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Spinal Cord Injuries and Evaluation of Treatments Amanda Nelson

1. Introduction

Spinal cord injuries (SCI), as the name suggests, are any damage to the spinal cord. The spinal cord is a large bundle of nerves that relays information between the brain and the periphery. It sends sensory information to the brain and sends motor function information to the periphery; therefore, it is a critical part of the body for normal functioning and personal autonomy. This is the reason why a successful treatment is needed to help people recover after SCI. Older treatments include surgery, pharmacotherapy, and physical therapy, while newer treatments include bionics, electric stimulation, and the use of stem cells. The older treatments are still used today and can be effective based on the SCI, but in this paper, the newer treatments will be examined more in depth and evaluated to identify which one is the best.

In 2013, the average number of SCI each year was 250,000 to 500,000 people with the average age of males being from 20 to 29 years old and older than 70, while the average age of females was 16 to 19 years old and older than 60 (WHO 2013). The 2016 data for the United States indicates there are around 17,000 new cases each year, and that there are currently 282,000 people living with SCI (NSCISC 2016). This is a lot of people in the world living with some deficit for an injury that has no successful treatment yet.

The most common causes of SCI are vehicular (38%) and falls (30.5%), while the other 31.5% of causes comes from violence, sports, medical or surgical mishaps, and other causes (NSCISC 2016). Almost all SCI cause some sort of permanent damage; only 0.4% of SCI

actually have no long-term deficits (NSCISC 2016). The main categories used to describe SCI are complete or incomplete and paraplegic or tetraplegic. A complete SCI means the affected person has lost all sense of feeling and all motor function below the level of injury, while an incomplete SCI means that the affected person has lost all motor function, but retained some degree of sensation (NSCISC 2016). A paraplegic SCI is when only the lower extremities are affected, while a tetraplegic SCI is when all extremities are affected (NSCISC 2016). A successful treatment for SCI is needed so affected people can return to their normal lives.

A person with SCI is not only physically affected, but also mentally and emotionally distressed. The World Health Organization (2013) states that 30% of people living with an SCI are diagnosed with clinical depression, but that does not include the statistic for those living with SCI that have moods affected to a lesser extreme. Living with deficits always has an impact on the person, but this could be eliminated with the use of a successful treatment. A person with any type of SCI is also two to five times more likely to die prematurely and they have a high risk of developing fatal secondary conditions (WHO 2013). Selvarajah et al. (2014) conducted an analysis on SCI to determine the specific impacts this type of injury has. It was discovered that from 2007 to 2009, an average of 12,939 SCI cases were sent to the emergency department, which was a large increase from data collected in the 1970s. It is suggested that this trend will continue to rise, which means even more people will suffer from SCI in the future than previous decades. The death rate for patients with SCI was 5.7%, or 2,458 people, from the 2007 to 2009 years (Selvarajah et al. 2014). This puts people with SCI at an unnecessary high risk, which could be eliminated with a successful treatment.

The physical, psychological, and social burdens that arise from SCI not only affect the person with the condition, but also the family members and friends close to that person (WHO 2013). The person with SCI will mostly likely become dependent on their family and friends or at least in need of some assistance from them. If SCI can be fixed, the burdens caused by these injuries can be reduced.

2. SCI Physiology

There are significant changes that happen in the spinal cord after an SCI that can be categorized into a primary and secondary phase. The primary phase is what happens right at the time of the injury and in the first two hours afterwards. This is also called the hyperacute phase. During this phase, the neuronal and endothelial tissue in the spinal cord is damaged. The myelinated axons are usually more disrupted than the unmyelinated axons, which is the cause of motor deficits (Mortazavi et al. 2015).

The secondary phase starts around three hours after the injury. This phase can be broken down into three parts: the acute phase, the intermediate phase, and the late phase. The acute phase lasts from three hours to three days after injury; the intermediate phase lasts from three days to weeks after the injury; the late phase lasts from weeks to months after the injury. The secondary phase as a whole is characterized by necrosis and apoptosis. As the time after injury progresses, the cells being affected by apoptosis dwindle from all cell types to usually just oligodendrocytes and myelinated cells. Remyelination does occur during this phase as well, however, it usually only preserves the spared intact axons and does not actually repair axons that have been disrupted. A glial scar and mesenchymal scar form at the site of injury starting just

two weeks after the initial injury, which make the regeneration of neural cells much more difficult as the scar is an obstruction in the spinal cord now (Mortazavi et al. 2015). Because of these changes in the microenvironment of the spinal cord, treatment soon after the injury is crucial. The most motor function will be regained if the treatment is given before the formation of the scars (Mortazavi et al. 2015).

3. Treatment Options

3.1. Older Treatment Options

3.1.1. Surgery

One of the earliest methods to treat SCI is surgery. There are two different surgeries that can be done: a laminectomy or a bone graft. A laminectomy is when the posterior arch of the spinal column is removed so the pressure on the spinal cord is lessened (Kotulak 1970). The pressure on the spinal cord causes pain, so the primary goal of this surgery is to reduce pain. The other surgery is a bone graft, which is when a piece of another bone, usually the femur, is used as a brace on the spinal column to provide more support (Kotulak 1977). The primary goal of this surgery is to stabilize the spine so that no further damage can be done by moving the spinal cord. In the 1970s, a British physician by the name of Dr. Ludwig Guttman thought that the surgeries did more harm than good and that they should not be performed anymore (Kotulak 1970). The reasoning behind this claim was that the invasiveness of the surgeries was worse for the patients than just leaving the injury alone and allowing it to heal on its own time. Nonetheless, surgery for SCI is still a popular treatment option, especially since the methods for these procedures have advanced along with the technologies of the medical world.

3.1.2. Pharmacotherapy

Another early method for treatment of SCI is pharmacotherapy, which is also still a popular treatment option today. One of the earliest drugs used to treat SCI is methylprednisolone, which in the 1990s, was one of the top ten advances in this era of medicine (Kotulak 1991). The main focus of this drug is to reduce the secondary effects that occur within the spinal cord after injury, including apoptosis and neurosis. On average, nerve damage was reduced by 20% when this drug was administered to the patients within eight hours following the injury (Kotulak 1991). Other drugs used to positively impact the state of the spinal cord after injury are chondroitinase and FGF, where the main focus is to encourage the spinal cord to regrow on its own (Carmichael 2013). Chondroitinase ABC is also used, with the intention of degrading the glial scar that forms (Sarveazad et al. 2016). A natural chemical that can be used for treatment of SCI is brain-derived neurotrophic factor (BDNF), which is supposed to provide neuroprotective effects on the spinal cord (Uchida et al. 2016). BDNF has also been shown to promote nerve regeneration when applied to the injury site (Uchida et al. 2016).

3.1.3. Physical Therapy

Physical therapy is also a treatment option for SCI. This is the least invasive treatment method for these types of injuries. The goal of physical therapy is to improve flexibility, strength, and mobility, while also reducing pain (Gómara-Toldrà et al. 2014). Physical therapy is performed in a clinic that mostly consists of exercises targeting the previously stated goals. Each patient has different goals and starting abilities, so a difficult factor for the physical therapists is

creating a personalized program for each patient they see. The best results of physical therapy for SCI have been seen when a behavioral intervention program is included (Nooijen et al. 2016). A behavioral intervention program is designed to help the patient change the way he/she thinks about the physical activities needed to prevent relapse of the SCI condition and to promote an active lifestyle after discharge from the physical therapy clinic (Nooijen et al. 2016). Physical therapy is a long process and requires much determination and patience from both the patient and physical therapist to achieve the intended goals.

3.2. Newer Treatment Options

3.2.1. Stem Cell Therapy

Of the newer treatment options that are available today, stem cell therapy is receiving the most attention. Stem cells themselves have been around since the 1960s when the first stem cell was found (Murnaghan 2016). It was not until 1978 when the first stem cell was discovered in human blood, and then it took until the 1990s to discover there are different types of stem cells with the discovery of embryonic stem cells and induced pluripotent stem cells (Murnaghan 2016). In the 2000s, it was determined that pluripotent stem cells could be manipulated into specific types of cells depending on the interest of the scientists at work (Murnaghan 2016). The mechanisms of how stem cell manipulation are not fully understood, but it is hoped that this knowledge will be attained soon (Murnaghan 2016). Nonetheless, stem cells are used to regrow the spinal cord to alleviate the deficits caused by SCI. There are four main types of stem cells, each with different characteristics and ethical concerns.

One type of stem cell is a neural stem cell. These are pluripotent stem cells that develop into the different types of neural cells and glia during development (Muheremu et al. 2016). Yokota et al. (2015) performed a study on neural stem cells and how they promote functional recovery after SCI. In this experiment, they gave SCI of varying levels (mild, moderate, or severe) to mice at the ninth thoracic vertebrae and then measured hindlimb motor function via the Basso Mouse Scale, footprint analysis, and grip walk test. The mice were injected with neural stem cells for treatment of the SCI or they were left alone if in the control group. The mild and moderate SCI groups showed better functional recovery after stem cell transport than the control group; the severe group did not show significant improvements on functional recovery. The researchers also reported that preconditioning the injury site to receive the stem cells resulted in a more significant functional recovery than no preconditioning. The stem cells differentiated into adequate cells for the spinal cord and interacted with the spared neurons. It is believed that the functional recovery was strongly influenced by the number of spared neurons in the spinal cord; the severe SCI group, did not have many spared neurons so the functional recovery was not significant (Yokota et al. 2015). These results show encouragement for using neural stem cells as a treatment for SCI, but only if it is a mild or moderate SCI.

Another type of stem cell that is under consideration for the treatment of SCI is the embryonic type. Because of where they are harvested, there are many ethical concerns regarding these types of stem cells. The majority of these stem cells are taken from aborted fetuses, which is why they are not a popular choice among the public (Muheremu et al. 2016). However, they have shown positive results in experimental studies because they are a very early type of stem cell to arise in development. Adeeb et al. (2015) wrote a review on the use of embryonic stem

cells for SCI. These researchers state that using embryonic stem cells is a successful way to treat SCI because they have a high differentiation and proliferation potential. This is important because the stem cells need to become all the types of cells in the spinal cord. Many studies in their review focused on embryonic stem cell transplantation in mice and stated that successful integration and differentiation of the stem cells was seen, as well as a large number of remyelinated axons. Significant motor function improvements were also observed and the progression of these improvements was much faster than the control group of mice that did not receive any stem cells treatment after injury (Adeeb et al. 2015). The experimental trials of mice are a great start to the understanding of how effective embryonic stem cells are, but human clinical trials are needed as well.

Shroff and Gupta (2015) conducted a study on five human patients with varying SCI who received treatment with embryonic stem cells. Significant improvements were seen in all patients and none of them developed tumors. Some of the improvements seen were being able to stand after not having that ability, increased control of bladder and bowel movement, and improved deep sensation in the lower limbs when sensation was little or nonexistent. The patients were also not given an immunosuppressant drug, which indicates that the embryonic stem cells were not rejected by the body since no adverse reactions were seen. At this point in time, large scale clinical trials are needed to report the safety and effectiveness of these types of stem cells (Shroff and Gupta 2015). These clinical trials are essential to the progression of stem cells as a treatment for SCI because although there have been many positive studies on mice, humans are slightly different so the results cannot be fully extended to human subjects.

Mesenchymal stem cells also show promise for being effective in the treatment of SCI. These stem cells are usually derived from bone marrow or adipose tissue of the person with the SCI, therefore, the ethical concerns are close to none (Muheremu et al. 2016). There are fewer reports on the adipose-derived mesenchymal stem cells, but it has been shown that they can differentiate into neuronal cells, so the potential is there (Muheremu et al. 2016). In a study by Sarveazad et al. (2016), human adipose-derived stem cells were used to treat SCI in rat models. They found that transplantation of these stem cells promoted remyelination and functional recovery, which is significant for the treatment of the injury (Sarveazad et al. 2016).

There have been more reports on the bone marrow-derived mesenchymal stem cells. Morita et al. (2016) performed a study on the effects of these stem cells on functional recovery in rat subjects. One important find that they made was the remyelination of motor neurons in the spinal cord. They know that the axons were remyelinated because axons are usually myelinated with oligodendrocytes, but after the stem cell treatment, some axons were myelinated with a Schwann cell-like pattern. It is also suggested that over time, mesenchymal stem cells could protect the spinal cord tissue and reduce fluid build up, which is important for functional recovery. This research team noted that some therapeutic effect of mesenchymal stem cell therapy was seen up to ten weeks after the injury (Morita et al. 2016).

Gu et al. (2017) also investigated the effects of bone marrow-derived mesenchymal stem cells after SCI, but were more focused on the neural apoptosis that happens after injury. The experimental group of mice that received the stem cells showed significant improvement in motor function after only 6 days as compared to the control group that did not receive treatment. The number of apoptotic cells was dramatically decreased in the experimental group (Gu et al.

2017), which is important to note because the apoptosis of cells after injury is more detrimental to motor functioning than the injury itself. The apoptosis spreads in the spinal cord making the lesion bigger than the initial trauma (Mortazavi et al 2015). Gu et al. (2017) also noted that they were able to save damaged motor neurons in the spinal cord after injury, but only up to eight hours after injury. Once the injury was left untreated for more than twelve hours, the motor neurons could no longer be saved via bone marrow-derived stem cell therapy (Gu et al. 2017).

The fourth main type of stem cells is not natural, but formed when cells are converted back to their stem cells form. For this reason, they are called induced pluripotent stem cells (Muheremu et al. 2016). They have all the potential of a natural stem cell, so differentiating into neuronal cells is not a problem. Nori et al. (2011) researched functional recovery in mice after SCI following transplantation of induced pluripotent stem cells. They observed that the induced pluripotent stem cells were able to survive in the injury site and that half of the cells transplanted were able to differentiate into neurons. These transplanted cells also showed a greater preservation of motor neurons when compared with the control group of mice that did not receive stem cell transplantation. When measuring functional recovery of the two groups of mice, more functional recovery was seen in the experimental group. The mice that received stem cell transplantation were also able to run longer and at a faster speed on the treadmill than the control group. It is important to note that the researchers did not observe tumor formation in any of the mice that received stem cell transplantation and that the transplanted cells showed normal differentiation (Nori et al. 2011). One concern about this type of stem cell is their high rate of tumor formation because of having to reprogram the cells and then induce them into another

specific type of cell (Adeeb et al. 2015). Using these types of stem cells overcame the ethical issues that are involved with human embryonic stem cells (Nori et al. 2011).

Liu et al. (2017) investigated also this type of stem cell for SCI therapy. They found that they could induce cells to become neural stem cells that have the same ability to give rise to all the types of cells in the spinal cord. The researchers noted that even eight weeks after transplanting these cells into the injury site, they survived and also integrated into the spinal cord and differentiated into the proper cells needed. They also did not observe tumor formation in any of the mice they tested (Liu et al. 2017). This is another study that did not see the high rate of tumor formation that is associated with this stem cell type (Adeeb et al. 2015). These researchers also noted that transplanting a combination of neural and glial progenitors into the injury site yielded optimal effects for stem cell survival and motor function recovery (cited Liu et al. 2017).

3.2.2. Bionics

Another newer treatment for SCI is bionics, which includes the use of exoskeletons as assistance to help people with SCI walk again. These powered exoskeletons consist of leg braces and a waist strap, along with arm crutches (Grush 2014). These suits can detect weight shifts by the person using it to assist him/her with stepping forward (Gush 2014). The significance of these suits is that they are able to get the patient up and moving soon after their injury, which some believe is better for healing by speeding up the recovery time (Grush 2014). As of now, exoskeletons are not available to the general public, but can be used in some physical therapy clinics as long as the physical therapists are trained on how to use the suits (Grush 2014).

Esquenazi et al. (2017) reviewed ten different exoskeletons and compared all of them for effectiveness, cost, and fitting. These bionic suits are not just for patients with SCI, but for any individual that has a gait deficiency, and are now capable of moderate walking speeds to simulate a more normal gait for the user. There are short-term benefits that users have experienced such as improved bladder and bowel function, psychological experience, mobility, and cardiopulmonary function, which all lead to an improved quality of life. Long-term benefits have not yet been determined as lengthy clinical trials have not been completed. Though these suits have already been very beneficial in the little time they have been around, there are still many improvements that need to be made on these, such as automated fall prevention if a system failure occurs and more mobility for uneven ground and stairs. As these bionic suits are innovated, they will hopefully simulate the human gait more closely and have faster walking speeds so that they become more realistic options than wheelchairs, whether powered or manual. The team of Esquenazi and colleagues (2017) state that in the future "soft robotics" may be developed which are bionic suits made of softer material with less rigid edges. These softer suits are intended for those patients who cannot fit into the hard, rigid exoskeletons produced today. This research team also hopes that in the future further development is focused on the upper limb robotics for people with tetraplegia (Esquenazi et al. 2017).

3.2.3. Electric Stimulation

The third new treatment option for SCI is electric stimulation. This is using electrical currents to make the intended neurons fire since the SCI is obstructing the pathway and the signals from the brain cannot get to the intended part of the body (Maldarelli 2016). It has been

suggested that this actually reawakens intact connections between the brain and the body that were not destroyed during the injury (Willyard 2014). This works by the brain sending signals that are collected and interpreted by a computer. The computer then transfers the information to the electrodes implanted in the spinal cord below the level of injury. These electrodes then send electrical currents to the nerves of the intended muscles, which causes muscular contractions (Maldarelli 2016). This system allows a person to move his/her damaged limb(s) again. In 2014, these systems were wired, which caused some problems with tangling wires and having to carry around a backpack for the computer (Willyard 2014). Fortunately in 2016, these systems became wireless, which made them a lot easier to carry around and now the patient does not have to worry about tangling or breaking wires (Maldarelli 2016). Currently these systems are focused on broad muscle movement, like moving an entire limb, and not yet designed for intricate movements like those of the fingers and hand (Maldarelli 2016).

In a study done by Rejc et al. (2015), the effects of electrical stimulation on the lumbosacral part of the spinal cord were evaluated. Four patients participated in this study, none of which could stand or move their legs before the electrical stimulation. While receiving electrical stimulation to the lumbosacral part of the spinal cord, all four participants were able to stand in a completely weight-bearing stance, when the machine was on. These participants still needed some assistance with balance, using a horizontal bar, and when the machine was turned off, they held themselves up by the weight-bearing action of their arms on the horizontal bar (Rejc et al. 2015). This shows that with the correct configuration of the electrical stimulation machine for each participant, they were able to overcome the deficit of not being able to stand.

This is not only important for a person to regain motor function, but to also avoid secondary complications that arise from a lack of movement (Rejc et al. 2015).

Another study evaluating the effects of electrical stimulation on gait deficits after SCI was conducted by Capogrosso et al. in 2016. Soon after hooking the SCI monkeys up to the wireless electrical stimulation machine, the monkeys regained their weight-bearing motor function. The monkeys were also able to walk on a treadmill and on real ground, and with more time using the machine, they experienced almost no gait deficits anymore. This research team has noted that a machine like this can also be used to help patients with complete tetraplegia move robotic arms (Capogrosso et al. 2015). This was not simulated here as the monkeys only had paraplegia, but it is a possibility depending on where the electrodes are placed in the spinal cord.

4. Combination of Treatments

It has been suggested by many that a combination of treatments would be even more beneficial to treat SCI than just one treatment individually. Possible combinations of treatments that have been suggested are stem cell therapy and gene therapy, stem cell therapy and a tissue scaffolding to help the stem cells grow, stem cell therapy and electrical stimulation, and stem cell therapy with pharmacotherapy. One specific example of combining treatments can be seen in a study by Sarveazad et al. (2016) where they used human adipose-derived mesenchymal cells and Chondroitinase ABC (ChABC). These researchers studied the effects of both the stem cell therapy and the ChABC treatments individually, but also the combination of the two. In both the individual treatments, a significant improvement was seen in the animals' motor functioning, but

a greater improvement was seen after the combination therapy. There was also much more remyelination in the combination therapy group than either of the individual treatments. The reason the combination therapy worked much better was because ChABC is an enzyme that disintegrated the glial scar in the injury site. This allowed the stem cells to grow and mature without having to go through or around the glial scar, so their growth was as normal as during development (Sarveazad et al. 2016). If other combination treatments can rid the injury site of the glial scar too, the best results for regaining motor functioning after SCI would be seen.

5. Evaluation of Treatments

Now that all of the treatments have been explained as to what they are and if they are effective, an evaluation of these treatments is needed. Surgery as a treatment for SCI is widely available because of all the hospitals and surgeons in the world. Also, medicine is advancing rapidly, so the techniques for SCI surgery are improving. On the other hand, SCI surgery is an invasive procedure that may take a while to recover from. The surgery also has to be feasible depending on the location of the injury, which is not always the case. Sometimes the injury is not accessible, so surgery is not even an option for those specific cases. Since surgery is so widely available, the surgeon needs to have an opening in his/her daily schedule to perform the surgery. Sometimes, this is not soon after the injury, so the injury could progress, making symptoms worse before any treatment. Also, surgeries are not usually performed without some type of pre-surgical preparation, usually in the form of physical therapy. This would add time to the recovery process.

Pharmacotherapy is also a part of the medicinal world that is advancing rapidly. This means that there are a lot of potential drugs that can be used for SCI treatment, including expensive drugs and inexpensive drugs. This allows the patient to choose which drug to take depending on which one(s) are in his/her price range. This could mean, though, that the best drugs for a patient are too expensive and therefore, another drug with less effectiveness must be substituted. Another good thing about using drugs is that this is not an invasive procedure like surgery is, however, this does mean that the patient must be compliant when taking these drugs. The drugs must be taken at the correct time of day, taken in the correct dosage, and taken for the correct amount of time.

Physical therapy, like the previous two forms of SCI treatment, is widely available as well and does not require an invasive procedure. Unfortunately, a specific program must be developed for each patient as physical therapy is a highly individualized treatment. This can be a positive or a negative about this treatment type. It is good in the fact that it will be specific to the person receiving the therapy, but this also means that no data can be used to project what the outcomes will be and when the patients will hit their goals. Physical therapy also takes a lot of patient compliance because the patient must show up to physical therapy and also continue to do the exercises assigned at home. Patients and physical therapists must both be determined in this process because the results take a long time before they start to show.

Stem cell therapy is the only new treatment reviewed in this paper that actually treats the injury, rather than just finding a way for the patient to work around it or learn to live with it and the deficits from the injury. This is an invasive procedure that may require the patient to go back for multiple transplants. This procedure is not widely available yet because ethical concerns

regarding some stem cells have halted their research or because not enough of certain types of stem cells have been harvested. Most of the human clinical trials are small groups of people that do not have an experimental group and a control group, which means that no definitive conclusions can be made. However, from the animal clinical trials, the results are encouraging. It seems that all the types of stem cells promote neural regeneration and also improve functional recovery.

Of the four types of stem cells reviewed in this paper, the embryonic stem cells have the most ethical concerns associated with them. This is because they are harvested from unborn fetuses, which opens up a large debate on whether or not we should continue research with them. The other three types of stem cells seem to have less ethical concerns attached to them because they are harvested from the patient who is receiving the treatment. The induced pluripotent have a concern of tumor formation when used, though not seen in any of the studies explained in this paper. The adipose-derived mesenchymal stem cells and the neural stem cells need more research conducted on them to confirm their effectiveness. Therefore, because of the reasons stated above, the best type of stem cell to use now, if stem cell therapy is the treatment of choice, would be the bone marrow-derived mesenchymal stem cells.

The bionic exoskeletons are another treatment option that does not require an invasive procedure. These suits are also relatively easy to use, however, they do need some major improvements in the near future. First of all, the suits right now are very bulky and some patients do not fit into them. Luckily, "soft robotics" are being developed to combat these concerns. The suits also do not treat the injury itself, but rather help the patient get around the deficits that are caused by the SCI. Patients are able to return to fairly normal lives, but their lives would be even

more normal if the treatment would target the injury directly. As of now, the bionic suits are not available to the general public, but they are available in some physical therapy clinics if a physical therapist at that facility is properly trained on how the suits work.

The electric stimulation treatment option is easier to use now than when they were first developed. Since moving to a wireless system, the patient with this machine does not have to worry about tangling wires or breaking them, nor do they have to worry about moving around because the wireless system eliminated the need for a large backpack to house the computer. This computer provides the same input to specific parts of the body that the brain would if the spinal cord was working properly. This means that the patient with the electric stimulation machine can move in real time and does not have to rely on feedback all the time. The downside to this treatment option is that it is an invasive procedure to place the computer in the brain and the electrodes in the spinal cord. This treatment option also does not target the injury directly, but finds a way for the patient to live with the deficits that the injury caused. These electrical stimulation machines are also not widely available, but can be used in some physical therapy clinics if the physical therapist is trained on how to use these machines.

One main concern with all of these treatments is the cost. Not all insurance companies will cover these treatments, especially if they are new developments. Insurance plans vary greatly and in order to know if a specific plan will cover any of these treatments, additional research into each individual's insurance plan is required. The more invasive procedures will be more expensive up front, but they are very short, so there will be no long term payments. If the treatment is a long process, like physical therapy, the costs may be lower each visit, but a lot of visits will eventually add up to a large amount of money. The older treatments may be more

likely to be covered by insurance because more research has been developed about them, while little research to support the newer treatments could mean it is very likely that the insurance companies will not cover them. Each individual insurance plan may also only cover part of the procedures, whether it is after a person has paid a certain amount out of pocket or if the company will put a cap on how much they are willing to pay for "necessary treatment". This situation is most commonly seen with physical therapy where the patient needs this treatment, but after the initial plan and extension of that plan, the patient may want more treatment. The insurance companies could deem this extra physical therapy as simply a "want" by the patient and not an actual "need". Depending on which treatment(s) are covered by his/her specific insurance plan, that may change the patient's treatment choice compared to all the treatments being available financially.

6. Conclusion

Spinal cord injuries (SCI) account for 250,000 to 500,000 new cases around the world each year. In the United States alone, there are approximately 282,000 people living with SCI each year. There are significant physical deficits that come as a result of SCI, as well as psychological, social, and economic burdens for the people with SCI and their surrounding friends and family. It is important that a successful treatment for SCI is found so that these impacts can be avoided. Older treatment options for SCI include surgery, pharmacotherapy, and physical therapy, while newer treatment options include stem cell therapy, bionics, and electrical stimulation. Of these options for treating SCI, the best choice is stem cell therapy using bone marrow-derived mesenchymal stem cells. This is because these stem cells do not have ethical

concerns regarding their use since they are derived from the patients themselves, and also prevent apoptosis of cells at the injury site, promote remyelination of neurons in the spinal cord, and improves functional recovery. However, since this treatment is still in Phase I trials and is not available to the general public yet, the best option currently available to treat SCI is pharmacotherapy. This is another treatment that is directly targeting the injury by promoting cell growth, inhibiting apoptosis, or disintegrating the glial scar to allow for a normal regrowth pattern. The future holds the key to the treatment of SCI with the use of stem cells, but the science and medical fields are not quite there yet; however, they will be there soon.

Sources Used

- Adeeb N, Deep A, Hose N, Rezaei M, Fard SA, Tubbs RS, Yashar P, Liker MA, Kateb B, Mortazavi MM. 2015. Stem cell therapy for spinal cord injury: The use of oligodendrocytes and motor neurons derived from human embryonic stem cells. Transl Res Ana. 1(1): 17-24.
- Capogrosso M, Milekovic T, Borton D, Wagner F, Moraud EM, Mignardot JB, Buse N, Gangar J, Barraud F, Xing D, Rey E, Duis S, Jianzhong Y, Ko WKD, Li Q, Detemple P, Denison T, Micera S, Bezard E, Bloch J, Courtine G. 2016. A brain-spine interface alleviating gait deficits after spinal cord injury in primates. Nature. 539(1): 284-288.
- Carmichael J. [Internet]. 2013 Jun 26. Scientists regrow severed spinal cords in rats; [2017 Jan 10]. Available from: http://www.popsci.com/science/article/2013-06/regrowing-rats-severed-spinal-cords.
- Esquenazi A, Talaty M, Jayaraman A. 2017. Powered exoskeletons for walking assistance in persons with central nervous system injuries: A narrative review. PM R. 9(1): 46-62.
- Gómara-Toldrà N, Sliwinski M, Dijkers MP. 2014. Physical therapy after spinal cord injury: A systematic review of treatments focused on participation. J Spinal Cord Med. 37(4): 371-379.
- Grush L. [Internet]. 2014 Dec 5. Robotic exoskeletons are here, and they're changing lives; [2017 Jan 10]. Available from: http://www.popsci.com/watch-paralyzed-man-take-stroll-bionic-exoskeleton-video.
- Gu C, Li H, Wang C, Song X, Ding Y, Zheng M, Liu W, Chen Y, Zhang X, Wang L. 2017. Bone marrow mesenchymal stem cells decrease CHOP expression and neuronal apoptosis after spinal cord injury. Neuro Let. 636(1): 282-289.
- Kotulak R. 1970. Briton is critical of standard spinal cord treatment in U.S. Chicago Tribune:11. Kotulak R. 1977. Urge quick surgery for spine injury. Chicago Tribune: 6B.
- Kotulak R. 1991. Giant steps: The top 10 advances of an extraordinary era in medicine. Chicago Tribune: SMA6.
- Liu Y, Zheng Y, Li S, Xue H, Schmitt K, Hergenroeder GW, Wu J, Zhang Y, Kim DH, Cao Q. 2017. Human neural progenitors derived from integration-free iPSCs for SCI therapy. Stem Cell Res. 19(1): 55-64.
- Maldarelli C. [Internet]. 2016 Nov 11. Wireless brain implants are helping paralyzed monkeys walk again; [2017 Jan 10]. Available from: http://www.popsci.com/paralyzed-monkey-walks-with-help-wireless-brain-implant.
- Mortazavi MM, Jaber N, Adeeb N, Deep A, Hose N, Rezaei M, Fard SA, Kateb B, Yashar P, Liker MA, Tubbs Rs. 2015. Engraftment of neural stem cells in the treatment of spinal cord injury. Transl Res Ana. 1(1): 11-16.
- Morita T, Sasaki M, Kataoka-Sasaki Y, Nakazaki M, Nagahama H, Oka S, Oshigiri T, Takebayashi T, Yamashita T, Kocsis JD, Honmou O. 2016. Intravenous infusion of

- mesenchymal stem cells promotes functional recovery in a model of chronic spinal cord injury. Neurosci. 335(1): 221-231.
- Muheremu A, Peng J, Ao Q. 2016. Stem cell based therapies for spinal cord injury. Tiss & Cell. 48(1): 328-333.
- Murnaghan I. [Internet]. 2016 6 Dec. Explore stem cells; [2016 Dec 13]. Available from: http://www.explorestemcells.co.uk/historystemcellresearch.html.
- National Spinal Cord Injury Statistical Center. [Internet]. 2016. Facts and figures at a glance; [2017 Jan 8]. Available from: https://www.nscisc.uab.edu/Public/Facts%202016.pdf.
- Nooijen CFJ, Stam HJ, Bergen MP, Bongers-Janssen HMH, Valent L, van Langeveld S, Twisk J, Act-Active Research Group, van den Berg-Emons RJG. 2016. A behavioural intervention increases physical activity in people with subacute spinal cord injury: a randomised trial. J Phys. 62(1): 35-41.
- Nori S, Okada Y, Yasuda A, Tsuji O, Takahashi Y, Kobayashi Y, Fujiyoshi K, Koike M, Uchiyama Y, Ikeda E, Toyama Y, Yamanaka S, Nakamura M, Okano H. 2011. Grafted human-induced pluripotent stem-cell-derived neurospheres promote motor functional recovery after spinal cord injury in mice. PNAS. 108(40): 16825-16830.
- Rejc E, Angeli C, Harkema S. 2015. Effects of lumbosacral spinal cord epidural stimulation for standing after chronic complete paralysis in humans. PLoS ONE. 10(7): 1-20.
- Sarveazad A, Babahajuan A, Bakhtiari M, Soleimani M, Behnam B, Yari A, Akbari A, Yousefifard M, Janzadeh A, Amini N, Agah S, Fallah A, Joghataei MT. 2016. The combined application of human adipose derived stem cells and Chondroitinase ABC in treatment of a spinal cord injury model. Neuropep. xxx(1): xxx-xxx.
- Selvarajah S, Hammond ER, Haider AH, Abularrage CJ, Daniel Becker D, Dhiman N, Hyder O, Gupta D, Black III JH, Schneider EB. 2014. The burden of acute traumatic spinal cord injury among adults in the United States: An update. J Neurotr. 31(1): 228-238.
- Shroff G, Gupta R. 2015. Human enbryonic stem cells in the treatment of patients with spinal cord injury. Annals Neurosci. 22(4): 208-2016.
- Uchida S, Hayakawa K, Ogata T, Tanaka S, Kataoka K, Itaka K. 2016. Treatment of spinal cord injury by an advanced cell transplantation technology using brain-derived neurotrophic factor-transfected mesenchymal stem cell spheroids. Biomat. 109(1): 1-11.
- Willyard C. [Internet]. 2014 Jul 9. How it works: A system that reverses paralysis; [2017 Jan 10]. Available from:
 - http://www.popsci.com/article/science/how-it-works-system-reverses-paralysis.
- World Health Organization. [Internet]. 2013 Nov. Spinal cord injury; [2017 Jan 8]. Available from: http://www.who.int/mediacentre/factsheets/fs384/en/.
- Yokota K, Kobayakawa K, Kubota K, Miyawaki A, Okano H, Ohkawa Y, Iwamoto Y, Okada S. 2015. Engrafted neural stem/progenitor cells promote functional recovery through synapse reorganization with spared host neurons after spinal cord injury. Stem Cell Rep. 5(1): 264-277.