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The Long-term Effects of Uncultured Omental Adipose-derived Nucleated Cells Fraction and Bone-marrow Stromal Cells on Sciatic Nerve Regeneration

Saeed Azizi[*1], Behnam Heshmatian[2], Saman Mahmoudpour[1], Abbas Raisi[3]

Abstract

Objective- Adipose tissue is an appropriate source for isolation of cells with stem-cell–like properties. In the present long-term study, the effects of the omental adipose-derived nucleated cells (OADNCs) fraction were compared to those of the undifferentiated cultured bone marrow stromal cells (BMSCs) on sciatic nerve regeneration.
Design- Experimental *in vivo* study.
Animals- Fifty male White Albino rats.
Procedures- The rats were divided into four experimental groups, randomly: Normal control (NC), inside-out vein graft (IOVG), the OADNC and the BMSC groups. A 10-mm sciatic nerve defect was bridged using an inside-out vein graft. In OADNC and BMSC groups, the vein was filled with OADNCs and BMSCs, respectively. Functional studies of sciatic function index, electrophysiologic, morphometric and immunohistochemistry assessments were performed at 16, 20 and 24 weeks after surgery.
Results- There was no significant differences ($P > 0.05$) between BMSC and OADNC groups concerning recovery of the regenerated nerves, amplitude and time delay of electromyography. Compared to IOVG, OADNCs enhanced the nerve regeneration similar to undifferentiated BMSCs.
Conclusion and Clinical Relevance- It was concluded the long-term morphometric results could be more reliable in histological study of sciatic nerve regeneration.
Key Words- BMSCs, OADNCs, Sciatic nerve regeneration, Rat.

Introduction

Reconstruction and satisfactory functional recovery of a damaged nerve is a major challenge for neurosurgeons. Generally, to enhance the nerve regeneration, combinations of nerve bridging and cell-based supportive therapies are widely accepted. Nevertheless, autologous nerve grafting is the most commonly used clinical tool to repair peripheral nerve defects.
Adipose tissue has been found to possess a population of multipotent stem cells that can be differentiated to a Schwann-cell phenotype.[1] The non-adipocyte cells, known as the stromal vascular fraction, when loaded in a vein graft, have been successfully improved peripheral nerve regeneration and functional recovery as well.[2]

[1] Department of Veterinary Surgery and Diagnostic Imaging, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.
[2] Neurophysiology research center, Urmia University of Medical Sciences, Urmia, Iran.
[3] Department of Clinical Sciences, Faculty of Veterinary Medicine, Lorestan University, Khoramabad, Iran
Address all correspondence to to Dr. Saeed Azizi (DVM, DVSc)
E-mail: s.azizi@urmia.ac.ir
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The mesenchymal stem cells (MSCs) originated from bone marrow, as a main source of stem cells, have been widely used in tissue repair including peripheral nerve regeneration. Also, these cells under appropriate conditions can be selectively differentiated into Schwann cells.[3]
In our previous short-term study (4-12 weeks after surgery), we showed that omental adipose-derived nucleated cells fraction can enhance sciatic nerve regeneration similar to undifferentiated cultured bone marrow stromal cells.[4] No statistically significant differences were observed between the experimental groups measuring SFI values, muscle mass and immunohistochemistry observations throughout the study. However, in the quantitative histomorphometric analyses of the regenerated nerves a significant difference in myelin sheath thickness was observed between the groups in favor of OADNCs at the end of study period (12 weeks after surgery).
The aim of the present study was to conduct a long-term study (16-24 weeks after surgery) to compare the beneficial effects of OADNCs with BMSCs on sciatic nerve regeneration through inside-out vein graft in a rat sciatic nerve transection model.

Assessment of nerve regeneration was based on functional walking track analysis, electrophysiological, histomorphometric and immunohistochemistry (Schwann-cell detection by S100 expression) criteria at 16, 20 and 24 weeks after surgery.

Materials and Methods

Experimental Design

Fifty male White Albino rats, weighing approximately 290 g, were divided into four experimental groups randomly: Normal control (NC) (n=5), inside-out vein graft (IOVG) (n=15), the omental adipose-derived nucleated cell fraction (OADNC) (n=15), and the undifferentiated bone marrow stromal cell (BMSC) group (n=15). IOVG, OADNC and BMSC groups were further subdivided into three subgroups of five animals each. Forty-five rats, weighing 300–350 g, were used as vein graft donors. Four of the donor rats were assigned to OADNC fraction preparation and four others were assigned to isolation and preparation of undifferentiated BMSCs. Two weeks before and through-out the experimental period the animals were housed in individual plastic cages at an ambient temperature almost 23 ºC, with even humidity and a natural day/night cycle. The rats had free access to standard rodent laboratory food and tap water.

Preparation of OADNCs fraction and Isolation and Culture of BMSCs

The techniques of omentum tissue collection and cell-harvesting procedure for preparing of OADNC and also adult BMSCs isolation technique are described in our previous study.[4]

Grafting Procedure

Animals were anesthetized by intraperitoneal administration of ketamine–xylazine (ketamine 5% at 90 mg/kg, and xylazine 2% at 5 mg/kg). The procedures were carried out based on the guidelines of the ethics committee of the International Association for the Study of Pain.[5] The University Research Council approved all experiments. A 15-mm segment of right external jugular vein was harvested on a tube after the donor animals had been anesthetized, shaved and prepared aseptically[6]. Grafts were washed in physiologic solution and left at room temperature for 30–40 min. A subtle retraction of 1 mm was already expected. Each graft was inverted inside-out to prevent any potential branching of axons through the side branches during regeneration.[6]
After surgical preparation, in the NC group, the left sciatic nerve was exposed through a gluteal muscle incision and after careful hemostasis the muscle was sutured with absorbable 4/0 sutures, and the skin with 3/0 nylon. In the other experimental groups, following left sciatic nerve exposure it was transected proximal to the tibioperoneal bifurcation, where a 8-mm segment was excised, leaving a gap of about 10 mm due to retraction of nerve ends. Proximal and distal stumps were each inserted 2 mm into the graft, and two 10/0 nylon sutures were placed at each end of the cuff to fix the graft in place and leave a 10-mm gap between the stumps.

Transplantation of OADNCs and BMSCs to Sciatic Nerve

In the OADNC group, the inside-out vein graft was filled with 10µl of omental adipose-derived nucleated cells fraction aliquot (2×10^7 cells/ml) using a syringe, and sterile Vaseline was used to seal the ends of the tubes to avoid leakage. In the BMSC group, the graft was filled the same way with 10µl of undifferentiated cultured BMSC aliquot (2×10^7 cells/ml) and in the IOVG group, the inside-out vein graft was filled with 10µl of Phosphate-buffered saline (PBS).

Functional Assessment of Nerve Regeneration

Walking track analysis was performed at 16, 20, and 24 weeks after surgery based on work by Bain et al.[7] The lengths of the third toe to its heel (PL), the first to the fifth toe (TS), and the second toe to the fourth toe (IT) were measured on the experimental side (E) and the contralateral normal side (N) in each rat. The sciatic function index (SFI) in each animal was calculated by the following formula:
SFI= -38.3×(EPL-NPL)/NPL+ 109.5× (ETS-NTS)/NTS +13.3×(EIT-NIT)/NIT-8.8
In general, the SFI oscillates around 0 for normal nerve function, whereas around -100 SFI represents total dysfunction. The SFI was assessed based on the IOVG group and the normal level was considered as 0. The SFI was a negative value, and a higher SFI meant better function of the sciatic nerve.

Electrophysiological measurements

The animals were subjected to in vivo electrophysiological studies using Nacro bio system 320-3760 A trace 80 (USA) at the end of study for each group. Data acquisition and analysis performed by Power Lab instrument (AD Instrument Australia) and Lab Chart 7 software. Under general anesthesia (see earlier) firstly, rat was fixed on a table and body temperature was kept constant at 37°C. Then, the previous surgical site at the mid-thigh level was opened and the regenerated sciatic nerve cable was exposed. Electromyographic (EMG) assessment was carried out by stimulating both proximally and distally to the regenerated nerve (unresorbed nylon sutures were taken as selection points).[8] Single electrical pulses (at

supramaximal intensity) were delivered via bipolar electrodes placed in turn at the proximal and distal trunk of the regenerated nerve cable and EMG was recorded by inserting an electrode into the belly of gastrocnemius muscle. After EMG recording, amplitude and latency of EMG in the proximal and distal sites of stimulation was measured.

Histologic Preparation and Quantitative Morphometric Studies

Under general anesthesia (see above) the animals were euthanized with transcardial perfusion[9] of a fixative containing 2% paraformaldehyde and 1% glutaraldehyde buffer (pH 7.4) at 16, 20 and 24 weeks after surgery.
Mid-graft segments of the experimental groups were harvested and fixed in 2.5% glutaraldehyde. The grafts were then embedded in paraplast paraffin, cut in 5-µm slices, and stained with toluidine blue. Morphometric analysis was carried out using image analysis software (Image Pro Express, version 6.0.0.319; Media Cybernetics, Silver Spring, Maryland). Equal opportunity, systematic random sampling and two-dimensional dissector rules were followed with sampling-related, fiber-location–related, and fiber-size–related biases.[10]

Immunohistochemical Analysis

In the present study, anti- S100 (1:200; DAKO) was used as a marker for axon and myelin sheath. Prior to immunohistochemistry, specimens were postfixed with 4% paraformaldehyde for 2 h and embedded in paraffin. After non-specific immunoreactions were blocked, sections were incubated in S100 protein antibody solution for 1 h at room temperature. They were washed three times with PBS and incubated in biotinylated anti-mouse rabbit IgG solution for 1 h. Horseradish peroxidase–labeled secondary antibody was developed using the diaminobenzidine method. The results of immunohistochemistry were examined under a light microscope. The immunohistochemical results were analyzed qualitatively using positive, more positive and clearly more positive terms.[6]

Statistical Analysis

Experimental results were expressed as mean ± SD. Statistical analyses were performed using PASW, v18.0 (SPSS, Inc., Chicago, Illinois). Model assumptions were evaluated by examining the residual plot. Results were analyzed using a factorial analysis of variance (ANOVA) with two between-subjects factors. The Bonferroni test for pairwise comparisons was used to examine the effect of time and treatments. Differences were considered significant at $P < 0.05$.

Results

Recovery of Sciatic Nerve Function

The SFI value, 16 weeks after the surgery, decreased from normal (around 0) to -45.5 ± -3.43, -25.7±3.16 and -25.7±-1.6 in the IOVG, the BMSC and the OADNC groups, respectively. Following 20 weeks, SFIs increased to -27.8 ± -2.23 in the IOVG group, -16.7 ± -2.21 in the BMSC group and to -12.5±-2.54 in the OADNC group. The improvement of SFI in the BMSC and the OADNC groups were significantly better than IOVG group at the end of 16 and 20 weeks after surgery ($P < 0.05$). Twenty four weeks after surgery SFI values of the IOVG, the BMSC and the OADNC groups reached -12.9±-3.47, -8.5±-1.4 and -8.7±-2.8, respectively. When the mean SFI values in the BMSC and the OADNC groups were evaluated, no statistically significant differences ($P > 0.05$) were detected during the study period (Fig. 1).

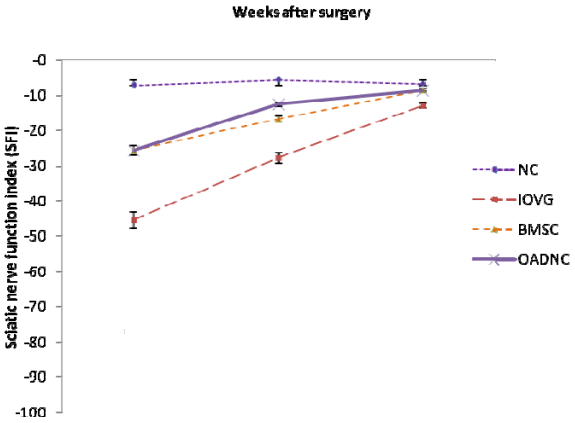

Figure 1- The effects on sciatic nerve function index (SFI). Treatment with bone marrow stromal cells (BMSCs) and the omental adipose-derived nucleated cells (OADNCs) gave better results in functional recovery of the sciatic nerve index.

Electrophysiological measurements

All experimental rats showed successful muscle contraction. The amplitude of EMG in the OADNC group and BMSC group was significantly higher than of IOVG group in both proximal and distal of the regenerated nerve cable throughout the study period ($P<0.05$). There was not any statistically significant difference between EMG amplitude between the OADNC group and BMSC group ($P>0.05$). The average of amplitude in 16, 20 and 24 weeks after surgery for proximal and distal sites is shown in Table 1. The EMG amplitudes patterns in distal and proximal stimulation point almost overlapped each other which confirmed the absence of signal dispersion and the good conductivity of the regenerated nerves.

In measurement of time delay, the gastrocnemius muscle response to nerve stimulation was decreased over time in both proximal and distal sites in all three transected groups. Since the difference in time delay was not statistically significant between the OADNC and BMSC groups, EMG time delay of these groups were significantly higher (P<0.05) than that of IOVG group (Table 2). All recorded values of latency in distal site were shorter and not statistically more significant than proximal site (P > 0.05). These data confirmed the sciatic nerve fibers regeneration.

Histological and morphometric findings

Table 3 shows quantitative morphometric analyses of the regenerated nerves for each of the experimental groups. Statistical analysis by one-way ANOVA showed that the increase in number of fibers, diameter of fibers, and diameter of axons, as well as the increase in mean myelin sheath thickness were not statistically significant between BMSC and OADNC groups in the study period (P>0.05). However, these indices were significantly different (P<0.05) between IOVG group with BMSC and OADNC groups in 16 weeks after surgery. The mean number of fibers was significantly different (P<0.05) between IOVG group with BMSC and OADNC groups in 20 weeks after surgery.

A factorial ANOVA with two between-subjects factors (group-time) showed an interaction across time in the experimental groups. The fiber number showed significant increase in BMSC and OADNC groups in 16 and 20 weeks after surgery and this increase was seen throughout the study period for the IOVG group (P<0.05). Significant increases were seen in fiber diameter, axon diameter and mean thickness of myelin sheath in the IOVG group between 16 and 20 weeks (P < 0.05). Ratio of axon diameter to fiber diameter (G-ratio) was calculated in each group to show the effects of time and treatment on the maturation of nerve fibers.

Immunohistochemistry

Immunoreactivity to S-100 protein was extensively observed in the cross-sections of regenerated nerve segments. The expression of S-100 protein signal was located mainly in myelin sheath. The axon also showed a weak expression, indicating that Schwann cell-like phenotype existed around the myelinated axons (Fig. 2). The structure and function of regenerated axons and myelin sheath in both BMSC and OADNC groups were far more similar to those of normal nerve compared to IOVG group. Overall, the expression of S-100 resembled those of the histologic evaluations in all experimental groups.

Table 1. EMG amplitudes of the regenerated sciatic nerve for each of the experimental groups.

	Proximal amplitude (mV)			Distal amplitude (mV)		
Weeks	**16**	**20**	**24**	**16**	**20**	**24**
Groups						
NC	13.87±0.8*†	13.87±0.8*†	13.87±0.8*	13.87±0.8*†	13.87±0.8*†	13.87±0.8*
IOVG	5±0.8	5.48 ± 0.82	8.46 ± 0.56	5±0.8	5.08±0.75	8.05±0.6
OADNC	7.09 ± 0.85*	7.46 ± 0.9*	11.8 ± 1.02*	6.69 ± 1.06*	7.24 ± 0.95*	11.58 ± 1.22*
BMSC	7.64±0.62*	8.22± 0.54*	11.64 ± 1.1*	7.04± 0.9*	8.12±0.36*	11.01±1.2*

* P<0.05 vs IOVG group, † P<0.05 OADNC and BMSC groups. Values are given as mean ± SD.
NC: Normal control, IOVG: Inside-out vein graft, BMSC: bone marrow stromal cell,
OADNC: omental adipose-derived nucleated cells

Table 2- Electromyographic time delay of the regenerated sciatic nerve for each of the experimental groups.

	Proximal Latency (s)			Distal Latency (s)		
Weeks	**16**	**20**	**24**	**16**	**20**	**24**
Groups						
NC	0.048±0.012*†	0.048±0.012*†	0.048±0.012*†	0.048±0.012*†	0.048±0.012*†	0.048±0.012*†
IOVG	0.212±0.014	0.183 ± 0.018	0.164 ± 0.019	0.202±0.08	0.178±0.015	0.155±0.04
OADNC	0.18 ± 0.01*	0.169 ± 0.012*	0.134 ± 0.02*	0.169 ± 0.016*	0.145 ± 0.03*	0.124 ± 0.011*
BMSC	0.184±0.018*	0.167± 0.01*	0.142 ± 0.03*	0.182± 0.012*	0.16±0.032*	0.132±0.03*

* P<0.05 vs IOVG group, † P<0.05 vs OADNC and BMSC groups. Values are given as mean ± SD
NC: Normal control, IOVG: Inside-out vein graft, BMSC: bone marrow stromal cell, OADNC: omental adipose-derived nucleated cells

Table 3- Morphometric analyses of regenerated nerves for experimental groups (mean ± SD)

Groups	NC	IOVG			BMSC			OADNC		
Weeks	**24**	**16**	**20**	**24**	**16**	**20**	**24**	**16**	**20**	**24**
N	8224 ± 308	4285 ± 291	6453 ± 312	8256 ± 423	7142 ± 273†	8194 ± 257†	8213± 304	7390 ± 247†	8373 ± 183†	8254 ± 272
D	12.06 ± 0 .11	9.47 ± 0.34	11.72 ± 0.49	11.89 ± 0.29	11.54 ± 0.39†	12.08 ± 0.21	12.11 ± 0.03	11.77 ± 0.12†	12.21 ± 0.04	12.03 ± 0.02
d	7.06 ± 0.12	5.74 ± 0.73	6.97 ± 0.28	7.08 ± 0.52	6.67 ± 0.41†	7.02 ± 0.47	7.07 ± 0.15	6.72 ± 0.36†	6.98± 0.41	7.02 ± 0.33
T	2.54 ± 0.01	1.86 ± 0.04	2.37 ± 0.12	2.40 ± 0.06	2.43 ± 0.08†	2.53 ± 0.03	2.52 ± 0.02	2.50 ± 0.05†	2.61 ± 0.02	2.52 ± 0.04
G-ratio	0.585	0.606	0.595	0.595	0.578	0.581	0.583	0.571	0.572	0.584

N: Number of fibers, D: Diameter of fibers (µm), d: Diameter of axon (µm), T: Thickness of myelin sheath (µm).
†Results were significantly different at p<0.05.
G-ratio: Ratio of axon diameter to fiber diameter.NC: Normal control, IOVG: Inside-out vein graft, BMSC: bone marrow stromal cell, OADNC: omental adipose-derived nucleated cells

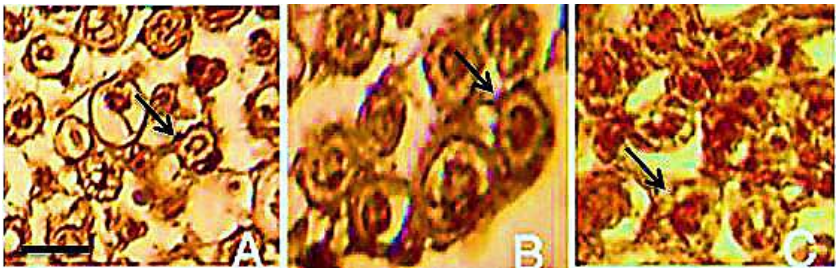

Figure 2- Immunohistochemical analysis of the regenerated nerve 20 weeks after surgery. (**A**) indicates the Inside-out vein graft (IOVG) group, (**B**) for the bone marrow stromal cells (BMC)group and (**C**) for the omental adipose-derived nucleated cells (OADNC) group. There is clearly more positive staining for the myelin sheath–associated protein S100 (arrow) within the periphery of nerve, indicating well-organized structural nerve reconstruction in both of BMCs and (C) OADNC groups compare to IOVG group. Scale bar = 10 µm.

Discussion

In the present long-term study, we compared the effect of OADNCs and undifferentiated BMSCs on peripheral nerve regeneration in sciatic transection model in rat. The results showed similar enhancement of functional recovery, electrophysiologic function and nerve regeneration with bridging an inside-out vein graft loaded with OADNCs and undifferentiated BMSCs.

All methods of fixation change the structure of neural tissue. Hence, it is necessary to study the potential for artifact and distortion, even for well-established techniques because avoiding artifacts in laboratory data is of utmost importance.[11] There are several methods for tissue fixation that two of the most common are transcardial perfusion and immersion. In the neuroscience literature perfusion fixation has been proposed to be the gold standard for studies of neural tissue.[9]

The advantages like no donor morbidity, the ease of harvesting and transplanting, availability, affordability and no foreign reactions make vein graft an attractive alternative to other standard grafts.[12] Adventitial wall of the vein promotes nerve regeneration by providing an environment rich in collagen and laminin thereby promoting increased vascularization of the new nerve[13].

The results of the present study showed significant improvement of SFI in BMSC and OADNC groups than of IOVG group at 16 and 20 weeks after surgery. When the mean SFI values in the BMSC and the OADNC groups were evaluated, no statistically significant differences were detected during the study period which was similar to the results of our previous short-term study. However, a very minor difference, although not statistically significant, was observed in the SFI between the two groups in favor of the OADNC group at the present long-term study which was in contrast with the results of our previous study. In the late short-term study better recovery function was in favor of BMSC group at 12 weeks after surgery.[4] Overall, it seems cell therapy with OADNC when loaded topically into inside-out vein graft is able to produce more rapid and better functional recovery in transected regenerated sciatic nerve.

In the present study, in order to evaluate the degree of reinnervation, we performed gastrocnemius muscle EMG measurements. Compound muscle action potentials (CMAPs) were recognized to have a resolving power when evaluating nerve regeneration and electrical functionality of the grafted or regenerated nerves.[14] Compound muscle action potential can be measured only when enough regenerated nerve fibers grow across the nerve gap to innervate the distal target muscle. Amplitude of the EMG is directly proportional to the number of nerve fibers innervating the muscle that allows the conduction velocity of the motor nerve to be calculated.[15] In the present study, the regenerated nerve cable in all rats showed electrical viability, but differences in recorded amplitudes were present among the groups. It has been reported reductions of amplitude and releasing of latency are mainly due to axonal loss or presence of smaller caliber axons. However, these might be also influenced by demyelination when this leads to temporal dispersion or partial distal conduction blocks.[16] In the present study, the indices for EMG amplitude and time delay showed substantial improvement in nerve regeneration in all experimental groups. These indices were lower (for amplitude) and higher (for latency) in IOVG group compared to OADNC and BMSC groups that might be correlated with multiple factors such as the smaller diameter of the regenerating axons, thinner myelin sheaths and immaturity of myelinated nerve fibers as a whole [15,17] which was consistent with the morphometric findings. When CMAPs were recorded after stimulation distal to the regenerated nerve, absolute values were generally conserved (see results section for details), with maintained relationships among the groups. This confirms that, even with differences between different groups, the gap was crossed by functional fibers, with no blocks or irregularities in conductivity.

In the our previous short-term study [4], we showed a significant difference between groups concerning the mean thickness of the myelin sheath at the end of study period (week 12) and a general faster improvement in diameter of fibers and axons in favor of the OADNC group was observed throughout the study period. However, in the present long-term study, a significant increase was observed in number of fibers in OADNC group compared to BMSC group at 16 and 20 weeks after surgery. An overall increase in the mean diameter of fibers, mean diameter of axons and myelin sheath thickness in favor of OADNC group might indicate more beneficial effects of OADNCs on sciatic nerve regeneration.

The significant increase of the histologic indices in both BMSC and OADNC groups at 16 weeks after surgery and also significant increase of the mean number of fibers in both BMSC and OADNC groups at 20 weeks after surgery compared to IOVG group could show the same beneficial effect of the these type of cell therapy on sciatic nerve regeneration as well. Furthermore, a 16 week post-operative assess could be desirable for histological study in peripheral nerve regeneration of sciatic nerve transection model in rat.

Good expression of axon and myelin sheath special proteins in both of BMSC and OADNC groups compared to IOVG group indicated its normal histologic structure. These immunohistochemistry findings support the histological findings as well.

The beneficial effects of undifferentiated BMSCs on peripheral nerve regeneration have been reported with some technical limitations and disadvantages by others.[4,18,19,20] However, OADNCs, as an alternative source of multipotent cells, have been reported to show technical simplicity as an injectable, readily accessible,

and cost-saving instantly available source of cells in large quantities for clinical application.[4, 21, 22] Even though our study showed the beneficial effect of local OADNCs and BMSCs in peripheral nerve injuries, determining the molecular mechanisms leading to the these positive action remains and needs to be investigated. This may be considered as a limitation to our study.

It was concluded that OADNCs and undifferentiated cultured BMSCs when loaded in an inside-out vein graft have similar beneficial effects on sciatic nerve regeneration in rat transection model. In histomorphological study of the sciatic nerve regeneration long-term results could be more desirable and reliable.

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چکیده

اثرات طولانی- مدت سلول‌های هسته‌دار جداشده از بافت چربی چادرینه و سلول‌های استرومال مغز استخوان بر روی رژنراسیون عصب سیاتیک

سعید عزیزی*[۱]، بهنام حشمتیان[۲]، سامان محمودپور[۱]، عباس رئیسی[۳]

[۱] گروه جراحی و تصویربرداری تشخیصی، دانشکده دامپزشکی دانشگاه ارومیه، ارومیه، ایران.
[۲] مرکز تحقیقات نروفیزیولوژی، دانشکده علوم پزشکی دانشگاه ارومیه، ارومیه، ایران.
[۳] گروه علوم درمانگاهی، دانشکده دامپزشکی دانشگاه لرستان، خرم آباد، ایران.

هدف- بافت چربی یک منبع مناسب برای استحصال سلول‌های با ویژگی‌های سلول‌های بنیادی می‌باشد. در مطالعه حاضر تاثیر طولانی- مدت سلول‌های هسته‌دار جداشده از بافت چربی چادرینه با سلول‌های استرومال کشت شده تمایز نیافته جداشده از مغز استخوان بر روی رژنراسیون عصب سیاتیک مورد مقایسه قرار گرفت.

طرح مطالعه- مطالعه تجربی درون-زیستی

حیوانات- ۴ قطعه موش صحرایی نژاد آلبینوی سفید

روش کار- موش‌های صحرایی در شکل تصادفی به چهار گروه کنترل نرمال، گروه گرافت ورید از داخل برگردانده شده، گروه سلول‌های هسته‌دار جدا شده از بافت چربی چادرینه و گروه سلول‌های استرومال کشت شده تمایز نیافته جداشده از مغز استخوان تقسیم شدند. محل نقیصه عصبی با گرافت ۱۰ میلی‌متری ورید از داخل برگردانده شده ارتباط داده شد. در گروه سلول‌های هسته‌دار جداشده از بافت چربی چادرینه و در گروه سلول‌های استرومال کشت شده تمایز نیافته جداشده از مغز استخوان به ترتیب داخل ورید با سلول‌های زیربط پر گردید. مطالعات عملکردی ضریب عملکرد سیاتیک، مطالعات الکتروفیزیولوژیکی، ارزیابی‌های ریخت‌شناسی و ایمونوهیستوشیمی در هفته‌های ۱۶، ۲۰ و ۲۴ بعد از جراحی به انجام رسید.

نتایج- اختلاف معنی‌دار($P>0.05$) از لحاظ عملکرد اعصاب رژنره، دامنه و زمان تاخیر الکترومیوگرافی در مقایسه دو گروه، گروه سلول-های هسته‌دار جداشده از بافت چربی چادرینه و گروه سلول‌های استرومال کشت شده تمایز نیافته جداشده از مغز استخوان، مشاهده نشد. ولی در مقایسه با گروه گرافت ورید از داخل برگردانده شده هر دو گروه سلول‌های هسته‌دار جداشده از بافت چربی چادرینه و گروه سلول-های استرومال کشت شده تمایز نیافته جداشده از مغز استخوان افزایش رژنراسیون عصبی یکسانی از خود نشان دادند.

نتیجه‌گیری و کاربرد بالینی- در مطالعه بافت شناسی روند رژنراسیون عصب سیاتیک می‌توان نتیجه‌گیری کرد که نتایج ریخت‌شناسی مطالعه طولانی- مدت آن بیشتر قابل اعتماد باشد.

کلید واژگان- سلول هسته‌دار جداشده از بافت چربی چادرینه بزرگ، سلول استرومال کشت شده تمایز نیافته جداشده از مغز استخوان، رژنراسیون عصب سیاتیک، موش صحرایی.