Efficacy of chitosan nanoparticles and mesenchymal stem cells in rabbit models for sciatic nerve regeneration

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Abstract

Peripheral nerve injuries (PNI) are frequently caused by several circumstances, including trauma and iatrogenic operations, and there are limited therapy options to help with functional recovery. This study aimed to compare in vivo adipose-derived stem cells (ASCs) to chitosan nanoparticles (CS NPs) in rabbit sciatic nerve defect regeneration. Twenty healthy rabbits of local breed randomly enrolled in two equal groups split into two groups at random: The critical size defect was bridged with a 14 mm conduit from acellular bovine urinary bladder impacted with chitosan nanoparticles (CS NPs) semi-gel 1mg/ml as the first group, and the critical size defect was bridged with mesenchymal stem cells (MSCs) 5x10^6 in the second group. At the end of 56 and 112 days, assessment of the nerve regeneration, motor and sensory function, and histopathological assessment of the sciatic nerve were investigated. According to the findings, the motor and sensory capabilities of the sciatic nerve increased faster in the mesenchymal stem cells (MSCs) group. In the mesenchymal stem cells group repairing a 10mm sciatic nerve defect, histopathological examination revealed basophilic nuclei of proliferated Schwann cells with thick myelin sheath, suitable orientation nerve fibers, dense axon population, large axon diameter, nerve fiber myelination, and low fibrous tissue at the epineurium compared to chitosan nanoparticles (CS NPs). It is concluded that effect mesenchymal stem cells (MSCs) promote regeneration of the sciatic nerve defect compared to chitosan nanoparticles (CS NPs).

Keywords: Conduit, CS NPs, ASCs, PNI, Rabbit

Introduction

Peripheral nervous injuries (PNI) are common causes of disabilities, like these injuries that occur from the wrong injection during treatment. Treatment for PNS injuries remains a challenging clinical issue, with many proposed strategies yielding unsatisfactory outcomes, highlighting the need for novel treatment approaches (1,2). Cell therapy shows great promise as a potential approach to repairing damaged peripheral nerves. These cells can create a conducive environment that limits damage and fosters regeneration through immunoregulatory mechanisms via direct cellular interaction and releasing dissolved substances, including TGF-β, IL-10, and others (3). Several cell types have been studied for their potential to promote healing of damaged peripheral nerves, including embryonic stem cells (ESCs), neural stem cells (NSCs) (4), and mesenchymal stem cells (MSCs) (5). Another approach for peripheral nerve regeneration involves using biomaterials to repair damaged tissues (6). Chitosan, a cationic polysaccharide derived from chitin through deacetylation, has been extensively studied as a scaffold for cell growth, anti-adhesive substances, differentiation, integration, immunomodulators, and action against microorganisms (7-9). Numerous studies have reported the beneficial effects of chitosan on nerve regeneration (10,11). Researchers used a nerve conduit containing lyophilized human umbilical cord powder seeded with human umbilical cord mesenchymal
stem cells in a canine sciatic nerve model with a 10mm lesion, indicating the efficiency of this technique for peripheral nerve injury (12).

This work looks at the ability of mesenchymal stem cells and CS NPs to regenerate sciatic nerve lesions in rabbit models using a decellularized urine bladder matrix conduit.

Materials and methods

Ethical approval

The work was approved by Baghdad University’s College of Veterinary Medicine’s Scientific Ethic Committee (no: 1305/PG on Jan 18, 2023).

Experimental design

Twenty healthy adult male local breed rabbits between 5 and 7 months old and weighing between 1.3 and 1.9 Kg were collected from the animal house of the College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq. Animals were kept in specially designed cages, one rabbit in each cage, for fifteen days before the experiment. The rabbits were fed a typical diet and water ad libitum. The animals were randomly divided into two groups, each consisting of ten individuals. A critical size defect (CSD) was created in the left sciatic nerve using a 10 mm transaction. The defect was then repaired by connecting a 14 mm conduit to each proximal and distal end of the nerve defect using 6.0 nylon epineural simple interrupted sutures. In the first group of CS NPs, the CSD was impacted with a semi-gel solution containing CS NPs at 1mg/ml concentration mesenchymal stem cells (MSCs) from the second group, with a quantity of 5x10^6.

Anesthetic protocol

Before the surgical protocol, the rabbit was denied food for two hours. Rabbits were anesthetized with xylazine 5mg/kg (Holland, Xylazine 2%, Alfasan™) and ketamine 35mg/kg (Holland, ketamine 10%, Alfasan™) from alfasan company after an intramuscular injection of acepromazine 1 mg/kg (Holland, Neurotranq, Alfasan™) (13,14).

Surgical protocol

Prepare the lateral side of the thigh for aseptic surgery and make longitudinal skin incision length parallel posterior-lateral thigh about 3 cm from the caudolateral to the greater trochanter to expose the sciatic nerve splitting the biceps femoris and semitendinous muscle by blunt dissection (Figure 1). A wooden tongue depressor was gently placed under the nerve, and the nerve was severed using a scalpel blade. A critical size defect to the nerve was created by a 10 mm transaction (Figure 1) and coaptated with a 14 mm conduit connected in each nerve segment with 6.0 nylon epineural simple interrupted sutures (Figure 1). The subcutaneous tissue and skin were closed routinely, and a broad-spectrum antibiotic injection of ceftriaxone 20mg/kg was given IM twice daily for five days.

Figure 1: The procedure for doing sciatic nerve neurotmesis. A. The sciatic nerve is isolated from the surrounding tissues. B. A 10mm section of the sciatic nerve is cut. C. The proximal end of the conduit was secured to the stump using 6-0 nylon sutures. D. The conduit end was sutured to the distal site of the nerve.

Preparation of chitosan nanoparticles (CS NPs)

The preparation method of nanomaterials uses the chemical process using the sol-gel technique with certain modifications mentioned by Ghadi et al. (15), which entailed dissolving 1 g of chitosan (Sigma-Aldrich) in 200 ml deionized distilled water and subjecting it to ultrasonic bath for 30 min. The pH of the solution was then raised to 10 with NaOH (1N) drop by drop and stirred using a magnetic stirrer on a rotor. The pH was then decreased to 4 using HCL (1N), added drop by drop, and stirred using a magnetic stirrer on a rotor for 60 minutes at room temperature to form a clear solution. Finally, the pH was adjusted to 7 using NaOH (1N) drop by drop and stirred using a magnetic stirrer on a rotor for 60 minutes at room temperature.

Characterization of prepared nanoparticles

Based on Van der Waals or other attracting and repulsive forces, Atomic Force Microscopy (AFM) provides two- and three-dimensional surface topography (16). After being dried in an incubator throughout the previous night, chitosan nanoparticles FT-IR spectra were examined (17).
Preparation and characterization of allogeneic mesenchymal stem cells

The ASCs collected from the adipose tissue from the nape of the neck of a male indigenous breed rabbit were prepared according to Arana et al. (18), identified, differentiated following the procedure described in (19).

Conduit fabrication from bovine urinary bladder matrix (UBM)

In creating the urine bladder matrix (UBM), fresh urinary bladders were collected in their whole from slaughtered cows at a local abattoir using the procedure described (20). The conduit was made using procedure (21), and it was cut into appropriate sizes before being wrapped around ECM with a stainless-steel pin that was doubled up depending on the diameter of the tube, which had a 0.18 mm wall thickness. A basic digital caliper measured it. The tube's two edges were joined with a biological adhesive of egg albumen (22).

Evaluation of motor functions

All experimental animals were examined daily to determine their clinical signs or abnormal clinical signs such as walking style, which includes crouching, crawling on the heel, normal, and knuckling. The severity of these behaviors was classified as severe, moderate, mild, or common. The force of muscle contraction was assessed on a grad ranging from mild to moderate to strong (23).

Evaluation of sensory functions

The sensory functions of the conducting sciatic nerves were tested weekly throughout the study. The presence or absence of a toe spreading reflex, the presence or absence of toe pinch, toe prick, and lateral aspect leg sensation were evaluated. Additionally, the lateral aspect of leg sensation was assessed using foot withdrawal and vocalization activities. Positive responses to toe pinching and pricking have been observed, indicating recovery and improved function (24).

Preparing and assessing histology

The nerve tissue specimens were fixated using a 10% neutral buffered formalin solution, and the specimens were dehydrated using a series of ethanol, followed by clearing in xylene. The specimens were then embedded in paraffin and cut into sections with a thickness of 5 μm. Finally, these sections were stained using hematoxylin and eosin. Microscopic examination of nerve tissue sections was used to determine the excellent orientation of nerve fibers, basophilic nuclei of proliferated Schwann cells with thick myelin sheath, presence of vacuolated degenerate nerve fibers, dense axon population, nerve fiber myelination, and low fibrous tissue.

Statistical data analysis

The data was analyzed, and the results were presented as means and standard errors. One-way ANOVA and post hoc tests were used for statistical comparisons between groups, and the Statistical Package for the Social Sciences (SPSS) version 26 software was used, with a significance level of P<0.05.

Results

Chitosan nanoparticles (CS NPs) group

The animals Returned to normal walking abilities on day 80 post-operation (PO), which was a significant discovery. Mild knuckling remained until the end of the study. The muscular contraction force was strong (Table 1). Skin feeling eventually advanced from the foot to the fetlock joint over time. There was no toe spreading reflex, lateral leg feeling, toe pinch, or toe prick sensation (Table 2).

Mesenchymal stem cells (MSCs) Group

On the 56th post-operation, all animals walked usually, which was a significant discovery. Furthermore, the disappearance of knuckling was observed on the 62 days, and there was a notable increase in muscle force contraction on the 63 days post-operation (Table 1). Sensory improvements were also observed, with the sensation of toe spread becoming evident on day 90 post-operation, the appearance of lateral aspect leg response on day 81 post-operation, and the presence of the pinch on day 73 post-operation, as well as toe prick on day 67 post-operation (Table 2).

Sensory clinical functional tests

Sensory clinical indicators such as toe spread, lateral leg sensation, toe pinch, and toe prick did not show sensory responses on day 112 PO in the CS NPs and MSCs groups (Table 3).

Table 1: Meantime rates of motor functional tests on 112 in CS NPs and MSCs groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Onset</th>
<th>Walking</th>
<th>Type of gait</th>
<th>Knuckling</th>
<th>Muscle contraction Force</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Crouch</td>
<td>Crawl</td>
<td>Nor.</td>
</tr>
<tr>
<td>CS NPs</td>
<td>4.6</td>
<td>5.8</td>
<td>14.4</td>
<td>27</td>
<td>56.8</td>
</tr>
<tr>
<td>MSCs</td>
<td>2.6</td>
<td>3.8</td>
<td>11</td>
<td>24</td>
<td>53</td>
</tr>
</tbody>
</table>

Nor: normal. N: None. Mod: Moderate.
Table 2: Sensory Function tests during 112 days in CS NPs and MSCs groups

<table>
<thead>
<tr>
<th>Groups/days</th>
<th>Toe spread</th>
<th>Lateral Aspect Leg Sensation</th>
<th>Toe Pinch</th>
<th>Toe prick</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS NPs</td>
<td>+98</td>
<td>+87</td>
<td>+78</td>
<td>+72</td>
</tr>
<tr>
<td>MSCs</td>
<td>+90</td>
<td>+81</td>
<td>+67</td>
<td>+73</td>
</tr>
</tbody>
</table>

Table 3: The mean time (days) during 112 sensory clinical observations in CS NPs and MSCs groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Toe spread</th>
<th>Lateral Aspect Leg Sensation</th>
<th>Toe Pinch</th>
<th>Toe prick</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS NPs</td>
<td>98.2±0.96 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>87.4±1.82 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>78.2±0.86 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>72.2±1.31 &lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MSCs</td>
<td>89.8±1.59 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>80.6±0.92 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>67.4±1.36 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>73.4±0.97 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

LSD Value: 4.63, 4.29, 2.94, 3.86

At a significance level of P<0.05, a, b (Mean SE) with separate superscripts within the same row indicate statistically significant differences.

Histopathological study of the proximal portion of the sciatic nerve in the CS NPs group 56 days postoperatively showed vacuolated nerve fibers in degeneration. Also, collagen fibers impeded the nascent nerve development. The stem cell group showed that the remyelinated new nerve was arranged as a longitudinal neural fiber with angiogenesis in the affected area. However, a small vacuolation was observed (Figure 2).

Histopathological study of the middle segment of the sciatic nerve in the CS NPs group at 56 days postoperatively showed incomplete remyelination of the injured nerve. In the impacted region, vast voids were seen. The stem cells group showed complete remyelination of the middle area injured. However, small vacuoles were observed in the nerve axon (Figure 3).

Histopathological examination of the distal section of the sciatic nerve in the CS NPs group at 56 days postoperatively showed insufficient growth of the injured nerve. Collagen fiber tissue surrounds the new growth nerve's terminal and interrupts the new growth nerve (Figure 4). The stem cells group showed complete growth of the injured nerve. However, spaces between nerve fibers were observed (Figure 4).

Figure 3: A photomicrograph of the middle segment of 56 days post sciatic nerve defect. A. Chitosan nanoparticles group, incomplete remyelination process area of the injured nerve. Large spaces (thick arrow) were observed in the affected area and unaligned the regenerative fiber (thin arrow). B. Stem cells group, complete remyelination of the middle area injured. However, small vacuoles (arrows) were observed in the nerve axon. H&E, X100.

Figure 4: A photomicrograph of the distal segment of 56 days post sciatic nerve defect. A. Chitosan nanoparticles group, insufficient nerve growth. The collagen fiber tissue (arrow) that surrounds the terminal of the new growth nerve severed the new growth nerve. B. Stem cell group, degenerated nerve fibers of the affected area (arrow) and enhanced parallel of the nerve fibers. H&E, X100.

Figure 2: A photomicrograph of the proximal segment of 56 days post sciatic nerve defect. A. Chitosan nanoparticles group, the healing process of the affected nerve shows vaculation within the neural axon. Collagen fibers (arrow) also disrupt the nascent nerve development. B. Stem cell group, remyelinated new nerve, was structured as a longitudinal neural fiber (thin arrow) with angiogenesis activity in the afflicted location. However, small vacuolation (thick arrow) was observed in these new nerves. H&E, X100.

Figure 4: A photomicrograph of the distal segment of 56 days post sciatic nerve defect. A. Chitosan nanoparticles group, insufficient nerve growth. The collagen fiber tissue (arrow) that surrounds the terminal of the new growth nerve severed the new growth nerve. B. Stem cell group, degenerated nerve fibers of the affected area (arrow) and enhanced parallel of the nerve fibers. H&E, X100.
Histopathological study of the proximal segment of the sciatic nerve in the CS NPs group on 112 days postoperatively showed a poor healing process of the sciatic nerve was observed, where low density of neural axons with the presence of large spaces internodal and scar in the affected area was noted (Figure 5). The stem cells group showed Schwann cells at the epineurium and perineurium. However, collagen fibers were observed in the healing area that occupied some nerve areas. Also, the angiogenesis activity was noted (Figure 5).

Histopathological study of the middle segment of the sciatic nerve in the CS NPs group on 112 days postoperatively showed vacuoles in new growth nerve that were discovered in neural fibers of the posterior section of the sciatic nerve, indicating a poor healing process in the wounded sciatic nerve (Figure 6). In the stem cells group, the complete healing process of the sciatic nerve was observed: a large space (black arrow) that separated neural fibers (Figure 6).

Figure 5: A photomicrograph of the proximal segment of 112 days post sciatic nerve defect. A. Chitosan nanoparticles group. Poor healing process of the sciatic nerve was observed, where low density of neural axons with large spaces (arrow) in the affected area was noted. B. Stem cells group, Schwann cells(thine arrow) at the epineurium and perineurium, degenerated nerve fibers (thike arrow), and the angiogenesis activity (head arrow) were noted. H&E, X100.

Figure 6: A photomicrograph of the middle segment of 112 days post sciatic nerve defect. A. Chitosan nanoparticles group. Note the vacuoles (arrow) in new growth nerve observed in neural fibers of the proximal segment. B. Stem cells group, a complete healing process of the sciatic nerve, was observed. However, a large space (arrow) separated neural fibers. H&E, X100.

Histopathological study of the distal segment of the sciatic nerve in the CS NPs group on 112 days postoperatively showed an incomplete healing process of the sciatic nerve was observed, where the neural fibers were interrupted by collagen fibers surrounding the neural fibers (Figure 7). The stem cells group showed good remyelination regeneration of the nerve fibers. Also, angiogenesis activity was noted, where new blood vessels were observed between neural fibers (Figure 7).

Figure 7: A photomicrograph of distal segment of 112 days post sciatic nerve defect. A. Chitosan nanoparticles group, an incomplete healing process of the sciatic nerve, was observed, where the neural fibers were interrupted by collagen fibers (arrow) that surrounded the neural fibers. B. Stem cells group shows good remyelination and regeneration of the nerve fibers; also, angiogenesis activity was noted (thick arrows), where new blood vessels were observed between neural fibers with increased Schwann cells (thin arrows). H&E, X100.

Discussion

This investigation showed that the start of limb movement and walking in MSC animals was faster than in the CS NPs group. All the animals returned to normal gait; however, the MSCs group (53 days) regained normal gait faster than the CS NPs group (57 days). The disappearance of knuckling in the MSCs (62 days) groups differed substantially (p 0.05) from that of the CS NPs (74 days). Muscle contraction forces were significant in both groups; however, contraction started earlier in the MSCs (62 days) group than in the CS NPs (64 days). The ability of the animal to walk on its operated left hind foot was assessed based on the intensity of the discomfort, which was categorized as neuropathic or inflammatory. According to the outcomes of this study, all animals in the MSCs group progressed to normal gait, which was faster than those in the CS NPs group. This finding implies that MSCs have therapeutic potential and may play a role in neuropathic pain and faulty sciatic nerve regeneration. Previous research found that implantation of adipose-derived stem cells reduced neuropathic pain, perhaps due to the production of neurotrophic, angiogenic, and anti-apoptotic substances (24,25).
Another study found that injecting stem cells around the sciatic nerve lesion reduced the development of mechanical and thermal allodynia (26). Muscle contraction was related to muscle denervation and disuse, and greater muscle contraction force was connected with improved sciatic nerve motor function. Due to the facilitation of reinnervation, the MSC animals regained muscular force contraction more quickly than the CS NPs group because a sciatic nerve lesion hindered muscle force contraction. (27) discovered that muscular innervation-maintained muscle contraction force. Sensory reactivity, particularly toe spreading, improved with time, and peroneal nerve function returned (28). As a result, rabbit sciatic nerve regeneration was considered an indication of functional recovery. Implantation of fibroblast-like MSCs improved active healing of the damaged sciatic nerve in the MSCs group. MSCs have been found to express trophic factors and supporting substances such as nerve growth factor, brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, collagen, fibronectin, and extracellular matrix components, all of which influence endogenous neural cell activity (29,30).

In this study, the histological obtained at 56 days post-operation revealed variations in the rate of nerve regeneration among the treatment groups, likely attributed to differences in the quantity and quality of cells and the release of various neurotrophic factors supporting myelin sheath formation, neovascularization, and reduced inflammatory reaction, all contributing to the regeneration process. Particularly noteworthy was the CS NPs group, which showed an increased number of Schwann cells at 56 days post-operation, similar to the Stem cells group, due to a higher concentration of stem cells in the conduit. It is worth mentioning that the nerve conduit employed in this investigation had a high concentration of stromal stem cells (31). This conduit delivered factors directly to the transected peripheral nerve, resulting in increased angiogenesis and the release of growth factors such as VEGF and FGF, creating a favorable environment for stem cell differentiation into Schwann cells (32-34). Previous research has established the crucial role of Schwann cells in removing myelin and axon debris, with a codependent interaction with macrophages, where macrophages stimulate Schwann cell growth and collaborate in providing essential trophic and trophic factors for regenerating axons (35).

These findings align with a study conducted which evaluated the use of a decellularized bovine urinary bladder matrix conduit as a nerve guidance conduit, revealing an abundance of nerve fibers and enhanced radial function, elongation, and bridging of a 10 mm nerve gap in dogs. Similarly, another investigation involved the implantation of a xenogeneic acellular nerve matrix (ANM) into the sciatic nerve of rats, with the removal of a 1 cm nerve segment. The results demonstrated significant nerve regeneration properties of the constructed nerve graft, indicating its potential as a promising alternative to autologous grafts for repairing peripheral nerve defects at PN repair sites (36,37).

Various stem cell-based tissue engineering techniques have been used, training the environment to offer elements that encourage nerve regeneration (38,39). The findings of this study are consistent with a previous study (40) involving the implantation of mesenchymal stem cells into the gap of the sciatic nerve, bridged with a conduit in rats, resulting in enhanced motor function recovery, improved nerve regeneration, and reduced muscle atrophy.

The mechanisms behind neovascularization and axon regeneration after peripheral nerve injury are unclear (41). Despite this, several studies show a close link between angiogenesis and neurogenesis, which is mediated by the innate immune response to peripheral nerve injury (42). Macrophages are assumed to play a key role in responding to and guiding endothelial cell migration, leading to the formation of new blood vessels in hypoxic tissues. These newly created blood vessels are thought to direct Schwann cells and enable axon regeneration over peripheral nerve damage (43).

Surprisingly, after 112 days, the portions of the proximal segment in the stem cell group showed no evidence of degeneration or vacuolation. Instead, there was an increase in Schwann cells, proper nerve fiber alignment, and little scar tissue in the epineurium. Significant angiogenesis, nerve fiber alignment, and myelination were seen in the proximal, middle, and distal parts. These findings indicate that combining UBM conduits with MSCs promotes regeneration and increases functional recovery in sciatic nerve damage. This impact is linked to the production of various neurotrophic factors, which aided in developing more myelin sheaths in the middle segment, enhanced neovascularization, and decreased inflammatory responses. When combined with MSCs, a functional UBM conduit can support regenerating nerve fibers and control their growth in the ideal direction to bridge the nerve gap. As expected, employing both UBM conduits with MSCs resulted in better functional recovery than UBM conduits with chitosan conduits alone, exhibiting greater regeneration capacity. This discovery is consistent with a recent work (44) that used chitosan conduits with bone marrow mesenchymal stem cells (BMSCs) to bridge a fundamental gap in adult rat sciatic nerves in addition, combining MSCs with chitosan conduits expedited sciatic nerve regeneration and enhanced functional recovery compared to employing chitosan alone.

Furthermore, a study explored the effectiveness of nanofibrous nerve conduits supplemented with nerve growth factors and Bone Marrow stem cells (45). However, due to the limited accessibility of Schwann cells (SCs) and inadequate coverage of seeded cells on the nerve guidance conduits (NGCs), nerve regeneration across long gaps and achieving full functional recovery can be challenging. Nonetheless, the study indicated that mixing diverse parts improves peripheral nerve regeneration by boosting
neurotrophic factor production, especially in situations with extensive nerve damage intervals. Research on the other hand, found that using nerve guidance conduits (NGCs) in conjunction with adipose-tissue-derived multipotent mesenchymal stromal cells (ADMSCs) improves nerve regeneration in a Wistar rat model with a 12-mm sciatric nerve defect gap. After 112 days of therapy, regeneration was detected (46).

Furthermore, a research discovered that the presence of Schwann-like cells was increased in the sciatric nerve treated with BMSCs (47). BMSCs, like Schwann cells, have been postulated to prevent neuronal cell death and promote directed axonal growth. They form longitudinal columns known as Bungner bands as they multiply to take up home in the endoneuria sheaths (48,49). Within a few days of the damage, Schwann cells start division and form dedifferentiated daughter cells without axon interaction. They downregulate the expression of their normal proteins, such as peripheral myelin protein-22 (PMP-22), myelin basic protein (MBP), myelin-associated glycoprotein (MAG), and connexin-32 (50), to change into a premyelinating cell phenotype.

The Schwann cells undergo a process of dedifferentiation, proliferation, and redifferentiation. Their crucial role in guiding axon regeneration and the influence of neurotrophins, which communicate through paracrine receptor-mediated signals (51), Nerve growth factor (NGF), neurotrophic factors, cytokines, and other substances are examples. This increase stimulates Schwann cell development and proliferation, critical in avoiding neuronal death following damage. Furthermore, it promotes Schwann cell migration, adherence to axonal outgrowth, and the major augmentation of neovascularic withdrawal in any inflammatory process and subsequent promotion of regeneration time (52-54).

Conclusions

The study evaluated the impact of CS NP implantation within an acellular urinary bladder matrix conduit (AUBM) on repairing peripheral nerve regeneration defects. Although the implanted CS NPs in AUBM showed improvement in regeneration, the recovery rate was relatively lower. On the other hand, the implantation of ASCs within an acellular urinary bladder matrix conduit (AUBM) demonstrated a more significant effect in repairing a 10mm peripheral nerve gap in rabbits, particularly for sciatric nerve defects.

Acknowledgments

The College of Veterinary Medicine, University of Baghdad provided the study materials.

Conflicts of interest

According to the authors, there is no conflict of interest.

References


تعتبر إصابة الأعصاب المحيطية من أكثر الإصابات حدوثًا في الحيوانات والتي يسببها عدد من العوامل، ومنها الصدمات والعمليات العلاجية، والخليارات العلاجية تكون محدودة للمساعدة في التعافي الوظيفي لهذه الحالات. كان الهدف من هذه الدراسة هو مقارنة الخلايا الجذعية المشتقة من الدهون والجزيئات النانوية لتجديد العصب الوركي المقطوع للأرانب. حيث تم تقسيم عشرين أرنبًا من السلالات المحلية إلى مجموعتين بشكل عشوائي حيث تم سد القطع المحدث بإعطاء solução شبه الهلام 1 ملغ/ملي المجموعة الأولى، وتم إعطاء الجزيئات النانوية لخلية الكيتوسان في المجموعة الثانية. وفي نهاية اليوم السادس والخمسون واليوم المئة وأثني عشر، تم فحص الأعراض السريرية والوظيفة الحركية والحساسية والتقدم السنتي في العصب الوركي. وفقًا للتحليل، زادت الفترات الحركية والحساسية للعصب الوركي بشكل أسرع في مجموعة الخلايا الجذعية. في مجموعة الخلايا الجذعية لمصلحة القطع المحدث في العصب الوركي بقياس عشرة ملم، وتكشف الفحص الطبي المركزي عن نواة قاعديًا للخلايا شوان المتكاثرة مع عقد المايلين سميكة والألياف العصبية جيدة التوجه ومجموعة محورية كثيفة وقطرة محوري كبير ونخاع ألياف كبيرة والتنوعة التي متخصصة. وخلص إلى أن تأثير الخلايا الجذعية يعزز تجديد العصب الوركي المقطوع بجزيئات الكيتوسان النانوية.