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Original Article

Effects of vitamin B12 adjuvant therapy on neural recovery after replantation of severed fingers

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Abstract: Objective: To investigate the effects of vitamin B12 adjuvant therapy on neural recovery after replantation of severed fingers. Methods: We retrospectively analyzed 227 patients admitted to our hospital for replantation of severed fingers. We performed the following tests on all patients 8 weeks after treatment: Return of finger pulp pressure sensation (25 g), touch sensation (4 g), pain sensation (4 g), and discrimination sensation (>5 mm). Results: A week after treatment, 7.6%, 15.1%, 32.8% and 44.5% of patients from the test group showed excellent, good, fair, and poor recovery, respectively. In contrast, 0.9%, 6.5%, 16.7% and 75.0% of patients from the control group showed excellent, good, fair, and poor recovery, respectively, ($P<0.05$). Three weeks after treatment, 18.5% of patients in the test vs. 8.3% of patients in the control group showed excellent recovery ($P<0.05$). Five weeks after treatment, 71.4% of patients in the test vs. 44.4% of patients in the control group showed excellent or good recovery ($P<0.05$). Eight weeks after treatment, neurological testing showed that in comparison of the test and the control group, return of pressure sensation was observed in 80.7% vs. 48.1% of patients, respectively; return of touch sensation was observed in 70.6% vs. 39.8% of patients, respectively; and return of pain sensation in 60.5% vs. 39.8% of patients, respectively. Conclusions: Vitamin B12 adjuvant therapy effectively improved the recovery of neurological function in fingers after replantation of severed fingers and should be promoted in clinical practice.

Keywords: Vitamin B12, severed finger replantation, finger nerves, adjuvant therapy

Introduction

Replantation of severed fingers is a surgical repair procedure used for the management of complete or incomplete severing of fingers from a patient's palm secondary to various kinds of trauma/injuries [1]. Replantation of severed fingers is associated with extremely stringent requirements in terms of the time lapse between the onset of the injury and the intervention. Additionally, surgery and surgeon-related factors might contribute to a delay in intervention, necessitating an amputation [2]. Rapid advances in modern medical science and technology have led to improvements in the management of severed fingers and replantation techniques. Based on the statistical results of studies performed by Tang et al. [3] approximately 72.2% of patients globally achieved good rehabilitation results following replantation surgeries performed annually for the management of severed fingers. Repairing and reconnecting the injured nerves constitute the most important components of the reconstructive procedure because they determine whether the severed finger can be restored to the pre-injury activity level [4]. Usually, replantation procedures may not completely and perfectly repair the damaged nerves in a severed finger. Therefore, post-replantation rehabilitation therapy of the finger nerves with maintenance of good nerve anastomosis has become an extremely important issue in clinical settings. Presently, neuro-regeneration therapy and/or administration of nerve-growth stimulants are being increasingly used as adjuvant therapy after limb amputation [5]. Related studies [6, 7] have shown that vitamin B12, as an endogenous neurotrophic factor, could effectively promote repair and reconstruction of injured nerves. Therefore, it is viewed as an extremely valuable adjuvant therapeutic agent in several replantation techniques. However, there is lack of relevant literature proving the efficacy of vitamin B12 to treat patients undergoing replantation of severed fingers.

Therefore, we retrospectively analyzed the data relating to patients who underwent replantation of severed fingers and were then treated with vitamin B12. We aimed to prove that vitamin B12 plays a useful role in the repair of nerves to restore neurological function in patients undergoing replantation of severed fingers. We believe that our study adds reliable and effective information to the literature to serve as a future reference for the clinical management of patients presenting with severed fingers.

Materials and methods

Patients

We retrospectively analyzed 227 patients who underwent replantation of severed fingers at Department of Hand Surgery, The First Hospital of Jilin University between March 2010 and October 2016. Our study group comprised 156 men and 71 women aged between 18 and 55 years, mean age 38.65±12.74 years. Based on the treatment administered after replantation of severed fingers, patients were divided into a test (routine treatment and additional vitamin B12 administration: 119 patients) and a control group (routine treatment alone: 108 patients).

Inclusion and exclusion criteria

Inclusion criteria: Those who underwent replantation of severed fingers at our hospital, those who were willing to cooperate with our hospital staff, those in whom complete medical records were available, and those aged between 18 and 55 years. Exclusion criteria: Those diagnosed with comorbidities such as cardiovascular and/or cerebrovascular diseases, upper respiratory and/or lower respiratory tract diseases/infections, those who were referred to other hospitals during treatment, and those in whom we detected unauthorized use of drugs and/or therapy not provided by our hospital. All patients included in this study signed the informed consent form.

Methods

All patients included in this study were hospitalized for treatment after replantation of severed fingers. Patients in the control group received routine nursing and postoperative treatment such as smoking and drinking restrictions, maintenance of room temperature, immobilization of the affected limb, and regular antibiotic injections to prevent infection, pain and other wound-related adverse conditions. In addition to the treatment administered to patients belonging to the control group, patients belonging to the test group also received vitamin B12 (intramuscular injection at a dose of 500 ug/injection), injected every 3 days over 3 weeks. Adverse drug reactions, recovery of finger function, and length of hospitalization were recorded in patients from both groups. Based on the results of a study performed by Sears et al. [5], sutures were removed 8 weeks after the replantation procedure had been performed. Finger pulp pressure sensation (25 g), touch sensation (4 g), pain sensation (4 g), and discrimination sensation (>5 mm) tests were performed in all patients to evaluate the differences in efficacy of intervention between the study groups.

Criteria for evaluation of recovery

Excellent recovery was defined as a flexible finger without pain or a tearing sensation, and showing active flexion and extension. Good recovery was defined as a relatively flexible finger without significant pain or tearing sensation, and showing slow active flexion and extension. Fair recovery was defined as inability to perform active and passive movements of the finger, and a fair degree of pain. Poor recovery was defined as inability to perform active and passive movements of the finger with obvious pain when exposed to external forces.

Statistical methods

SPSS 22.0 statistical software was used for statistical analysis of data. The length of hospitalization is presented as mean ± SD and was analyzed using the t test. Clinical characteristics of patients, evaluation of efficacy of the intervention, and results showing return of neurological function of the finger are presented as rates, and were tested using the χ^2 test. $P < 0.05$ was considered statistically significant.

Results

Clinical data

We compared gender, age, place of residence, marital status, cause, and severity of injury, as well as admission time (duration between the occurrence of injury and preliminary treatment

Table 1. Clinical data comparison in two groups of patients [n (%)]

	Test group (n=119)	Control group (n=108)	$\chi^{2(P)}$
Gender			4.084 (0.251)
Male	79 (66.4)	77 (71.3)	
Female	40 (33.6)	31 (28.7)	
Age (year old)			4.124 (0.238)
<30	59 (49.6)	49 (45.4)	
≥30	60 (50.4)	59 (54.6)	
Residence			2.534 (0.448)
City	76 (63.9)	68 (63.0)	
Countryside	43 (36.1)	40 (37.0)	
Marital status			2.227 (0.487)
Married	99 (83.2)	86 (79.6)	
Unmarried	18 (15.1)	19 (17.6)	
Widowed	2 (1.7)	3 (2.8)	
Injured			3.692 (0.345)
Cutting	45 (37.8)	39 (36.1)	
Mechanical	39 (32.8)	44 (40.7)	
Tearing	25 (21.0)	19 (17.6)	
Extrusion	10 (8.4)	6 (5.6)	
Fracture situation			3.887 (0.369)
Complete	39 (32.8)	30 (27.8)	
Incomplete	80 (67.2)	78 (72.2)	
Treatment time (hour)			4.078 (0.256)
<5	76 (63.9)	69 (63.9)	
≥5	43 (36.1)	39 (36.1)	
Smoking			3.707 (0.341)
Yes	69 (58.0)	62 (57.4)	
No	50 (42.0)	46 (42.6)	
Drinking			3.564 (0.375)
Yes	74 (62.2)	69 (63.9)	
No	45 (37.8)	39 (36.1)	
Exercise habits			2.051 (0.436)
Yes	58 (48.7)	49 (45.4)	
No	61 (51.3)	59 (54.6)	
Body weight (kg)			4.574 (0.249)
<70	66 (55.5)	59 (54.6)	
≥70	53 (44.5)	49 (45.4)	

in hospital), smoking, drinking, exercise habits, and body weight between the study groups to minimize the role of other factors that could have interfered with our results. No significant intergroup differences were observed in the factors that could have affected the study results except the use of different treatment methods (P>0.05), which enhanced the accuracy of our study results, as shown in **Table 1**.

Recovery

To compare the recovery of finger function between the study groups, we performed simple evaluation in patients at 1, 3 and 5 weeks after treatment. Our results have been presented as follows: A week after treatment, 7.6%, 15.1%, 32.8% and 44.5% of patients from the test group showed excellent, good, fair, and poor recovery, respectively. In contrast, 0.9%, 6.5%, 16.7% and 75.0% of patients from the control group showed excellent, good, fair, and poor recovery, respectively, (P<0.05), as shown in **Table 2**. Three weeks after treatment, 18.5% of patients in the test vs. only 8.3% of patients in the control group showed excellent recovery (P<0.05), as shown in **Table 3**. Five weeks after treatment, 71.4% of patients in the test vs. only 44.4% of patients in the control group showed excellent or good recovery (P<0.05). Moreover, several patients in the control group showed only fair (38.9%) and poor (22.2%) recovery, as shown in **Table 4**.

Nerve tests

To compare the recovery of neurological function of the fingers between the study groups, neurological tests assessing finger function were performed on all patients. Eight weeks after treatment, neurological testing showed that in comparing the test and the control group, return of pressure sensation was observed in 80.7% vs. 48.1% of patients, respectively; return of touch sensation was observed in 70.6% vs. 39.8% of patients, respectively; and return of pain sensation in 60.5% vs. 39.8% of patients, respectively. Recovery of neurological function of the fingers in the test group was significantly better than that observed in the control group (P<0.05). Only 2.5% of the patients in the test group showed development of adverse reactions at the wound (inflammation), whereas 15.7% of patients in the control group showed development of fever, purulence, and other adverse reactions (P<0.05). The length of hospitalization in the test (14.24±5.27 days) was significantly shorter than that observed in the control group (23.57±7.21 days, P<0.05), as shown in **Table 5**.

Discussion

The hand is an extremely important organ in the human body and plays an irreplaceable role

Table 2. Week 1 recovery in two groups of patients [n (%)]

Level	Test group (n=119)	Control group (n=108)	$X^{2(P)}$
Excellent	9 (7.6)	1 (0.9)	13.82 (0.039)
Good	18 (15.1)	7 (6.5)	14.05 (0.035)
General	39 (32.8)	18 (16.7)	15.37 (0.026)
Failed	53 (44.5)	81 (75.0)	16.52 (0.015)

Table 3. The third week of recovery in two groups of patients [n (%)]

Level	Test group (n=119)	Control group (n=108)	$X^{2(P)}$
Excellent	22 (18.5)	9 (8.3)	15.77 (0.026)
Good	29 (24.4)	16 (14.8)	14.29 (0.034)
General	32 (26.9)	41 (38.0)	11.32 (0.042)
Failed	36 (30.3)	42 (38.9)	9.86 (0.057)

Table 4. Week 5 recovery of patients in both groups [n (%)]

Level	Test group (n=119)	Control group (n=108)	$X^{2(P)}$
Excellent	42 (35.3)	21 (19.4)	14.12 (0.037)
Good	43 (36.1)	27 (25.0)	10.67 (0.045)
General	27 (22.7)	42 (38.9)	10.92 (0.042)
Failed	7 (5.9)	24 (22.2)	16.07 (0.020)

in several aspects. Finger injuries primarily include mechanical cutting and crush injuries caused by use of fingers at the workplace [8]. In modern times, the equipment that needs to be manually operated at different workplaces is gradually being replaced by integrated computer settings. However, there exist a few risks associated with the use of machines/equipment. Moreover, with an increasing number of vehicles in use, an increasing number of patients are presenting to our hospital with severed fingers caused by car accidents. Trauma-induced limb severing usually includes complete and/or incomplete severing of the limbs [9], which is accompanied by peripheral nerve injury, and the best treatment for this condition is replantation surgery [2, 10]. Although reconstruction of severed limbs is not very difficult, it is extremely difficult to repair and reconnect severed nerves [11]. Anatomically, fingers demonstrate an extremely complicated and dense nerve distribution in the human body [12]. Repair of damaged nerves and proper restoration of finger flexibility following the reconnection of severed fingers and the restoration of pre-injury finger shape, is a topic that lends itself to comprehensive clinical studies/research. Based on the popularity of neurotrophic drugs used as adjuvant therapy in patients undergoing replantation [13], we hypothesized in this study that vitamin B12, a representative neurotrophic agent, could achieve good results in those undergoing nerve repair after replantation performed for severed fingers. In this study, patients were screened in strict accordance with the inclusion and exclusion criteria and were treated in strict accordance with the operating guidelines, changes observed/reported by patients during treatment were closely monitored and recorded, and the most advanced statistical software was used for data analysis. The objective of this study was to prove our hypothesis and provide a reference and guidelines for future clinical studies.

The results of this study show that the use of vitamin B12 as adjuvant therapy is superior to the use of routine treatment in terms of recovery of neurological function of the severed and replanted finger, adverse reactions, length of hospitalization, and efficacy of the intervention. The differences between these treatment approaches could be attributed to the effects of vitamin B12. Vitamin B12, as a cobalt-containing water-soluble vitamin B, can participate in synthesis and metabolism of several compounds such as nucleic acid, methionine, choline, fat, and sugar in the human body, and demonstrates a strong cohesive action to maintain the integrity of erythrocytes and myelination of nerves [14]. At the molecular level, structurally, the cobalt atom linked to the methyl group in the center of the methyl vitamin B12 actively promotes conversion of the methyl group and synthesis of nucleic acid and protein [15].

Additionally, vitamin B12 can be used as an auxiliary enzyme in the synthesis of amino acids to serve as a methyl donor during the conversion of homocysteine into methionine. It can provide the methyl group for thymine synthesis, and participate in synthesis of DNA [16, 17]. As an active participant in the synthesis of axonal structural proteins present in nerve cells, methyl vitamin B12 stimulates the regeneration of axons, and easily enters neuronal organelles, thereby facilitating and regulating the division of Schwann cells around neurons and the synthesis of neuro lecithin to promote the recovery

Table 5. Finger nerve test results in two groups of patients [n (%)]

	Test group (n=119)	Control group (n=108)		P
Pressure feel	96 (80.7)	52 (48.1)	χ^2=13.47	0.012
Tactile	84 (70.6)	42 (38.9)	χ^2=13.32	0.014
Pain	72 (60.5)	43 (39.8)	χ^2=12.55	0.020
Adverse reactions	3 (2.5)	17 (15.7)	χ^2=11.59	0.038
Hospitalization time (d)	14.24±5.27	23.57±7.21	t=3.57	0.027

and growth of axons and forms a circular chain until axons show recovery. The results of this study also showed that adjuvant therapy using vitamin B12 achieved better overall recovery compared to routine treatment without associated neurological adverse reactions reported in patients (it was speculated that inflammation noted was caused by bacterial infection at the wound site and resolved after disinfection). Therefore, vitamin B12 could effectively promote the repair of peripheral nerves after replantation of severed fingers. The results of this study are in agreement with the results of studies listed in the references mentioned in the literature describing the use of vitamin B12 in replantation [18-21]. Therefore, administration of vitamin B12 after replantation of severed fingers needs to be actively promoted in clinical practice.

In this study, we retrospectively analyzed the recovery of 227 patients who underwent replantation for severed fingers and analyzed the effects of vitamin B12 on nerve repair. However, some discrepancies could not be excluded from our study results due to the limitations of our study, such as the small number of subjects analyzed, an incomprehensive study population, and a short study period. We intend to continue to improve our testing methodology and perform more accurate and comprehensive analyses.

In summary, vitamin B12 adjuvant therapy effectively improved the recovery of neurological function in fingers after replantation of severed fingers and should be widely promoted in clinical practice.

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Disclosure of conflict of interest

None.

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