Journal of Stem Cell Research

Genesis-JSCR-5(1)-57
Volume 5 | Issue 1
Open Access
ISSN: 2582-8797

Mesenchymal Stem Cells and their Effect on Scoliosis Treatment

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Citation: Kelly FG, Gallicchio VS. (2024) Mesenchymal Stem Cells and their Effect on Scoliosis Treatment. J Stem Cell Res. 5(1):1-9.

Received: May 02, 2024 | **Published**: May 23, 2024

Abstract

Scoliosis is an abnormal curvature of the spine that can lead to many issues, including significant chronic pain. While the exact cause of scoliosis hasn't been clearly identified, new data advocates for the incorporation of stem cell research and therapy within the scoliosis field. Scoliosis does not tend to be a fatal chronic illness, so it has not been prioritized in the research on stem cells. Not many concrete conclusions can be drawn based on the lack of data, but new correlations have been found that suggest malfunctions in stem cells may be the cause of scoliosis and could potentially be used to correct scoliosis. Expanding upon that, a study on a young boy showed improvement in the curvature of his spine when doctors implanted mesenchymal stem cells. A different type of scoliosis also saw improvement when using MSCs to perform a spinal fusion. This paper aims to compare the effects that MSCs can have on causing scoliosis while also compiling the research that proposes stem cells can assist in pain management and even correct curvature. The current treatment for scoliosis can have severe complications, and there is no guarantee that it can correct the spine. With more research done analyzing the effect stem cells can have on scoliosis, we can hopefully begin to find the cause to create more efficient and ethical treatment.

Keywords
Mesenchymal stem cells (MSCs); scoliosis, spinal fusion; stem cell therapy; neuropathic

Abbreviations

AIS: Adolescent Idiopathic Scoliosis, CS: congenital scoliosis, DS: degenerative scoliosis, MSCs: Mesenchymal stem cells.

Introduction

What is scoliosis?

Scoliosis affects 2-3% of the population, making it prevalent in many lives [1]. The spine is one of the most important parts of the human body and acts as the central support system [2]. The complex structure of the spine comprises ligaments, nerves, spinal disks, bones, and more [3]. Among the spine are different planes that work in a 3-dimensional manner to allow movement in many directions [4]. The cervical, lumbar, and thoracic regions have a naturally occurring curve for shock absorbance and movement [5]. Scoliosis is seen on the frontal or coronal plane, where an atypical curvature takes place [1]. Scoliosis can be identified for different reasons, but the most prevalent types include idiopathic, congenital, and degenerative scoliosis [6]. Adolescent Idiopathic Scoliosis is the most popular type of scoliosis that is seen in adolescents between the ages of 10-18 [7]. The cause of AIS is unknown, but some theories include hormone issues, an imbalance of muscles, or even genetic factors [8]. Congenital scoliosis has been identified as a curvature of the spine stemming from the time of development in the womb [9]. CS is a defect present at the birth of the child due to complications in bone formation that may progress throughout their childhood [10]. Degenerative scoliosis is seen in adults, where the curvature of the spine develops as the individual ages and the joints and discs present in the spine wear down [11]. While all three of these types of scoliosis have different origins and symptoms, they each have a curvature of the spine where stem cells can be explored in finding a cure or providing better care (Figure 1).

Figure 1: Shows the X-Rays of three types of scoliosis, AIS [12], CS [13], DS [14].

Current Standard of Care

All the way dating back to the 5th century, physicians have worked to find relief for scoliosis patients [15]. From then on, different procedures with rods were introduced, as well as bracing, beginning in the 1500s. Today, bracing and surgery are the only two cures globally recognized [16]. The archaic process of bracing for AIS patients uses constriction of bones and muscles throughout puberty to stop the curve of the spine from progressing. Bracing cannot work after the child is done growing [17], so invasive surgery or spinal fusion is used for most patients. It is often used to prevent the spine from getting worse, as opposed to correcting the curvature. It also has a significant failure rate, with 25% of patients having to get surgery [18]. The quality of life is also difficult, with the brace expected to be worn for over 20 hours a day in many cases [19]. When bracing doesn't work, patients must get a spinal fusion, which can be associated with extreme medical complications that can even result in death [20] (Figure 2).

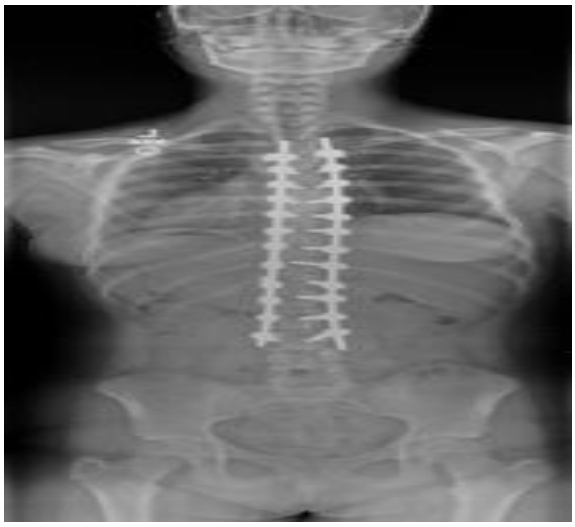

Figure 2: Shows spinal fusion [21].

Mesenchymal Stem Cells

Mesenchymal stem cells or better known as MSCs, are seen in many types of regenerative care [25]. These stem cells can be derived from the umbilical cord, bone marrow, blood, adipose tissue, and more [26]. The revolutionary aspect of MSCs is their ability to self-renew and can be seen repairing skeletal tissues and muscles [27]. They can develop into different cells seen in bones, tissues, or fats through differentiation [28]. MSCs can also be seen assisting with signaling cells for repair and calming down inflammation [29]. These multifaceted cells have just begun to be researched within the scoliosis field for assisting with surgery, healing, or even correction (Figure 3).

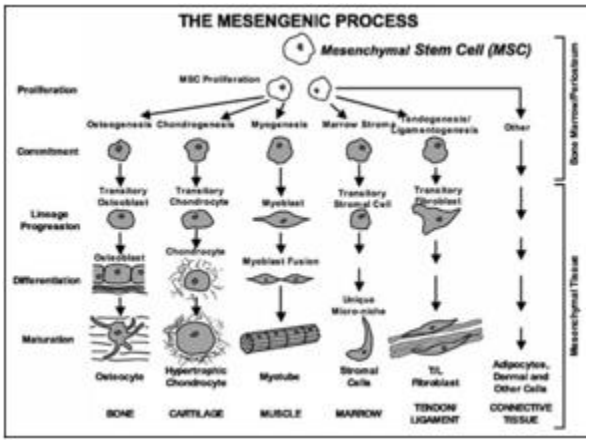

Figure 3: Differentiation and development of MSCs [30].

Methods and Discussions

Tissue Repair with MSCs

MSCs in scoliosis research show they can assist in tissue repair [31]. A recent study involving rabbit tendons incorporated MSCs to allow the Achilles to heal better. What was found after 12 weeks was an increase in productivity around collagen organization as well as less stress and inflammation. It allowed for a faster and easier recovery for the rabbit [32]. The stem cells show a unique lineage that allows for the onset of new cells that can support healing [33]. While human studies with tissue repair in Achilles haven't been finalized, these results can show a promising future for proper healing and potentially correction within the scoliosis industry.

What are the theories for the cause of scoliosis?

To properly form conclusions on stem cell involvement in the scoliosis industry, many scientists are looking for the actual cause of it [34]. Each type of scoliosis has many theories that are currently being researched. For AIS, studies have shown a link between scoliosis and the embryonic development of genes [35]. It was found that in people with AIS, the cells around that curve are acting like nerve cells instead of bone cells [36]. By investigating the coding of genes and the ability for them to turn on and off, scientists believe that when genes are turned off in the womb, they can cause scoliosis. This idea was later supported using chickens. When they intervened with turning genes on and off, like how they present in people with AIS, there was a curvature of the spine seen as they aged. If this data is further researched, it could signify that the underlying issues with scoliosis are an epigenetic problem. Stem cell therapy could potentially later be used to help the differentiation of cells and allow for proper coding (Figure 4).

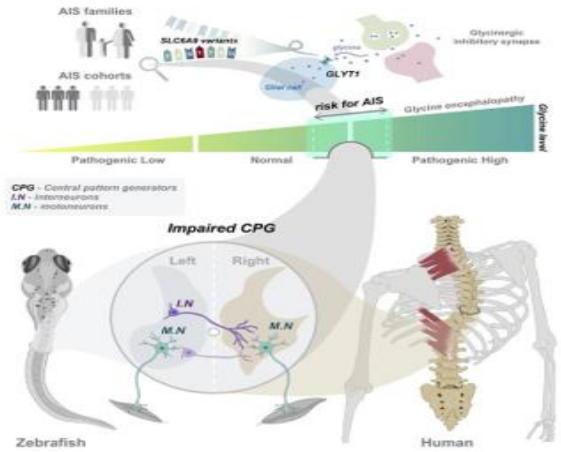

Figure 4: Outlines potential cause of scoliosis through gene coding [37].

Another theory for the origin of AIS is abnormalities in MSCs [38]. While there have been major discussions on MSCs research for treating scoliosis or managing pain, the cells might be the cause of the spinal deformity. As previously mentioned, MSCs work as cells that can develop into bone cells, tissue cells, and more [39]. In a recent study, the gene expression, protein levels, melatonin levels, and non-coding RNA in patients with AIS were different when compared to healthy spines. All these factors allow for MSCs to properly differentiate and develop into the correct cells. Low bone density as well as abnormal bone growth are seen when MSCs aren't properly developing. These differences in protein levels and abnormalities in the MSCs also appear in DS [40]. This data is very important because if it is proven accurate, then scientists can begin seeing how to prepare these functions (Figure 5).

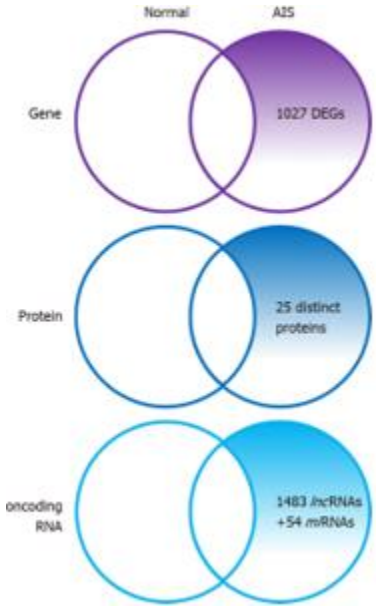

Figure 5: Gene expression seen in someone with AIS [38].

Animal Studies

Animal studies that involve scoliosis are difficult to replicate. Due to the unique bilateral composition of our bodies, our spines are structured differently from animals that are usually studied [41]. They also don't have intervertebral discs, which could affect the comparison to humans. Chickens were found to have the most similar type of spine, and scoliosis can be seen under certain conditions. Following the trends of neuropathic problems seen in the experiments with humans, researchers performed a pinealectomy on chickens. In animals, the pineal gland produces melatonin [42]. A pinealectomy is when the pineal gland is removed, and no more melatonin is produced [43]. Melatonin is significant due to its role in regulating bone formation and contributing to the development of bones. In patients with scoliosis, the melatonin levels were low [44]. Once the pinealectomy was finished, they found that many chickens with scoliosis had the pinealectomy. While it was enough to consider the data significant, it will be hard to form conclusions about humans until further studies are performed (Figure 6).

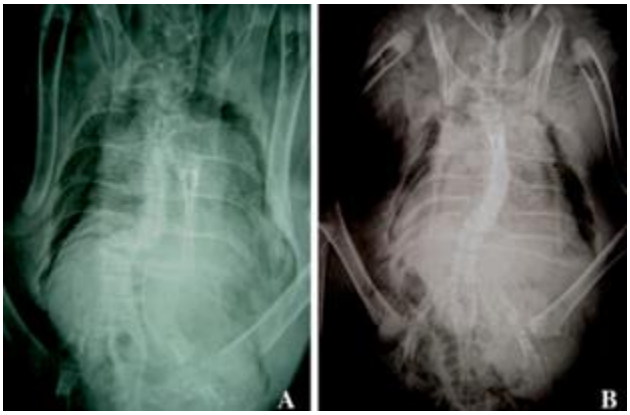

Figure 6: Scoliosis in chickens after pinealectomy [42].

Human Studies

While stem cell research is just beginning, there are human studies exploring stem cells and scoliosis. The stem cells are shown to assist in recovery for those who have had spinal fusion surgery, correction of the curve, and even pain management for scoliosis symptoms.

CS and MSCs

As mentioned previously, congenital scoliosis is a spinal deformity present from birth due to bones in the vertebrae forming improperly [45]. In a study with a two-year-old boy diagnosed with scoliosis, he had a segmented hemivertebra [46]. Umbilical cord derived MSCs were implanted into this bone defect. After three years, not only did this patient show significant improvement and correction in the curve of the spine, but his hemivertebra ratio was also improved. These results can allow progress to be made in the use of stem cells to correct the curve in different types of scoliosis (Figure 7).

Figure 7: CS in a young boy showing improvement after MSCs therapy [46].

DS and MSCs

Degenerative scoliosis is seen in adults who have developed curvature of the spine due to stress on the joints and discs in the spine [47]. This leads to extreme pain in patients, and new stem cell therapy has begun to be tested. The procedure, Percutaneous Scolioplasty, is a minimally invasive procedure used to treat DS. Dr. Christopher J. Centeno began injecting autologous biologics into targeted places in the spine. What makes this different is that past procedures used metal pieces to add structural support to the spine [48]. His goal is to provide that structure to take place using stem cells from bone marrow to allow for regenerative care [49]. Among his trials, he had a 70-year-old patient with severe DS. She couldn't stand for longer than 20 minutes before her procedure. After the Percutaneous Scolioplasty, her spine saw 85% improvement and had regained her strength to be able to stand for as long as she wants. He predicts these findings will be revolutionary to the scoliosis industry and can be explored with AIS in the future (Figure 8).

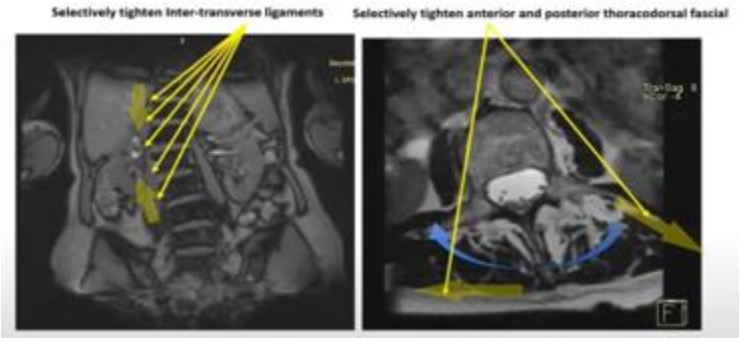

Figure 8: Demonstrates the use of stem cells to fuse the spine [49].

Spinal Fusion and MSCs

Spinal fusion is used to correct AIS [50]. As previously mentioned, this procedure has many complications, and doctors have been attempting to find ways to improve the surgery. Instead of using metals to help fuse the bones during the surgery, they are exploring using MSCs and other stem cells.

While the procedure doesn't have enough data to form conclusions, there seems to be a lot of hope in the outcome. MSCs can differentiate and become bone cells. If doctors find a way to place the cells in the proper place, they hope it will help fuse the bones. More clinical trials and research are needed, but this is a great step in the right direction for the industry.

Summary and Conclusions

Next steps

The cause of scoliosis has been a topic of debate for many years. Finding the actual root of the deformity could prove to be detrimental to improving the care of patients all over the world. New studies show there could be a correlation between genetic factors in stem cells and development within the womb. As more trials are run, hopefully more conclusions can be drawn to start discovering a cure and looking deeper into stem cells and scoliosis.

Conclusion

The scoliosis industry hasn't changed much in centuries, and new stem cell research aims to provide a better quality of life for those battling scoliosis [51]. This paper aimed to explore the potential causes of scoliosis, new forms of treatment for scoliosis, and tissue regeneration all while focusing on the use of stem cells. While there is little research on the effects stem cells can play with scoliosis, there seems to be great hope for the future.

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