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Wei Li*

Pharmacodynamic comparison of butylphthalide and edaravone dexborneol in acute cerebral infarction – a mechanism-based subgroup analysis focusing on culprit vessel and etiology

Фармакодинамичко поређење бутилфталида и едаравон-дексборнеола код акутног исхемијског можданог удара – анализа подгрупа према етиологији и одговорној артерији

Lixin County People's Hospital, Department of Neurology, Bozhou, Anhui, China

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***Correspondence to:**
Wei LI
Department of Neurology, Lixin County People's Hospital, Intersection of Feihe Avenue and Wenzhou Avenue, Lixin County, Bozhou, Anhui 236700, China
E-mail: **17730359572@163.com**

Pharmacodynamic comparison of butylphthalide and edaravone dexborneol in acute cerebral infarction – a mechanism-based subgroup analysis focusing on culprit vessel and etiology

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SUMMARY

Introduction/Objective This study compared the pharmacodynamics of butylphthalide and sodium chloride (BSC) with those of edaravone dexborneol (ED) in middle-aged and elderly patients with acute cerebral infarction (ACI), focusing on etiology and culprit vessel stratification.

Methods A total of 138 middle-aged and elderly patients with ACI admitted to our hospital from January 2023 – June 2025 were enrolled and randomly assigned to the BSC group (n = 69) and the ED group (n = 69). Both groups received standard ACI treatment; the BSC group received BSC injection (25 mg twice daily), and the ED group received ED injection (30 mg twice daily). The main outcome measures were the National Institutes of Health Stroke Scale (NIHSS) score, modified Rankin Scale score, and mean velocity (Vm) of the middle cerebral artery before and after treatment. The secondary indices included coagulation-related parameters (PLT, white blood cell count) and safety evaluation. Subgroup analyses were based on culprit vessel type (large-vessel disease / small-vessel disease) and etiologic category (atherosclerotic infarction / cardioembolism).

Results Findings revealed that, compared with the ED group, the BSC group had a significantly lower NIHSS score ($p < 0.05$) and a significantly higher Vm in the middle cerebral artery, especially in the large-vessel disease subgroup ($p < 0.05$). Coagulation profiles showed that after seven days of treatment, platelet counts were lower in the BSC group compared with the ED group ($p < 0.05$). In the atherosclerosis subgroup, BSC resulted in lower PLT than ED ($p < 0.05$). Safety assessments indicated comparable adverse event rates and liver/kidney function between the groups ($p > 0.05$), with no cases of serious bleeding or organ damage.

Conclusion BSC exerts a pathologic type-dependent therapeutic effect via its multi-target mechanism (vascular endothelial growth factor-mediated collateral augmentation and platelet-activating factor-dependent platelet inhibition), demonstrating significant etiology-specific efficacy, and supporting its prioritization in large-vessel or atherosclerotic ACI subtypes.

Keywords: butylphthalide; edaravone dexborneol; acute cerebral infarction; middle-aged and elderly adults; neuroprotection; hemodynamics

САЖЕТАК

Увод/Циљ Ова студија је упоредила фармакодинамику бутилфталида и натријум-хлорида (*BSC*) са едаравоном дексборнеолом (ЕД) код средовечних и старијих болесника са акутном церебралном инфаркцијом (АЦИ), са фокусом на стратификацију према етиологији и одговорној артерији.

Методе Укупно 138 средовечних и старијих болесника са АЦИ хоспитализованих у нашој болници од јануара 2023. до јуна 2025. укључено је и случајно подељено у *BSC* групу ($n = 69$) и ЕД групу ($n = 69$). Обе групе су добиле стандардно лечење акутне церебралне инфаркције; *BSC* група је примила инјекцију бутилфталида и натријум-хлорида (25 *mg* два пута дневно), а ЕД група инјекцију едаравон-дексборнеола (30 *mg* два пута дневно). Основне мере исхода биле су скор на Скали за мождани удар Националних института за здравље (*NIHSS*), скор на модификованој Ранкиновој скали (*mRS*) и средња брзина (*Vm*) средње мождане артерије пре и после лечења. Секундарни индекси укључивали су функцију коагулације (*PLT*, *WBC*) и процену безбедности. Подгрупне анализе засноване су на типу одговорне артерије (болест великих судова / болест малих судова) и етиолошкој категорији (атеросклеротска инфаркција/кардиоемболизам).

Резултати Резултати су показали да је, у поређењу са ЕД групом, *BSC* група имала значајно нижи скор на скали *NIHSS* ($p < 0,05$) и значајно вишу средњу брзину (*Vm*) средње мождане артерије, посебно у подгрупи са болешћу великих судова ($p < 0,05$). Профил коагулације показао је да је након седам дана лечења број тромбоцита био нижи у *BSC* групи у односу на ЕД групу ($p < 0,05$). У подгрупи са атеросклерозом, примена *BSC* довела је до нижих вредности *PLT* у односу на ЕД ($p < 0,05$). Процене безбедности указале су на упоредиве стопе нежељених догађаја и функцију јетре/бубрега између група ($p > 0,05$), без озбиљних крварења или оштећења органа.

Закључак *BSC* испољава терапијско дејство зависно од патолошког типа путем свог вишецилног механизма (побољшање колатералног крвотока посредовано *VEGF*-ом + инхибиција тромбоцита зависна од *PAF*), показујући значајну етиолошки специфичну ефикасност, што подржава приоритетну примену ове терапије код подтипова АЦИ везаних за велике судове или атеросклерозу.

Кључне речи: бутилфталид; едаравон-дексборнеол; акутни исхемијски мождани удар; средовечна и старија популација; неурозаштита; хемодинамика

INTRODUCTION

As the global population ages, the incidence of acute cerebral infarction (ACI), a leading cause of disability and mortality worldwide, continues to rise; Li et al. (2023) pointed out that aging has significantly increased the global disease burden of ACI and related long-term disability [1]. Middle-aged and elderly patients (≥50 years) face a particularly heightened risk of unfavorable outcomes. This vulnerability is attributed to age-related physiological decline, including reduced vascular compliance, diminished collateral circulation compensation capacity, and a higher burden of comorbidities [2]. Consequently, tailoring neuroprotective therapy to individual patients is paramount for improving clinical outcomes. Butylphthalide and sodium chloride (BSC) and Edaravone Dexborneol (ED) are commonly employed neuroprotective drugs. Their clinical benefits are well-established, supported by extensive clinical validation. For example, a Phase III clinical trial by Zhang et al. (2023) on BSC demonstrated its efficacy in significantly reducing the 90-day National Institutes of Health Stroke Scale (NIHSS) score and improving daily living activities in individuals with mild-to-moderate ACI [3]. Meanwhile, ED was shown in a multicenter study to suppress oxidative stress during the acute phase and shorten the time to neurological function recovery [4]. Clinical pharmacological studies have shown that BSC exerts neuroprotection by promoting collateral circulation and inhibiting glutamate excitotoxicity [5], while ED mainly targets oxidative stress [6]. Existing studies on BSC or ED, however, are predominantly conducted across broad age groups, overlooking the distinct considerations relevant to middle-aged and elderly patients [7, 8]. There is a lack of pharmacodynamic comparison between BSC and ED in elderly ACI patients, especially based on the mechanism of etiological stratification. The diminished cerebral hemodynamic reserve commonly seen in these patients may alter how pharmacological agents influence cerebral arterial flow, differing from the effects observed in younger adults [9]. Second, clinical effectiveness is considerably modulated by the high degree of heterogeneity in this group, influenced by factors like infarct location and culprit vessel [10].

While ED primarily scavenges free radicals via Nrf2/ARE pathway activation, BSC simultaneously modulates VEGF/Notch-mediated angiogenesis and suppresses COX-2/P-selectin-dependent platelet adhesion. We hypothesize that such multi-target pharmacology confers broader efficacy in elderly ACI patients with complex vasculopathy, particularly those with large artery atherosclerosis where hemodynamic rescue and thromboregulation are critical. Therefore, an innovative aspect of this investigation is its concentrated examination of heterogeneity in the middle-aged and elderly ACI population. The findings of this study will help to fill the evidence gap of stratified pharmacology and provide the basis for precision medicine.

METHODS

Study population

The sample size calculation was based on the expected between-group difference in the modified Rankin Scale (mRS) score, the primary outcome measure. Based on prior research, a between-group difference of

0.5 points in mRS scores was assumed, with a standard deviation (SD) of 1.2, referring to the study of Shi et al. (2022) [11], a between-group difference of 0.5 points in mRS scores was assumed, with a standard deviation (SD) of 1.2. Given a two-sided alpha of 0.05 and 80% power (1–β), the calculation conducted with PASS 15.0 showed that 58 patients are needed per group. To allow for an estimated 20% dropout rate (including loss to follow-up, early withdrawal, or non-adherence to the protocol), the sample size was increased to 69 per group, yielding a minimum total of 138 participants. Patient selection for this study involved 138 ACI-affected individuals, admitted to our hospital from January 2023 to June 2025. This cohort size was finalized after estimating the required sample size and implementing the specified inclusion and exclusion protocols. The clinical data of the two groups are shown in Table 1, and there was no significant difference between the two groups (P>0.05).

Inclusion and exclusion criteria

Inclusion criteria: Age between 50 and 90 years; Time from stroke onset ≤48 hours; Radiologically confirmed new cerebral infarction (lesion diameter ≥1 cm) on cranial magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI). Exclusion criteria: Presence of intracranial hemorrhage (e.g., intracerebral, subarachnoid) or tumor-related stroke; Severe cerebral herniation (GCS score ≤8) or terminal illness (life expectancy <3 months); Significant hepatic/renal dysfunction; Coagulopathy; Allergy to BSC or ED; Recent participation (within 3 months) in other therapeutic drug trials; Pre-existing psychiatric or cognitive disorders that would impede study assessments.

Grouping and blinding

Using a centralized randomization system integrated with electronic medical records, participants were allocated in a 1:1 ratio to receive either BSC injection (BSC group) or ED injection (ED group). Block randomization (computer-generated sequence) was used, and assessors were blinded to minimize bias. The study adopted a single-blind design, in which both patients and outcome assessors were unaware of group assignments; statistical analysts were also blinded to treatment allocation throughout the analysis process. Baseline clinical characteristics showed no significant intergroup differences (P>0.05), as summarized in Table 1.

Treatment protocols

Standard treatment for acute ischemic stroke was provided to both groups, consisting of antiplatelet agents (aspirin or clopidogrel), statins for plaque stabilization, and management of blood pressure and blood glucose. In addition, the BSC group was administered BSC injection (H20100041, CSPC-NBP Pharmaceutical Co., Ltd.) 25 mg (100 mL) per bottle, 25 mg per dose, twice daily, intravenously, with each infusion lasting ≥30 min. ED Injection (H20200007, Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd.)

10 mg: 2.5 mg: 5 mL per dose; 30 mg (15 mL) twice daily, intravenously, with each infusion lasting ≥30 min. All participants received treatment for 6-10 days, beginning within 48 hours after symptom onset. Concurrent use of additional neuroprotective drugs, including citicoline and oxiracetam, was not permitted. Administration of the trial drug was halted and documented if severe adverse events occurred, including elevation of liver enzymes greater than three times the upper limit of normal (ULN). The dose was based on the previous pharmacokinetic study [12, 13] to ensure that the blood concentration reached the therapeutic window.

Outcome measures

The study conducted (within 24 hours after admission) and post-treatment (within 24 hours after the end of the 6-10 day treatment course) assessments of neurological status via the NIHSS [14] and mRS [15], where higher scores signify worse neurological function. The peak systolic velocity (Vs), mean flow velocity (Vm), and pulsatility index (PI) of middle cerebral artery (MCA) was measured by transcranial Doppler ultrasound (TCD) within 48 hours after admission and after treatment to evaluate the improvement of cerebral blood flow. Blood samples obtained from patients were analyzed for coagulation (APTT, TT, INR, WBC, PLT) and biochemical parameters (ALT, AST, CREA, UREA). All adverse reactions during treatment were documented. Subgroup analyses further explored variations among patients categorized by culprit vessel type (large vs. small vessel disease) and stroke etiology (atherosclerotic infarction vs. cardiogenic embolism).

Statistical analysis

The statistical evaluation was carried out utilizing SPSS, Version 31.0. For categorical measures, group differences were examined via the Chi-square test or Fisher's exact test. The distribution of continuous data was verified with the Shapiro-Wilk normality test; normally distributed data were presented as mean ± standard deviation (SD), with intergroup comparisons performed using independent-samples t-test and intragroup pre-post comparisons using paired t-test. Non-normally distributed continuous data were presented as median (interquartile range, IQR), with intergroup comparisons performed using Mann-Whitney U test and intragroup pre-post comparisons using Wilcoxon signed-rank test. Results with P-values below 0.05 were deemed statistically significant.

Ethics: The investigation was performed following approval by the Lixin County People's Hospital' Ethics Committee and after acquiring informed consent from all subjects.

RESULTS

Assessment of neurological improvement

Both patient cohorts had similar neurological impairment at baseline based on NIHSS and mRS scores ($P>0.05$). The BSC intervention produced greater neurological improvement than ED treatment ($P<0.05$), with subgroup analysis identifying this advantage specifically in the large vessel disease subgroup ($P<0.05$) and atherosclerotic infarction subgroup ($P<0.05$), but not in small vessel or cardioembolic cases ($P>0.05$) (Figure 1 and Table 2).

Evaluation of cerebral hemodynamics enhancement

Hemodynamic improvements were observed following treatment, with both groups demonstrating increased blood flow velocities in MCA (increased Vs and Vm) and decreased PI compared with baseline values ($P<0.05$). No significant between-group difference was observed in the improvement of Vs ($P>0.05$). The PI decreased significantly in both groups after treatment ($P<0.05$), with no significant between-group difference ($P>0.05$). A markedly greater increase in Vm was recorded in the BSC group (52.16 ± 6.05 cm/s) compared to the ED group ($P<0.05$). Specifically, the increase in Vm in the BSC group was significantly more pronounced in the large vessel disease subgroup ($P<0.05$). Given that mean flow velocity (Vm) is the most stable and representative indicator for evaluating cerebral perfusion status in ischemic stroke, which directly reflects the blood supply of the ischemic penumbra, this study focused on Vm as the core hemodynamic outcome for subgroup analysis. Further analysis by subgroup demonstrated that the superiority of BSC in significantly enhancing Vm was confined to patients diagnosed with large vessel disease and atherosclerotic infarction ($P<0.05$) (Figure 2 and Table 3).

Monitoring of coagulation parameters

No intergroup differences in coagulation profiles were observed at baseline ($P>0.05$). Post-intervention, parameters including PT, APTT, and INR showed no notable alterations ($P>0.05$). Conversely, both WBC and PLT counts declined statistically from initial levels ($P<0.05$). A more marked decrease in PLT was noted in the BSC group versus the ED group ($P<0.05$). Subgroup analysis showed that the BSC group had a significantly lower WBC count after treatment than the ED group in all subgroups ($P<0.05$). However, in the macrovascular disease and atherosclerosis subgroups, the PLT in BSC group was lower than that in ED group ($P<0.05$) (Figure 3 and Table 4).

Comparison of hepatic and renal function

No marked variations in liver and kidney function markers (ALT, AST, CREA, UREA) were detected in either group following treatment ($P>0.05$). The stability of these parameters implies minimal hepatorenal impact from both drugs (Figure 4).

DISCUSSION

ACI stands as a predominant contributor to disability and death among middle-aged and elderly individuals. Its pathophysiological mechanisms encompass multidimensional damage such as oxidative stress, inflammatory cascade activation, and impaired cerebral perfusion [16]. BSC and ED are known to provide neuroprotection in diverse age groups; however, older patients may respond differently due to age-related vascular stiffness, compromised collateral compensation, and multiple coexisting conditions. The central pharmacological finding of this study is that the efficacy advantage of BSC is not universal but is achieved by targeting the vascular pathology - its PLT inhibition effect interacts with the platelet hyperreactivity of atherosclerotic lesions in a precise way, which provides a mechanistic basis for personalized medicine.

BSC, an emerging dual-target agent, provides neuroprotection via microcirculatory reconstruction—promoting collateral flow and suppressing glutamate excitotoxicity—and by boosting energy metabolism; meanwhile, BSC can not only up-regulate VEGF to promote collateral circulation, but also inhibit platelet activating factor (PAF) [5, 17], which explains its advantage in macrovascular disease. This study found greater post-treatment NIHSS and mRS reductions with BSC, consistent with a previous Phase III clinical trial in mild-to-moderate ACI [12]. ED, a free-radical scavenger and inflammation suppressor, showed robust anti-inflammatory activity in previous reports [18]. Yet, it leads to limited short-term neurological improvement, possibly due to delayed inflammatory modulation. Future pharmacodynamic monitoring is needed for validation. Regarding coagulation parameters, PLT was lower in the BSC group post-treatment, potentially due to BSC's inhibitory effect on platelet-activating factor (PAF)-mediated adhesion and aggregation; the decrease in PLT observed in the BSC group in this study may be related to its PAF inhibition mechanism [19]. The simultaneous improvement of Vm and PLT by BSC suggests a synergistic effect of both revascularization and thromboprophylaxis pathways, while the single antioxidant mechanism of ED is difficult to cover multiple pathological links.

Furthermore, in-depth subgroup analysis revealed significant associations between drug efficacy and specific pathophysiological features: (1) Hemodynamic-specific improvement in the large vessel disease subgroup: Occlusions in large vessels (e.g., internal carotid artery, middle cerebral artery trunk) frequently result in significant hypoperfusion. BSC addresses this via a two-pronged mechanism: it enhances collateral circulation by upregulating vascular endothelial growth factor (VEGF), which promotes the opening of pial anastomoses [20], thus enhancing perfusion in the ischemic penumbra. Concurrently, as shown in animal experiments by Guo ZN et al., BSC modulates calcium channels to attenuate vascular smooth muscle contraction [17], mitigating secondary ischemia due to large vessel spasm. The greater increase in Vm observed in the large vessel disease subgroup of the BSC group, compared to the ED group, is consistent with prior evidence demonstrating that BSC enhances intracranial large vessel hemodynamics [21]. (2) Previous studies have confirmed that BSC can stabilize atherosclerotic plaques by suppressing MMP-9 to stabilize the fibrous cap [22], , and the findings in this study may be relevant to this mechanism, which may underlie the observed differential outcomes in the atherosclerotic subgroup. (3) Targeted

modulation of platelet activation: The more pronounced PLT reduction with BSC may result from its targeted inhibition of platelet activation. As noted, BSC competitively binds to the PAF receptor, suppressing collagen-induced platelet aggregation [19]. It also downregulates COX-2 and reduces thromboxane A2 synthesis [23]. Since platelet hyperactivity is common in atherosclerosis [24], BSC's platelet-modulating effects are particularly evident in these patients.

Therefore, our recommendation is to prioritize BSC in the management of middle-aged and elderly ACI patients, especially in cases of large vessel disease or atherosclerotic stroke, to achieve prompt restoration of cerebral perfusion. Vigilant monitoring of PLT is warranted throughout this treatment, particularly for high-risk patients, to guard against hemorrhagic tendencies. Furthermore, the complementary mechanisms of BSC and ED present a rationale for examining sequential or combined administration regimens. This approach holds promise for addressing the multifaceted pathology of ACI.

Key limitations of this work include its restricted scale (n = 138) and observation period (7 days), preventing analysis of long-term prognosis (e.g., 90-day mRS) and recurrence, and possibly masking the drug's full therapeutic potential. The study also omitted quantitative evaluation of pivotal indicators like infarct volume and collateral circulation grading, which could obscure subgroup heterogeneity. Moreover, the failure to track longitudinal changes in biomarkers related to inflammation or oxidative stress impedes a complete delineation of the drug's pharmacodynamic pathways.

Limitations

This study has several limitations. First, it was conducted at a single center with a relatively modest sample size, which may limit external validity and statistical power for subgroup analyses. Additionally, the sample size of some subgroups (e.g., cardiogenic embolism subgroup with n = 23) was relatively small, which may lead to insufficient statistical power for the corresponding subgroup analyses. Second, follow-up was short, precluding assessment of longer-term functional outcomes and the durability of observed effects. Third, quantitative imaging metrics (e.g., infarct volume and collateral status) were not systematically incorporated, limiting evaluation of radiological heterogeneity. This indicator was not recorded systematically at the time of data collection. Finally, dynamic monitoring of inflammation- and oxidative stress–related biomarkers was not performed, which constrained mechanistic interpretation of the findings.

CONCLUSION

BSC shows a pathological type-dependent therapeutic effect in middle-aged and elderly patients with ACI through a multi-target mechanism (collateral circulation activation and platelet activity regulation). Its significant efficacy in the large vessel/atherosclerosis subgroup suggests that future efficacy evaluation of neuroprotective agents should integrate vascular biological classification and pharmacokinetic parameters, rather than relying on clinical phenotype alone.

Availability of data and materials: The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of interest: None declared.

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Table 1. Baseline data of the study groups

Parameter	BSC group (n = 69)	ED group (n = 69)	t or χ^2	p
Age	69.23 ± 12.81	68.45 ± 11.45	0.378	0.706
Male/Female	42/27	45/24	0.280	0.597
Time from stroke onset (h)	26.06 ± 11.59	29.38 ± 12.84	1.594	0.113
History of smoking Yes/no	34/35	30/39	0.466	0.495
History of drinking Yes/no	22/47	25/44	0.294	0.590
Large/small vessel disease	39/30	37/32	0.117	0.732
Atherosclerotic infarction / cardiogenic embolism	42/27	46/23	0.502	0.479

Table 2. Subgroup analysis of neurological function (NIHSS and mRS)

Subgroups		Groups	Before	After
NIHSS	Large vessel disease	BSC (n = 39)	7.87 ± 2.4	3.79 ± 1.08
		ED (n = 37)	8.35 ± 2.52	5.00 ± 1.29#
	Small vessel disease	BSC (n = 30)	8.30 ± 1.97	3.93 ± 1.08
		ED (n = 32)	8.16 ± 2.46	4.25 ± 1.27
	Atherosclerotic infarction	BSC (n = 42)	7.98 ± 2.45	3.81 ± 1.06
		ED (n = 46)	8.17 ± 2.59	4.89 ± 1.18#
	Cardiogenic embolism	BSC (n = 27)	8.19 ± 1.82	3.93 ± 1.11
		ED (n = 23)	8.43 ± 2.27	4.04 ± 1.46
mRS	Large vessel disease	BSC (n = 39)	2.92 ± 0.81	1.69 ± 0.89
		ED (n = 37)	2.76 ± 0.89	2.24 ± 0.95#
	Small vessel disease	BSC (n = 30)	2.77 ± 0.97	2.10 ± 0.66
		ED (n = 32)	2.69 ± 0.82	2.19 ± 0.74
	Atherosclerotic infarction	BSC (n = 42)	2.95 ± 0.82	1.74 ± 0.91#
		ED (n = 46)	2.76 ± 0.85	2.26 ± 0.93
	Cardiogenic embolism	BSC (n = 27)	2.7 ± 0.95	2.07 ± 0.62
		ED grop (n = 23)	2.65 ± 0.88	2.13 ± 0.69

BSC – butylphthalide and sodium chloride; NIHSS – National Institutes of Health Stroke Scale; mRS – modified Rankin Scale; ED – edaravone dexborneol;

#$p < 0.05$ compared with BSC group

Table 3. Subgroup analysis of cerebral hemodynamics (Vm)

Subgroups	Groups	Before	After
Large vessel disease	BSC (n = 39)	43.64 ± 7.63	52.29 ± 5.57
	ED (n = 37)	44.11 ± 6.84	46.38 ± 7.28[#]
Small vessel disease	BSC (n = 30)	45.09 ± 5.76	51.99 ± 6.71
	ED (n = 32)	46.04 ± 6.34	50.95 ± 6.05
Atherosclerotic infarction	BSC (n = 42)	44.36 ± 6.75	53.04 ± 5.97
	ED (n = 46)	44.61 ± 6.25	48.22 ± 7.11[#]
Cardiogenic embolism	BSC (n = 27)	44.12 ± 7.19	50.8 ± 6.02
	ED (n = 23)	45.79 ± 7.43	49.06 ± 7.12

[#]$p < 0.05$ compared with BSC group

Table 4. Subgroup analysis of coagulation function (WBC and PLT)

Subgroups		Groups	Before	After
WBC (× 10^9/L)	Large vessel disease	BSC (n = 39)	12.31 ± 1.82	8.37 ± 1.79
		ED (n = 37)	12.37 ± 2.49	10.1 ± 2.12#
	Small vessel disease	BSC (n = 30)	12.34 ± 1.72	7.83 ± 1.69
		ED (n = 32)	12.56 ± 2.37	10.6 ± 2.58#
	Atherosclerotic infarction	BSC (n = 42)	12.20 ± 8.27	8.27 ± 1.69
		ED (n = 46)	12.52 ± 2.4	10.21 ± 2.26#
	Cardiogenic embolism	BSC (n = 27)	12.53 ± 1.72	7.93 ± 1.86
		ED (n = 23)	12.32 ± 2.49	10.56 ± 2.53#
PLT (× 10^9/L)	Large vessel disease	BSC (n = 39)	291.24 ± 33.13	231.43 ± 35.29
		ED (n = 37)	287.49 ± 36.89	254.05 ± 33.45#
	Small vessel disease	BSC (n = 30)	294.38 ± 38.75	223.63 ± 24.61
		ED (n = 32)	292.93 ± 28.96	223.63 ± 21.94
	Atherosclerotic infarction	BSC (n = 42)	292.5 ± 32.41	234.23 ± 33.78
		ED (n = 46)	291.26 ± 34.54	249.1 ± 33.8#
	Cardiogenic embolism	BSC (n = 27)	292.77 ± 40.36	218.41 ± 24.04
		ED (n = 23)	287.53 ± 31.34	221.62 ± 19.16

#$p < 0.05$ compared with BSC group

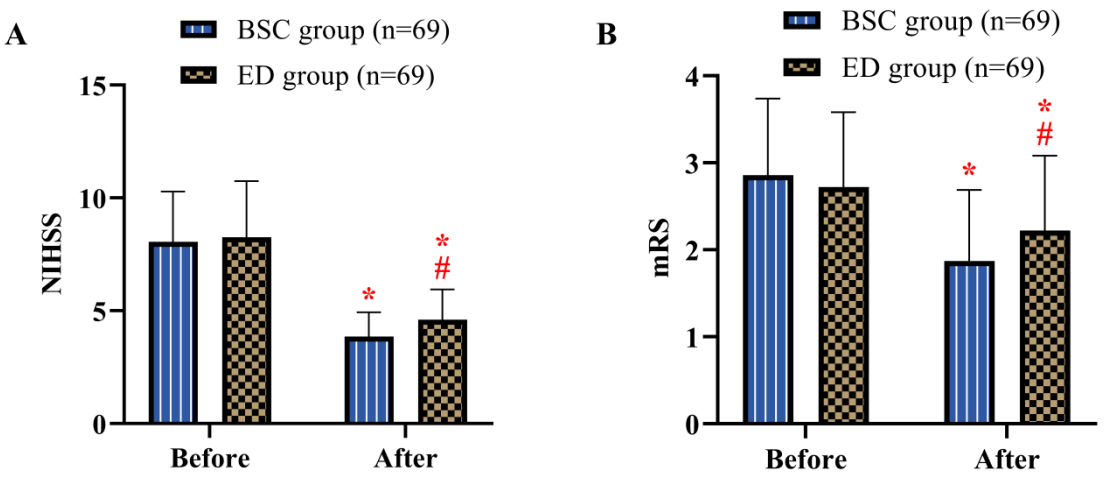

Figure 1. Comparison of neurological functions; (A) NIHSS before and after treatment; (B) mRS before and after treatment;

BSC – butylphthalide and sodium chloride; NIHSS – National Institutes of Health Stroke Scale; ED – edaravone dexborneol;

*$p < 0.05$ compared with before treatment;

$^{\#}p < 0.05$ compared with BSC group

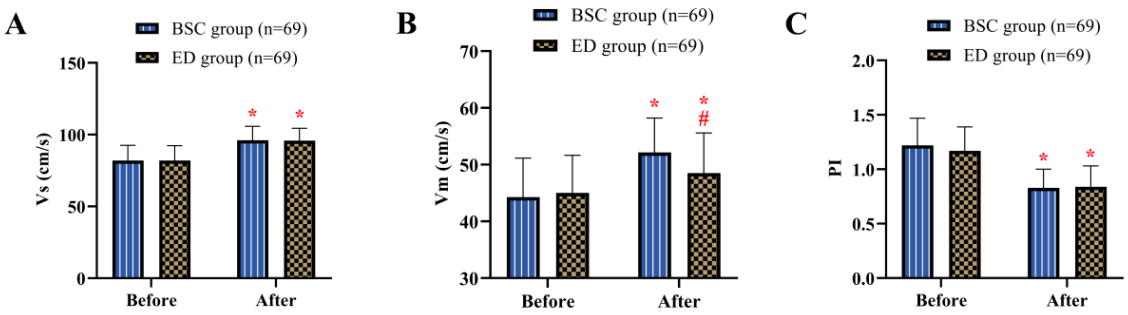

Figure 2. Comparison of cerebral hemodynamics; (A) Vs before and after treatment; (B) Vm before and after treatment; (C) PI before and after treatment;

Vs – peak systolic velocity; Vm – mean flow velocity; PI – pulsatility index;

*$p < 0.05$ compared with before treatment;

#indicates $p < 0.05$ compared with BSC group

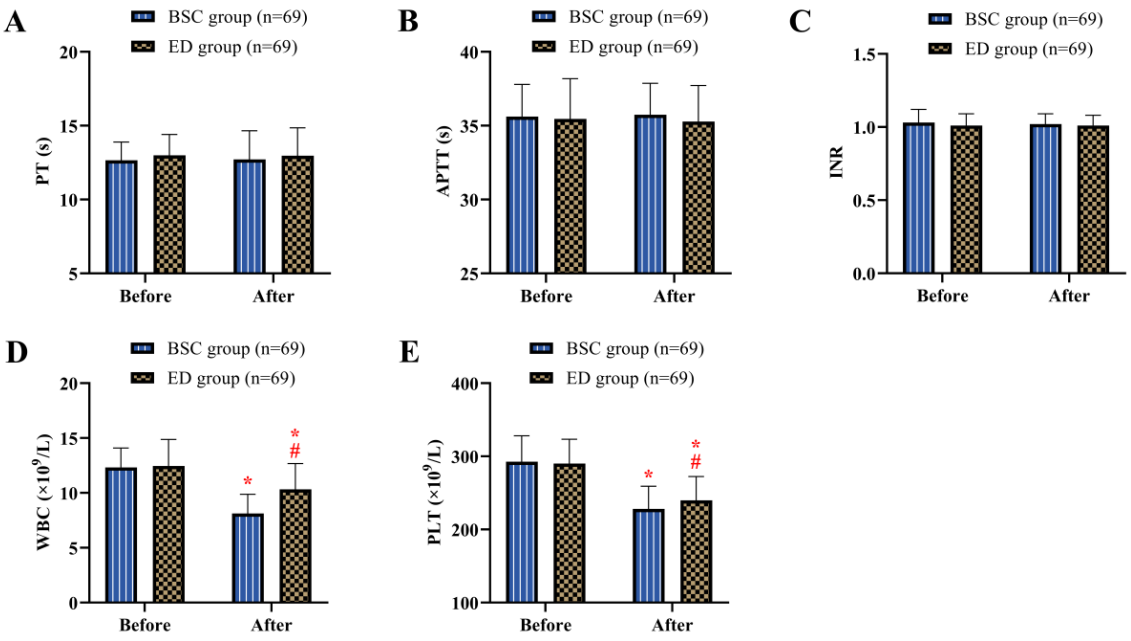

Figure 3. Comparison of coagulation function; (A) PT before and after treatment; (B) APTT before and after treatment; (C) INR before and after treatment; (D) WBC before and after treatment; (E) PLT before and after treatment;

APTT – activated partial thromboplastin time; TT – thrombin time; INR – international normalized ratio; WBC – white blood cell count; PLT – platelet count;

*$p < 0.05$ compared with before treatment;

#$p < 0.05$ compared with BSC group

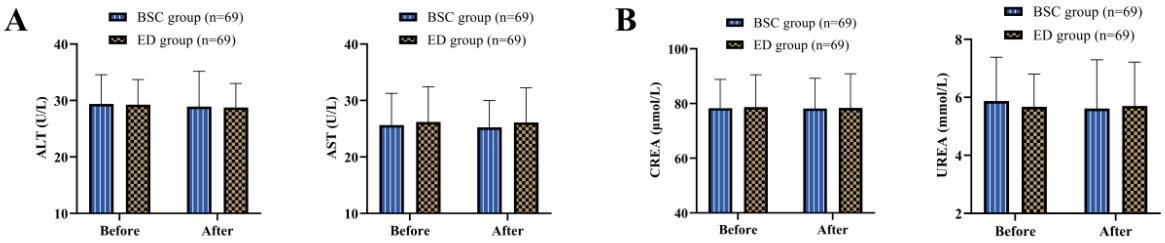

Figure 4. Comparison of liver and kidney functions; (A) ALT, AST before and after treatment; (B) CREA, UREA before and after treatment;

ALT – alanine aminotransferase; AST – aspartate aminotransferase; CREA – creatinine; UREA – urea;

*$p < 0.05$ compared with before treatment;

$^{\#}p < 0.05$ compared with BSC group;

