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Original Article

Comparison of intermittent pneumatic compression and shenmai injection in prevention of venous thromboembolism after cerebral apoplexy and its influence on coagulation function of patients

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Abstract: Objective: To probe into the effects of drug prophylaxis regimen and physical intervention regimen on the prevention of venous thromboembolism (VTE) after stroke and the coagulation function of patients. Methods: 104 cerebral apoplexy patients treated in our hospital between May 2017 and May 2019 were selected as the research objects and randomly divided into the drug prophylaxis group (Shenmai injection was given intravenously) and physical intervention group (adopted intermittent pneumatic compression) (n=52 for each). The incidence of VTE was compared between the two groups of patients, and the changes in coagulation function-related indicators before and after treatment were compared between the two groups of patients as well. Results: After color doppler ultrasound examination, no pulmonary thromboembolism (PTE) was found in the two groups of patients and the venous thrombosis in both groups was peripheral; the incidence of lower-limb DVT of drug prophylaxis group was significantly lower than that of physical intervention group [5 (9.62%), 13 (25.00%), X^2=4.2997, P=0.0381)]; there were 2 cases of mild diarrhea in the drug prophylaxis group and 1 case of mild diarrhea in the physical intervention group. All patients relieved spontaneously after 2 days [2 (3.85%), 1 (1.92%), X^2=0.0000, P=1.0000]. There were no obvious adverse drug reactions caused by drug allergy, bleeding, gastrointestinal tract reaction or other physical discomfort symptoms in the patients of both groups. Conclusion: The results suggested that drug prophylaxis regimen has better preventive effect on VTE after stroke than physical intervention regimen.

Keywords: Cerebral apoplexy, venous thromboembolism, coagulation function

Introduction

Cerebral apoplexy is a common disease that occurred frequently in clinical neurology. It is divided into three types, i.e. hemorrhagic, ischemic and mixed cerebral apoplexy. Among them, ischemic cerebral apoplexy takes up the highest proportion of about 60-80% [1]. As China's aging population increases and people's lifestyle changes in recent years, the incidence of cerebral apoplexy increases rapidly, and gradually becomes one of the major public health problems [2, 3]. According to statistics, over two million new cases of cerebral apoplexy occur in China every year, and the rate continues to increase at an annual rate of 8.7%, which is far higher than the global average rate [4, 5]. Due to the factors such as the effects of disturbance of consciousness, complicated viscera damage of important organs, and long-term bed rest, the activity of patients with cerebral apoplexy decreases obviously, which is likely to cause venous blood reflux disorders and abnormal blood coagulation in the deep veins of the lower limbs, eventually leading to the formation of DVT [6, 7]. Despite its insidious onset, DVT progresses fast. If patients with DVT were not treated in time, it might lead to ischemia and necrosis in their body [8, 9]. Moreover, the thrombus may fall off at any time, which will result into severe pulmonary thromboembolism (PTE) [10]. Once PTE occurs, patients may develop functional disorders of the circulatory system and respiratory system, resulting in the occurrence of sudden death. DVT and PTE are collectively referred to as venous thromboem-

bolism (VTE), which severely threatens the quality of life and health of patients [11, 12]. The key to reduce the mortality and disability of patients with cerebral apoplexy is to prevent the occurrence of VET. Currently the intervention measures such as low molecular weight heparin method or stretch socks, and intermittent pneumatic compression are often used to prevent the occurrence of VTE [13, 14]. The low molecular weight heparin method has achieved notable preventive effects since it was applied to the prevention of VTE, but it has been restricted for usage because of its adverse effects, including neurological deterioration, bleeding, and poor compliance [15, 16]. Intermittent pneumatic compression is a kind of physical method which will not cause bleeding complications, and prevent the occurrence of VTE. Meanwhile, it has the advantages of simplicity, convenience, low cost and so on [17]. However, there are reports indicated that the usage of the intermittent pneumatic compression has limited preventive effects on VTE, especially in high-risk patients [18]. Shenmai injection originated from the ancient Chinese herbal medicine Shenmai drink. Experimental studies have confirmed that Shenmai injection can reduce platelet aggregation, effectively improve the body's microcirculation disorders and blood hypercoagulability to reduce thrombosis, and thus play an anticoagulant effect [19-21]. It has been reported in the literatures [22, 23] that the treatment of patients with acute stroke and complicated VET using Shenmai injection can significantly reduce the incidence of hemiplegia, improve the scores of some dimensions of patients' life function assessment scale (BI), and improve the prognosis. However, there are few reports about the effect of Shenmai injection on the prevention of VTE after cerebral apoplexy and its influence on the coagulation function of patients. By exploring the effects of drug prophylaxis group (intravenous drip of Shenmai injection) and physical intervention group (intermittent pneumatic compression) on the prevention of VTE after cerebral apoplexy and the coagulation function of patients, this study aims to provide a reference for the clinical prevention of VTE after cerebral apoplexy.

Materials and methods

General data

104 cerebral apoplexy patients treated in our hospital between May 2017 and May 2019 were selected as the research objects, among which there were 55 males and 49 females. The average age was 67.53±7.11 years, body mass index (BMI) 23.15±3.14 kg/m^2, course of disease 27.05±9.38 h, and the types of diseases included 32 cases of cerebral hemorrhage, 72 cases of cerebral infarction. 35 cases with diabetes, 67 cases with hypertension, 55 cases with hyperlipidemia, 44 cases with hyperhomocysteinemia and 38 cases with anemia. This study was conducted in accordance with the regulations of the Declaration of Helsinki concerning clinical trial research and was approved by the ethics committee of our hospital. The cases were randomly divided into the drug prophylaxis group and the physical intervention group (n=52 for each).

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients included in the study were all conformed to the clinical diagnosis of cerebral apoplexy; (2) Patients had clinical symptoms of disturbance of consciousness, limb numbness, nausea, and dizziness, etc.; (3) Age ≥ 18 years old; (4) Disease onset time ≤ 72 h; (5) Patients and their families voluntarily signed informed consent.

Exclusion criteria: (1) Patients who were allergic to the drugs used in this study; (2) Patients who had a history of venous thromboembolism; (3) Patients with epilepsy and mental illness; (4) Pregnant and lactating women; (5) Patients with severe diseases of important organs such as liver or kidney; (6) Patients with collagenosis and joint disease; and (7) Patients with severe endocrine and hematopoietic diseases.

Methods

The two groups of patients were routinely treated after admission based on their specific conditions. Rationally controlled blood glucose and blood pressure levels, and maintained the vital signs of the patients. Gave the routine treatments like intra-arterial thrombolysis, anti-infection, dehydration and nutritional support, and basic care to prevent pressure sores; Performed proper lower-limb exercises independently or with the assistance of patients' families/therapists. Based on the routine treatment, the patients of drug prophylaxis group also received intravenous drip of Shenmai injection (G.Y.Z.Z. Z51021879, China Resources Sanjiu (Ya'an) Pharmaceutical Co., Ltd.) by 50

Table 1. Comparison of the general data of the two groups of patients

Item	Drug prophylaxis group (n=52)	Physical intervention group (n=52)	t/X^2	P
Gender (Male/Female)	27/25	28/24	0.0386	0.8442
Age ($\bar{x}$ ± sd, Age)	68.25±8.39	67.04±6.12	0.8402	0.4028
Body mass index (BMI) ($\bar{x}$ ± sd, kg/m^2)	23.94±2.28	22.88±3.67	1.7692	0.0799
Course of disease (x ± sd, h)	26.95±8.46	27.75±6.67	0.5355	0.5935
Type of disease (Cerebral hemorrhage/cerebral infarction)	18/34	14/38	0.7222	0.3954
Complicated diabetes (Yes/No, Case)	16/36	19/33	0.3876	0.5336
Complicated hypertension (Yes/No, Case)	35/17	32/20	0.3776	0.5389
Complicated hyperlipidemia (Yes/No, Case)	28/24	27/25	0.0386	0.8442
Complicated hyperhomocysteinemia (Yes/No, Case)	20/32	24/28	0.6303	0.4272
Anemia (Yes/No, Case)	18/34	20/32	0.1659	0.6838

ml, one dose a day for 14 days. The patients of physical intervention group who were based on the routine treatment were given 40 mmHg intermittent pneumatic compression, 30 min/time, twice a day for total of 14 days.

Observation of indicators

This study primarily observed the difference of the two methods in the prevention of VTE after cerebral apoplexy (Color doppler ultrasound examination was performed respectively on the first day of hospitalization and after treatment). The secondary observations were the effects of two sets of preventive measures on the coagulation function-related indexes of patients, such as D-Dimer, fibrinogen, plasma viscosity and red blood cell volume (Fasting venous blood was measured within 24 hours of hospitalization and 14 days after treatment. D-Dimer was determined by immunoturbidimetric method, fibrinogen was determined by coagulation method, plasma viscosity was measured by SA-600 automatic hemorheology tester, and red blood cell volume was measured using an XE-3000 blood cell analyzer).

Statistical method

SPSS19.0 statistical software were used to conduct statistical analysis and processing. The measurement data were all expressed as mean ± standard deviation (x ± sd). The intra-group before-after comparison was performed by paired sample t-test, and the comparison between the two groups was performed by independent sample t-test. The enumeration data were expressed as percentage and analyzed with the X^2 test. P<0.05 indicated that the difference was statistically significant.

Results

The general data comparison

There was no statistically significant difference between the two groups in the general data refer to gender, age, course of disease, type of disease, comorbid diseases and so on (P>0.05, **Table 1**).

Occurrence of DVT of the patients in the two groups

After color doppler ultrasound examination, no PTE was found in the two groups of patients. 5 patients in the drug prophylaxis group showed obvious DVT with an incidence of 9.62%, which was significantly lower than 25.00% (13/52) of physical intervention group. The difference was statistically significant (X^2=4.2997, P=0.0381, **Table 2**).

Occurrence and distribution of DVT of the two groups of patients

DVT occurred in 5 cases in the drug prophylaxis group, and 13 cases in the physical intervention group. See **Table 3** for details.

Changes in coagulation function-related therapy before-after treatment in the two groups of patients

The levels of D-Dimer, fibrinogen, plasma viscosity, and red blood cell volume of the patients in the two groups after treatment were significantly lower than those before treatment, and the decreases in the levels of D-Dimer, fibrinogen, and plasma viscosity of the patients in the drug prophylaxis group were significantly great-

Table 2. Comparison of the incidence of vet between the two groups

Group	Case	Number of VET cases	Incidence rate (%)	X^2	*P*
Drug prophylaxis group	52	5	9.62	4.2997	0.0381
Physical intervention group	52	13	25.00		

Table 3. Occurrence and distribution of DVT of the two groups of patients (case)

Group	DVT did not occur	DVT occurred		
		Simple intermuscular thrombosis	Popliteal vein thrombosis with intramuscular thrombosis	Femoral vein thrombosis
Drug prophylaxis group (n=52)	47	3	2	0
Physical intervention group (n=52)	43	4	3	2
X^2			1.3206	
P			0.2505	

Table 4. Changes in coagulation function-related therapy before and after treatment in the two groups of patients (x ± sd)

		D-Dimer (mg/L)	Fibrinogen (g /L)	Plasma viscosity (mPa/S)	Red blood cell volume (%)
Drug prophylaxis group (n=52)	Before treatment	0.37±0.07	3.89±1.14	1.92±0.13	54.46±7.12
	After treatment	0.16±0.04*	2.88±0.91*	1.43±0.04*	43.52±5.17
	t	18.7830	4.9931	25.9784	8.9657
	P	0.0000	0.0000	0.0000	0.0000
Physical intervention group (n=52)	Before treatment	0.35±0.08	3.91±1.23	1.93±0.17	53.58±7.29
	After treatment	0.24±0.05	3.13±1.05	1.62±0.09	45.67±6.14
	t	8.4081	3.4780	11.6215	5.9845
	P	0.0000	0.0007	0.0000	0.0000

Note: Comparison with the physical intervention group, *$P<0.05$.

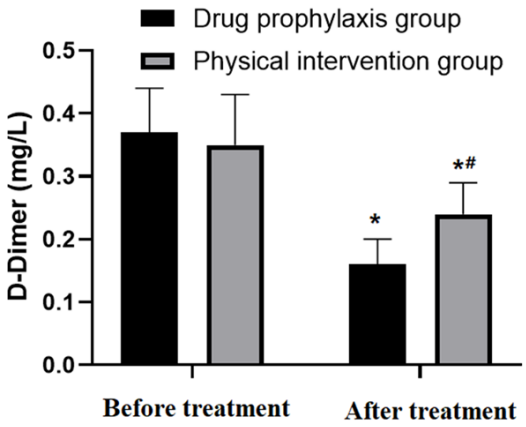

Figure 1. Comparison of D-dimer levels between the two groups before and after treatment. Comparison with the same group before treatment, *$P<0.05$. Comparison with drug prophylaxis group, #$P<0.05$.

er than those of the physical intervention group ($P<0.05$); There was no statistical difference in the levels of red blood cell volume between the two groups after treatment ($P>0.05$). Details are listed in **Table 4** and **Figures 1**-**4**.

Comparison of adverse reactions between the two groups

Comparison of adverse reactions of the two groups: Except for 2 cases of mild diarrhea in the drug prophylaxis group and 1 case of mild diarrhea in the physical intervention group, who relieved spontaneously after 2 days [2 (3.85%), 1 (1.92%), X^2=0.0000, P=1.0000], there was no drug-induced allergic reaction, bleeding, gastrointestinal reaction, and other physical discomfort in the patients of the two groups (**Table 5**).

Discussion

In this study, there are 13 cases with lower limb vein thrombus in the control group who used

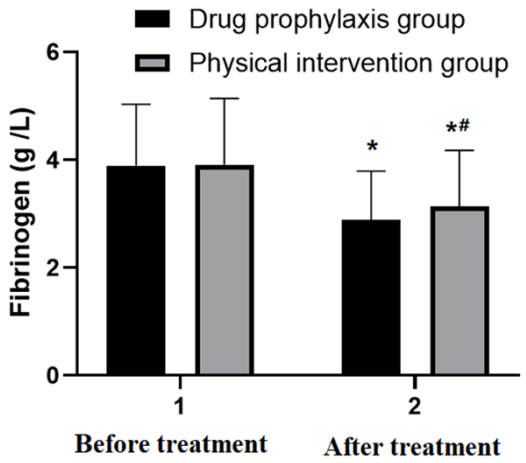

Figure 2. Comparison of Fibrinogen levels between the two groups before and after treatment. Comparison with the same group before treatment, **P<0.05*. Comparison with drug prophylaxis group, *#P<0.05*.

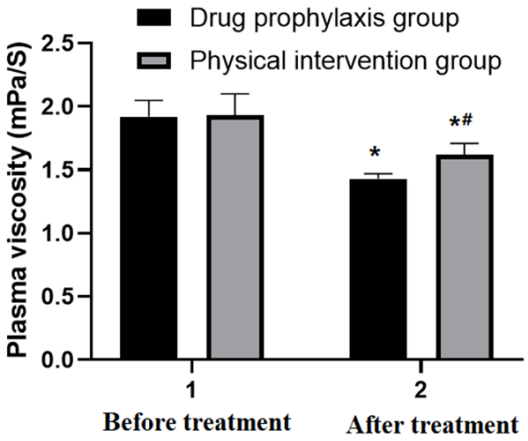

Figure 3. Comparison of plasma viscosity levels between the two groups before and after treatment. Comparison with the same group before treatment, **P<0.05*. Comparison with drug prophylaxis group, *#P<0.05*.

intermittent pneumatic compression for physical intervention, with incidence higher than the research results of Wan Feng et al. [24]. The reason may be related to the fact of some differences in the source of the patients included in the study, the implementation plan of the physical intervention, and the time point of making physical intervention. Moreover, the incidence is also higher than the drug prophylaxis group measured with Shenmai injection in this study, suggesting that the preventive effect of intermittent pneumatic compression on VTE after cerebral apoplexy is not as good as that of intravenous drip of Shenmai injection. The reasons are as follows: The prevention of physical intervention group focuses on the lower extremities, where the source of thrombus is the most, while drug prevention focuses on the whole body, with different prevention mechanisms. The mechanism of intermittent pneumatic compression of physical intervention group is mechanical and biochemical effect [25, 26]. The mechanical effect is mainly to change the vascular structure and hemodynamics of patients' lower extremities through intermittent uniform gas charging and outgassing. The biochemical effect is reflected in that the pressure in the gap of the tissues increases by increasing the pressure of the muscles and subcutaneous soft tissues of the patients. It is conducive to the return of the tissue fluid to decrease the degree of edema of the patients' lower limbs, and then reduce the tension of the soft tissues; moreover, intermittent pneumatic compression can increase blood flow to the vascular tension and shear stress caused by the increased tensile stress and the NOS activity, so as to promote the increase of NO content in the blood, thus inhibiting platelet adhesion and aggregation and improving the role of microcirculation. The mechanism of preventing VTE after cerebral apoplexy by Shenmai injection in the drug prophylaxis group has not been fully clarified. It may be related to the effects of improvement of the patients' microcirculation by Shenmai injection, reduction in blood viscosity and fibrinogen content and anti-platelet aggregation [27, 28]. The two preventive measures have their own

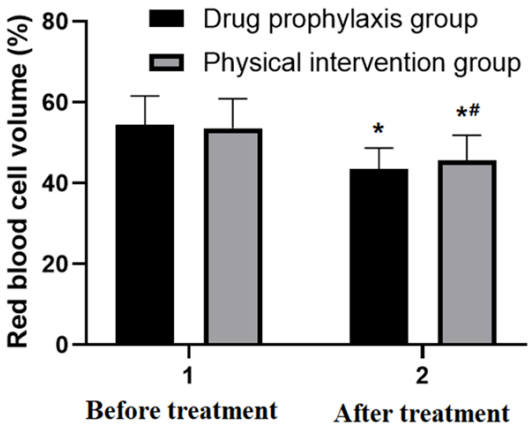

Figure 4. Comparison of red blood cell volume levels between the two groups before and after treatment. Comparison with the same group before treatment, **P<0.05*. Comparison with drug prophylaxis group, *#P<0.05*.

Table 5. Comparison of adverse reactions between the two groups

Group	Case	Number of adverse reactions	Incidence rate (%)	X^2	*P*
Drug prophylaxis group	52	2	3.85	0.0000	1.0000
Physical intervention group	52	1	1.92		

characteristics and should be used flexibly in clinical application according to the risk of thrombosis.

The results of this study showed that the D-Dimer content of patients in both groups was significantly reduced after treatment. The figure of the D-Dimer content in drug prophylaxis group was lower than that of the physical intervention group, suggesting that Shenmai injection decreased D-Dimer content more significantly than intermittent pneumatic compression and decreased more notably for the risk of thrombosis in patients with cerebral apoplexy. The results of this study showed that fibrinogen content, plasma viscosity and red blood cell volume of patients in the two groups significantly were decreased after treatment compared with those before treatment. The fibrinogen content and plasma viscosity of patients in the prophylaxis group after treatment were lower than those of physical intervention group, suggesting that Shenmai injection greatly reduced the fibrinogen and plasma viscosity of patients. It has been reported in the literature [29] that when plasmin and Shenmai injection are used to treat cerebral infarction, the former is not as effective as plasmin, but it can dramatically improve fibrinogen content, plasma viscosity, platelet aggregation rate, and hematocrit in patients with cerebral infarction. This has corroborated the results of this study, indicating that the drug prophylaxis group has a positive preventive effect on VTE after cerebral apoplexy. Studies have shown that Shenmai injection is better than physical intervention for improving the coagulation function of patients with cerebral apoplexy. It provides certain reference value for the clinical application of Shenmai injection. No significant adverse drug reactions occurred in the two groups of patients in the study, indicating that Shenmai injection is safe to some extent.

In conclusion, drug prophylaxis regimen has better preventive effect on VTE after cerebral apoplexy than physical intervention regimen. It better improves patients' coagulation function than physical intervention regimen. However, the study has certain limitations: (1) The respondents came from a single center under a small sample size. The results of the two groups of VTE and the incidence of adverse reactions need to be further studied in multiple centers with larger sample size; and (2) This study only observed the short-term preventive effect of VTE after cerebral apoplexy, but not the long-term preventive effect, which needs to be further explored.

Disclosure of conflict of interest

None.

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References

[1] Stark K, Schubert I, Joshi U, Kilani B, Hoseinpour P, Thakur M, Grünauer P, Pfeiler S, Schmidergall T, Stockhausen S, Bäumer M, Chandraratne S, von Brühl ML, Lorenz M, Coletti R, Reese S, Laitinen I, Wörmann SM, Algül H, Bruns CJ, Ware J, Mackman N, Engelmann B and Massberg S. Distinct pathogenesis of pancreatic cancer microvesicle-associated venous thrombosis identifies new antithrombotic targets in vivohighlights. Arterioscler Thromb Vasc Biol 2018; 8: 104638-104653.

[2] Hultcrantz M, Björkholm M, Dickman PW, Landgren O, Derolf ÅR, Kristinsson SY and Andersson TML. Risk for arterial and venous thrombosis in patients with myeloproliferative neoplasms: a population-based cohort study. Ann Intern Med 2018; 168: 317-325.

[3] Behrouzi R and Punter M. Diagnosis and management of cerebral venous thrombosis. Clin Med (Lond) 2018; 18: 75-79.

[4] Rezoagli E, Martinelli I, Poli D, Scoditti U, Passamonti SM, Bucciarelli P, Ageno W and Dentali F. The effect of recanalization on long-term neurological outcome after cerebral venous thrombosis. J Thromb Haemost 2018; 16: 718-724.

[5] Needleman L, Cronan JJ, Lilly MP, Merli GJ, Adhikari S, Hertzberg BS, DeJong MR, Streiff MB and Meissner MH. Ultrasound for lower extremity deep venous thrombosis: multidisciplinary recommendations from the society of radiologists in ultrasound consensus conference. Circulation 2018; 137: 1505-1515.
[6] Gao L, Xu W, Li T, Yu X, Cao S, Xu H, Yan F and Chen G. Accuracy of magnetic resonance venography in diagnosing cerebral venous sinus thrombosis. Thromb Res 2018; 167: 64-73.
[7] Matsuda Y, Owai Y, Kakishita K and Nakao N. A novel combined approach using a Penumbra catheter and balloon catheter for cerebral venous sinus thrombosis. BMJ Case Rep 2018; 26: 18-22.
[8] Shu XJ, Li ZF, Chang YW, Liu SY, Wang WH and Li X. Different doses of folic acid and vitamin B12 to treat rabbits with deep venous thrombosis and hyperhomocysteinemia. Exp Ther Med 2018; 15: 2874-2878.
[9] Danwang C, Mazou TN, Tochie JN, Tankeu R and Bigna JJ. Global epidemiology and patterns of cerebral venous thrombosis: a systematic review and meta-analysis protocol. BMJ Open 2018; 8: 939.
[10] Cascio V, Hon M, Haramati LB, Gour A, Spiegler P, Bhalla S and Katz DS. Imaging of suspected pulmonary embolism and deep venous thrombosis in obese patients. Br J Radiol 2018; 91: 20170956.
[11] Ishak MN, Nik-Abdul-Ghani NM and Mohamad I. Sudden bilateral sensorineural hearing loss secondary to cerebral venous thrombosis. Iran J Otorhinolaryngol 2018; 30: 113-116.
[12] Hanson SE, Mitchell MB, Palivela N, Peng SA, Feng L, Largo RD, Butler CE and Garvey PB. Smaller-diameter anastomotic coupling devices have higher rates of venous thrombosis in microvascular free tissue transfer. Plast Reconstr Surg 2017; 140: 1293-1300.
[13] Chirakkara SKP, Bakhsh ARA, Pariyadath AK and Rathinavelu B. Cerebral venous sinus thrombosis in a patient with meningococcal meningitis. Oman Med J 2018; 33: 61-64.
[14] Feng X, Zhao T, Liu J and Zhou C. Cerebral venous sinus thrombosis with cerebral hemorrhage presenting with status epilepticus in early pregnancy. Clin Lab 2018; 64: 611-614.
[15] Lakha S, Png CYM, Chun K and Ting W. Recurrent iliofemoral venous thrombosis in the setting of may-thurner syndrome as the presenting symptom of Behcet's disease. Ann Vasc Surg 2018; 49: 315.
[16] Mendes PD, Lopes CLDS, França DM, Reis JC, Santos ACJ and Darwich RZ. The dilemma of anticoagulating patients with cerebral venous thrombosis who underwent decompressive craniectomy. World Neurosurg 2018; 114: 168-171.
[17] Xia ZN, Zhou Q, Zhu W and Weng XS. Low molecular weight heparin for the prevention of deep venous thrombosis after total knee arthroplasty: a systematic review and meta-analysis. Int J Surg 2018; 54: 265-275.
[18] Lidegaard Ø. Severely biased review of studies assessing the risk of venous thrombosis in users of drospirenone-containing oral contraceptives. BJOG 2018; 125: 929-931.
[19] Vila I, Brea-García B, Fernández-Marcos AA, Hurtado-Ruzza HA, Couto-González I and Taboada-Suárez A. Discussion: smaller-diameter anastomotic coupling devices have higher rates of venous thrombosis in microvascular free tissue transfer. Plast Reconstr Surg 2018; 141: 780e.
[20] Chen YL, Shou LH and Zhang ZX. Association of interleukin-18 gene polymorphism and its protein expression with the lower extremity deep venous thrombosis in the Chinese Han population: a case-control study. J Clin Lab Anal 2018; 32: e22345.
[21] Vecht L, Zuurbier SM, Meijers JCM and Coutinho JM. Elevated factor VIII increases the risk of cerebral venous thrombosis: a case-control study. J Neurol 2018; 265: 1612-1617.
[22] Roriz M, Crassard I, Lechtman S, Saadoun D, Champion K, Wechsler B, Chabriat H and Sène D. Can anticoagulation therapy in cerebral venous thrombosis associated with Behcet's disease be stopped without relapse. Rev Neurol (Paris) 2018; 174: 162-166.
[23] Arivazhagan A, Mundlamuri RC, Shreedhara AS, Bharath RD, Mahadevan A, Sinha S, Rao MB and Satishchandra P. Remote contralateral side cerebral venous thrombosis following intracranial surgery: a rare complication in an unusual setting. Neurol India 2018; 66: 520-522.
[24] Lefrère B, Stepanian A, Itzhar-Baïkian N, Charles P, Hadj-Ali A, Joly B, Alhenc-Gelas M, Drouet L, Veyradier A and Siguret V. Deep venous thrombosis treated by rivaroxaban in a young patient with type Ia carbohydrate-deficient glycoprotein (CDG) syndrome. Ann Biol Clin (Paris) 2018; 76: 217-223.
[25] Garland J, Kesha K, Vertes D, Modahl L, Milne D, Ruder T, Stables S and Tse R. Empty delta sign on unenhanced postmortem computed tomography scan in cerebral venous thrombosis. Am J Forensic Med Pathol 2018; 39: 360-363.
[26] Harrington LB, Blondon M, Cushman M, Kaunitz AM, Allison MA, Wang L, Sullivan S, Woods NF, LaCroix AZ, Heckbert SR, McKnight B, Rossouw J and Smith NL. Vasomotor symptoms and the risk of incident venous thrombosis in postmenopausal women. J Thromb Haemost 2018; 16: 886-892.

[27] Taha MA, Busuttil A, Bootun R and Davies AH. A systematic review on the use of deep venous stenting for acute venous thrombosis of the lower limb. Phlebology 2018; 34: 115-127.
[28] Kravtsov PF, Katorkin SE and Melnicov MA. Clinical experience with the use of rivaroxaban in the treatment of cancer patients with venous thrombosis. Khirurgiia (Mosk) 2018; 57-63.
[29] Mizoguchi S, Sawai T, Hirota A, Yamamoto S, Nakajima H, Makino K, Takase K and Ito M. Trousseau's syndrome causing refractory deep venous thrombosis. Intern Med 2018; 57: 623-626.