

Sanhuang ointment prolongs indwelling time and promotes vein injury repair in patients receiving intravenous infusion via peripheral venous indwelling needles

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Abstract: We investigated the effect of Sanhuang ointment on the indwelling time and vein injury repair in patients receiving intravenous infusion via peripheral venous indwelling needles. Patients (n=120) who received infusion via peripheral venous indwelling needles were randomized into Sanhuang ointment, Hirudoid, and blank control groups. The indwelling time, venous injury and repair rate, venous intimal roughness rate, vascular wall thickening rate, thrombosis rate, and blood flow velocity were compared within 24h and on day 4 post-needle removal. The indwelling time in the Sanhuang ointment group was 7 (6,8) days, significantly longer than that in the Hirudoid (5(4,6) days) and blank control groups (4(3,5) days) ($P<0.01$). Within 24h of needle removal, differences in venous injury and repair grades, intimal roughness, wall thickening, thrombosis and blood flow were not significant ($P>0.05$). On day 4, the rates of venous intimal roughness, vascular wall thickening and thrombosis were significantly lower, while the blood flow velocity and venous repair rates were significantly higher in the Sanhuang ointment group than those in the Hirudoid and blank control groups ($P<0.05$). Sanhuang ointment application extends peripheral venous indwelling time and promotes vein repair without increased injury risk.

Keywords: Indwelling time, peripheral venous indwelling needle, Sanhuang ointment, venous injury, venous repair.

INTRODUCTION

Peripheral venous indwelling needle, a widely used intravenous infusion device, is characterized by its soft cannula, convenient operation, and long indwelling time (Buyukyilmaz *et al.*, 2019; Pinelli & Pittiruti, 2021; Weiss *et al.*, 2019). However, venipuncture not only disrupts the integrity of the skin, but also has a high risk of complications such as phlebitis, vascular injury and indwelling needle-related infection (Guenezan *et al.*, 2019; Oragano *et al.*, 2019). Venous injury is a local venous wall chemical inflammatory reaction caused by infusion. It may also be caused by repeated punctures of the same vein or indwelling needle irritation, mainly manifested as vein narrowing, decreased elasticity (hardening), or even disappearance of the vein after needle removal (Li *et al.*, 2010; Zhao *et al.*, 2019). Phlebitis is mostly a sterile inflammation of the venous intima, clinically manifested as local pain, redness, or local cord-like structures at the infusion site and even inflammatory changes such as induration after intravenous infusion (Braga *et al.*, 2018; Yang *et al.*, 2021). It has been shown that local phlebitis is associated with the severity of vascular injury (Zhao *et al.*, 2019;

Zhao *et al.*, 2015). A higher level of phlebitis post-infusion corresponds to increased vascular damage severity, thereby complicating vascular recovery. The superficial peripheral veins are the most common infusion channel for patients. However, these veins are limited in number and after moderate to severe injury, the veins become thin or even disappear, affecting the re-establishment of peripheral access. Furthermore, in cases where peripheral venous damage remains unrepaired, central venous catheterization becomes necessary, albeit with inherent substantial risks (Opperman *et al.*, 2022). The repair of peripheral venous injury may impede drug leakage, alleviate edema in the punctured limb, and sustain optimal peripheral blood circulation (Bithal *et al.*, 2022). Additionally, due to complications such as venous injury, peripheral venous indwelling needles often fail before completion of treatment, leading to prolonged hospital stays, necessitating patients to undergo repeated venous punctures and increasing patient discomfort and healthcare costs (Oragano *et al.*, 2019). Therefore, it is necessary to minimize the frequency of venipuncture in clinical practice.

Studies have recommended the removal of peripheral venous indwelling needles according to clinical indications (Alloubani *et al.*, 2019; American Society of

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Nursing for Intravenous Infusion, 2016; Webster *et al.*, 2019). The average indwelling time of peripheral venous indwelling needles in admitted patients is 3.7 days (Hopkinson *et al.*, 2020). Moreover, the average cost of peripheral venous indwelling needles during hospitalization is 64.60~121.25 RMB/person (Ming *et al.*, 2021; Yuan *et al.*, 2018). If complications such as venous injury occur, the peripheral venous indwelling needles become unusable and re-venipuncture is required, thus increasing the discomfort and medical burden (Guenezan *et al.*, 2019). Therefore, it is crucial in intravenous treatment to prolong the indwelling time, reduce venipuncture discomfort, and repair venous damage.

Hirudoid is one of the clinically recognized drugs for the prevention and treatment of phlebitis. In China, Hirudoid is commonly considered as a control in clinical trials (Hu *et al.*, 2018; Zhang, 2017). It has the effects of anti-infection, anti-exudation and pain relief. Its main component is polysulfonic acid mucopolysaccharide, which can inhibit various catabolic enzymes, promote blood circulation, reduce swelling and pain, and inhibit thrombosis (Li *et al.*, 2018; Zhang *et al.*, 2018). Long-term infusion via peripheral venous indwelling needles is always required in hospitalized patients. However, the data on the available drugs that can prolong the indwelling time of peripheral venous indwelling needles and promote repair of injured veins is limited.

Topical administration of traditional Chinese medicine has been confirmed to prevent venous injury and prolong the indwelling time of peripheral venous indwelling needles (Chen & Zheng, 2019; Wang *et al.*, 2021; Wen, 2018; Yang *et al.*, 2019; Zeng, 2020; Zhao, 2020; Zhong & Ji, 2021). Sanhuang ointment is a compound traditional Chinese medicine composed of Chinese rhubarb, *Scutellaria baicalensis* and *Cortex Phellodendri Chinensis*. Chinese rhubarb is the *principal* herb and its external use has the effect of activating blood circulation and removing stasis. *Scutellaria baicalensis* and *Cortex Phellodendri Chinensis* are adjuvant herbs, which have the effects of relieving swelling and pain (Ying *et al.*, 2005). Our previous studies in rabbits (Bao *et al.*, 2013; Feng *et al.*, 2016a; Feng *et al.*, 2012; Feng *et al.*, 2011; Lang, 2014; Ying *et al.*, 2005) confirmed that the immediate application of Sanhuang ointment following peripheral venous indwelling needle placement could effectively alleviate phlebitis and vein injury. Clinical studies have confirmed that the topical administration of Sanhuang ointment in the early stage can effectively prevent phlebitis caused by peripheral venous indwelling needles and increase patient comfort (Feng *et al.*, 2016a; Feng *et al.*, 2012; Feng *et al.*, 2011; Yang *et al.*, 2019; Ying *et al.*, 2005).

In this study, we further evaluated the role of Sanhuang ointment in prolonging indwelling time and promoting venous injury repair in patients receiving infusion via

peripheral venous indwelling needles. Our findings may provide a novel strategy to minimize repeated venipunctures during hospitalization and alleviate the nursing burden resulting from intravenous fluid management.

MATERIALS AND METHODS

Study design, ethics and clinical registration

This study is a randomized controlled trial, which was approved by the Institutional Ethics Committee of Hangzhou Hospital of Traditional Chinese Medicine (Approval No. 2020LH004). All methods were performed following the Declaration of Helsinki. Written informed consent was obtained from each enrolled patient. This study has been registered in the Chinese Clinical Trials Registry (ChiCTR2000041304).

Participants

Hospitalized patients who received peripheral venous infusion via indwelling needles from October 2020 to April 2021 were recruited. Inclusion criteria: 1) age ranging from 18 years to 85 years; 2) the pH value of infused medication was between 5 and 9 and the osmotic pressure was below 600 mOsm/L; 3) venipuncture site was located in thick and straight veins below the elbow of the upper limb; 4) the daily infusion volume was less than 1500mL and the infusion rate was approximately 60 drips/min; 5) vessels were classified as Hagle Me 0-1 level (Lang, 2014); 6) successful primary venipuncture. The exclusion criteria: 1) patients with a hospital stay of less than 4 days after needle removal; 2) patients with blood diseases and coagulation dysfunction. The criteria for censored cases: 1) accidental failure of peripheral venous indwelling needle placement; 2) non-compliance with the intervention plan and color ultrasound examination; 3) allergic reactions to Sanhuang ointment.

Randomization

All enrolled patients were randomized into the Sanhuang ointment group, Hirudoid group, and control group using the random number table method.

Preparation of the Sanhuang ointment

The Sanhuang ointment was prepared by our team, as previously described (Feng *et al.*, 2016b). Briefly, 100 g each of Chinese rhubarb, *Scutellaria baicalensis*, and *Cortex Phellodendri Chinensis* were ground into a fine powder and mixed. Subsequently, 700g of vaseline was heated to 120-125°C until fully melted, then filtered and cooled to 100°C. The vaseline was then thoroughly mixed with the pre-prepared fine powder and stirred until solidification, thereby forming the Sanhuang ointment.

Nursing care for patients receiving peripheral venous indwelling needles

All enrolled patients received routine nursing care for peripheral venous indwelling needles, which included

health education regarding intravenous infusion protocols. Patients were informed that they were not permitted to adjust the drip rate arbitrarily during infusion, should avoid excessive movement of the needles, refrain from lifting heavy objects, avoid twisting towels or other actions that could dislodge the needle, were advised against bathing to prevent local infection at the puncture site, and were instructed to take precautions to prevent dislodgement. If intravenous therapy was required after needle removal, a different vein on the opposite limb was selected for puncture.

For patients in the Sanhuang ointment group, in addition to routine nursing care, the topical administration of Sanhuang ointment was immediately conducted after the intravenous infusion. The ointment was applied from 2 cm in front of the puncture point to 6 cm of the proximal end along the centripetal direction of the vein, with a 4cm wide and 0.3 thickness. Then, the skin with Sanhuang ointment was covered with gauze. After 6h, the Sanhuang ointment was wiped off with a saline cotton ball. Sanhuang ointment was applied once daily. If there were clinical symptoms in the indwelling site, administration of Sanhuang ointment was continued once a day following removal of the peripheral venous indwelling needles, for 4 days. The color ultrasound was conducted on the fourth day.

For patients in the Hirudoid group, in addition to routine care, topical application of Hirudoid (Germany) was conducted, following the same intervention method as the Sanhuang ointment group.

Data collection

The demographic and clinicopathological characteristics, including sex, age, disease type, arm with indwelling needle, medication, total amount of fluid infusion, indwelling time, time point of needle removal, and phlebitis grade, were collected. Phlebitis grade was evaluated based on the 2016 version of the phlebitis evaluation criteria of the Infusion Nurses Society (American Society of Nursing for Intravenous Infusion, 2016).

Outcome measurement

The indwelling time and vein injury repair in patients with peripheral venous indwelling needles were defined as the primary outcomes. The indwelling time was determined as the duration from successful placement to removal of the peripheral venous indwelling needle (American Society of Nursing for Intravenous Infusion, 2016).

Based on our previous studies (Lang, 2014) and others (Goel *et al.*, 2020; Ma, 2013; Malgor & Labropoulos, 2013; Wang, 2016; Xu *et al.*, 2015; Zhang *et al.*, 2017), we designed the Local Venous Injury and Repair Grade table for patients with peripheral venous indwelling

needles to evaluate the grade of venous injury and repair. The following information was evaluated: the intima smoothness, the thickness of the vascular wall, thrombosis, and blood flow. The grading of venous injury and repair: Grade 0 (venous repair) - characterized by smooth intima, absence of wall irregularities or thrombosis and uninterrupted blood flow; Grade I (mild injury) - featured a rough intima and thickened vascular wall; Grade II (moderate injury) - indicated luminal thrombosis and blood flow hindrance; Grade III (severe injury) - marked by vascular occlusion, extensive thrombosis and near no detectable blood flow.

The venous repair rate was calculated as the number of cases with repaired veins on the 4th day after needle removal / the number of cases with injured veins within 24h of needle removal.

Secondary outcomes were defined as venous intimal roughness, vascular wall thickening, thrombosis and blood flow velocity, which were all evaluated by color Doppler examination (fig. 1).

STATISTICAL ANALYSIS

All statistical analyses were conducted by using the SPSS 20.0 software (IBM SPSS, USA). A two-sided $p < 0.05$ was considered as statistically significant. The distribution and homogeneity of variance of the data were evaluated. Continuous variables of normal distribution and with homogeneity of variance are expressed as mean \pm SD and were compared by one-way ANOVA and LSD. Continuous variables of non-normal distribution and without homogeneity of variance were presented as median (P25, P75) and analyzed with the *Kruskal-Wallis* rank sum test and *Bonferroni* correction. Categorical variables, which are expressed as frequencies and percentages, were analyzed with Pearson chi-square test or Fisher's exact test. Ordinal data were compared with the *Kruskal-Wallis* rank sum test and *Bonferroni* correction.

RESULTS

General characteristics

A total of 120 patients who received infusion via peripheral venous indwelling needles were recruited. Among them, 1 case in the Sanhuang ointment group was excluded due to accidental detachment of peripheral venous indwelling needles, 1 in the Hirudoid group case was censored due to allergy and 2 cases in the blank control group were excluded due to incompliance with color ultrasound examination. Finally, 116 cases were enrolled. Their baseline characteristics are shown in table 1. There were no significant differences in sex, age, disease type, arm with the indwelling needle, vascular grade, medication, total amount of fluid infusion, indwelling time, time point of needle removal and phlebitis grade at needle removal among groups.

Table 1: Baseline characteristics

		Sanhuang ointment group (n=39)	Hirudoid group (n=39)	Blank control group (n=38)	Statistical values	P
Gender	Male	19(48.7)	22(56.4)	16(42.1)	12.557 ^{a)}	0.276
	Female	20(51.3)	17(43.6)	22(57.9)		
Age (years)		71.08±11.69	73.95±11.72	75.05±7.27	1.488 ^{c)}	0.230
Type of disease	Cardiovascular disease	19(48.7)	19(48.7)	20(52.6)	0.157 ^{a)}	0.925
	Respiratory disease	20(51.3)	20(51.3)	18(47.4)		
Arm with indwelling needle	Left forearm	20(51.3)	21(53.8)	20(52.5)	0.067 ^{a)}	0.967
	Right forearm	19(48.7)	18(46.2)	18(47.5)		
Vascular grade	Level 0	33(84.6)	32(82.1)	30(78.9)	0.414 ^{b)}	0.813
	Class I	6(15.4)	7(17.9)	8(21.1)		
	Class II	0(0.0)	0(0.0)	0(0.0)		
	Grade III	0(0.0)	0(0.0)	0(0.0)		
Medications	Antibiotics	10(25.6)	11(28.2)	9(23.7)	0.886 ^{a)}	0.990
	Chinese medicine for activating blood circulation and removing stasis	8(20.5)	9(23.1)	7(18.4)		
	Chinese medicine for alleviating cough and reducing phlegm	10(25.6)	8(20.5)	9(23.7)		
Total amount of fluid infusion	Antiarrhythmics	11(28.2)	11(28.2)	13(34.2)	1.580 ^{b)}	0.454
		250 (250, 250)	250 (250, 250)	250 (250, 250)		
Grade of phlebitis	Level 0	33(84.6)	31(79.5)	25(65.8)	4.495 ^{b)}	0.106
	Class I	5(12.8)	6(15.4)	8(21.1)		
	Class II	1(2.6)	2(5.1)	5(13.1)		
	Grade III	0(0.0)	0(0.0)	0(0.0)		

Note: ^{a)} χ^2 value; ^{b)} *H* value, ^{c)} *F* value.

Table 2: Comparison of indwelling time of peripheral venous indwelling needles among three groups (*M*(*P*₂₅, *P*₇₅)).

	Number of cases	Indwelling time (days).	<i>H</i>	<i>P</i>
Sanhuang ointment group	39	7 (6, 8)	45.501	<0.001
Hirudoid group	39	5 (4, 6) ^{a)}		
Blank control group	38	4 (3, 5) ^{a, b)}		

Note: ^{a)}*P*<0.001 compared to the Sanhuang ointment group, ^{b)}*P*>0.05 compared to the Hirudoid group.

Table 3: Comparison of venous injury and repair grade (n/%) within 24h and on day 4 after indwelling needle removal among three groups.

	Number of cases	Venous injury and repair grade			
		Grade 0	Grade I	Grade II	Grade III
Indwelling needle removal within 24h					
Sanhuang ointment group	39	1 (2.5)	31 (77.5)	8 (20.0)	0 (0)
Hirudoid group	39	0 (0)	24 (61.5)	13 (33.3)	2 (5.1)
Blank control group	38	0 (0)	24 (63.1)	11 (28.9)	3 (7.9)
<i>H</i>					4.603
<i>P</i>					>0.05
Day 4 after indwelling needle removal					
Sanhuang ointment group	39	29 (74.4)	10 (25.6)	0 (0)	0 (0)
Hirudoid group	39	13 (33.3)	19 (48.7)	5 (12.8)	2 (5.1)
Blank control group	38	2 (5.3)	26 (68.4)	7 (18.4)	3 (7.9)
<i>H</i>					39.512
<i>P</i>					<0.001

Table 4: Venous injury and repair under color ultrasound within 24h and on day 4 after indwelling needle removal.

	Sanhuang ointment group	Hirudoid group	Blank control group	F/x ²	P
Indwelling needle removal within 24h					
Venous intimal roughness rate (%)	84.6	92.3	92.1	1.486	0.589
Vascular wall thickening rate (%)	97.4	97.4	100	1.225	1
Thrombosis rate (%)	23.1	33.3	36.8	1.849	0.397
Blood flow velocity (cm/s).	4.23±0.57	3.90±1.11	3.76±0.96	2.583	0.080
Day 4 after indwelling needle removal					
Venous intimal roughness (%)	23.1	61.5	81.6	27.596	<0.001
Vascular wall thickening rate (%)	25.6	64.1	89.5	33.060	<0.001
Thrombosis rate (%)	2.6	25.6	31.6	11.442	0.003
Blood flow velocity (cm/s)	4.41±0.54	3.93±1.19	3.60±1.29	5.663	0.005
Venous repair rate (%)	76.3	33.3	35.3	39.557	<0.001



Fig. 1: Rating of venous injury and repair on color Doppler ultrasound. (A) The rough intima of the vein at the indwelling site was shown. (B) The arrow indicates that the vascular wall was not uniformly thickened, resulting in different vascular diameters at the proximal and distal ends. (C) The incompressible echo area under the longitudinal view of color Doppler ultrasound was shown. The yellow arrow indicates venous thrombosis. (D) The incompressible echo area under the cross-sectional view of color Doppler ultrasound was shown. The yellow arrow indicates venous thrombosis. (E) The blood flow velocity calculated under color ultrasound was 4.14 cm/s.



Fig. 2: Color Doppler ultrasound findings of veins in cases with severe venous injury after removal of peripheral venous indwelling needles. (A) Within 24h after needle removal, the vascular lumen was dilated and there was thrombosis. The thrombus was large (17.3mm *1.63mm) and occluded the lumen. A severe venous injury was diagnosed. (B) On day 4 after needle removal, the venous thrombosis decreased to 6.77 mm *1.32 mm, but it was not dissolved. A severe venous injury was diagnosed. (C) On day 10 after needle removal, the blood flow in one severe case was not obvious and the vein disappeared on ultrasound.

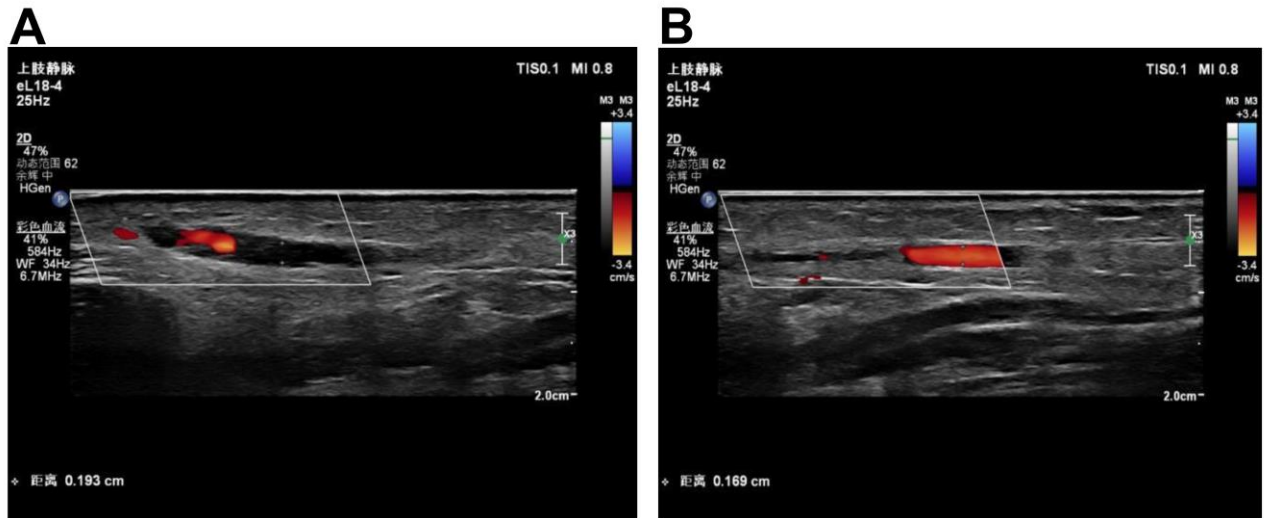


Fig. 3: Color Doppler ultrasound analysis of veins in cases with moderate venous injury vascular wall after removal of peripheral venous indwelling needles. (A) Within 24h after needle removal, the vascular wall was thickened, the lumen diameter was slightly expanded to 1.9mm and there was mural thrombosis. Moderate venous injury was diagnosed. (B) On day 4 after needle removal, the thickening of the vein wall was reduced and the lumen diameter was restored to 1.69 mm, but it was still in a slightly dilated state and the thrombus was not dissolved. Moderate venous injury was diagnosed.

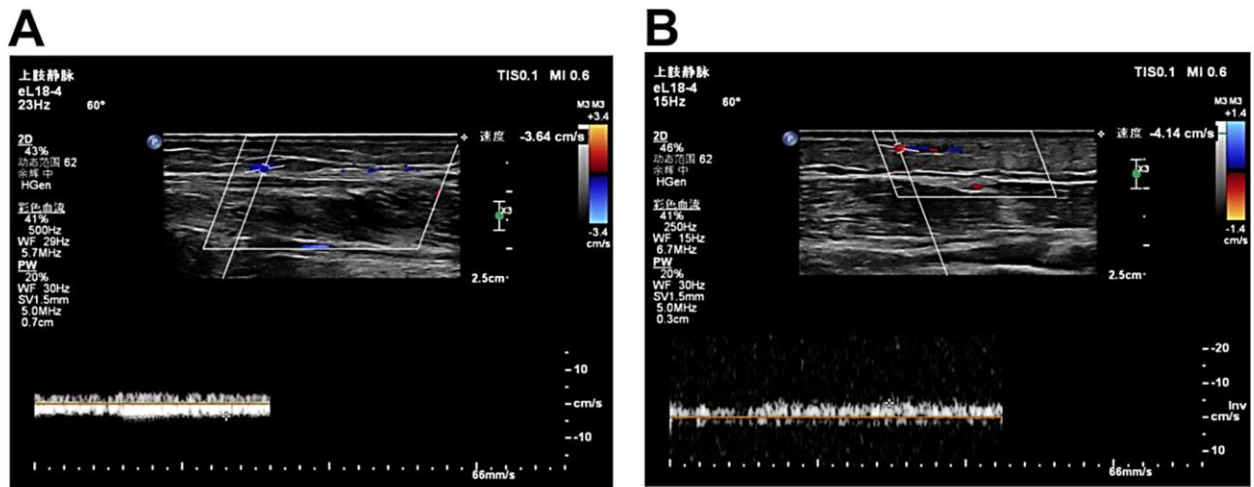


Fig. 4: Color Doppler ultrasound findings of venous repair after removal of peripheral venous indwelling needles. (A) Within 24 h after needle removal, there was thrombosis in the vein and the blood flow velocity was 3.64 cm/s. Moderate venous injury was diagnosed. (B) On day 4 after needle removal, there was no thrombus in the vein and the blood flow velocity was 4.14 cm/s, suggesting repair of the vein.

Indwelling time of peripheral venous indwelling needles

The median indwelling time in the Sanhuang ointment group was 7 (6,8) days, which was longer than that of the Hirudoid group ((5 (4,6) days) and the blank control group (4 (3,5) days) ($P < 0.01$) (table 2). The results of the *Bonferroni* correction showed that the difference in the indwelling time among the three groups was statistically significant ($P < 0.01$). There was no significant difference in the indwelling time between the Hirudoid group and the blank control group ($P = 0.226$, table 2). This indicates

that Sanhuang ointment could prolong the indwelling time of peripheral venous indwelling needles.

Venous injury and repair grade

Within 24h following removing peripheral venous indwelling needles, there was no significant difference in the grade of venous injury among groups ($P > 0.05$) (table 3). However, on day 4 post-removal, significant differences in the levels of venous injury and repair were observed among the three groups ($P < 0.01$). There was

also a significant difference between the Hirudoid group and the blank control group ($P=0.047$), as shown in table 3. Thus, Sanhuang ointment could promote the repair of injured veins caused by peripheral venous indwelling needles.

There were 2 cases of severe venous injury (grade III) in the Hirudoid group, while 3 cases were observed in the blank control group. Moreover, in these patients, venous repair was not observed by Color Doppler on the 4th day following the removal of peripheral venous indwelling needles (fig. 2). Due to the significant size of the thromboembolus and subsequent occlusion of the vascular lumen, the topical administration of Hirudoid also failed to dissolve the intravenous thrombus (fig. 3). Thus, we suppose that continuous topical administration of Sanhuang ointment after removing indwelling needles can promote the filling of blood flow and thrombolysis and thus facilitate the repair of venous intima and vascular wall (fig. 4).

Color Doppler evaluation

Within 24 h following the removal of peripheral venous indwelling needles, there were no significant differences in venous intimal roughness, vascular wall thickening rate, and thrombosis rate among groups ($P>0.05$) (table 4). On day 4 following the removal of peripheral venous indwelling needles, the venous intimal roughness rate, vascular wall thickening rate, and thrombosis rate of the Sanhuang ointment group were lower than those in the Hirudoid group and the blank control group ($P<0.05$) (table 4). However, the Sanhuang ointment group had a significantly higher venous injury repair rate than the Hirudoid group and the blank control group ($P<0.05$).

DISCUSSION

In this study, we found that there were 2 cases and 3 cases of severe venous injury (grade III) in the Hirudoid group and the blank control group, respectively. Furthermore, venous repair was not observed by Color Doppler in these patients. It has been shown that there is endothelial dysfunction and damaged vascular wall structure in severely damaged blood vessels, which may induce endothelial cell necrosis, increase vascular permeability, promote platelet activation and coagulation and finally cause thrombosis (Oo *et al.*, 2022). Similarly, large thromboemboli adherence to the vessel intima could result in luminal narrowing, semi-occlusion, or complete occlusion, adversely affecting venous function (Zhao *et al.*, 2014). We have obtained consistent results in this study. We found that on the 4th day after the removal of peripheral venous indwelling needles, patients with severe venous injury (grade III) had lumen occlusion, non-evident blood flow and disappearance of veins on ultrasound (data not shown). Additionally, there was collateral circulation, indicating that the repair of severe

damage to veins is challenging. Therefore, severe venous injury may be irreversible. In the clinical nursing practice, we should pay attention to the protection of peripheral veins to prevent severe venous injury.

Topical application of Sanhuang ointment before placement of peripheral venous indwelling needles can prolong the indwelling time without increasing the risk of phlebitis, thus reducing the discomfort of patients with multiple punctures and lowering hospitalization costs. It has been recommended that the peripheral venous indwelling needles should be removed according to clinical indications (American Society of Nursing for Intravenous Infusion, 2016; Li *et al.*, 2020b; Webster *et al.*, 2019). Failure of peripheral venous indwelling needles before the end of treatment is mostly associated with the occurrence of complications, such as phlebitis, vascular injury, indwelling needle-related infection, etc. (Guenezan *et al.*, 2019; Oragano *et al.*, 2019). The occurrence of complications may not only increase the discomfort of patients but also prolong the hospital stay and increase medical costs. It has been reported that the estimated total treatment fee for phlebitis in 96 patients was approximately 866.18 US dollars (Furlan & Lima, 2020). In this study, we followed the recommendations for the removal of the peripheral venous indwelling needles (American Society of Nursing for Intravenous Infusion, 2016; Li *et al.*, 2020b; Webster *et al.*, 2019), and found that the indwelling time in the Sanhuang ointment group was 7(6,8) days, which was significantly longer than that in Hirudoid group (5(4,6) days) and blank control group (4(3,5) days). There was no significant difference between the Hirudoid and the blank control group. Therefore, we concluded that topical administration of Sanhuang ointment could prolong the indwelling time, and was better than that of Hirudoid. Moreover, there was no significant difference in the grade of venous injury and repair among groups within 24 h following removal of peripheral venous indwelling needles, indicating that the topical administration of Sanhuang ointment immediately following infusion did not increase the risk of venous injury. These findings further confirmed the advantages of Sanhuang ointment in reducing the number of punctures, alleviating discomfort and reducing nursing workload.

The indwelling time of peripheral venous indwelling needles is affected by various factors, such as infused medication, indwelling site, and venous conditions (Chen *et al.*, 2021; Liu *et al.*, 2021). This duration cannot be blindly extended. Chen *et al* showed that the indwelling time of patients from the oncology department was (43.51 ± 30.91) h (Chen *et al.*, 2021), which was shorter than the indwelling time of this study. This may be related to the application of hypertonic solution in the study by Chen *et al.* The infusion of hyperosmolar solution may impair indwelling needle function and irritate the

indwelling vein, leading to shortened indwelling time. The indwelling time of peripheral venous indwelling needles in elderly stroke patients was (7.77±1.87) days (Xiao *et al.*, 2020), which is similar to the results of this study. Thus, the clinical indications for the removal of peripheral venous indwelling needles should be closely monitored to achieve the optimal protection of peripheral veins.

In this study, we showed that there were no significant differences in venous intimal roughness, vascular wall thickening rate, blood flow velocity and thrombosis rate among three groups within 24h following removal of peripheral venous indwelling needles. On day 4 post-removal, color ultrasound detection showed the venous intimal roughness rate, vascular wall thickening rate and thrombosis rate in the Sanhuang ointment group were lower than those in the Hirudoid group and the blank control group, but the blood flow velocity and venous recovery rate were higher. Thus, we suppose that continuous topical administration of Sanhuang ointment after removing indwelling needles can facilitate the repair of venous intima and vascular wall, and promote the filling of blood flow and thrombolysis. It has been reported that venipuncture can cause mechanical injury to the blood vessels, which then may promote platelet activation and lead to the imbalance of coagulation and anticoagulation as well as abnormal vasomotor activity, resulting in thrombosis (Gilardi *et al.*, 2024). In the Sanhuang ointment, the herb Chinese rhubarb has good effects in anti-vasodilation, anti-thrombosis, and improvement of blood circulation (Bai *et al.*, 2019). *Scutellaria baicalensis* and *Cortex Phellodendri Chinensis* can inhibit platelet aggregation and have anticoagulant, antithrombotic, antibacterial, anti-inflammatory, and antipyretic effects (Jiang, 2018; Li *et al.*, 2019; Wang & Zhang, 2014). The combination of three herbs can improve blood circulation. Furthermore, venous injury caused by peripheral venous indwelling needles is mainly due to venous spasm caused by mechanical stimulation and inflammation of the venous vascular wall (Li *et al.*, 2020a). Sanhuang ointment has anti-inflammatory, antioxidant, sedative, and analgesic effects, and can promote the recovery of vascular endothelial cells. Our results have confirmed that continuous topical administration of Sanhuang ointment after the removal of peripheral venous indwelling needles could repair the damage to the vascular intima and wall. Hirudoids can rapidly penetrate the skin tissue and have the effects of reducing tissue edema, anti-infection, anti-exudation, and promoting the proliferation of locally damaged tissues (Yue, 2022). However, its effects on the chronic inflammation after the thickening of the venous vascular wall may be insufficient.

In this study, although we confirmed that Sanhuang ointment was superior to Hirudoid in promoting

thrombolysis, there was still 1 case without thrombolysis after the topical administration of Sanhuang ointment, whereas 10 cases without thrombolysis after topical administration of Hirudoid. The size of the thrombosis and patient factors will affect the outcome of thrombolysis (Li *et al.*, 2020a). When the complete thrombosis is formed, the vein would be occluded. Therefore, in clinical nursing work, we should prevent complete thrombosis.

There are several limitations in this study. First, this was a single-center-based study, with a relatively small sample size. Secondly, due to technical limitations, visual observation was used for vascular grading before vein puncture instead of objective evaluation by color Doppler ultrasound. Third, the mechanism by which Sanhuang ointment promotes the repair of damaged veins in patients with indwelling needles remains unclear. Further multi-center large-sample studies are needed to verify the findings of this study.

CONCLUSION

In this study, we evaluated the efficacy of topical administration of Sanhuang ointment in reducing intravenous injury and promoting venous recovery in patients receiving infusion via peripheral venous indwelling needles. We found that Sanhuang ointment prolonged the indwelling time and promoted venous injury repair. Our findings further confirm the advantages of Sanhuang ointment in prolonging the indwelling time, enhancing the safety of intravenous treatment, reducing medical costs, and alleviating discomfort.

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