IJMA

International Journal of Medical Arts

Volume 6, Issue 4, April 2024

P- ISSN: 2636-4174
E- ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Plastic Surgery]

Original Article

The Role and Efficacy of Fibrin Glue in Repair of Peripheral Nerves; Meta-Analysis Study

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Article information

Received: 16-06-2023

Accepted: 27-03-2024

DOI: 10.21608/IJMA.2024.218070.1711.

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Citation: Helmy Y, Hassan MA, Youssif SH. The Role and Efficacy of Fibrin Glue in Repair of Peripheral Nerves; Meta-Analysis Study. IJMA 2024 April; 6 [4]: 4323-4328. doi: 10.21608/ IJMA.2024.218070.1711.

ABSTRACT

Background: Fibrin glue has gained popularity in the field of peripheral nerve surgery as a substitute for traditional microsurgical suture repair. Fibrin glue began to have benefits for nerve reconstruction in the form of technical simplicity, reduced tissue manipulation, and quicker procedure timeframes. Although fibrin glue appears to be a promising substitute for traditional microsurgical repair, additional knowledge regarding the results of nerve healing is crucial.

The aim of the work: This meta-analysis aimed to assess the technical efficiency and outcome of Fibrin glue in the repair of peripheral nerves.

Methods: Clarivate -Scopus, PubMed, Cochrane, and Rigster TCT listed papers were searched for literature. EKB was one of many search engines employed by this investigation to download articles from the previous year.

Results: Seven studies assessed sensory recovery and showed that there were insignificant differences between these studies as patients had excellent sensory recovery [p-value 0.0735]. Seven studies assessed motor recovery and showed that there were significant differences between these studies as patients had good motor recovery [p-value <0.0001].

Conclusion: In this study, a complete assessment of the material on fibrin glue for peripheral nerve restoration is conducted. According to the study's findings, suture repairs and repairs using fibrin glue may both result in nerve regeneration, although repairs using fibrin glue take less time to complete.

Keywords: Peripheral nerve injury; Fibrin glue; Suture; Nerve repair; Nerve regeneration.

INTRODUCTION

Despite these early observations, fibrin glue wasn't widely used for peripheral nerve healing until the 1970s, when it was made commercially available [1]. The practice of using tissue adhesives to heal peripheral nerves is not new; accounts of its application date back to the 1940s. Before this, the norm for mending peripheral nerves was microsurgical suturing, despite evidence that it may induce damage and inflammatory reactions that alter results and may greatly impair survival [2].

When compared to sutures, fibrin is significantly quicker and easier to use during surgical procedures. Its role as a physiological component of tissue repair prevents nerve regrowth and does not cause a foreign body reaction [3]. Additionally, because the fibrin glue approach is less stressful than micro suturing, it results in less inflammation, fibrosis, and granuloma formation. It might also help disperse tensile forces more evenly over the healing site [4].

Due to its various benefits, fibrin glue has considerably increased the quality of peripheral nerve repairs. When new developments occur, fibrin glue and its alternatives will likely play an important role in nerve reconstruction [5, 6].

This meta-analysis study addressed carefully the technical efficiency and outcome of Fibrin Glue in the repair of peripheral nerves.

METHODS

We performed a systematic review of the subject according to the PRISMA guidelines

Literature search strategy

Clarivate -Scopus, PubMed, Cochrane, and Register TCT listed papers were searched for literature. For this investigation, the publications from the previous year were downloaded using a variety of search engines, including EKB. The following keywords were used for search strategy formation [Peripheral nerve repair, nerve graft, nerve reconstruction, neurorrhaphy, and fibrin glue].

Eligibility criteria

Screening of the studies was done in two steps: 1] title and abstract screening, 2] Full-text screening. We included all RCTs, retrospective and prospective studies match with the following inclusion criteria:

Population: Patients with peripheral nerve injury.

Intervention: Fibrin glue.

Comparator: Any comparator.

Outcomes: DASH score, sensory recovery, motor recovery and complications.

All articles that were not meeting the inclusion criteria were excluded. Also, exclusion occurred when the data researched are lacking or unreliable in the studies.

Data extraction

It was carried out methodically by two independent reviewers. Disagreements were resolved by a third senior author. The effectiveness of its repair compared to other methods of repair was examined in this meta-analysis study, which also examined peripheral nerve injuries, types of repair, fibrin glue preparation, and the role of fibrin glue in repairing peripheral nerves.

Data analysis

For outcomes that constitute dichotomous data, the frequency of events and the total number of patients in each group were pooled as risk ratio between the two groups in the Mantel Hanzel [M-H] random-effect model. All statistical analyses were done by Stata/MP version 17 for Microsoft Windows. Statistical heterogeneity among studies was evaluated by the Chi-square test [Cochrane Q test]. Then, the chi-square statistic, Cochrane Q, was used to calculate the I-squared according to the equation:

$$I2=\left(\frac{Q-df}{Q}\right)x100\%.$$

A Chi-square P value less than 0.1 was considered significant heterogeneity. I-square values ≥ 50% were indicative of high heterogeneity.

RESULTS

In this meta-analysis, 181 suitable articles were found during the literature search. After applying inclusion and exclusion criteria, we found that the total number of articles that might be included was 16 studies, nine of which were animal experiments, which were excluded. Seven studies were a human study were included in the final analysis [Figure 1]. The mean follow-up period in the three studies was 20.44 months as shown in Table 1. DASH score was assessed by 2 studies with insignificant differences after treatment p-value of 0.6414 [Table 2].

Seven studies assessed sensory recovery and showed that there were insignificant differences between these studies as patients had excellent sensory recovery p-value of 0.0735 [Table 3]. All studies assessed motor recovery and showed that there were significant differences between these studies as patients had good motor recovery p-value <0.0001 [Table 4].

All studies assessed motor recovery and showed that there were significant differences between these studies as patients had no recovery p-value of 0.3552. Table [5] and [Figure 2]. Seven studies assessed motor recovery and showed that there were insignificant differences between these studies as patients had complications p-value of 0.21791 [Table 6].

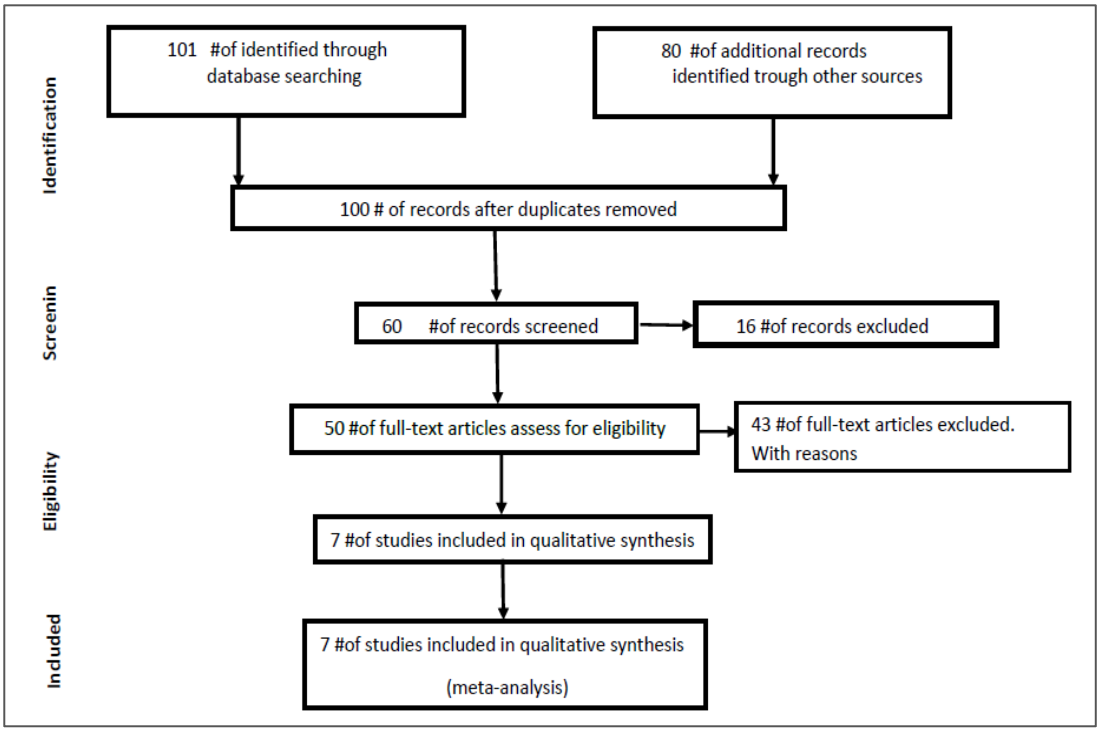

Figure [1]: Prisma Flow diagram

Table [1]: Follow-up period

Author	follow up\mn
Sallam *et al.* [7]	15.2
Armaiz Flores and Wang [8]	28.2
Hweidi *et al.* [9]	18

Table [2]: Meta-analysis for DASH

Study	Estimate	Standard Error	95% CI	Z	p
Schwaiger *et al.* [10]	29.600	28.00	-25.280 – 84.480		
Flores [11]	43.200	8.30	26.932 – 59.468		
Total [fixed effects]	42.101	7.958	26.504 – 57.699	5.291	<0.001
Total [random effects]	42.101	7.958	26.504 – 57.699	5.291	<0.001
	Test for heterogeneity				
Q	0.2169				
DF	1				
Significance level	0.6414				
I^2 [inconsistency]	0.00%				
95% CI for I^2	0.00 – 0.00				

Q: Total variance for heterogeneity. **I^2:** Observed variance for heterogeneity. **CI:** Confidence interval [LL: Lower limit–UL: Upper Limit].

Table [3]: Meta-analysis for excellent sensory recovery

Study	Total number	Event	Event rate [%] [Proportion]	95% CI of rate [%]
Sallam *et al.* [7]	43	0	0.000	0.000 – 8.221
Schwaiger *et al.* [10]	12	0	0.000	0.000 – 26.465
Armaiz Flores and Wang [8]	20	0	0.000	0.000 – 16.843
Hweidi *et al.* [9]	15	0	0.000	0.000 – 21.802
Wolfe *et al.* [12]	20	0	0.000	0.000 – 16.843
Flores [11]	5	2	40.000	5.274 – 85.337
Aberg *et al.* [13]	6	1	16.667	0.421 – 64.123
Total [fixed effects]	**121**		2.263	0.451 – 6.580
Total [random effects]	**121**		3.428	0.337 – 9.563
Test for heterogeneity				
Q	11.5245			
DF	6			
Significance level	0.0735			
I^2 [inconsistency]	47.94%			
95% CI for I^2	0.00 – 78.01			

Q: Total variance for heterogeneity. **I^2:** Observed variance for heterogeneity. **CI:** Confidence interval [LL: Lower limit–UL: Upper Limit].

Table [4]: Meta-analysis for good motor recovery

Study	Total number	Event	Event rate [%] [Proportion]	95% CI of rate [%]
Sallam *et al.* [7]	43	0	0.000	0.000 – 8.221
Schwaiger *et al.* [10]	12	0	0.000	0.000 – 26.465
Armaiz Flores and Wang [8]	20	2	10.000	1.235 – 31.698
Hweidi *et al.* [9]	15	10	66.667	38.380 – 88.176
Wolfe *et al.* [12]	20	18	90.000	68.302 – 98.765
Flores [11]	5	5	100.000	47.818 – 100.000
Aberg *et al.* [13]	6	0	0.000	0.000 – 45.926
Total [fixed effects]	**121**		22.186	15.323 – 30.379
Total [random effects]	**121**		32.438	4.185 – 71.340
Test for heterogeneity				
Q	116.8509			
DF	6			
Significance level	<0.0001			
I^2 [inconsistency]	94.87%			
95% CI for I^2	91.65 – 96.84			

Q: Total variance for heterogeneity. **I^2:** Observed variance for heterogeneity. **CI:** Confidence interval [LL: Lower limit–UL: Upper Limit].

Table [5]: Meta-analysis for no recovery

Study	Total number	Event	Event rate [%] [Proportion]	95% CI of rate [%]
Sallam *et al.* [7]	43	3	6.977	1.463 – 19.061
Schwaiger *et al.* [10]	12	0	0.000	0.000 – 26.465
Armaiz Flores and Wang [8]	20	4	20.000	5.733 – 43.661
Hweidi *et al.* [9]	15	0	0.000	0.000 – 21.802
Wolfe *et al.* [12]	20	2	10.000	1.235 – 31.698
Flores [11]	5	0	0.000	0.000 – 52.182
Aberg *et al.* [13]	6	0	0.000	0.000 – 45.926
Total [fixed effects]	**121**		7.903	3.874 – 14.009
Total [random effects]	**121**		7.793	3.556 – 13.491
Test for heterogeneity				
Q	6.6423			
DF	6			
Significance level	0.3552			
I^2 [inconsistency]	9.67%			
95% CI for I^2	0.00 – 74.07			

Q: Total variance for heterogeneity. **I^2:** Observed variance for heterogeneity. **CI:** Confidence interval [LL: Lower limit–UL: Upper Limit].

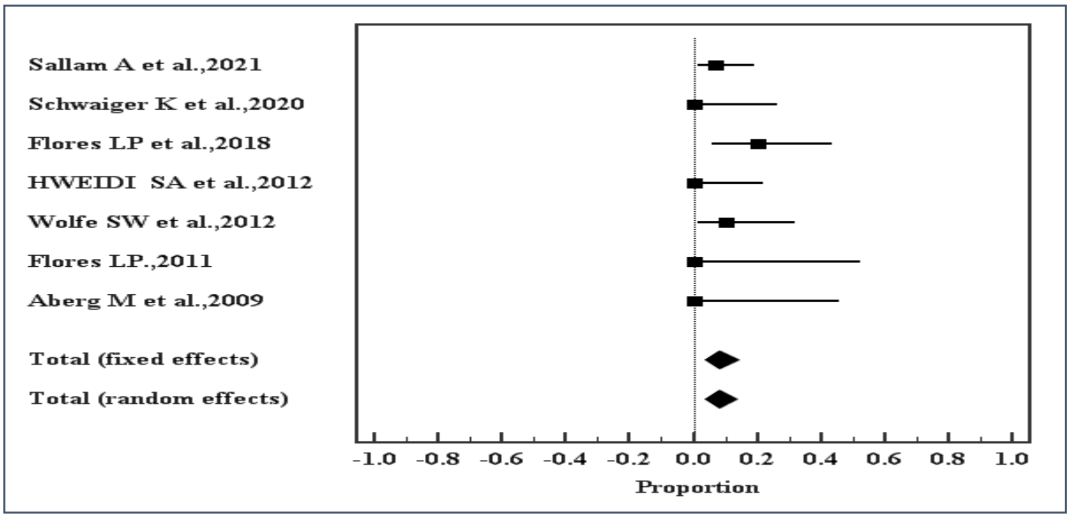

Figure [2]: Forest plot for no recovery [Motor recovery]

Table [6]: Meta-analysis for complications

Study	Total number	Event	Event rate [%] [Proportion]	95% CI of rate [%]
Sallam *et al.* [7]	43	6	13.953	5.298 – 27.932
Schwaiger *et al.* [10]	12	0	0.000	0.000 – 26.465
Armaiz Flores and Wang [8]	20	0	0.000	0.000 – 16.843
Hweidi *et al.* [9]	15	0	0.000	0.000 – 21.802
Wolfe *et al.* [12]	20	0	0.000	0.000 – 16.843
Flores [11]	5	0	0.000	0.000 – 52.182
Aberg *et al.* [13]	6	0	0.000	0.000 – 45.926
Total [fixed effects]	**121**		4.854	1.841 – 10.142
Total [random effects]	**121**		4.080	0.926 – 9.328
Test for heterogeneity				
Q	8.2861			
DF	6			
Significance level	0.2179			
I^2 [inconsistency]	27.59%			
95% CI for I^2	0.00 – 68.70			

Q: Total variance for heterogeneity. **I^2:** Observed variance for heterogeneity. **CI:** Confidence interval [LL: Lower limit–UL: Upper Limit].

DISCUSSION

Our study showed that; there were 121 total cases; the majority of them were men, and the average age was 38.3 years. In three investigations, the average follow-up time was 20.44 months.

According to **Sallam *et al.*** [7] the bulk of the population they looked at was made up of men, with a mean age of 36. In **Armaiz Flores and Wang** [8], the mean age of the patients was 28 years. The mean time from injury to intervention was 4.6 months, and the mean follow-up length was 28.2 months. Regarding the side of affection, 1 of the 52 instances involved a bilateral ailment, while 17 involved a left-side ailment. In terms of the nerves affected, these include the ulnar, median, combined median and ulnar, Sural, radial, axillary, and suprascapular nerves. The mean period from injury to intervention in **Wolfe *et al.*** [12], was 5.2 months. The ulnar nerve, axillary nerve, suprascapular nerve, and sural nerve were the afflicted nerves. Additionally, **Aberg *et al.*** [13], from 8 showed that the lesion affected the ulnar, median, and ulnar and median nerves.

In the study in our hands, the DASH score was assessed by 2 studies with insignificant differences after a treatment p-value of 0.64. Five of the six patients who were followed up on in the study by **Schwaiger *et al.*** [10], had a DASH score of 0.05. One patient received a 50. It was anticipated that healthy people of the same age should have a DASH score between 2.23 and 17.87. Between the measured and predicted DASH scores, there were no statistically significant differences [$p > 0.05$]. Moreover, **Flores** [11] found no genuinely critical varieties between the Scramble score before and following treatment. As per the concentrate by **Hweidi *et al.*** [9], tangible recuperation after fringe nerve wounds treated with a fibrin stick was 100 % [15 out of 15 nerve components], 80% [12 out of 15 patients] had great tactile recuperation, and 20% [3 out of 15 patients] had fair tangible recuperation. As per **Sallam et al** [7], 24 of 42 patients in the miniature stitch gathering and 26 of 43 patients in the fibrin stick bunch both experienced valuable tactile recuperation [P, .76].

Concerning the mean % recuperation of grasp and squeeze qualities and Michigan Hand Result scores, the two gatherings were tantamount, as indicated by **Sallam *et al.*** [7], 63 exchanges [17 patients] were accessible for a 2-year follow-up assessment in the **Wolfe *et al.*** [12], preliminary.

Every one of the 10-nerve course-based moves showed clinical improvement and electromyographic reinnervation at two years. Of the 20 exchanges conveyed managed without conductors, clinical recuperation was found in 18 of them. Moreover, neither of the treatments was believed to be conceivable or presumably related to any un-favourable occasions or major antagonistic occasions, as per the concentrate by **Aberg *et al.*** [13].

In the **Sallam *et al.*** [7] study, postoperative issues happened in 26% of the 43 patients who got fibrin sticks contrasted with 8% of the 42 patients who got micro sutures. Two patients in the fibrin stick bunch detailed shallow injury diseases, and four patients had fixed finger irregularities because of delicate tissue contracture. Two patients in the miniature stitch bunch experienced shallow injury contaminations, and six patients had long-lasting irregularities.

Conclusion: This meta-analysis study showed that fibrin glue could be a reasonable alternative for microsurgery suturing in nerve repair. It has a similar outcome; however, it may carry the following advantages being quicker, Due to its physiological role in tissue repair, it doesn't inhibit nerve regeneration or create foreign body reactions. Its atraumatic nature also contributes to decreased inflammation, fibrosis, and granuloma development. It also increases the distribution of tensile force over the repair site.

Conflict of interest: None.

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International Journal of Medical Arts

Volume 6, Issue 4, April 2024

P- ISSN: 2636-4174
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