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Original Article

The comparative study on therapeutic effects of intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke

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Abstract: Objective: To compare the therapeutic effects of intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke. Methods: One hundred and twenty patients of acute ischemic stroke who were treated in our hospital from January 2015 to January 2017 were selected and separated into intravenous alteplase thrombolytic treatment group (Group A, n=40), intravenous urokinase thrombolytic treatment group (Group B, n=40) and interventional urokinase thrombolytic treatment group (Group C, n=40), according to the random number table method. The National Institutes of Health Strike Scale (NIHSS) scores, clinical efficacy, adverse reactions, long-term therapeutic effects of the patients in three groups were statistically analyzed. Results: The differences of NIHSS scores before and after treatment among the three groups were not statistically significant (P=0.125 and P=0.230 respectively); the total effective rates of the three groups were 97.5% (39/40), 95% (38/40), 92.5% (37/40) respectively, the differences of which were not significant in statistics (F=2.77, P=0.223>0.05). The adverse reaction rates of the three groups were 7.5% (3/40), 10% (4/40), 12.5% (5/40) respectively and there were no significant differences (F=4.11, P=0.256>0.05); The differences of recanalization rates, good prognosis rates, mortality rates among the three groups had no statistical significance (F=0.32, 0.45, 0.41, P=0.421, 0.467, 0.362>0.05). Conclusion: Intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke have equivalent therapeutic effects.

Keywords: Acute ischemic stroke, intravenous alteplase, urokinase thrombolysis, interventional urokinase thrombolysis, therapeutic effects

Introduction

In 2008, the results of the third National Death Cause Investigation found by the Ministry of Health showed that cerebrovascular diseases has become the first cause of death in urban and rural residents in China [1]. Eighty percent of cerebrovascular diseases were cerebral infarction, the disability rate and mortality rate of which was around 50% and 10% respectively. Now in clinical treatment, it is widely acknowledged that thrombolytic treatment is the only therapeutic method and other drug therapy all belongs to systemic protective treatment and prevention from relapse [2]. Thrombolytic drug therapy can reestablish the circulation of ischemic region in patients at ultra-early stage of cerebral infarction, consequently promote perfusion, narrow infarct size, mitigate patients' clinical symptoms and improve life quality. In this study, the therapeutic effects of intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke were studied and compared, and the results implied that all these three methods had equivalent therapeutic effects.

Materials and methods

General information

This study was approved by Ethics Committee of our hospital. The clinical data of 120 cases

of acute ischemic stroke patients who were treated in our hospital from January 2015 to January 2017 were conducted with randomized controlled trial.

Inclusion criteria: All the patients who got attacked by acute ischemic stroke for the first time; all the patients who were confirmed as acute ischemic stroke by computed tomography (CT) and magnetic resonance imaging (MRI) or had normal coagulation mechanisms; all the patients whose symptoms were in line with the diagnostic criteria for acute ischemic stroke and whose onset time were within 6 hours; all the patients who signed Informed Consent Form [3].

Methods and groups

Before thrombolytic treatment, all the patients should be selected carefully. To accurately grasp the indications of thrombolytic treatment, what we should pay attention to were as follows. Inclusion criteria: Patients with acute ischemic stroke within 3-6 h would be the qualified candidates for thrombolytic treatment; patients who were clinically diagnosed as acute cerebral infarction; patients whose cranial CT excluded brain hemorrhage; patients without corresponding lesion of nerve function defect; patients aged less than 80 years old; patients whose blood pressure was less than 160/100 mmHg; patients without hemorrhagic disease or coma. In clinical treatment, it was widely acknowledged that the earlier patients received thrombolytic treatment, the better the therapeutic effects would achieve. Therefore, 6 h is the main time window for clinical selection [4].

Exclusion criteria: Patients with bleeding or hemorrhagic diseases or severe general complications; patients who did not take any platelet inhibitors or other drugs in recent time; patients who did not have acute infective endocarditis medical history or acute gastrointestinal ulcer; patients who had normal blood coagulation mechanisms. Before and during thrombolytic treatment, the blood pressure of patients should be under 185/110 mmHg and 185/95 mmHg respectively.

Patients in intravenous alteplase thrombolytic treatment group (Group A) received intravenous alteplase thrombolytic treatment. Patients were given intravenous injection of 0.9 mg/kg alteplase (Bohringer Ingelheim Pharma GmbH & Co. KG, Germany) and 10 ml physiological saline, which should be finished within 1 h.

Patients in intravenous urokinase thrombolytic treatment group (Group B) received intravenous urokinase thrombolytic treatment. After being diagnosed as stroke, patients' coagulation function was checked and their heads were examined by CT, in order to open a green channel for thrombolytic treatment. First, patients were given intravenous drip of plasma volume expanders and further given 1.09 million U urokinase (Tianjin Biochemical Pharmaceutical Co., Ltd., China) plus 100 ml physiological saline, and the injection was finished within 0.5 h.

Patients in interventional urokinase thrombolytic treatment group (Group C) received interventional urokinase thrombolytic treatment. The femoral artery catheterization technique was used to puncture and insert the catheter sheath. Through the minipump in micro catheter, 1.09 million U urokinase was injected into the specific vascular occlusion site, and the thrombolysis was performed within 2 h.

The specific operations were as follows: after local anesthesia, Seldinger femoral artery catheterization technique was used to puncture and insert the 6 F catheter sheath, and systemic heparin was applied. After the first DSA examination, the vascular occlusion site was found out. Under the guide of roadmap and micro-wire, the micro catheter was sent to thrombus site and its distal. Contrast medium was handly push to find out the size, length and accurate site of thrombus. Destruction of thrombus was done with a micro-wire machine with a soft head end. The head end of the micro catheter was placed at the thrombus site, and the micro pump in the micro catheter was used to inject urokinase into the thrombus. For the first time, 200 thousand U urokinase was added into the 60 mL saline and then injected continuously into the micro catheter within 15 min. Next, the liquid of the same concentration was pumped continuously at the speed of 3 ml/min until the blood vessel was opened. The general dosage was from 0.5 million U to 1.2 million U, the thrombolysis should be completed within 2 h as far as possible. If the total dose of urokinase reached 1.5 million U, the thrombolysis

Table 1. Comparison of general information of patients in the three groups

Items	Assortment	Group A (n=40)	Group B (n=40)	Group C (n=40)	F or X^2	P
Gender					2.71	0.255
	Male	25 (62.5)	24 (60.0)	26 (65.0)		
	Female	15 (37.5)	16 (40.0)	14 (35.0)		
Age		67.0±11.2	68.2±11.1	68.0±11.0	1.886	0.564
Time from onset to thrombolysis (h)		3.0±0.3	3.5±0.5	3.3±0.1	1.638	0.521
Degree of neurologic impairment					4.61	0.561
	Mild	13 (32.5)	14 (35.0)	13 (32.5)		
	Moderate	23 (57.5)	21 (52.5)	22 (55.0)		
	Severe	4 (10.0)	5 (12.5)	5 (12.5)		
Complications	Diabetes	15 (37.5)	13 (32.5)	14 (35.0)	1.32	0.165
	Hyperlipidemia	5 (12.5)	6 (15.0)	5 (12.5)	1.39	0.236
	Atrial fibrillation	2 (5.0)	3 (7.5)	3 (7.5)	2.37	0.152

Table 2. Comparison of NIHSS scores among the three groups of patients before and after treatment (scores, $\bar{x}$ ±s)

Groups	Cases	Before treatment	After treatment	D-Value	F	P
Group A	40	19.7±3.5	11.3±1.5	8.3±1.5	4.303	0.023
Group B	40	19.3±3.1	11.1±1.4	8.1±1.3	3.182	0.030
Group C	40	19.5±3.3	11.2±1.3	8.2±1.8	2.776	0.041
F		1.533	1.476	1.365		
P		0.345	0.214	0.204		

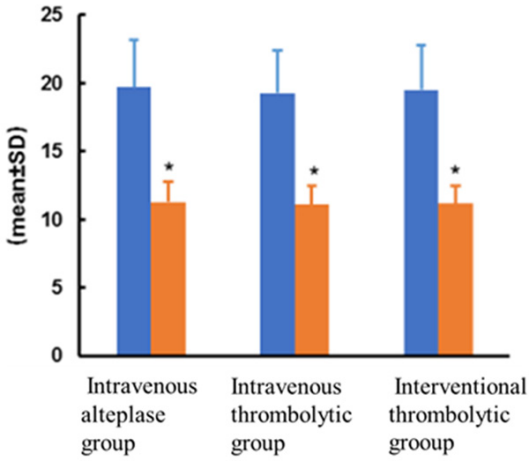

Figure 1. Comparison of NIHSS scores of the three groups of patients before and after treatment. Compared with before treatment in the same group, *P<0.05.

would be stopped even without recanalization. The cranial CT was reexamined immediately to see if there was any bleeding.

The neurological evaluation of three groups of patients were conducted by neurological surgeon before surgery, 2 h after surgery and 30 d after surgery, and were expressed by NIHSS scores. The criteria of Thrombolysis in Myocardial Infarction were used to evaluate the recanalization of vessels after thrombolysis.

Patients in three groups took MRI examination one day later. In the absence of cerebral hemorrhage, patients were asked to take 0.5 g aspirin (Hefei Jiulian Pharmaceutical Co., Ltd., China) orally once a day (10 days for a course of treatment) and then after one course reduced the drug dose to 0.1 g once a day for long-term use.

Observation indexes

The follow-up visits of patients were held once a week, which lasted for one month. One month before and after treatment, the neurological impairment degrees of patients in three groups were judged by National Institutes of Health Strike Scale (NIHSS). The scores ranged from 0 to 42 points. The degrees of patients' neurological impairment and scores were positively correlated, that is to say 0 points represented normal neurological function and 42 points represented severe impairment of neurological function [5]. Meanwhile, the numbers of patients with subcutaneous ecchymosis, gingival bleeding, hemoptysis, intracranial hemorrhage and other adverse reactions in two groups were counted. In addition, three groups of patients'

Table 3. Comparison of clinical efficacy of three groups of patients (cases/%)

Groups	Cases	Basic cure	SP	Progress	Stable	Det	TEC
Group A	40	11 (27.5)	15 (37.5)	13 (32.5)	1 (2.5)	0 (0)	39 (97.5)
Group B	40	11 (27.5)	14 (35.0)	13 (32.5)	2 (5.0)	0 (0)	38 (95.0)
Group C	40	10 (25.0)	14 (35.0)	13 (32.5)	2 (5.0)	1 (2.5)	37 (92.5)
X^2							2.77
P							0.235

Note: SP: Significant progress; Det: Deterioration; TEC: Total effective cases.

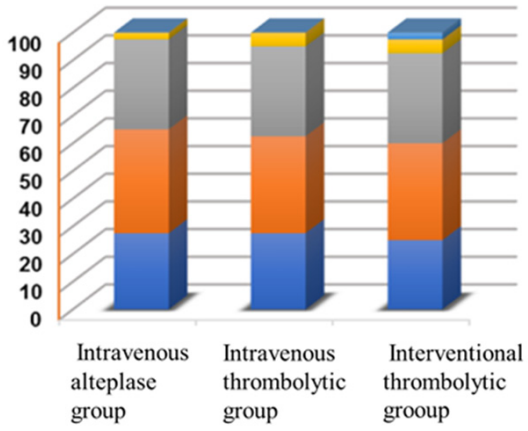

Figure 2. Comparison of clinical efficacy of three groups of patients.

recanalization, good prognosis, death were observed and recorded in order to assess its long-term therapeutic effects.

Efficacy evaluation criteria

The clinical efficacy of patients in three groups was assessed according to NIHSS score reduction rate. The NIHSS score reduction rate = NIHSS scores before treatment/NIHSS scores after treatment to NIHSS scores before treatment (91%-100% for basic cure, 46%-90% for significant progress, 18%-45% for progress, 0%-17% for stable, -18%-0% deterioration) [6].

Statistical analysis

The data were analyzed by SPSS20.0. The clinical efficacy, adverse reactions, long-term therapeutic effects and other enumeration data of the three groups of patients were expressed by adoption rate (%). And the differences between two groups were analyzed by X^2 test. The NIHSS scores of the three groups of patients before and after treatment were expressed by standard variance ($\bar{x} \pm s$) and the difference between pairs was analyzed by variance. Test standard: a=0.05.

Results

Comparison of general information of patients in the three groups

According to random number table method, these patients were divided into Group A (n=40), Group B (n=40) and Group C (n=40). The general information of patients in the three groups was not significantly different (P>0.05). See **Table 1**.

Comparison of NIHSS scores among the three groups of patients before and after treatment

For the three groups of patients, the NIHSS scores before and after treatment all had no significant difference. See **Table 2** and **Figure 1**.

Comparison of clinical efficacy of three groups of patients

The total effective rate of three groups of patients was 97.5% (39/40), 95.0% (38/40), 92.5% (37/40) respectively, and all the difference among them was not significant (F=2.77, P=0.223>0.05). See **Table 3** and **Figure 2**.

Comparison of adverse reactions among the three groups of patients

The incidence of adverse reactions for the three groups of patients was 7.5% (3/40), 10.0% (4/40), 12.5% (5/40) respectively, and all the difference among them was not significant (F=4.11, P=0.256>0.05). See **Table 4**.

Comparison of long-term therapeutic effects of three groups of patients

There was no significant difference in the rate of recanalization, good prognosis and mortality among the three groups of patients (F=0.32, 0.45, 0.41, P=0.421, 0.467, 0.362>0.05). See **Table 5**.

Table 4. Comparison of adverse reactions among the three groups of patients (cases/%)

Groups	Cases	SE	GB	Hemoptysis	IH	Total
Group A	40	1 (2.5)	1 (2.5)	0 (0)	1 (2.5)	3 (7.5)
Group B	40	1 (2.5)	1 (2.5)	1 (2.5)	1 (2.5)	4 (10.0)
Group C	40	1 (2.5)	1 (2.5)	1 (2.5)	2 (5.0)	5 (12.5)
X^2		1.39	2.37	3.36	4.35	4.11
P		0.263	0.302	0.420	0.630	0.154

Note: SE: Subcutaneous ecchymosis; GB: Gingival bleeding; IH: Intracranial hemorrhage.

Table 5. Comparison of long-term therapeutic effects of three groups of patients (cases/%)

Groups	Cases	Recanalization	Good prognosis	Mortality
Group A	40	31 (77.5)	28 (70.0)	2 (5.0)
Group B	40	31 (77.5)	28 (70.0)	1 (2.5)
Group C	40	30 (75.0)	29 (72.5)	1 (2.5)
X^2		0.32	0.45	0.41
P		0.654	0.416	0.325

Discussion

The mechanisms of intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke

Alteplase is a tissue plasminogen activator (t-PA) produced by gene recombination technology. As compared with the natural t-PA, the enzyme can activate the plasmin that binds to fibrin, which can be converted into plasmin more efficiently than the activated plasminogen in circulating blood. Its main function is to digest local fibrin clots. Alteplase could get satisfactory therapeutic effects and 70% of patients received thrombolytic treatment benefit from alteplase [7]. In the treatment of acute ischemic stroke, intravenous alteplase thrombolysis had high effectiveness and safety [8]. However, because of the influence of thrombolytic drugs' continuous promotion and popularization, new thrombolytic approaches have been booming in recent years, especially arterial thrombolysis and digital subtraction angiography technology, which have been achieving dramatic development. Urokinase thrombolysis is effective and safe [9]. Urokinase is a protein enzyme, its site of action is endogenous fibrinolytic system, after the catalytic cracking of plasminogen into plasmin, the plasmin dissolves fibrin clots, reduces the concentrations of the blood coagulation factor V and blood coagulation factor VIII and fibrinogen in blood circulation, and thereby the thrombolytic takes effect. Arterial thrombolysis and intravenous thrombolysis, had 63.2%, 46.2% vascular recanalization rate respectively [10]. However, the use of angiography techniques in thrombolysis may cost a lot and lack high effectiveness, so it is difficult to make full use of angiography technology in the thrombolysis. Some scholars have compared the effects of intravenous thrombolysis and arterial thrombolysis in the treatment of acute ischemic stroke in internal carotid artery system and found that the two methods had similar 3-month good prognosis [11]. However, those studies didn't take the following important variables into consideration: matched treatment time window, gender, age, time window and so on. And the study did not compare the therapeutic effects of two groups of patients receiving alteplase thrombolysis treatment alone. Hence, the effectiveness difference between different thrombolysis approaches might be overestimated or underestimated. Compared with intravenous thrombolysis patients within 4.5 hours after onset, patients with arterial thrombolysis had higher rate of 3-month good prognosis within 6 hours after onset [12]. However, mechanical auxiliary fragmentation had been fully utilized in arterial thrombolysis. At present, there has been no exact data to support the differences in effectiveness and safety between alteplase and urokinase.

Comparative studies on therapeutic effects of intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke

Related studies showed that intracranial hemorrhage and ischemia reperfusion injury were the main complications of thrombolytic treatment [13]. In the treatment of acute stroke, intracranial hemorrhage is the most severe complication, whose pathogenesis has not been clear yet in clinic. However, most relevant medical scholars thought that secondary coag-

ulation dysfunction and collateral circulation have caused direct and profound impact on acute stroke [14]. Therefore, to improve the therapeutic effectiveness and safety, the key was to select out the appropriate treatment window. For the treatment of arterial occlusion in brain tissue, arterial thrombolysis had better therapeutic effects [15]. Although the incidence of bleeding is higher in thrombolytic treatment, it will not affect mortality rate of patients. However, because of arterial thrombolysis' technical and equipment limitations, it is impossible to carry out large-scale clinical trials in our country, and there is no uniform standard for inclusion criteria, drug dosage, angiography and technical operation. Therefore, the clinical efficacy remains to be further observed. In recent years, with the continuous development and improvement of medical technology, compared with arterial thrombolysis, intravenous thrombolysis (with treatment time window within 6 hours) has lower symptomatic bleeding rate, better therapeutic effects and higher safety [16]. The mechanisms of ischemia reperfusion injury is that oxygen free radicals metabolize abnormally when penumbra brain tissue cannot make full use of oxygen after treatment. To reduce the incidence of this situation, patients can be given ultra-early treatment and cerebral cytoprotective agents can be applied scientifically and rationally [17-20]. After treatment, vascular re-occlusion has complex mechanisms. On the one hand, it involves the redeposition of fibrin; on the other hand, it involves platelets aggregation, which mainly involves fibrinolysis showing hypercoagulable state when tissue factors are exposed. In clinic, thrombolytic should be used in small dose successively after treatment, in order to effectively prevent the re-occlusion of blood vessels. The results of this study showed that there was no significant difference in the NIHSS scores before and after treatment, total effective rate, the incidence of adverse reactions, recanalization rate, good prognosis rate and mortality rate among the three groups were (all $P>0.05$), which were consistent with the related medical research results mentioned above.

However, since this study had a relatively small sample capacity, the results might not be representative enough. So, our relevant medical scholars need to increase sample capacity for further studies.

To summarize, intravenous alteplase thrombolysis, intravenous urokinase thrombolysis and interventional urokinase thrombolysis for acute ischemic stroke have equivalent therapeutic effects.

Disclosure of conflict of interest

None.

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References

[1] Fugate JE and Rabinstein AA. Absolute and relative contraindications to IV rt-PA for acute ischemic stroke. Neurohospitalist 2015; 5: 110-121.

[2] Seiffge DJ, Hooff RJ, Nolte CH, Bejot Y, Turc G, Ikenberg B, Berge E, Persike M, Dequatre-Ponchelle N, Strbian D, Pfeilschifter W, Zini A, Tveiten A, Naess H, Michel P, Sztajzel R, Luft A, Gensicke H, Traenka C, Hert L, Scheitz JF, De Marchis GM, Bonati LH, Peters N, Charidimou A, Werring DJ, Palm F, Reinhard M, Niesen WD, Nagao T, Pezzini A, Caso V, Nederkoorn PJ, Kagi G, von Hessling A, Padjen V, Cordonnier C, Erdur H, Lyrer PA, Brouns R, Steiner T, Tatlisumak T and Engelter ST. Recanalization therapies in acute ischemic stroke patients: impact of prior treatment with novel oral anticoagulants on bleeding complications and outcome. Circulation 2015; 132: 1261-1269.

[3] Bu X, Zhang Y, Bazzano LA, Xu T, Guo L, Wang X, Zhang J, Cui Y, Li D, Zhang F, Ju Z, Chen CS, Chen J and He J. Effects of early blood pressure reduction on cognitive function in patients with acute ischemic stroke. Int J Stroke 2016; 11: 1009-1019.

[4] Simonsen CZ, Sorensen LH, Juul N, Johnsen SP, Yoo AJ, Andersen G and Rasmussen M. Anesthetic strategy during endovascular therapy: general anesthesia or conscious sedation? (GOLIATH - General or Local Anesthesia in Intra Arterial Therapy) a single-center randomized trial. Int J Stroke 2016; 11: 1045-1052.

[5] Palomino A, Fernandez A, Romero I, Garcia JL, Vigil E and Jimenez MD. Starting bring the hospital to patients: accessibility and outcomes of therapy in acute ischemic stroke in southern Spain by telestroke. Int J Stroke 2016; 11: NP55-57.

[6] He AH, Churilov L, Mitchell PJ, Dowling RJ and Yan B. Every 15-min delay in recanalization by

intra-arterial therapy in acute ischemic stroke increases risk of poor outcome. Int J Stroke 2015; 10: 1062-1067.
[7] Messina LM. Toward a biological therapy to improve stroke outcomes after thrombolytic therapy. Circulation 2015; 132: 2201-2202.
[8] Jia H, Phipps M, Bravata D, Castro J, Li X, Ordin D, Myers J, Vogel WB, Williams L and Chumbler N. Inpatient stroke care quality for veterans: are there differences between veterans affairs medical centers in the stroke belt and other areas? Int J Stroke 2015; 10: 67-72.
[9] McKay C, Hall AB and Cortes J. Time to blood pressure control before thrombolytic therapy in patients with acute ischemic stroke: comparison of labetalol, nicardipine, and hydralazine. J Neurosci Nurs 2015; 47: 327-332.
[10] Mokin M, Morr S, Fanous AA, Shallwani H, Natarajan SK, Levy EI, Snyder KV and Siddiqui AH. Correlation between cerebral blood volume values and outcomes in endovascular therapy for acute ischemic stroke. J Neurointerv Surg 2015; 7: 705-708.
[11] Wang C, Yi X, Zhang B, Liao D, Lin J and Chi L. Clopidogrel plus aspirin prevents early neurologic deterioration and improves 6-month outcome in patients with acute large artery atherosclerosis stroke. Clin Appl Thromb Hemost 2015; 21: 453-461.
[12] Menon BK, Campbell BC, Levi C and Goyal M. Role of imaging in current acute ischemic stroke workflow for endovascular therapy. Stroke 2015; 46: 1453-1461.
[13] Christoforidis GA, Slivka AP, Karakasis C, Mohammad Y, Avutu B. Predictors of clinical improvement, angiographic recanalization, and intracranial hemorrhage after intra-arterial thrombolysis for acute ischemic stroke. Interventional Neuroradiology 2010; 16: 297-305.
[14] Amiri H, Bluhmki E, Bendszus M, Eschenfelder CC, Donnan GA, Leys D, Molina C, Ringleb PA, Schellinger PD, Schwab S, Toni D, Wahlgren N and Hacke W. European cooperative acute stroke study-4: extending the time for thrombolysis in emergency neurological deficits EC-ASS-4: ExTEND. Int J Stroke 2016; 11: 260-267.
[15] d'Esterre CD, Boesen ME, Ahn SH, Pordeli P, Najm M, Minhas P, Davari P, Fainardi E, Rubiera M, Khaw AV, Zini A, Frayne R, Hill MD, Demchuk AM, Sajobi TT, Forkert ND, Goyal M, Lee TY and Menon BK. Time-dependent computed tomographic perfusion thresholds for patients with acute ischemic stroke. Stroke 2015; 46: 3390-3397.
[16] Bennett MH, Weibel S, Wasiak J, Schnabel A, French C and Kranke P. Hyperbaric oxygen therapy for acute ischaemic stroke. Stroke 2015; 46: e109-e110.
[17] Llull L, Laredo C, Renu A, Perez B, Vila E, Obach V, Urra X, Planas A, Amaro S and Chamorro A. Uric acid therapy improves clinical outcome in women with acute ischemic stroke. Stroke 2015; 46: 2162-2167.
[18] Liang Z, Ren L, Wang T, Hu H, Li W, Wang Y, Liu D and Lie Y. Effective management of patients with acute ischemic stroke based on lean production on thrombolytic flow optimization. Australas Phys Eng Sci Med 2016; 39: 987-996.
[19] Berge E, Cohen G, Lindley RI, Sandercock P, Wardlaw JM, Sandset EC and Whiteley W. Effects of blood pressure and blood pressure-lowering treatment during the first 24 hours among patients in the third international stroke trial of thrombolytic treatment for acute ischemic stroke. Stroke 2015; 46: 3362-3369.
[20] Vahidy FS, Rahbar MH, Lal AP, Grotta JC and Savitz SI. Patient refusal of thrombolytic therapy for suspected acute ischemic stroke. Int J Stroke 2015; 10: 882-886.