered. I read this paper through several times, and it is not clear if they were injected into the spinal canal or exactly where & how the stem cells were deployed. But still, wow!

Spinal cord injury in rats treated using bone marrow mesenchymal stem-cell transplantation

Yu-Bing Chen, Quan-Zhang Jia, Dong-Jun Li, Jing-Hai Sun, Shuang Xi, Li-Ping Liu, De-Xuan Gao, Da-Wei Jiang
Int J Clin Exp Med 2015;8(6):9348-9354

This study aimed to analyze the repairing effects of BMSCs transplantation in spinal cord injury by assessing behavioral and histological data.

Methods: 192 rats were used. They were divided into 4 groups: control without SPC, control with SPC and no treatment, SC I+ BMSCs via tail vein injection, SCI + local transplantation of BMSCs at the site of the injury. Allografts were used in this study.

Results: Most of the transplanted cells migrated to the surrounding areas of lesions, neuronal and glial markers were expressed in some of the transplanted BMSCs, and motor functions of these rats were improved. Histological observations showed that edema was reduced 7 days after the treatment, inflammatory cell infiltration decreased, vacuolar degeneration improved, the morphology of nerve cells appeared normal, and intracellular structures were evenly arranged. The recovery of nerve cells and structural arrangement was observed by day 15 as compared to tissues examined 7 days post transplantation, indicating that BMSCs transplantation into the area of spinal cord injury can promote repair and regeneration of the injured spinal cord.

This experiment also indicated that BMSCs can penetrate the blood-spinal cord barrier and migrate to the injured spinal cord tissues after tail vein injection and promote repair by transforming into neurons.

Nonetheless, the migratory mechanism of BMSCs to the area of injury needs further investigation.

Why you should care…

So this study is interesting because of the two different methods of delivering the stem cells. Both were effective. It's also interesting because they used allografts versus auto-grafts.

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Heart Warming Dog Story: Swansea Jack

Swansea Jack was a black retriever who lived with his owner William Thomas near the River Tawe in Swansea, Wales, during the 1930s. One day, Jack saw a small boy drowning in the river and ran in, pulling the boy to shore by the scruff of his neck. There was no one around to see it, and had circumstances been different, the boy would probably have spent the rest of his life telling the story to people who would never believe him. But Jack wasn't done. Within a few weeks, Jack rescued another swimmer, this time with witnesses in attendance. And then another. And another. And so on. Over the course of the next decade, Jack was reported to have saved at least 27 people from, presumably, the most dangerous river and docks in Wales.

For his efforts over the course of his lifetime, Jack was given a silver collar by Swansea council, the Bravest Dog of the Year Award, a silver cup from the Mayor of London, and his very own statue. That's more accolades than your average Batman. And he's still recognized today—he was probably the inspiration for the nickname of Premier League football team Swansea FC, "The Swansea Jacks."

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Drop me a line! Send me your questions!

Four Leg Rehab Inc

PO Box 1581,
Cochrane, AB T4C 1B5
Canada

Laurie@Fourleg.com