

Evaluation of Vein Wrap Around Peripheral Nerve Repair: An Experimental Study

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ABSTRACT

Background: Scar tissue is an unavoidable result of peripheral nerve surgery. Extraneural and intraneural fibrosis might have an incapacitating effect on the regenerating nerve fibers. So, protecting accurately aligned nerve ends from surrounding fibrosis through nerve isolation or wrapping is more prone to achieve the ultimate goal for nerve repair.

Methodology: In this work, experimental study and histological evaluation of the effect of vein wrap around 2 different models of femoral nerve repair in rats with induction of an adhesion model around them (experiment groups n=20). In comparison to same models rats without induction of an adhesion model around them (control groups n=20).

Results: The results showed effective shielding of the repaired peripheral nerve from invasion by the surrounding scar tissue by the vein wrap. The results of this study with short term follow-up support further experimental study with long term evaluation of the vein wrap on the regenerating nerve fibers and their functional recovery.

Key Words: Vein wrap – Peripheral nerve repair.

INTRODUCTION

Current microsurgical techniques for peripheral nerve repair give functional results that are not always optimal [1]. The need to improve these results has led to the quest for alternative methods of nerve repair that would cause minimal interference with the internal environment of the injured nerve. The use of adhesives such as cyanoacrylate glue and fibrin glue had no remarkable improvement of the results [2,3].

Tissue welding with carbon dioxide lasers causes some amount of thermal damage to the nerve, experimental evidence that CO₂ laser-assisted nerve repair with welding of the protein with the absorbable suture may allow for healing with minimal foreign body reaction. Further experiments still

needed to refine laser-welding techniques to be ready for clinical applications [4,5,6].

Millesi, 1985, in his experimental work, reached a conclusion that the ultimate result of the nerve repair, regardless its type, is directly related to the amount of connective tissue proliferation at the site of repair. Extraneural and intraneural fibrosis might have an incapacitating effect on the regenerating nerve fibers [7].

Nerve tubulization offers an alternative method of repair of severed nerves with maximal coaptation and minimal injury. It is considered a more biological approach to nerve repair whereby the neural tissue is allowed to heal by its intrinsic capacity in a closed space with minimal surgical trauma. Tubulization has several advantages, as it protects regenerating fibers through reducing invasion and scarring of the nerve, and discourages the formation of neuromas. Lacing the transected nerve ends with a small gap separating the stumps allows for the collection of local neurotropic factors that enhance the nerve regeneration along a concentration gradient rather than allowing for diffusion from the target neural tissue [8]. Never the less, the factors that induce sensory/motor specificity regardless of the inter stump gap are ineffective when it comes to topographic specificity; axons are unable to find their own way to the correct topographic location [9-12]. Accurate alignment of axons in proximal and distal stumps thus remains a primary goal of the peripheral nerve surgeon [13,14].

So, protecting accurately aligned nerve ends from surrounding fibrosis through nerve isolation or wrapping is more prone to achieve the ultimate goal for nerve repair. Wrapping a peripheral nerve

had been experimentally studied and clinically tried in the last 3 decades in attempt to minimize the compressive manifestations that can result from nerve entrapment surgical treatment. Therefore, the same methods were used for nerve grafting and repair due to the encouraging results [15,16,17].

In this work, experimental study and histological evaluation of the effect of vein wrap around 2 different models of nerve repair with induction of an adhesion model around them (experimental groups). In comparison to same models rats with nerve wrap without injection of adhesive material (control groups).

MATERIAL AND METHODS

Experiments were performed in the animal lab of Faculty of Medicine, Cairo University from January 2015 to June 2016 on 40 rats (body weight approximately 150g). The animals were anaesthetized using a dose of 10mg/kg body weight of an intra peritoneal injection of ketamine. Two different models of nerve repair were used. In each model the right femoral nerve was used as the experiment side and the left femoral nerve as the control side. Exposure of the femoral nerve throughout its whole length in the thigh with its dissection and isolation from the femoral vessels (Fig. 1).

The first group, (n=20), underwent complete nerve transaction at its mid-thigh portion, then realignment using 10/0 Ethilon epineural stitches. The ipsilateral femoral vein was isolated, ligated at its both ends leaving about 3cm segment. The vein segment was transected at one end and left attached to the other facilitating manipulation. The isolated vein segment was laid open along its whole length then transected from the other end. Guided by the technique of Masear et al. [18], the vein segment, which is now converted into a sheet of venous wall with the intima on one side and the adventitia on the other side, was wrapped around the site of nerve repair in a spiral way with the intima facing inward (Fig. 2). The wrap was extended far enough proximally and distally to isolate the anastomotic site completely. A proximal and a distal 10/0 Ethilon stitch was used to secure the wrap in place. Meticulous care should be taken to ensure complete encircling of the nerve avoiding gaps in between the spirals, an approximating 10/0 Ethilon stitch was undertaken, to secure gapping if present.

In the second group (the adhesion model, n=20), the same was done as for group I with creation of

adhesion around the wrapped nerve using one cc ethanolamine oleate.

For each group, exactly the same technique was done on the contralateral femoral nerve but with no vein wrap.

Photos were taken, the wounds were closed and the animals allowed recovering from anaesthesia.

After 4 weeks, the rats were re-anaesthetized, the wound was re-opened, and the repair was explored on both sides. Both experimental and control nerves repaired were harvested with a cuff of surrounding tissue, and fixed with 10% formalin for 48 hr. The specimens were sectioned and stained with hematoxylin and eosin. Cross sections of 2µm were made of the nerves within the area of repair. Examination under light microscopy at x200 and x400 magnification was performed. Both sides of each group were compared followed by a comparison of both the vein wrapped repair in both groups and the unshielded repair in both groups.

RESULTS

Comparing both groups on the vein wrapped side:

By naked eye examination more dense adhesions in the experimental (group II) were revealed, where ethanolamine oleate was injected, than in the experimental (group I). The vein wrap could be identified under the operating microscope as a completely separable layer from the repaired nerve in both groups.

By histological examination, there were no signs of absorption or degradation of the vein graft in both groups.

In addition, there was no difference noted between the effects of vein shielding in both experimental groups, which reflect the effectiveness of the vein wrap in preventing fibrous adhesions from encroaching upon the site of nerve repair regardless the degree of fibrosis. Also there was no significant difference regarding the number of axonal regenerating in the two groups.

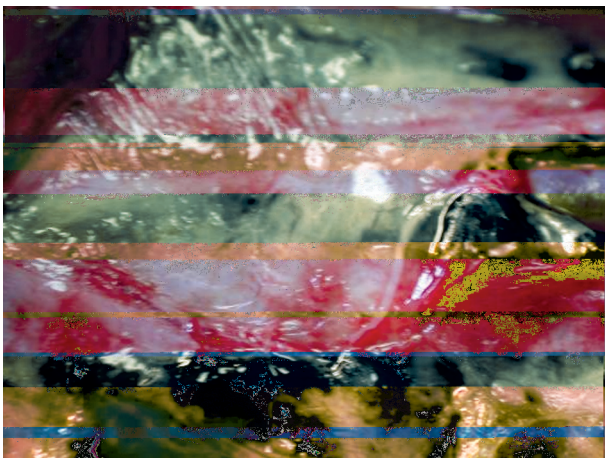
Furthermore, comparison of both sides of the experimental and control groups where no shielding wrap was used revealed a more dense thickness of adhesion in addition to an increase in the concentration of inflammatory cells around the area of nerve repair in both control groups, being more in the experiment group II, with no evidence of axonal regeneration being demonstrated.



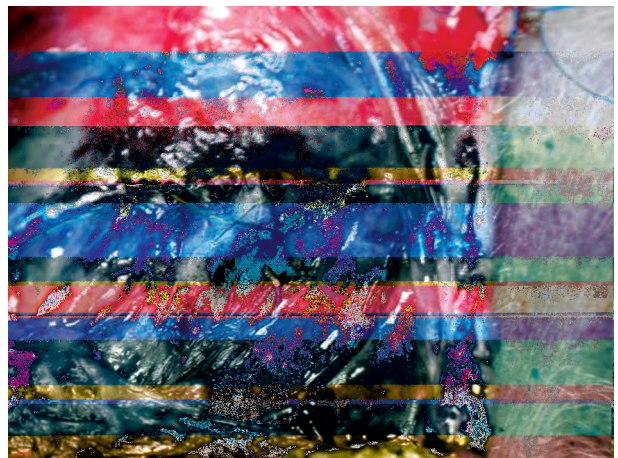
Fig. (1): Dissection of the neurovascular bundle showing the femoral nerve artery and vein.



Fig. (2): Showing wrapping of the femoral nerve repair with the vein.



(A)



(B)



(C)



(D)

Fig. (3): (A): Showing naked eye appearance of the unwrapped femoral nerve repair with sclerosant injection. (B): In the same rat the contralateral side with nerve wrapping and sclerosant injection. (C): Showing an unshielded femoral nerve repair. (D): On the contralateral side where a vein wrap was used.

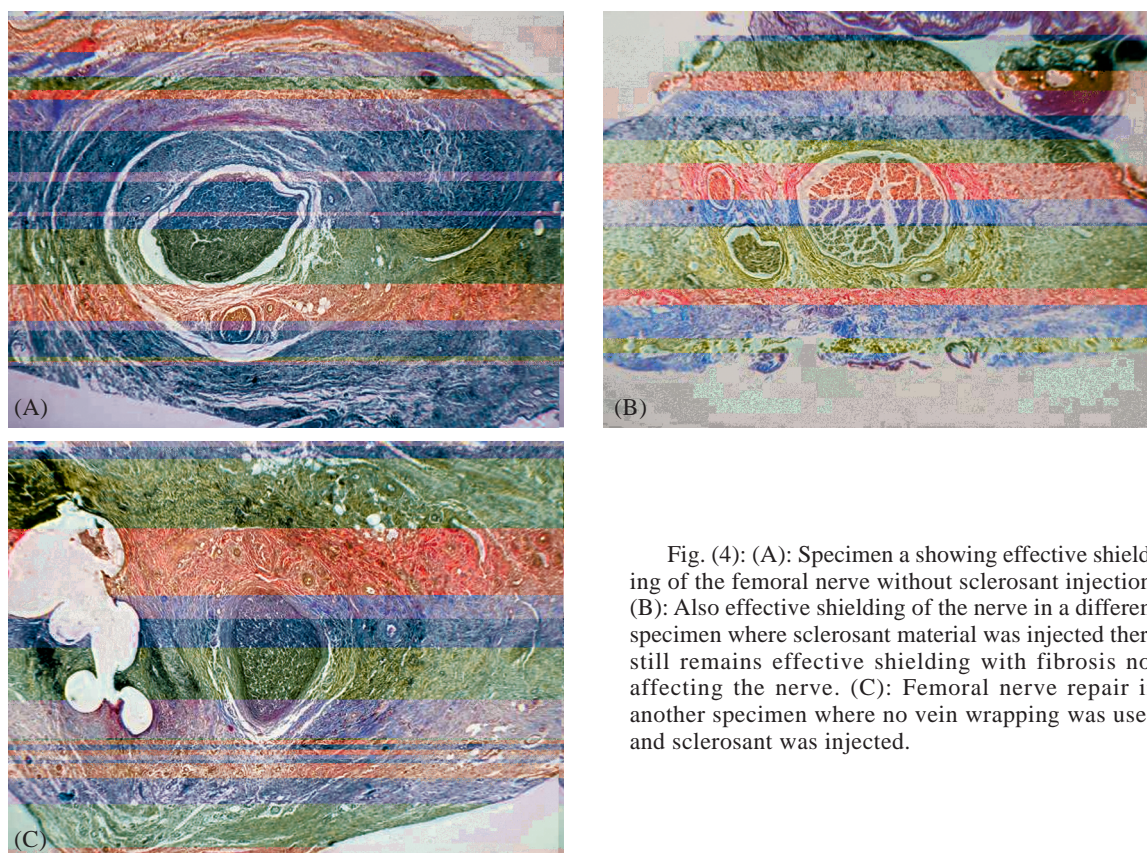


Fig. (4): (A): Specimen a showing effective shielding of the femoral nerve without sclerosant injection. (B): Also effective shielding of the nerve in a different specimen where sclerosant material was injected there still remains effective shielding with fibrosis not affecting the nerve. (C): Femoral nerve repair in another specimen where no vein wrapping was used and sclerosant was injected.

DISCUSSION

Surgical repair of the peripheral nerves is still full of challenges. Despite technical improvement in microsurgery, the present micro techniques seem to have reached its plateau with regard to capacity of available materials, technology and methodology. However, there is place for further development [14].

Several factors are now known to influence axon regeneration and the quality of recovery after nerve repair. A fair number of these factors cannot be controlled by surgery. However, a few of the factors that are influenced by surgery include tension, misdirectional axonal growth, perineural adhesions, foreign body scarring and granulomas [19,20].

In surgeries involving the peripheral nerves adhesion formations remain the utmost problem. The scar tissue that will form around the nerve postoperatively as a result of original trauma or the surgical intervention will sometimes interfere with nerve regeneration. Therefore, if the local muscle bed is not adequate, the use of a local muscle flap as a bed for an injured nerve or to change the environment of the nerve will allow that nerve to recover with minimal scar tissue [21,22].

Operative findings on exploration for delayed primary or secondary nerve repair always show the presence of a variable degree of perineural scarring. Also the recent attempts of following-up cases of nerve repair with persistent impairment of nerve function through high-resolution sonography showed some degree of nerve scarring that might be responsible, solely, or in conjunction with other factors for this dysfunction [23,24].

In attempt to reduce epineural scarring, several experimental research activities and clinical trials had been tried. These include the use of fibrin glue, alone or in conjunction with neurotropic factors, and laser welding instead of conventional micro sutures, the application of hyaluronic acid gel as a barrier around the nerve, the use of epineurial sleeve neurorrhaphy technique, the postoperative use of external beam irradiation (in low-dose) or laser therapy (low power biostimulation). The statistical analysis of the results of these modalities, though promising, yet could not achieve optimization of the functional outcome of nerve repair [3,5,21,25-28].

Recently alternatives to nerve suturing in the primary setting (i.e. when freshly transected) have been introduced, such as tubing (whether amnion tubes or vein tubes, or synthetic bio-absorbable

conduits, gortex tubes or silicon tubes). The introduction of these tubes aims to create an optimal environment that allows for biological regeneration of the transected nerve ends over a short space creeping through the tubal space protecting them from fibrosis. In such a procedure the surgical skill is minimized emphasizing the importance of the intrinsic healing capacity of the neural tissue and its capacity to regenerate. Nevertheless, controversy remains regarding the tube's existence as a foreign object that may lead to side effects such as nerve compression or inflammation. And despite encouraging primary results from contemporary studies, there are still concerns regarding the uncertainty surrounding these tubes functional results. The Functional impact of axonal misdirection remains the most critical issue that needs re-evaluation [9-12,29-33].

The application of vein wrap around peripheral nerve to isolate the interior microenvironment of the nerve creating a shield-like barrier between the nerve and its surrounding scarring in cases of nerve entrapment proved its efficacy in experimental trials that challenged peripheral nerve surgeons to adopt this modality extensively in clinical practice. Vein wrapping typically results in substantial improvements in the symptoms related to scar entrapment of peripheral nerve [14,16,34].

Clinical reproducibility of the vein wrap around peripheral nerves mandate a preliminary experimental study to evaluate the histological differences between wrapped and unwrapped repaired peripheral nerve, as well as the effectiveness of these wraps to shield the site of repair from the surrounding scar tissue during the phase of nerve regeneration.

In this study, creation of an adhesion model around repaired peripheral nerves using a sclerosing agent provided a reliable method to a comprehensive evaluation of the vein wrap around the site of repair. Also the comparison with the control side revealed a remarkable difference between the wrapped and un-wrapped side in regards of the invasion of the repair site with scar tissue and its effect on axonal regeneration.

The results of this study showed effective prevention of scar tissue invasion in the vein-wrapped groups, when compared to the control non-vein wrapped groups regardless the use sclerosant material.

The technique of vein wrapping around the site of repair of an injured peripheral nerve appears to be safe, feasible, and reliable. The short-term

results, as evaluated histologically, showed effective shielding of the repaired peripheral nerve from invasion by the surrounding scar tissue created by the adhesion model. The results support further experimental study with long-term evaluation of the vein wrap on the regenerating nerve fibers and their functional recovery.

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