

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Pharmacodynamic comparison of butylphthalide and edaravone dextroboenol 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 dextroboenol (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 to 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 (mRS) score, and mean flow velocity (V_m) of the middle cerebral artery before and after treatment. The secondary indices included coagulation-related parameters [platelet count (PLT) and white blood cell (WBC) count] and safety evaluation. Subgroup analyses were based on culprit vessel type (large-vessel / 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 V_m 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 atherosclerotic infarction subgroup, BSC resulted in lower PLT counts than in the ED group ($p < 0.05$). 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 pathology 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 dextroboenol; acute cerebral infarction; middle-aged and elderly adults; neuroprotection; hemodynamics

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. [1] pointed out that aging has significantly increased the global disease burden of ACI and related long-term disability. 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 dextroboenol (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 middle-aged and elderly patients with ACI, especially when stratified by etiological mechanism. The diminished cerebral hemodynamic reserve commonly seen in these

Received • Примљено:
November 11, 2025

Revised • Ревизија:
April 14, 2026

Accepted • Прихваћено:
April 15, 2026

Online first: May 12, 2026

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patients may alter how pharmacological agents influence cerebral arterial flow, differing from the effects observed in younger adults [9]. In addition, clinical effectiveness is considerably modulated by the high degree of heterogeneity in this group, influenced by factors such as infarct location and culprit vessel [10].

While ED primarily scavenges free radicals via Nrf2/ARE pathway activation, BSC simultaneously modulates vascular endothelial growth factor (VEGF) / notch-mediated angiogenesis and suppresses COX-2/P-selectin-dependent platelet adhesion. We hypothesize that such multi-target pharmacology confers broader efficacy in middle-aged and elderly patients with ACI 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 fill the evidence gap in stratified pharmacology and provide a 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, including the study by Shi et al. [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 were 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 patients with ACI, 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

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

dysfunction; coagulopathy; allergy to BSC or ED; recent participation (within three 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. The ED group received ED injection (H20200007, Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd.) 30 mg (15 mL) twice daily, intravenously, with each infusion lasting ≥ 30 minutes. 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 previous pharmacokinetic studies to ensure that the blood concentration reached the therapeutic window [12, 13].

Outcome measures

The study included baseline (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, where higher scores signify worse neurological function [14, 15]. The peak systolic velocity (V_s), mean flow velocity (V_m), and pulsatility index (PI) of the middle cerebral artery (MCA) were measured by transcranial Doppler ultrasound (TCD) within 48 hours after admission and after treatment to evaluate improvements in cerebral blood flow. Blood samples obtained from patients were analyzed for coagulation [activated partial thromboplastin time (APTT), thrombin time (TT), international normalized ratio (INR), white blood cell (WBC) count, and platelet count (PLT)] and biochemical parameters [alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (CREA), and urea (UREA)]. All adverse reactions during treatment were documented. Subgroup analyses further explored variations among patients categorized by culprit vessel type (large-vessel vs. small-vessel disease) and stroke etiology (atherosclerotic infarction vs. cardiogenic embolism).

Statistical analysis

The statistical evaluation was carried out using IBM SPSS Statistics, Version 31.0 (IBM Corp., Armonk, NY, USA). For categorical measures, group differences were examined via the χ^2 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 $\pm$ standard deviation (SD), with intergroup comparisons performed using the independent-samples t-test and intragroup pre-post comparisons using the paired t-test. Non-normally distributed continuous data were presented as median (interquartile range, IQR), with intergroup comparisons performed using the Mann–Whitney U test and intragroup pre-post comparisons using the 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).

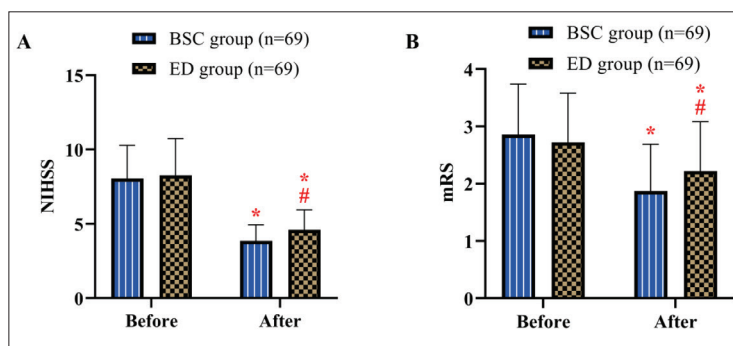


Figure 1. Comparison of neurological functions; (A) NIHSS before and after treatment; (B) mRS before and after treatment;

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

* $p < 0.05$ compared with before treatment;

$p < 0.05$ compared with the BSC group

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

Subgroups		Groups	Before	After
NIHSS	Large-vessel disease	BSC (n = 39)	7.87 $\pm$ 2.4	3.79 $\pm$ 1.08
		ED (n = 37)	8.35 $\pm$ 2.52	5 $\pm$ 1.29#
	Small-vessel disease	BSC (n = 30)	8.30 $\pm$ 1.97	3.93 $\pm$ 1.08
		ED (n = 32)	8.16 $\pm$ 2.46	4.25 $\pm$ 1.27
	Atherosclerotic infarction	BSC (n = 42)	7.98 $\pm$ 2.45	3.81 $\pm$ 1.06
		ED (n = 46)	8.17 $\pm$ 2.59	4.89 $\pm$ 1.18#
mRS	Large-vessel disease	BSC (n = 39)	2.92 $\pm$ 0.81	1.69 $\pm$ 0.89
		ED (n = 37)	2.76 $\pm$ 0.89	2.24 $\pm$ 0.95#
	Small-vessel disease	BSC (n = 30)	2.77 $\pm$ 0.97	2.10 $\pm$ 0.66
		ED (n = 32)	2.69 $\pm$ 0.82	2.19 $\pm$ 0.74
	Atherosclerotic infarction	BSC (n = 42)	2.95 $\pm$ 0.82	1.74 $\pm$ 0.91#
		ED (n = 46)	2.76 $\pm$ 0.85	2.26 $\pm$ 0.93
Cardiogenic embolism		BSC (n = 27)	2.7 $\pm$ 0.95	2.07 $\pm$ 0.62
		ED (n = 23)	2.65 $\pm$ 0.88	2.13 $\pm$ 0.69

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

mRS – modified Rankin Scale; ED – edaravone dextroboenol;

$p < 0.05$ compared with the BSC group

Evaluation of cerebral hemodynamics enhancement

Hemodynamic improvements were observed following treatment, with both groups demonstrating increased blood flow velocities in the MCA (increased V_s and V_m) and decreased PI compared with baseline values ($p < 0.05$). No significant between-group difference was observed in the improvement of V_s ($p > 0.05$). 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 V_m was recorded in the BSC group (52.16 ± 6.05 cm/s) compared with the ED group ($p < 0.05$). Specifically, the increase in V_m in the BSC group was significantly more pronounced in the large-vessel disease subgroup ($p < 0.05$). Given that mean flow velocity (V_m) is the most stable and representative indicator for evaluating cerebral perfusion status in ischemic stroke, which directly reflects the blood supply of

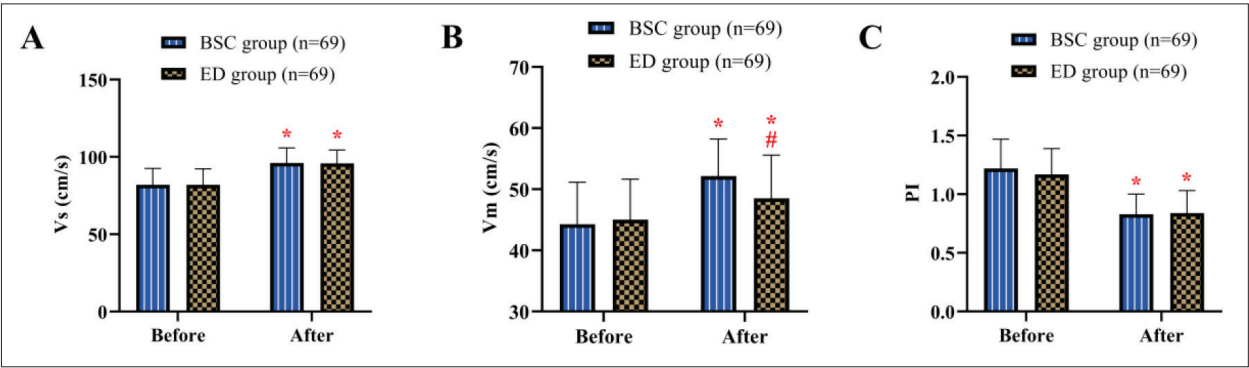


Figure 2. Comparison of cerebral hemodynamics; (A) Vs before and after treatment; (B) Vm before and after treatment; (C) PI before and after treatment;

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

*p < 0.05 compared with before treatment;

#indicates p < 0.05 compared with the 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 the 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
		ED (n = 37)	8.37 ± 1.79
		BSC (n = 37)	12.37 ± 2.49
		ED (n = 37)	10.1 ± 2.12#
	Small vessel disease	BSC (n = 30)	12.34 ± 1.72
		ED (n = 32)	7.83 ± 1.69
		BSC (n = 32)	12.56 ± 2.37
		ED (n = 32)	10.6 ± 2.58#
	Atherosclerotic infarction	BSC (n = 42)	12.20 ± 8.27
		ED (n = 46)	8.27 ± 1.69
PLT (× 10 ⁹ /L)		BSC (n = 46)	12.52 ± 2.4
		ED (n = 46)	10.21 ± 2.26#
	Cardiogenic embolism	BSC (n = 27)	12.53 ± 1.72
		ED (n = 23)	7.93 ± 1.86
		BSC (n = 23)	12.32 ± 2.49
		ED (n = 23)	10.56 ± 2.53#
	Large vessel disease	BSC (n = 39)	291.24 ± 33.13
		ED (n = 37)	231.43 ± 35.29
		BSC (n = 37)	287.49 ± 36.89
		ED (n = 37)	254.05 ± 33.45#
	Small vessel disease	BSC (n = 30)	294.38 ± 38.75
		ED (n = 32)	223.63 ± 24.61
		BSC (n = 32)	292.93 ± 28.96
		ED (n = 32)	223.63 ± 21.94
	Atherosclerotic infarction	BSC (n = 42)	292.5 ± 32.41
		ED (n = 46)	234.23 ± 33.78
		BSC (n = 46)	291.26 ± 34.54
		ED (n = 46)	249.1 ± 33.8#
	Cardiogenic embolism	BSC (n = 27)	292.77 ± 40.36
		ED (n = 23)	218.41 ± 24.04
		BSC (n = 23)	287.53 ± 31.34
		ED (n = 23)	221.62 ± 19.16

#p < 0.05 compared with the BSC group

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 significantly from baseline 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 large-vessel disease and atherosclerosis subgroups, the PLT count in the BSC group was lower than that in the 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 is 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, because its platelet-inhibitory effect interacts precisely with the platelet hyperreactivity of atherosclerotic lesions, 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 upregulate VEGF to promote collateral circulation, but also inhibit platelet-activating factor (PAF) [5,

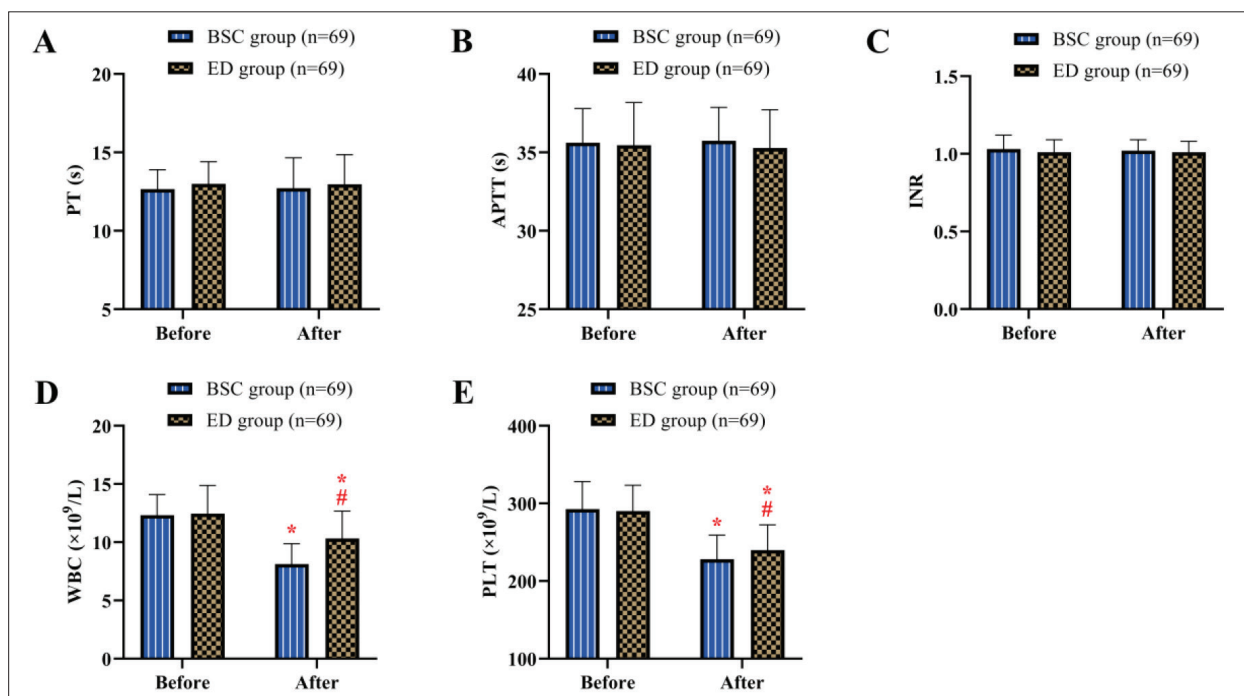


Figure 3. Comparison of coagulation function; (A) PT before and after treatment; (B) APTT before and after treatment; (C) INR before and after treatment; (D) WBC before and after treatment; (E) PLT before and after treatment;

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 the BSC group

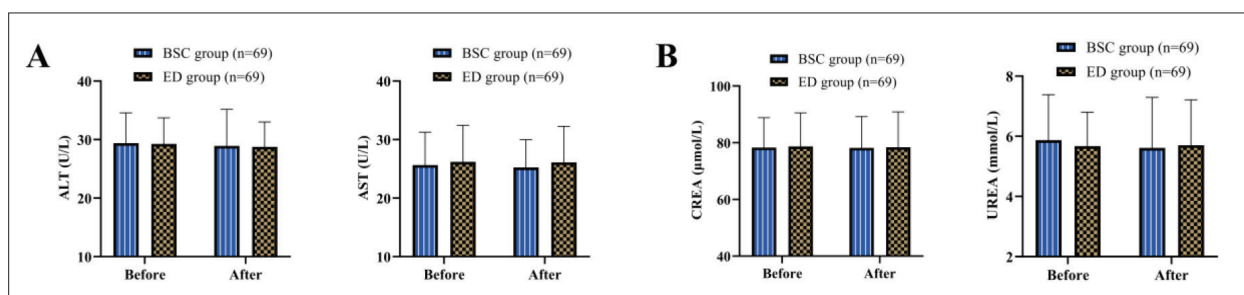


Figure 4. Comparison of liver and kidney functions; (A) ALT, AST before and after treatment; (B) CREA, UREA before and after treatment;

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

* $p < 0.05$ compared with before treatment;

$p < 0.05$ compared with the BSC group

17], which explains its advantage in large-vessel 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]. However, it may lead 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, whereas the single antioxidant mechanism of ED may not address multiple pathological pathways.

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 et al. [17], BSC modulates calcium channels to attenuate vascular smooth muscle contraction, mitigating secondary ischemia due to large-vessel disease spasm. The greater increase in Vm observed in the

large-vessel disease subgroup of the BSC group, compared with 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 patients with ACI, 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 small sample size ($n = 138$) and observation period of seven 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 such as 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.

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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, the 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. These indicators were 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 disease or atherosclerosis subgroup suggests that future efficacy evaluation of neuroprotective agents should integrate vascular biology 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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Фармакодинамичко поређење бутилфталида и едаравон-дексборнеола код акутног исхемијског можданог удара – анализа подгрупа према етиологији и одговорној артерији

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САЖЕТАК

Увод/Циљ У овој студији упоређена је фармакодинамика бутилфталида и натријум-хлорида (BSC) са едаравон-дексборнеолом (ЕД) код средовечних и старијих болесника са акутним исхемијским можданим ударом, са фокусом на стратификацију према етиологији и одговорној артерији.

Метод Укупно 138 средовечних и старијих болесника са акутним исхемијским можданим ударом хоспитализованих у нашој болници од јануара 2023. до јуна 2025. године насумично је распоређено у BSC групу ($n = 69$) и ЕД групу ($n = 69$). Обе групе су примиле стандардну терапију за акутни исхемијски мождани удар; BSC група је примала инјекције бутилфталида и натријум-хлорида (25 mg два пута дневно), а ЕД група инјекције едаравон-дексборнеола (30 mg два пута дневно). Основне мере исхода биле су скор на Скали за мождани удар Националног института за здравље, скор на модификованој Ранкиновој скали и средња брзина протока крви кроз средњу мождану артерију пре и после лечења. Секундарни параметри укључивали су параметре коагулације (број тромбоцита, број леукоцита) и процену безбедности. Анализе подгрупа засноване су на типу одговорне артерије (болест великих крвних судова / болест малих крвних судова) и етиолошкој категорији (атеросклеротски инфаркт / кардиоемболизам).

Резултати Резултати су показали да је, у поређењу са ЕД групом, BSC група имала значајно нижи скор на Скали за мождани удар Националног института за здравље ($p < 0,05$) и значајно вишу средњу брзину протока крви кроз средњу мождану артерију, посебно у подгрупи са болешћу великих крвних судова ($p < 0,05$). Анализа профила коагулације показала 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 броја тромбоцита у односу на ЕД ($p < 0,05$). Процене безбедности указале су на упоредиве стопе нежељених догађаја и функције јетре и бубрега међу групама ($p > 0,05$), без озбиљних крварења или оштећења органа.

Закључак BSC испољава терапијско дејство зависно од патолошког типа путем свог вишециљног механизма (побољшање колатералног крвотока посредовано фактором раста васкуларног ендотела и инхибиција тромбоцита зависна од фактора активације тромбоцита), показујући значајну етиолошку специфичну ефикасност, што оправдава приоритетну примену ове терапије код подтипова акутног исхемијског можданог удара повезаних са великим крвним судовима или атеросклерозом.

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