Fibrin Glue Versus Traditional Suturing in Treatment of Tibial Nerve Injury in Dogs: An Experimental Study

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Abstract

Recently, the most widely utilized strategies for repairing peripheral nerves are micro-sutures and fibrin glue, while the findings of experimental studies on both techniques have generated a debate. This prospective experimental trial aimed to evaluate the effectiveness of the fibrin glue and micro-suturing procedure in repairing peripheral nerves. In this study, eighteen male mongrel dogs in apparently good health condition were divided into two equal groups (n = 9). Group A, the tibial nerve was cut and healed using micro sutures. Group B, the tibial nerve was cut and mended using fibrin glue. Lameness evaluations of all dogs in both groups after repair did not reveal any statistically significant differences after 12 weeks. Group B (fibrin glue) had a much shorter operation time, but with a higher cost.

Regarding clinical recovery of limb function following nerve injury, fibrin glue and micro sutures are equivalent. For certain peripheral nerve repairs, fibrin glue can be an acceptable substitute. It is also effective in cases where several cable nerve grafts are required, many peripheral nerve lesions are present, or suture application is technically challenging or impossible.

Key words: fibrin glue, nerve injury, dog, peripheral nerve repair, tibial nerve.

Introduction

In veterinary practice, neurological and neuromuscular injuries are challenging clinical problems (***Fuchs et al., 2022***). Animals of any age can have traumatic nerve injuries, which are quite prevalent in small animal medicine. Limb rescue surgery is required when there is damage to the nerve branches in the fore and hind limbs. Veterinarians make decisions based on their knowledge of the causes of nerve damage and available treatment options in order to prevent irreparable nerve damage (***Anatolitou et al., 2012***).

Peripheral nerve injuries (PNI), which are usually caused by acute traumatic compression or crushing, limit function by causing myelin degeneration, denervation of muscle, and loss of axonal integrity. PNI is occasionally reversible, and researches are being done to identify treatments that hasten healing from these injuries. It is difficult to diagnose and treat these conditions, and it is difficult to predict which injuries may experience improved recovery (***Govindappa et al., 2020***).

Even after surgical nerve repair, dogs with PNI, particularly those with severe injury, frequently experience inadequate nerve regeneration and insufficient functional recovery, which results in partial or complete loss of motor, sensory, and autonomic function in the implicated body segments. Peripheral axons can regenerate after a nerve injury and provide a correct pathway, but without a correct pathway, the wounded nerve's proximal end may develop a neuroma and scar tissue, which will prevent the regenerated neuron from growing and result in insufficient functional recovery of PNI (***Elgazzar et al., 2007).***

An ideal nerve repair would prevent foreign body reactions, be minimally stressful to the previously damaged tissues, and quickly restore the normal endo-neural environment (***Lundborg, 2000*****).** For reconstruction following peripheral nerve injury, the use of suture combined with heterologous fibrin sealant has been emphasized, with the benefit of being safe for clinical application (***Leite et al., 2019***).

Suture application necessitates several passes of the needle into the fragile epineurium, which eventually caused trauma and structural disruption. When nonabsorbable suture material is present, a foreign body reaction occurs, causing granulomas and scar formation. End-to-end neurorrhaphy is the gold standard for reconstruction in this type of injury (***Rafijah et al., 2013; Wu et al., 2014***), Although the application of sutures may cause inflammatory reactions, such as the development of granulomas and neuromas, and chronic pain (***Chimutengwende-Gordon and Khan, 2012; Nakamura et al., 2004*****).**

Reducing the number of reconstruction points, was applied as an alternative to decrease the harm caused by suture use (***Biscola et al., 2017***). Due to its ability to adhere to tissues, fibrin glue is an excellent method in this regard and has been utilized extensively in the medical industry since the 1970s ***(Isaacs et al., 2008***).

Furthermore, sutures are only placed on a regular basis within the epineurium, leaving gaps that allow inflammatory cells to invade, and mediators necessary for nerve regeneration to escape ***(Johnson et al., 2007*).** These issues have prompted researchers to look for alternative methods of coapting severed nerves. Non-suture techniques, particularly fibrin glue, have recently received attention as a means of removing sutures from the repair site ***(Elgazzar et al., 2007; Johnson et al., 2007*)**.

The main objective of this study was to compare the efficacy of fibrin glue versus the micro-suturing technique in peripheral nerve repair.

Materials and methods

The Faculty of Veterinary Medicine's Institutional Animal Use and Care Committee reviewed and approved all experimental procedures. In this study, eighteen male monogrel apparently healthy dogs were divided into two equal groups: Group A, the tibial nerve was transected and sutured with micro-sutures, and Group B, the tibial nerve was transected and mended with fibrin glue (fibrin sealant consists of Human Thrombin 1000 IU/ml and Human Fibrinogen 6.5 g/dl produced by Cairo Medical Center Blood Bank) (**Fig. 1**).

Food was stopped 6-8 hours before surgery. Each dog was pre-medicated 15 minutes prior to induction of general anesthesia with IM injections of atropine sulphate at 0.1 mg/kg and chlorpromazine hydrochloride (Neurazine®) at 1 mg/kg **(*Hall et al., 2001*)**.

The operation site (caudo-lateral aspect of the thigh, upper to the stifle) was clipped, shaved, and disinfected with povidone iodine solution (Betadine®), and general anesthesia was administered via IV injection of thiopental sodium 2.5 percent solution until the main reflexes were absent. Except for the operation site, the animal was draped in a sterile towel. During surgery, a balanced electrolyte solution (Sodium Chloride 0.9 percent) was administered in a dose of 10 ml/kg/hr. Surgical exposure was performed in accordance with **(*Denny and Butterworth, 2008*)**. A lateral skin incision was made from below the greater trochanter at the mid-thigh level to the stifle to expose the sciatic nerve bifurcation. Just cranial to the biceps femoris, the fascia lata was incised. Sharp dissection between the vastus lateralis and biceps femoris muscles revealed the sciatic nerve bifurcation to tibial and fibular nerves, then tibial nerve was transected with a sharp blade.

In group A, the nerve was repaired with epi-neural micro-sutures using polyproline 8/0 with the aid of surgical loop, whereas in group B, the transected nerve was glued with fibrin glue applied to the epineurium of the nerve's proximal and distal stumps. The stumps were accurately coated and a maximum contact area between nerve ends was obtained. The glue was applied as a cuff rather than directly to the section surface. The nerve ends were stabilized for two minutes before the adjacent soft tissues were sutured and the surgical wound was closed routinely in both groups as shown in (**Fig. 2)**.

Postoperative evaluation

During the study period, dogs were clinically observed daily to record any postoperative complications. Our outcome measures included assessing the lameness score of all dogs in both groups one day post-operatively then at two, four, eight and twelve weeks post-operatively to evaluate functional disorders of the affected limb while walking.

Lameness assessment

Lameness was evaluated on a scale from 0 to 4 as showed at (**Table 1**) according to **(*Jandi et al., 2007*)**.

Fig. 1: Fibrin glue package.

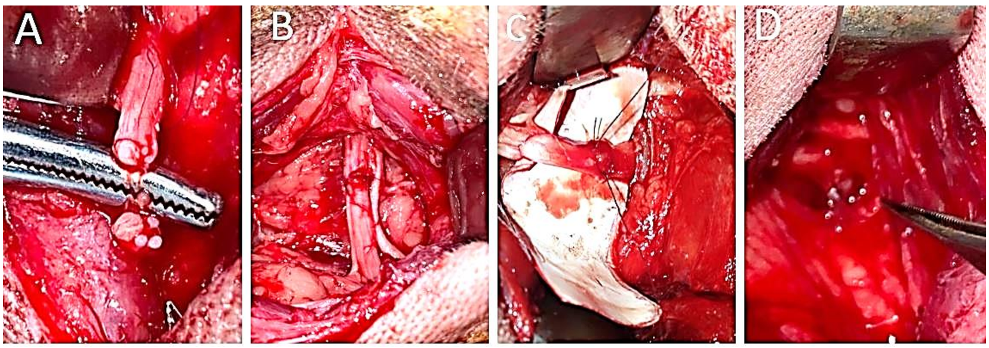

Fig. 2: A: complete transection of tibial nerve, B & C: Tow dogs from Group A with sutured nerve, D: Dog from Group B with applied fibrin glue

Table 1: *Lameness Scale*

Degree	Description
0	Normal attitude in station and walking without lameness.
1	Mild lameness or minor gait abnormality.

Results

Lameness assessment

The results in table 2 and figure 3, showed that, there are non-significant differences between groups A and B at different times for lameness scale, while between time interval for each group. Statistical analysis showed significant difference between time intervals at P < 0.05 in each group.

One day postoperatively, 100% for dogs had non-weight-bearing lameness (score-4) in the two groups.

After 2 weeks, in group A, 60% of dogs had non-weight-bearing lameness (score-4) and 40% had sever weight-bearing lameness (score-3), while in group B 40% of dogs had non-weight-bearing lameness (score-4) and 60% had sever weight-bearing lameness (score-3).

After 4 weeks, 80% of dogs had severed weight-bearing lameness (score-3) and 20% had moderate lameness or gait abnormality (score-2), dogs had weight-bearing lameness due to paralysis of muscles in the caudal compartment of the crus and dogs showed limping, dropped hock, external rotation of the footpad, overextended digits, knuckling of the digits and walking instability were observed in group A and B.

After 8 weeks, in group A, 90% of dogs had moderate lameness or gait abnormality (score-2) and 10% had mild lameness or minor abnormality (score-1) with dogs showed limping, dropped hock, and walking instability, while in group B, 50% of dogs had moderate lameness or gait abnormality (score-2) and 50 % had mild lameness or minor abnormality (score-1) dogs showed limping, dropped hock, and walking instability.

Finally, after 12 weeks, in group A, 10% of dogs had normal attitude in station and walking without lameness (score-0), 70% had mild lameness or minor abnormality (score-1) and 20% had moderate lameness or gait abnormality (score-2). While in group B, 10% of dogs had normal attitude in station and walking without lameness (score-0), 80% had mild lameness or minor abnormality (score-1) and 10% had moderate lameness or gait abnormality (score-2).

Table 2: *Lameness assessment findings (Comparison between groups and time intervals)*

	scores	Post		2w		4w		8w		12w		P values
		N	%	N	%	N	%	N	%	N	%	
Group A	0									1	10%	<0.001**
	1							1	10%	7	70%	
	2					2	20%	9	90%	2	20%	
	3			4	40%	8	80%					
	4	10	100%	6	60%							
Group B	0									1	10%	<0.001**
	1							5	50%	8	80%	
	2					2	20%	5	50%	1	10%	
	3			6	60%	8	80%					
	4	10	100%	4	40%							
P values		**1.00**		**0.383**		**1.00**		**0.57**		**0.739**		

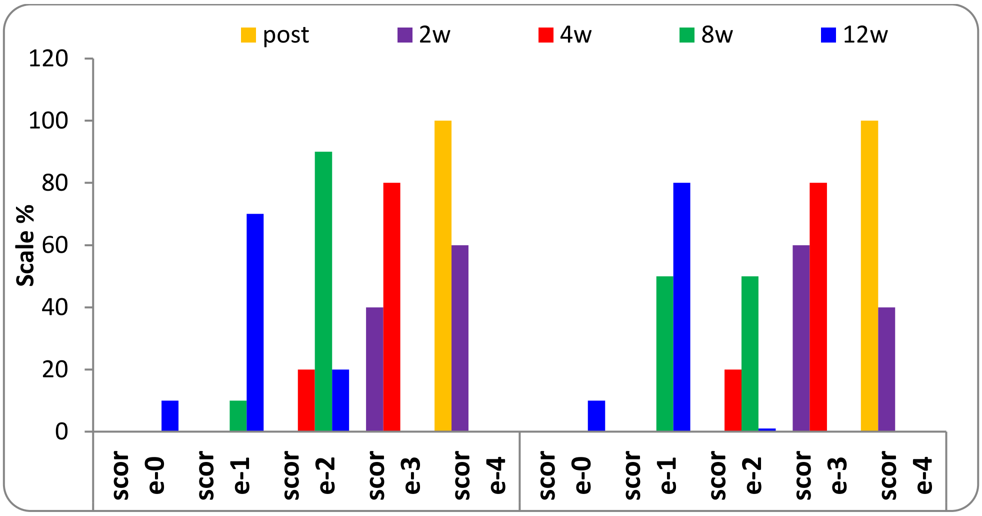

Fig. 3. Lameness score findings curve

Discussion

Accurate adaptation and apositioning of the various fascicles are critical in peripheral nerve microsurgery. Techniques such as epineural, perineurial, and interfascicular have been advocated. Microsurgical magnification and a better understanding of anatomy have improved the outcomes **(*Orgel, 1984*)**. Suture placement has been thought to obstruct sprouting axons and compress blood supply to fascicles, impairing regeneration of transected nerve ends after repair **(*Šmahel et al., 1987*).** Furthermore, the formation of suture granuloma inhibits myelin and axonal regeneration. These factors resulted in the development of various tissue sealants for atraumatic tissue repair. Fibrin glue is one of these materials which is the only natural sealant ***(Martins et al., 2005; Ornelas et al., 2006b; Elgazzar et al., 2007; Johnson et al., 2007; Sameem et al., 2011*)**. Theoretically, fibrin glue repair technique has some disadvantages, such as penetration of the adhesive through the suture line and distinct connective tissue reaction induced by glue, which cause nerve compression. However, ***Palazzi et al., (1995)*** demonstrated that fibrin glue is a sealant and not a nerve barrier. There is no appreciable clot retraction because the sealant does not contain thrombocytes. In this study, neither anastomotic dehiscence nor neuroma formation has been found in any of the nerves repaired by either technique. This has been also reported in the literature **(*Ornelas et al., 2006a; Anani and El-Sadek, 2009*).** However, **(*Wieken et al., 2003*)** stated that a tension-free repair is necessary with the use of glue, but that gapping may occur, limiting the use of the agent in promoting re-neurotization. We agree with them that tension free repair is a fundamental factor in preventing dehiscence in any technique used for nerve repair.**(*Choi et al., 2004*)** reported that stitches may shift toward the center of the cross-section and cause a foreign body reaction. We believe that this might be true if sutures were put under tension in agreement with **(*Anani and El-Sadek, 2009*)**.

This study showed no difference between both groups regarding the recovery of the nerve clinically on the operated dogs. This means that whatever the method used for nerve coaptation, the results will be satisfactory if the rules of nerve repair are followed and this agreed with (***Rowshan et al., 2004***). Good orientation of both nerve ends, good trimming of the unhealthy nerve ends, removal of any interfascicular blood clots, gentle nerve handling and repair without any tension are the crucial factors in obtaining satisfactory results in nerve repair rather than the method of repair, in accordance with **(*Rowshan et al., 2004; Anani and El-Sadek, 2009*)**. In the view of the similar results of both techniques, the crucial factor in the choice of either of them will be the operative time and costs.

Sulaiman and Kline (2006) and Anani and El-Sadek (2009) stated that, the spent time of nerve repair using fibrin glue was lower than that of microsuture technique. However, the costs were higher, and these were noticed in this study.

Conclusion

Based on the findings of this study, we can conclude that fibrin glue is a new trend for regeneration of nerve injury achieving easy non-invasive surgical maneuver rather than the invasive traditional suturing technique.

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الملخص العربي

صمغ الفبرين مقابل الخياطة التقليدية في علاج إصابة عصب قصبة الساق في الكلاب: دراسة تجريبية

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في الآونة الأخيرة، أصبحت تقنية الخياطة التقليدية باستخدام الخيوط الجراحية الدقيقة وتقنية استخدام صمغ الفيبرين من أكثر الاستراتيجيات المستخدمة على نطاق واسع لإصلاح اصابات الأعصاب الطرفية، وقد أثارت نتائج الدراسات التجريبية على كلا التقنيتين جدلاً واسعا عن ايهما أفضل. كان الهدف من هذه التجربة هو تقييم فاعلية استخدام صمغ الفيبرين وإجراء الخياطة التقليدية باستخدام الخيوط الجراحية الدقيقة في إصلاح الأعصاب الطرفية. تم استخدام ثمانية عشر كلبا (ذكور) في حالة صحية جيدة وتقسيمهم إلى مجموعتين متساويتين (ن = 9). في المجموعة أ، تم قطع وتوصيل عصب قصبة الساق باستخدام الخيوط الجراحية الدقيقة. وفي المجموعة ب، تم قطع عصب قصبة الساق وإصلاحه باستخدام صمغ الفيبرين. ثم تم تقييم درجة العرج لجميع الكلاب في كلا المجموعتين بعد اجراء العمليات. وقد اوضحت النتائج عدم وجود أي فروق ذات دلالة إحصائية بين المجموعتين خلال فترة التجربة (12 أسبوع) بينما استغرقت العمليات في المجموعة ب (صمغ الفيبرين) وقت أقصر بكثير من العمليات في المجموعة أ. بالنسبة لبعض حالات إصلاح الأعصاب الطرفية، يمكن أن يكون غراء الفيبرين بديلاً مقبولاً. كما أنه فعال أيضًا في حالات وجود العديد من إصابات الأعصاب الطرفية، أو في حالة صعوبة استخدام تقنية الخيوط الدقيقة.