Experimental research on preventing mechanical phlebitis arising from indwelling needles in intravenous therapy by external application of mirabilite

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Received May 18, 2017; Accepted September 25, 2017

DOI: 10.3892/etm.2017.5347

Abstract. Various types of complications arising from intravenous indwelling needles have become a challenge in clinical care. It is urgent to seek a simple and cost-effective method for prevention and treatment of phlebitis. We investigated the roles of mirabilite in preventing and treating phlebitis caused by intravenous indwelling needles and provide guidance for prevention and treatment of mechanical phlebitis caused by intravenous indwelling needles. A total of 57 healthy congeneric big-eared New Zealand rabbits were randomly divided into 3 groups: blank control, indwelling needle, and group with external application of mirabilite. The ear vein of each rabbit was punctured with an intravenous indwelling needle. The ear vein specimens were taken at 3, 5, and 7 days after indwelling. The hematoxylin and eosin stained pathological tissue sections of the ear veins of the rabbits in each group were observed. The expression levels of IL-1 and IL-6, and tumour necrosis factor-α (TNF-α) in the vascular tissue of the ear veins of the rabbits in each group were detected with the immunofluorescence method. In the blank control group, there was no inflammatory cellular infiltration and no proliferation of fibrous tissue around the vascular wall. With the increase of the indwelling time, proliferation of fibrous tissue in vascular wall, increased inflammatory cellular infiltration and organized thrombus in the vascular tissue occurred in the ear veins of the rabbits in the indwelling needle group and group with external application of mirabilite. Compared with the indwelling needle group, the group with external application of mirabilite had significantly decreased fibrous tissue in the vascular wall and significantly decreased inflammatory cellular infiltration. At the same point in indwelling time, the expression levels of IL-1, IL-6, and TNF-α in the indwelling needle and group with external application of mirabilite were significantly higher than that in the blank control group ($P<0.05$). The expression levels of IL-1, IL-6, and TNF-α in the group with external application of mirabilite were lower than that in the indwelling needle group ($P<0.05$). The expression levels of IL-1, IL-6, and TNF-α are positively correlated with the indwelling time within the same group at different points in time. In conclusion, external application of mirabilite can significantly decrease infiltration of venous inflammatory cells of the rabbit ear margin, proliferation of fibrous tissue and thrombosis in the vascular wall, significant decrease the expression levels of IL-1, IL-6, and TNF-α in the mechanical phlebitis caused by intravenous indwelling needles, and decrease the inflammatory responses of the ear veins of rabbits.

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Key words: indwelling needles, ear vein, phlebitis, mirabilite

Introduction

Intravenous indwelling needles are widely used in clinical practice due to their advantages. Meanwhile, the resulting various types of complications become one of the difficulties in clinical care. Research indicates that as the most common complication of indwelling needles phlebitis has an incidence rate of 77.5% (1). Phlebitis clinically presents as, local tissue pain, pyrexia, and swelling at the sites of puncture and transfusion, and even formation of a hard strip along the direction of the vein. The phlebitis caused by intravenous indwelling needles presents with various symptoms after the indwelling needles stimulate the inner wall of the blood vessels and produce a series of pathological and physiological responses (2,3). Mechanical phlebitis is most common and an acute aseptic inflammation (4). The phlebitis caused by intravenous indwelling needle severely affects patient's comfort. Reducing the time for use of indwelling needles would increase patient's pain in repeated puncture and the treatment cost. Thus, the prevention and nursing of the phlebitis caused by intravenous indwelling needles become the focus and difficulty in indwelling needle nursing. Magnesium sulfate wet compression is currently a widely used effective method for treatment of phlebitis in clinical practice but it is not acceptable in clinical practice and patients due to tis poor operability. Research (5) has reported that use of Comfeel hydrocolloid

dressings can effectively prevent occurrence of the phlebitis caused by intravenous indwelling needles but its high cost increases the economic burden on patients. Therefore, seeking a simple and cost-effective method for prevention and treatment of phlebitis has become a concern of the researchers.

External application of Chinese medicine is a method using the traditional Chinese medical theory. The medicine is absorbed into the lesions via skin for promoting circulation and removing stasis, clearing heat and removing toxicity, and subsidence of swelling. Mirabilite is a type of crystalline solid made from the sulfate mineral of the mirabilite family, mainly comprising hydrous sodium sulfate (Na_2SO_4 $10H_2O$). In the theory of traditional Chinese medicine, it is believed that mirabilite is bitter (6). Pharmacopeia of the People's Republic of China (7), edition 2010 states that mirabilite is mainly used to treat abdominal distension, dry stool. The research by Ke and Wang (8) demonstrates that external application of mirabilite can diminish inflammation, relieve pain, and prevent infections. In some clinical reports, mirabilite is used to treat phlebitis of various causes (9-11). However, the majority of these reports are clinical observations, which lack support of the experimental data.

At present, it is believed that the major cause of phlebitis is the mechanical stimulation of the venous vascular wall by the indwelling needle catheter. In terms of the pathological mechanism, the stimulation by the indwelling needle catheter and the drug can cause mechanical damage to the vascular intima, promote inflammatory reactions to occur in the venous wall and release inflammatory factors thus activating the inflammatory reaction chain (12). IL-1 and IL-6, and tumour necrosis factor-α (TNF-α) in the inflammatory factors are important proinflammatory factors that mediate the acute inflammatory responses (13). In the case of trauma and inflammation, the expression of IL-1, IL-6, and TNF-α increases. Particularly, the increase is more significant in inflammatory responses (14). The research by Li *et al* (15) demonstrated that the inflammatory factors promote occurrence of vascular inflammatory responses and increase vascular damage.

In the research, we observe the effect of external application of mirabilite on the pathological changes in the vascular tissue with phlebitis caused by indwelling needles at different points in time for indwelling of the intravenous indwelling needle using the animal experiment and hematoxylin and eosin (H&E) staining. We use the immunofluorescence method to detect the changes in the expression of IL-1, IL-6, and TNF-α in the vascular tissue and investigate their role in preventing mechanical phlebitis caused by intravenous indwelling needle thus providing experimental data for clinical prevention of phlebitis caused by indwelling needles.

Materials and methods

Grouping of the experimental animals and the treatment methods. A total of 57 healthy big-eared New Zealand rabbits weighing 2.5-3.0 kg, male or female, were divided into three groups using the random number table; blank control group, raised conventionally (Jinzhou Medical University, Jinzhou, China) without any treatment; indwelling needle group, conventionally punctured with indwelling needles; group with external application of mirabilite (Beijing Sanyao Science & Technology Development Co., Ltd., Beijing, China), punctured with intravenous indwelling needles followed by external application of mirabilite for intervention. The study was approved by the Ethics Committee of Jinzhou Medical University.

Operating procedures for intravenous indwelling needles. A total of 24 G positive pressure needle-free connecting type indwelling needles were used. Thick and straight venous blood vessels of rabbit ears were selected. The skin was disinfected with iodophor cotton ball according to the principles of sterile operation. The needle was directly inserted into the vein at an angle of 10-15˚C relative to the rabbit ear vein after the skin surface became dry. The puncture degree was decreased after blood returned. The rabbit ear was propped with the left hand. The catheter and the needle tip were pushed into the vein with the right hand with the supporting effect of the needle. The catheter was completely pushed into the vein while extracting the needle. It was then fixed with sterile adhesive tape.

Method for external application of mirabilite. A piece of sterile gauze was immersed in 10% mirabilite solution before intravenous infusion each day. The gauze was wrung until it did not drip. The gauze was applied in front of the punctured vein. The site was covered by preservative film and fixed by adhesive tape. The skin was exposed to the medicine for 6 h. A total of 20 ml of 0.9% sodium chloride injection was intravenously infused at a fixed time in sequence each day. A 3 ml pre-charged catheter (Beijing Beifang Pasture Biotechnology Research Institute, Beijing, China) irrigator was used for sealing the catheter under positive pressure. It was then properly fixed by bandage.

Collection of the tissue specimens. Three rabbits were randomly selected from the blank control group when the indwelling time was reached. Eight rabbits were randomly selected from the indwelling needle group and the group with external application of mirabilite, and the indwelling needles were extracted, respectively. They were subjected to intravenous anesthesia with 10% chloral hydrate and 4% paraformaldehyde perfusion. The rabbit ear vein was isolated. A segment of 1 cm-long ear vein was taken with the puncture point as the center and fixed in 4% paraformaldehyde solution.

H&E staining. The ear vein was routinely dehydrated and paraffined. The paraffined blocks were sectioned into 5 m-thick slices. After being baked for 15 min, the sections were dewaxed for 15 min with xylene (I) and xylene (II), respectively washed for 5 min with ethanol of different concentrations (100, 95, 90, 85, 80, 75 and 70%), washed 3 times for 3 min each with phosphate-buffered saline (PBS), immersed in hematoxylin for 5 min for staining, washed for 20 min with tap water, washed 3 times for 3 min each with PBS, washed for 1-3 sec with 1% acidic alcohol, washed for 3 sec with water, washed 3 times for 3 min each with PBS, stained for 1-3 min with 0.5% eosin solution, washed 3 times for 3 min each with PBS, immersed in: 100% alcohol for 10 min, 100% for 10 min, 95% for 5 min, 90% for 5 min, 85% for 5 min, 80% for 2 min, 75% for 2 min, 70% for 2 min, immersed in xylene (I) and xylene (II) for 5 min, respectively mounted with neutral gum, and observed under a microscope (Olympus Corp., Tokyo,

Table I. Percentages of IL-1 positive cells in various experimental groups (mean ± SD).

Groups	n=24		
	3 days	5 days	7 days
Blank	11.65±1.71	11.65±1.71	11.65±1.71
Indwelling needle	18.22±2.56[a,b]	33.68±1.62[a,b]	73.49±7.73[a,b]
Mirabilite intervention	13.78±1.87[a,b]	23.52±2.12[a,b]	56.8±5.54[a,b]

[a]Comparisons among various groups at the same point in time indicate P<0.05; [b]comparisons at different points in time in the same group indicate P<0.05; SD, standard deviation.

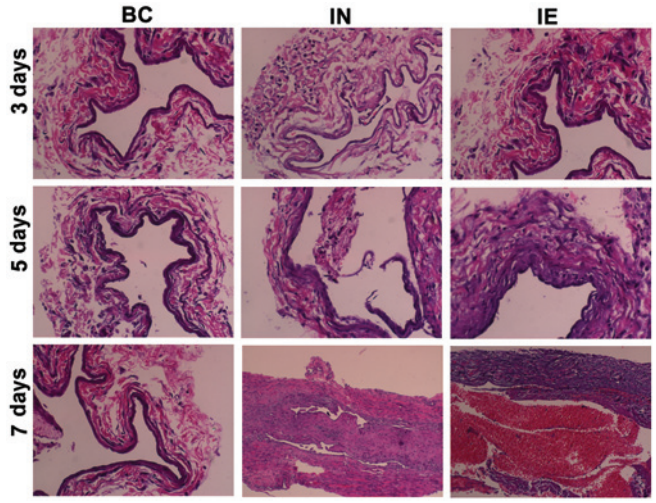

Figure. 1. H&E staining results in various experimental groups (200x). BC, blank control; IN, indwelling needle; IE, indwelling needle and external application of mirabilite; H&E, hematoxylin and eosin.

Japan). All reagents were purchased from Beijing Chemical Reagents Co., Ltd. (Beijing, China).

Immunofluorescence. The steps for preparation of paraffin sections were the same as mentioned above. The sections were baked for 60 min, dewaxed for 15 min with xylene (I) and xylene (II), respectively washed 3 times for 5 min each with 1x PBS, and blocked for 30 min with the antibody diluent. The sections were blocked with the goat serum. Primary antibodies of IL-1, IL-6, and TNF-α (purchased from Abcam, Cambridge, MA, USA) were added. Dilution was performed with the antibody diluent according to the dilution ratio. It was added to the tissue sections. The sections were incubated overnight at 4˚C, washed 3 times for 5 min each with 1x PBS. The fluorescence marked second antibody (Wuhan Boster Biological Technology Ltd., Wuhan, China) was added to the goat serum. Dilution was performed with the antibody diluent according to the dilution ratio. It was added to the tissue sections. The sections were incubated for 2 h at room temperature, washed 3 times for 5 min each with 1x PBS. The nucleus was 4', 6-diamidino-2-phenylindole (DAPI) stained for 15 min. The sections were washed 3 times for 5 min each with 1x PBS. The sections were mounted with glycerol, preserved away from light, and observed and photographed under the fluorescence microscope (Olympus Corp.).

Statistical analysis. The ImageJ software (Tree Star, Inc., Ashland, OR, USA) was used to count the tissue nuclei and positive cells of each section. The percentage of the count of the positive cells in the total number of all cells was computed as a comparison indicator. The SPSS 19.0 statistical software package (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis of the results. The one-way analysis of variance was used for comparison at different points in time within each group. The t-test was used for comparison of different groups at the same point in time. A P<0.05 was considered to indicate a significant analysis.

Results

Microscopic examination results of H&E staining in various experimental groups. In the blank group, no inflammatory cellular infiltration occurred in the vascular wall, and the no proliferation of fibrous tissue occurred around the vascular wall. A little inflammatory cellular infiltration occurred in both the indwelling needle group and the group with external application of mirabilite, and mild proliferation of fibrous tissue occurred around the vascular wall at 3 days. In both the indwelling needle and the mirabilite group, we could observe substantial inflammatory cellular infiltration in the vascular wall, proliferation of fibrous tissue in the vascular wall, and a little white thrombosis in the blood vessels at 5 days. In the indwelling needle group, we observed substantial inflammatory cellular infiltration around the vascular wall, significant fibrous tissue hyperplasia, and substantial thrombosis in the blood vessels at 7 days. Compared with the indwelling needle group, the group with external application of mirabilite had slight inflammatory cellular infiltration and thrombosis (Fig. 1).

Expression levels of IL-1 in the rabbit ear veins in various experimental groups. The detection results showed that with the increase of the indwelling time of the intravenous indwelling needles, the expression levels of IL-1 in the indwelling needle group and the group with external application of mirabilite increased. The expression levels in the indwelling needle and the group with external application of mirabilite were higher than that in the blank control group (P<0.05). The expression levels of IL-1 in the group with external application of mirabilite were lower than that in the indwelling needle group at 3, 5, and 7 days. The differences were statistically significant (Fig. 2 and Table I).

Expression of IL-6 in the rabbit ear veins in various experimental groups. The detection results showed that with the increase of the indwelling time of the intravenous indwelling needles, the expression levels of IL-6 in both the indwelling needle group and the group with external application of mirabilite increased. The expression levels in both the indwelling needle group and the group with external application of mirabilite were higher than that in the blank control group at 3, 5,

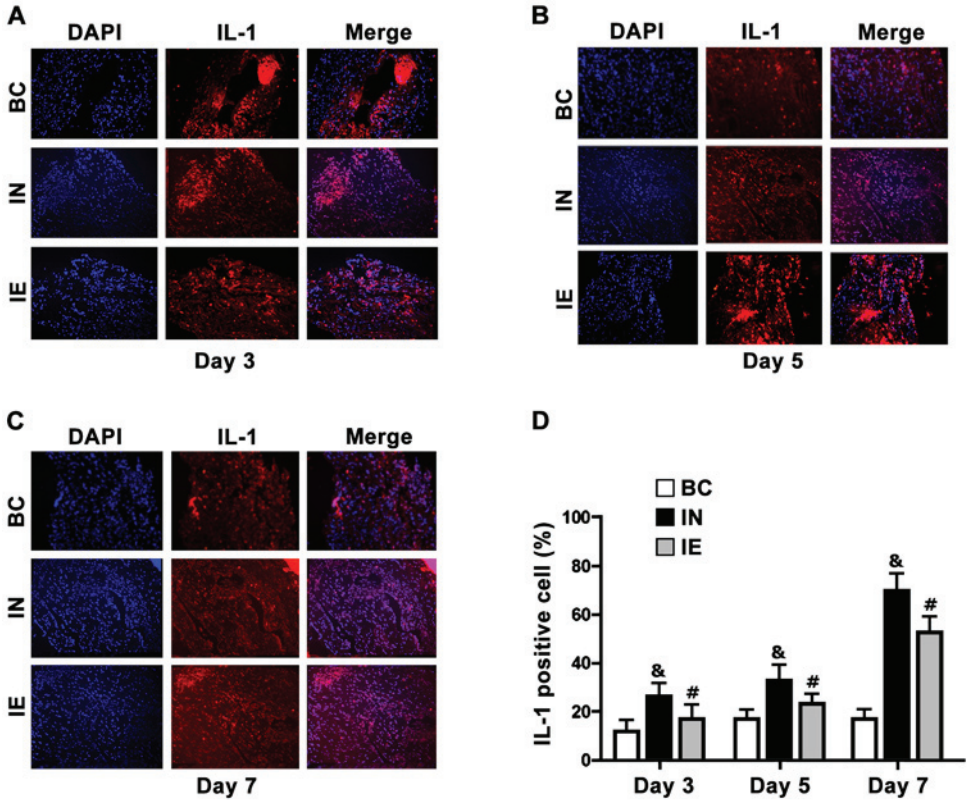

Figure 2. Expression of IL-1 in various experimental groups. (A) Expression of IL-1 in various experimental groups at day 3. (B) Expression of IL-1 in various experimental groups at day 5. (C) Expression of IL-1 in various experimental groups at day 7. (D) Statistical results of expression of IL-1 in various experimental groups. [&]Comparison with the control group P<0.05; [#]comparison with the indwelling needle group P<0.05; BC, blank control; IN, indwelling needle; IE, indwelling needle and external application of mirabilite.

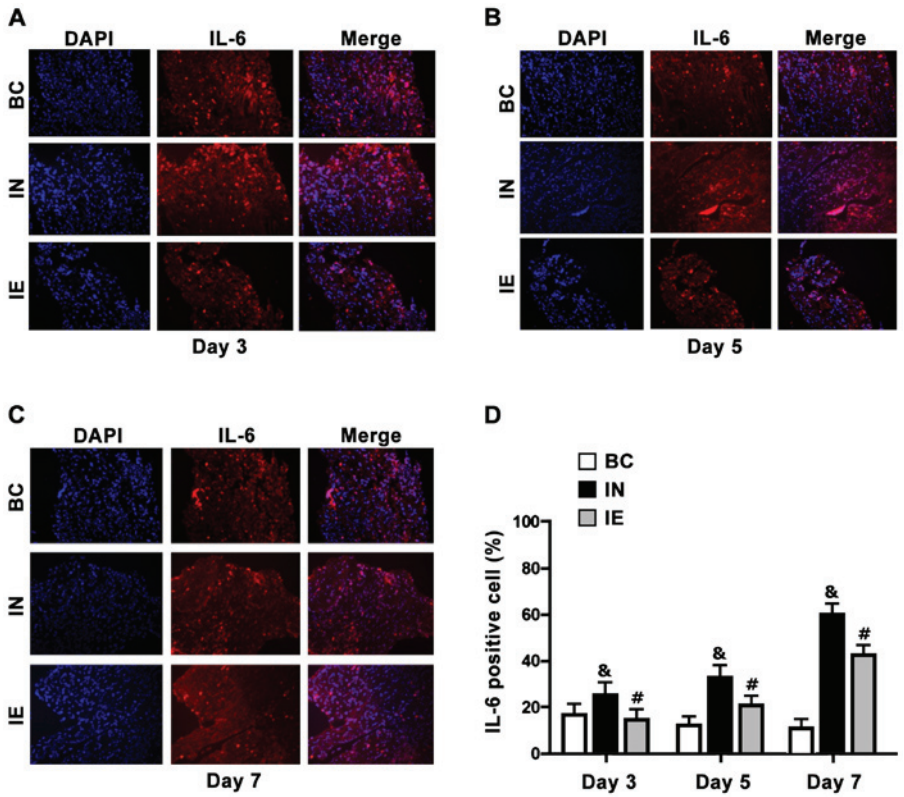

Figure 3. Expression of IL-6 in various experimental groups. (A) Expression of IL-6 in various experimental groups at day 3. (B) Expression of IL-6 in various experimental groups at day 5. (C) Expression of IL-6 in various experimental groups at day 7. (D) Statistical results of expression of IL-6 in various experimental groups. [&]Comparison with the control group P<0.05; [#]comparison with the indwelling needle group P<0.05; BC, blank control; IN, indwelling needle; IE, indwelling needle and external application of mirabilite.

Table II. Percentages of IL-6 positive cells in various experimental groups (mean ± SD) n=24.

Groups	3 days	5 days	7 days
Blank control	10.44±1.72	10.44±1.72	10.44±1.72
Indwelling needle	13.87±1.13[a,b]	31.17±1.61[a,b]	80.1±2.7[a,b]
With external application of mirabilite	12.26±1.7[a,b]	25.16±2.38[a,b]	69.4±2.77[a,b]

[a]Comparisons among various groups at the same point in time p<0.05; [b]comparisons at different points in time in the same group P<0.05; SD, standard deviation.

Table III. Percentages of the TNF-α positive cells in various experimental groups (mean ± SD) n=24.

Groups	3 days	5 days	7 days
Blank control	15.5±1.2	15.5±1.2	15.5±1.2
Indwelling needle	19.28±1.41[a]	37.22±1.78[a]	57.14±3.53[a]
With external application of mirabilite	17.67±1.57[a,b]	31.58±3.57[a,b]	46.0±4.53[a,b]

[a]Comparison among various groups at the same point in time indicates P<0.05; [b]comparison at different points in time within the same group indicates P<0.05; SD, standard deviation.

and 7 days. The expression of IL-6 in the group with external application of mirabilite was lower than that in the indwelling needle group. The differences were statistically significant (P<0.05) (Fig. 3 and Table II).

Expression of TNF-α in the rabbit ear veins in various experimental groups. The detection results indicated that with the increase of the indwelling time of the intravenous indwelling needles, the expression levels of TNF-α in both the indwelling needle group and the group with external application of mirabilite increased. The expression levels in the indwelling needle group and the group with external application of mirabilite were higher than that in the blank control group (P<0.05). The expression of TNF-α in the group with external application of mirabilite was lower than that in the indwelling needle group. The differences were statistically significant (P<0.05) (Fig. 4 and Table III).

Discussion

Venous transfusion is an important approach to clinical treatment. Intravenous indwelling needles have been substi-

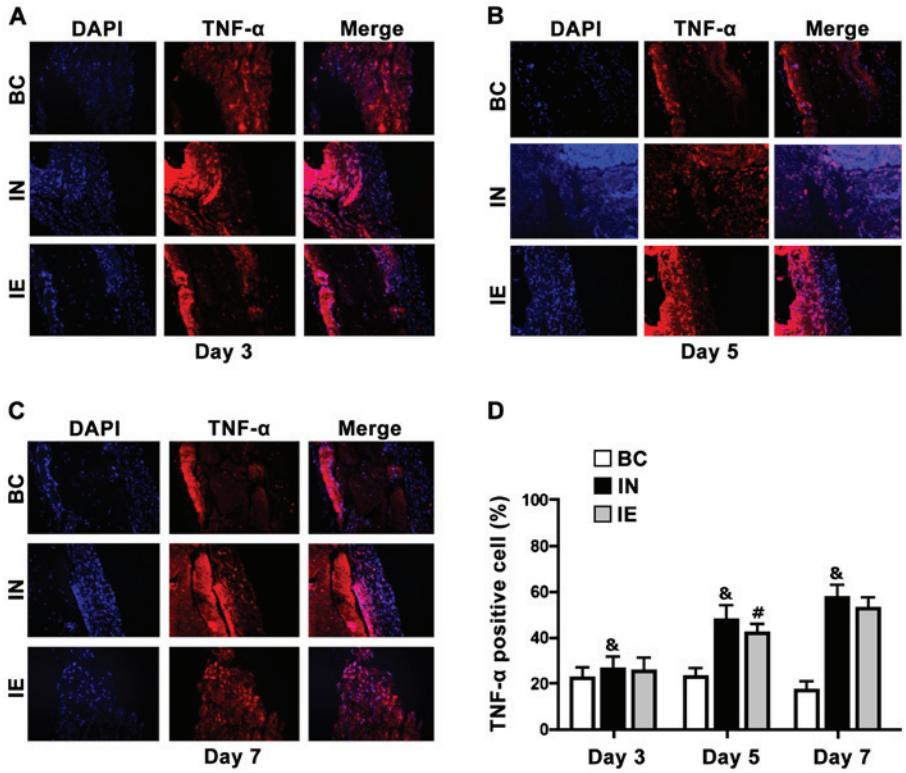

Figure 4. Expression of TNF-α in various experimental groups. (A) Expression of TNF-α in various experimental groups at day 3. (B) Expression of TNF-α in various experimental groups at day 5. (C) Expression of TNF-α in various experimental groups at day 7. (D) Statistical results of the expression of TNF-α in various experimental groups. [&]Comparison with the control group P<0.05; [#]comparison with the indwelling needle group P<0.05; BC, blank control; IN, indwelling needle; IE, indwelling needle and external application of mirabilite; TNF-α, tumor necrosis factor; DAPI, 4', 6-diamidino-2-phenylindole.

tuted for steel needles and become an important tool for clinical intravenous therapy due to their advantages. With the extensive application of indwelling needles in clinical treatment, the occurrence of various complications severely perplexed the clinical nursing personnel (16). In the complications caused by indwelling needles, phlebitis is the most common complication. Based on the clinical statistical data, the incidence of phlebitis is as high as 80% (17). Phlebitis can be divided into mechanical, chemical, and infectious by cause (18). The majority of the phlebitis cases caused by intravenous indwelling needles are mechanical phlebitis and acute aseptic inflammation. Mechanical phlebitis is an inflammatory response of the venous wall irritated by vasospasm and intimal injury arising from stimulation and friction of the vascular wall by the indwelling needle catheter (19). According to relevant literature (20-22), no phlebitis can be observed by naked eye if the indwelling time of the intravenous indwelling needles exceeds 3 days. Actually, inflammatory cellular infiltration occurs on the inner vascular wall. Thus, the indwelling time of the intravenous indwelling needles is considered as one of the important factors that influence the occurrence of phlebitis. In the experiment, significant inflammatory cellular infiltration could be observed in the venous tissue at 3 days after indwelling in the indwelling needle group, which is consistent with the relevant research result. With the increase of the indwelling time, the severity of phlebitis of the rabbit ear vein increases significantly, suggesting that the prevention of the mechanical phlebitis caused by indwelling needles should start as early as possible.

With the in-depth research on the pathological mechanism of phlebitis, it has been found that inflammatory responses play an important role in occurrence and progression of phlebitis (23). The mechanical stimulation of the vascular wall by intravenous indwelling needles can directly damage the vascular endothelial cells. The damaged vascular endothelial cells would increase the vascular permeability. The inflammatory cells effuse from the vascular wall thus leading to inflammatory responses under the action of chemotactic factors. Anti-inflammatory cytokines and pro-inflammatory factors are mutually conditioning thus forming a balance when no inflammatory responses occur in a normal organism (24). Various causes lead to an increase in pro-inflammatory factors. The balance would be damaged thus leading to inflammatory responses when the anti-inflammatory cytokines are insufficient to constrain the pro-inflammatory factors. In the experiment, the detection indexes of IL-1, IL-6, and TNF-α are the pro-inflammatory factors. The expression levels of the pro-inflammatory factors of IL-1, IL-6, and TNF-α increase abnormally when the indwelling time of the indwelling needles exceeds 7 days. Under the action of the chemotaxis of the pro-inflammatory factors, the inflammatory cells effuse to the extravascular tissue via the damaged vascular wall thus leading to inflammatory responses in the extravascular tissue.

IL-1 primarily comprises the inflammatory factors secreted by such phagocytes as macrophages, and monocytes. It has extensive biological activities. The biological activities mainly include: Promoting proliferation of lymphocytes, hematopoietic cells, and fibroblasts, promoting wound healing. In addition, IL-1 can promote adherence and infiltration of the leukocytes by inducing the endothelial cells to express adhesion molecules. The increase of the expression of IL-1 promotes the leukocytes to migrate to the vascular endothelial cells after adherence to wall. The leukocytes regularly release plasmin thus making the blood vessel endothelium shift from anticoagulation to coagulation accelerating and leading to development of phlebitis (25). In the experiment, the expression of IL-1 increases significantly when the indwelling time of indwelling needles exceeds 3 days. With the further increase of the indwelling time, the expression level also increases.

IL-6 is a glycosylated protein comprising 183 amino acids. IL-6 is produced by many types of cells including macrophages, T cells and B cells. It can regulate the growth and differentiation of many types of cells. It plays roles in regulation of immune responses, acute phase response, and hematopoiesis. It also plays an important role in anti-inflammation immune responses. IL-6 plays a vital role in occurrence of inflammation. In the experiment, the expression of IL-6 starts to increase when the indwelling time of indwelling needles exceeds 3 days. The expression at 7 days is significantly higher than that at 3 days.

TNF-α is synthesized by activated macrophages, monocytes, some T cells, and NK cells. It participates in such pathological processes as inflammatory reactions, immune responses, antitumor activity, endotoxic shock, arteriosclerosis, venous thrombosis, and vasculitis. It also plays an important role in the physiological processes of inflammation and immune responses. In the experiment, the expression of TNF-α starts to increase at 3 days of indwelling of the indwelling needles. It reaches the peak at 7 days.

Research demonstrates that inflammatory cells play roles in triggering and strengthening thrombosis. IL-1 and TNF-α can inhibit fibrinolysis. TNF-α can also inhibit the expression of the thrombomodulin of endothelial cells thus making the endothelial cells shift from an anticoagulation state to a pro-coagulation state. Therefore, the increased expression levels of IL-1 and TNF-α can not only promote progression of inflammations but also promote thrombosis.

Mirabilite is a white granular mineral medicine primarily hydrous sodium sulfate. In the traditional Chinese medicine, mirabilite has many functions. Modern research indicates external application of mirabilite plays roles in moisture absorption, subsidence of swelling, clearing heat and removing toxicity, and anti-inflammatory action. It is primarily used to treat pancreatitis, haemorrhoids and phlebitis.

The research results indicate that IL-1, IL-6, and TNF-α were highly expressed in the venous blood vessels of the rabbit ears at 3 days after the indwelling needles were indwelt. The expression increased with time. The expression increased significantly at 7 days, suggesting that infiltration of inflammatory cells occurred in the vascular tissue and the blood vessel endothelium released IL-1, IL-6, and TNF-α thus leading to local inflammatory responses under stimulation. The increase of the expression of IL-1 and TNF-α can induce the normal cells to produce IL-6. The increase of the expression of IL-6 further aggravates inflammatory responses. Continuous stimulation from the indwelling needle catheter makes the inflammatory factors to interact mutually thus aggravating phlebitis. Some research has indicated that the increase of inflammatory factors can lead to vasoconstriction and spasm, cause inflammatory responses to the blood vessels, and give

rise to blood damage (15), which is consistent with the above result.

Moreover, the research also demonstrates that external application of mirabilite can effectively decrease the expression of IL-1, IL-6, and TNF-α in the rabbit ear veins and decrease the severity of inflammatory responses, which is consistent with the result reported by Thao *et al* (26). Mirabilite may make the local blood supply sufficient by stimulating the nervous reflex, improve the blood circulation of the local tissue, accelerate local lymph circulation, strengthen the phagocytic functions of the reticuloendothelial cells, reduce local endothelial cell infiltration, strengthen anti-inflammatory function, recover the vascular functions, and alleviate phlebitis.

In conclusion, early application of mirabilite for prevention of mechanical phlebitis arising from intravenous indwelling needles is effective. Its specific action mechanism is expected to be further studied.

Acknowledgements

This study was financially supported by The Nature Science Foundation of Liaoning Provience (no. 201602283, for Yanyan Lu).

References

1. Kovalenko OM, Mal'tsev DV, Kazmirchuk VIe and Kovalenko AO: Studying of cytokine dynamics in injured persons with severe burns for estimation of severity and prognosis. Klin Khir 2: 49-53, 2014 (In Ukrainian).
2. Ray-Barruel G, Polit DF, Murfield JE and Rickard CM: Infusion phlebitis assessment measures: A systematic review. J Eval Clin Pract 20: 191-202, 2014.
3. Saunders H: Translating knowledge into best practice care bundles: A pragmatic strategy for EBP implementation via moving postprocedural pain management nursing guidelines into clinical practice. J Clin Nurs 24: 2035-2051, 2015.
4. Powell J, Tarnow KG and Perucca R: The relationship between peripheral intravenous catheter indwell time and the incidence of phlebitis. J Infus Nurs 31: 39-45, 2008.
5. Grange-Prunier A, Couilliet D, Grange F and Guillaume JC: Allergic contact dermatitis to the Comfeel hydrocolloid dressing. Ann Dermatol Venereol 129: 725-727, 2002 (In French).
6. Kourbeti IS, Vakis AF, Ziakas P, Karabetsos D, Potolidis E, Christou S and Samonis G: Infections in patients undergoing craniotomy: Risk factors associated with post-craniotomy meningitis. J Neurosurg 122: 1113-1119, 2015.
7. China Pharmacopoeia Committee: Pharmacopoeia of the People's Republic of China. China Medical Science Press, Beijing, 118-119, 2010.
8. Wang Y, Zhang X and Li C: Applying hot compresses with Rhubarb and mirabilite to reduce pancreatic leakage occurrence in the treatment of severe acute pancreatitis. Iran JPublic Health 46: 136-138, 2017.
9. Milutinović D, Simin D and Zec D: Risk factor for phlebitis: A questionnaire study of nurses' perception. Rev Lat Am Enfermagem 23: 677-684, 2015.
10. Abolfotouh MA, Salam M, Bani-Mustafa A, White D and Balkhy HH: Prospective study of incidence and predictors of peripheral intravenous catheter-induced complications. Ther Clin Risk Manag 10: 993-1001, 2014.
11. Hegerova LT, Leal AD, Grendahl DC, Seisler DK, Sorgatz KM, Anderson KJ, Hilger CR and Loprinzi CL: An analysis of fosaprepitant-induced venous toxicity in patients receiving highly emetogenic chemotherapy. Support Care Cancer 23: 55-59, 2015.
12. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ and Warren DK: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: Update by the Infectious Diseases Society of America. Clin Infect Dis 49: 1-45, 2009.
13. Ward-Kavanagh LK, Lin WW, Šedý JR and Ware CF: The TNF receptor superfamily in co-stimulating and co-inhibitory responses. Immunity 44: 1005-1019, 2016.
14. Ng PC, Li K, Leung TF, Wong RP, Li G, Chui KM, Wong E, Cheng FW and Fok TF: Early prediction of sepsis-induced disseminated intravascular coagulation with interleukin-10, interleukin-6, and RANTES in preterm infants. Clin Chem 52: 1181-1189, 2006.
15. Li WJ, Liu Y, Wang JJ, Zhang YL, Lai S, Xia YL, Wang HX and Li HH: 'Angiotensin II memory' contributes to the development of hypertension and vascular injury via activation of NADPH oxidase. Life Sci 149: 18-24, 2016.
16. Rickard CM, McCann D, Munnings J and McGrail MR: Routine resite of peripheral intravenous devices every 3 days did not reduce complications compared with clinically indicated resite: A randomised controlled trial. BMC Med 8: 53, 2010.
17. Zingg W and Pittet D: Peripheral venous catheters: An under-evaluated problem. Int J Antimicrob Agents 34: 38-42, 2009.
18. Karamanoglu A, Yumuk PF, Gumus M, Ekenel M, Aliustaoglu M, Selimen D, Sengoz M and Turhal NS: Port needles: Do they need to be removed as frequently in infusional chemotherapy? J Infus Nurs 26: 239-242, 2003.
19. Falkowski A: Improving the PICC insertion process. Nursing 36: 26-27, 2006.
20. Pandey D, Mehta S, Grover A and Goel N: Indwelling catheterization in Caesarean section: Time to retire it! J Clin Diagn Res 9: 01-04, 2015.
21. Mo XR, Luo XJ, Li CP, Pan XF and Zhou LL: Effect ofmannitol injection by intravenous catheter on ear vein endothelial cell apoptosis and venous thrombus in rabbits. Eur Rev Med Pharmacol Sci 19: 491-497, 2015.
22. Watanabe D, Fukunaga M and Yamamoto H: Verification of the injection pressure reduction effect using the novel indwelling needle for contrast-enhanced CT. Nihon Hoshasen Gijutsu Gakkai Zasshi 73: 267-272,2017.
23. dos Reis PE, Silveira RC, Vasques CI, and de Carvalho EC: Pharmacological interventionsto treat phlebitis: Systematic review. J Infus Nurs 32: 74-79, 2009.
24. Duan F, Yu Y, Guan R, Xu Z, Liang H and Hong L: Vitamin K2 induces mitochondria related apoptosis in human bladder cancer cells via ROS and JNK/p38 MAPK signal pathways. PLoS One 11: e0161886, 2016.
25. Park KH and Park WJ: Endothelial dysfunction: Clinical implications in cardiovascular disease and therapeutic approaches. J Korean Med Sci 30: 1213-1225, 2015.
26. Thao NP, Luyen BT, Koo JE, Kim S, Koh YS, Thanh NV, Cuong NX, Kiem PV, Minh CV and Kim YH: In vitro anti-inflammatory components isolated from the carnivorous plant *Nepenthes mirabilis* ELour. F Rafarin. Pharm Biol 54: 588-594, 2016.