Am J Transl Res 2025;17(12):9608-9618
www.ajtr.org /ISSN:1943-8141/AJTR0168275

Original Article

Efficacy and safety of blood purification in the treatment of autoimmune encephalitis: a meta-analysis

Minlu Wu[1], Mengmeng Wang[2], Wanning Li[1], Liyan Gu[1], Jie Wei[1], Jianhua Zhuang[3]

[1]Department of Neurology, No. 905 Hospital of People's Liberation Army Navy Affiliated to Naval Medical University, Shanghai 200052, China; [2]Department of Hyperbaric Oxygen and Neurology, Naval Medical Center, Shanghai 200052, China; [3]Department of Neurology, The Second Affiliated Hospital of Naval Medical University (Shanghai Changzheng Hospital), Shanghai 200003, China

Received August 21, 2025; Accepted December 3, 2025; Epub December 15, 2025; Published December 30, 2025

Abstract: Objective: To systematically evaluate the efficacy and safety of blood purification in the treatment of autoimmune encephalitis (AE). Methods: Databases including PubMed, Embase, and Cochrane Library were systematically searched. Prospective and retrospective cohort studies were included. Data on patients' baseline characteristics, interventions, and outcomes were extracted. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included studies. Meta-analysis was performed using RevMan 5.4 software. Results: Fifteen studies (531 patients) were included; NOS scores of 7-9 indicated high quality. Efficacy analysis showed that in studies with control groups, blood purification significantly increased the likelihood of clinical improvement (Odds Ratio (OR)=5.61, 95% Confidence Interval (CI) [2.72, 11.56], $P<0.00001$). In studies without control groups, most efficacy indicators (e.g., clinical improvement, modified Rankin Scale (mRS) score improvement) showed statistical significance. Safety analysis revealed that the risk of therapeutic plasma exchange (TPE)-related adverse events was significantly increased (Risk Difference (RD)=0.46, 95% CI [0.40, 0.52], $P<0.00001$). The risks of complications and seizures were also elevated (RD=0.57 and 0.74, respectively, both $P<0.05$). The risk of total adverse reactions per cycle was increased (RD=0.09, 95% CI [0.04, 0.14], $P=0.0004$). The 1-year relapse risk was significantly increased (RD=0.07, 95% CI [0.02, 0.11], $P=0.004$), while there was no significant difference in mortality ($P>0.05$). Publication bias was assessed via funnel plots and Egger's test, with no evidence of bias, and sensitivity analysis results were stable. Conclusion: Blood purification can significantly improve clinical outcomes in AE patients, but it is associated with higher risks of adverse events and relapse.

Keywords: Blood purification, autoimmune encephalitis, efficacy, safety, plasma exchange, immunoadsorption, hemoperfusion, adverse reactions, meta-analysis

Introduction

Autoimmune Encephalitis (AE) is a group of complex neuroinflammatory disorders characterized by the presence of autoantibodies targeting neuronal antigens, which can trigger various neurological symptoms such as seizures, cognitive dysfunction, psychiatric symptoms, and movement disorders [1]. Despite growing understanding of its pathophysiological mechanisms, the clinical management of AE remains challenging due to individual differences in patients' responses to standard immunotherapies like glucocorticoids, intravenous immunoglobulin, and rituximab. A considerable proportion of patients achieve incomplete recovery or experience relapses, highlighting the urgent need for alternative or adjuvant treatment strategies [2].

In recent years, blood purification (BP) techniques, including plasma exchange, immunoadsorption, and double plasma molecular adsorption, have gradually emerged as potential approaches for AE treatment. These techniques aim to directly remove circulating pathogenic autoantibodies, immune complexes, and proinflammatory mediators, thereby alleviating neuroinflammation and promoting neurological function recovery [3]. However, the current evidence supporting the efficacy and safety of BP in treating AE mainly comes from small-scale

observational studies, case series, and retrospective analyses, with results often conflicting. For instance, some studies [4] have shown that plasma exchange can significantly improve seizure control and cognitive function, while the incidence rates of adverse events such as hypotension, infection, and electrolyte disorders vary across different cohort studies [5].

Such inconsistencies in clinical outcomes can be attributed to multiple factors, including patient selection criteria, timing and duration of BP intervention, specific types of BP techniques used, and the combination with other immunotherapies. Additionally, the lack of large-scale randomized controlled trials has hindered the development of guidelines for the optimal application of BP in AE management. Consequently, clinicians face significant uncertainties when considering BP treatment, leading to variations in clinical practice and potential underutilization or inappropriate use of the techniques. Against this backdrop, this meta-analysis aims to systematically integrate existing evidence on the efficacy and safety of BP in treating AE. By pooling data from eligible studies, this analysis will address key issues such as the extent of BP-related clinical improvement, its impact on relapse rates, and overall safety - findings that are expected to standardize clinical practice and improve patient outcomes.

Materials and methods

Literature search strategy

This study was registered in PROSPERO (CRD-420251087020). A systematic search was conducted in PubMed, Embase, and the Cochrane Library, with the search period covering from the establishment of each database to May 2025. English search terms included “autoimmune encephalitis”, “blood purification”, “plasma exchange”, “immunoadsorption”, “dialysis”, “therapeutic apheresis”, and other relevant terms. Boolean operators were used for retrieval, and search strategies were adjusted appropriately for different databases. For example, the PubMed search strategy was: (((((autoimmune encephalitis [Title/Abstract]) AND (blood purification [Title/Abstract])) OR (plasma exchange [Title/Abstract])) OR (immunoadsorption [Title/Abstract])) OR (dialysis [Title/Abstract])) OR (therapeutic apheresis [Title/Abstract]).

Inclusion criteria for literature

(1) Study type: Prospective cohort studies and retrospective cohort studies were included. (2) Patients diagnosed with autoimmune encephalitis according to clear diagnostic criteria, regardless of age, gender, disease stage, and antibody subtypes (e.g., anti-N-methyl-D-aspartate (NMDA) receptor encephalitis, neuronal surface antibody-associated autoimmune encephalitis, anti-dipeptidyl peptidase-like protein 6 encephalitis, etc.). (3) Patients received at least one type of blood purification treatment (including but not limited to plasma exchange [Total Plasma Exchange (TPE)/ Double Plasma Molecular Adsorption System (DPMAS)], immunoadsorption, hemoperfusion, etc.), regardless of whether they were combined with other immunotherapies (e.g., glucocorticoids, immunoglobulin, etc.). (4) Main outcome indicators were as follows:

Efficacy: (1) Clinical improvement: Defined as a quantitative reduction in core symptoms of autoimmune encephalitis (e.g., reduction in seizure frequency by ≥50%, alleviation of consciousness disturbance from coma to confusion or clear-headedness, or resolution of psychiatric symptoms such as hallucinations/ delusions); or a ≥2-point decrease in the modified Rankin Scale (mRS) score compared to baseline (indicating improved functional independence) [6]. (2) Pathologies on MRI: Defined as the disappearance or ≥50% reduction in abnormal signal intensities (e.g., T2-weighted imaging/Fluid-Attenuated Inversion Recovery (FLAIR) hyperintensities in the temporal lobe, hippocampus, or basal ganglia) on brain MRI compared to pretreatment scans [7]. (3) Improvement in mRS: Specifically defined as ≥1-point decrease in the mRS score from baseline (minimum score: 0, indicating no disability; maximum score: 6, indicating death), reflecting enhanced daily living ability [8].

Safety: (1) TPE-related adverse events: Specific events including hypotension, allergic reactions (urticaria, anaphylaxis), hypocalcemia, catheter-related infections, and bleeding at the vascular access site [9]. (2) Adverse events/ adverse reactions/complications (non-TPE-related adverse events): General safety indica-

tors covering all treatment-related adverse manifestations (e.g., fever, headache, electrolyte disturbances) excluding TPE-specific events. (3) Clinical outcomes: Relapse during the year after initial treatment: Defined as recurrence of typical autoimmune encephalitis symptoms (e.g., re-emergence of seizures, impaired consciousness) within 12 months after initial symptom remission, confirmed by clinical evaluation and/or re-elevation of specific autoantibody titers [10].

Exclusion criteria for literature

(1) Case reports, reviews, case analyses, and other non-cohort study types. (2) Duplicate publications; the most recently published or informationally most comprehensive study is prioritized (duplicate studies are excluded). (3) Literature for which the full text is unavailable, and key data cannot be obtained even after contacting the authors. (4) Studies involving participants with comorbidities such as other central nervous system infections (e.g., viral encephalitis, bacterial meningitis), hereditary encephalopathy, metabolic encephalopathy, or definite cerebrovascular diseases; studies where blood purification was not targeted for autoimmune encephalitis itself (e.g., used merely for managing complications); or studies with incomplete participant data from which efficacy- and safety-related indicators cannot be extracted. (5) Unclear description of intervention measures. (6) Literature whose outcome indicators do not align with the predefined primary or secondary outcome indicators of this study.

Literature screening and data extraction

Two researchers independently conducted literature screening and data extraction. Initially, they screened titles and abstracts to exclude studies that obviously did not meet the inclusion criteria; those potentially eligible were further evaluated via full-text review to determine the final inclusion. Disagreements between the two researchers were resolved through discussion or consultation with a third independent researcher. The extracted data included the first author, year of publication, study type, sample size, baseline characteristics of participants (e.g., age, gender, AE subtypes), details of intervention measures, and relevant data on the predefined outcome indicators.

Quality assessment of literature

The Newcastle-Ottawa Scale (NOS) [11] was used to evaluate the quality of the included studies, with scoring based on dimensions including the selection of study population (e.g., representativeness of cases and controls, methods for defining cases and controls), comparability between groups (mainly considering the control of confounding factors), and outcome measurement (e.g., methods for determining outcomes, follow-up duration, and completeness of follow-up). The scoring system ranges from 0 to 9 points: studies with scores ≥7 are considered high-quality, those with 4-6 points are considered moderate quality, and those with ≤3 points are considered low quality.

Statistical analysis

Meta-analysis was performed using RevMan 5.4 software. All data were dichotomous variables, and Risk Difference (RD) or Odds Ratio (OR) with 95% Confidence Intervals (CI) was used as the effect indicator, with clear correspondence to specific outcome indicators:

For “Clinical improvement (with control group)”: OR reflects the difference in the proportion of patients achieving this efficacy endpoint between the blood purification group and the control group.

For “efficacy (without control group)”, “TPE-related adverse events”, “adverse events (in the number of cases)”, “adverse events (based on cycle counts)”, and “clinical outcomes”: RD reflects the difference in the incidence of these safety/clinical endpoints between the two groups.

Heterogeneity among studies was assessed using the χ^2 test and I^2 statistic. If $I^2<50\%$ and $P>0.1$, indicating low heterogeneity, a fixed-effects model was used for meta-analysis; if $I^2\geq50\%$ or $P\leq0.1$, indicating high heterogeneity, a random-effects model was applied.

By excluding low-quality studies and sequentially removing individual studies, the changes in the pooled effect size were observed. Direct visual assessment of publication bias was conducted using a funnel plot. The funnel plot presents the distribution of included studies, with the effect size as the abscissa and the stan-

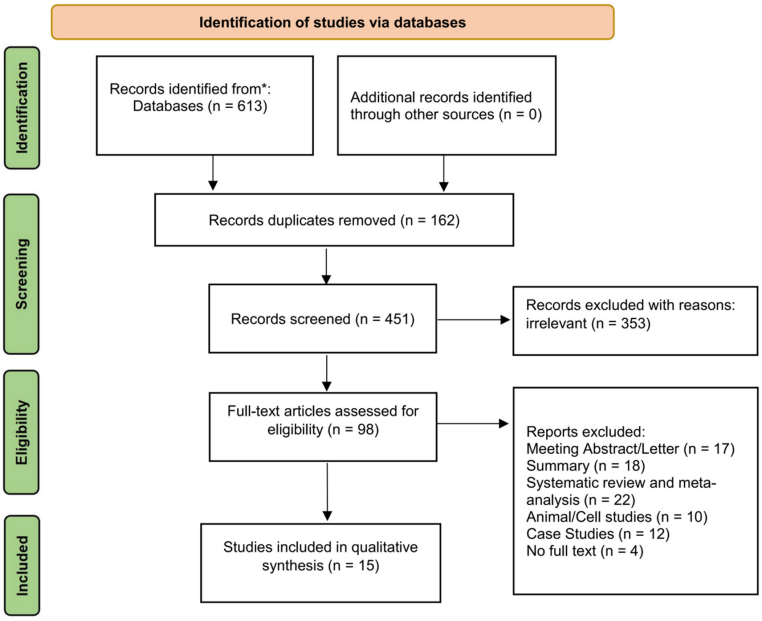

Figure 1. PRISMA flow diagram.

dard error as the ordinate. Ideally, in the absence of publication bias, the included studies should be evenly distributed on both sides of the funnel plot, forming a symmetric inverted funnel shape where study points converge towards the top of the funnel as the sample size increases (and the standard error decreases). Asymmetry in the funnel plot may indicate publication bias or other potential biases, and its interpretation should be combined with the results of sensitivity analyses to help evaluate the reliability of the study findings.

Results

Literature screening process and number of included studies

A total of 613 records were retrieved from the databases, with no additional records supplemented from other sources. After removing 162 duplicate records, 451 records entered the screening phase. Among these 451 records, 353 were excluded as "irrelevant" after initial screening, leaving 98 records for full-text evaluation. From the 98 full texts, 83 were excluded for reasons including "conference abstracts/letters (17), systematic reviews and meta-analyses (22), animal/cell studies (10), case reports (12), and unavailable full texts (4)". Finally, 15 studies were included in qualitative synthesis and subsequent meta-analysis (**Figure 1**).

Baseline characteristics and quality assessment of included studies

The 15 included studies [12-26] involved a total of 531 patients. The proportion of male patients ranged from 11% to 71.7%, with some data unspecified. The age of participants covered a wide range from children (1-17 years) to adults (e.g., 11-68 years). The main subtypes of AE were anti-NMDA receptor encephalitis and other subtypes, while some subtypes were not further subdivided. The anticoagulants administered were mainly heparin or ACDA, with some anticoagulants not reported. Blood purification was predominantly total plasma exchange (TPE), with a few studies using double filtration plasmapheresis (DFPP). The number of TPE cycles were mostly reported as total counts or ranges, and DFPP was mostly performed 3 (2-6) times; one study reported the replacement volume as 50.5±11.1 ml/kg per session.

Among the 15 studies, 3 were prospective cohort studies and 12 were retrospective cohort studies. Only 2 studies established control groups, and the rest did not. Outcome indicators included clinical improvement, adverse events, mRS scores, antibody titers, etc. The follow-up duration was 6-24 months, with some durations not specified. The NOS scores ranged from 7 to 9 points, indicating overall good quality (**Table 1**).

Meta-analysis of efficacy

Studies without control groups [13-15, 17, 21, 22, 26]: A random-effects model was used to calculate risk differences (RDs) for efficacy outcomes. The results showed that blood purification was associated with a significant improvement in clinical efficacy (RD=1.59, 95% CI [1.31, 1.94], P<0.00001) (**Figure 2A**).

Studies with control groups [12, 16]: A fixed-effects model was used for analysis, and the results revealed that the likelihood of clinical

Table 1. Baseline characteristics of patients

Number	Author Year	Country	n	Male	Age	Subtypes of AE	Anticoagulation	Blood purification	Cycles	Plasma exchange volume	Type	Set up a control	Outcome	Follow-up	NOS
[12]	Zhang 2021	India	57	30 (53%)	26 (21, 40)	No segmentation	Heparin	TPE	193	NA	Prospective	Yes	①②	12 months	8
[13]	Moser 2019	Austria	12	7 (58.33%)	45.1±18.8	No segmentation	NA	TPE	6.3±2.7	NA	Retrospective	No	③④⑦⑧	6 months	8
[14]	Crowe 2024	USA	37	23 (62.16%)	56 (28-77)	No segmentation	NA	TPE	5 (3-16)	NA	Retrospective	No	②⑨	NA	7
[15]	Nieto-Aristizábal 2020	Colombia	187	104 (55.6%)	50 (32-64)	No segmentation	ACDA	TPE	5 (5-5)	NA	Retrospective	No	⑩	NA	7
[16]	Zhang 2019	China	40	19 (47.5%)	28.1±12.6	anti-NMDA receptor encephalitis	NA	TPE	Total 118	NA	Retrospective	Yes	⑥⑩⑪	12 months	9
[17]	Liang 2024	China	26	17 (65.38%)	40 (16-72)	Neuronal surface antibody-associated autoimmune encephalitis	NA	DFPP	3 (2-6)	50.5±11.1 ml/kg/ session	Retrospective	No	①⑪⑫	6 months	8
[18]	Gupta 2025	India	53	38 (71.70%)	48 (11-68)	No segmentation	ACDA	TPE	Total 30	NA	Prospective	No	⑬	NA	8
[19]	Naik 2021	India	4	1 (25.00%)	9-14	anti-NMDA receptor encephalitis	ACDA	TPE	Total 20	NA	Retrospective	No	⑫⑯	12 months	7
[20]	Fateen 2023	Pakistan	24	11 (45.83%)	7.58±2.04	No segmentation	NA	TPE	Total 125	NA	Prospective	No	⑩	NA	9
[21]	Shah 2020	USA	18	11 (64.7%)	10.5 (1-17)	No segmentation	NA	TPE	Total 112	NA	Retrospective	No	①⑬	NA	7
[22]	Pham 2011	New York	9	1 (11.11%)	NA	anti-NMDA receptor encephalitis	ACDA	TPE	Total 56	NA	Retrospective	No	①⑩	12 months	8
[23]	Kong 2019	Taiwan, China	24	8 (33.33%)	16.62±7.39	anti-NMDA receptor encephalitis	NA	TPE	NA	NA	Retrospective	No	⑫⑭	6 months	8
[24]	Li 2024	China	20	NA	adult	anti-NMDA receptor encephalitis	NA	TPE	Total 82	NA	Retrospective	No	⑬	NA	9
[25]	Liu 2022	China	15	NA	24.27±9.00	anti-NMDA receptor encephalitis	NA	TPE	NA	NA	Retrospective	No	⑫⑮	24 months	8
[26]	Wan 2024	China	5	NA	adult	anti-dipeptidyl-peptidase-like protein 6 encephalitis	NA	DFPP	NA	NA	Retrospective	No	⑤⑦	NA	9

AE: Autoimmune Encephalitis; TPE: Total Plasma Exchange; DFPP: Double filtration plasmapheresis; ACDA: Acid-Citrate-Dextrose Anticoagulant Solution; NA: Not Available; NMDAR; GABA-BR: γ-aminobutyric acid receptor; LGI1: leucine-rich glioma inactivated 1. A: Not available. ① Clinical improvement, ② TPE-related adverse event, ③ Good clinical response, ④ Inflammatory CSF, ⑤ Elevated cerebrospinal fluid (CSF) protein levels, ⑥ NMDA receptor antibody titers in the CSF and/or plasma decreased or were negative, ⑦ Pathologies on MRI, ⑧ Seizures, ⑨ Improvement in mRS, ⑩ Complication, ⑪ mRS score, ⑫ Adverse event, ⑬ adverse reaction, ⑭ Clinical outcomes, ⑮ Relapse, ⑯ Died.

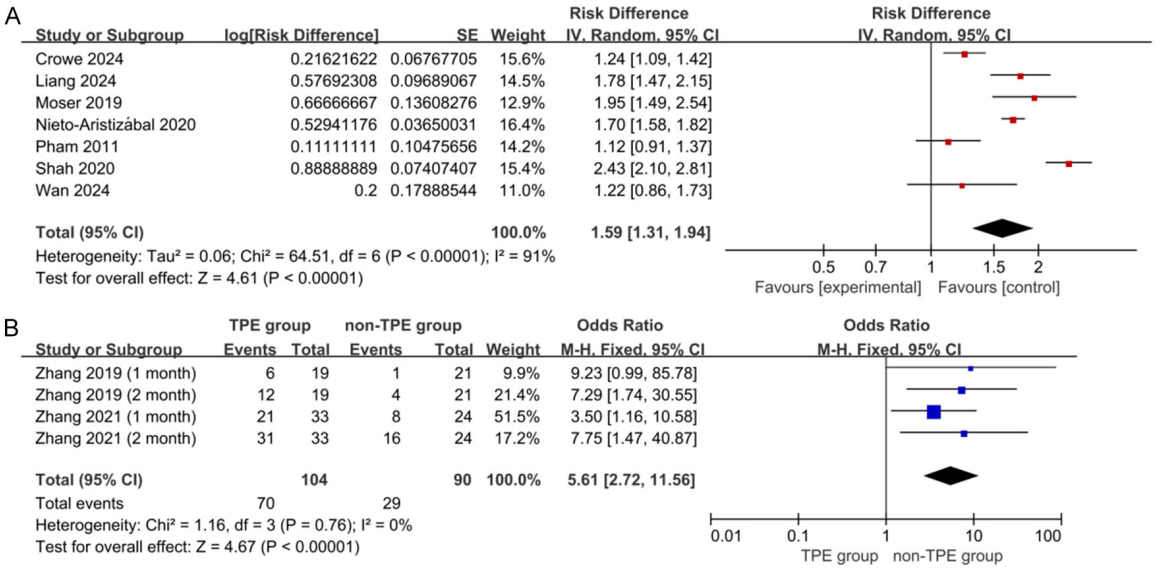

Figure 2. Forest plot of efficacy. A. Studies without control groups; B. Studies with control groups.

improvement was significantly higher in the blood purification group than in the control group (OR=5.61, 95% CI [2.72, 11.56], P< 0.00001) (**Figure 2B**).

Meta-analysis of safety

TPE-related adverse events [12, 14, 17, 23]: Risk differences (RDs) were calculated using a random-effects model. The results showed a statistically significant increase in the risk of TPE-related adverse events (RD=0.31, 95% CI [0.03, 0.59], P=0.03) (**Figure 3A**).

Non-TPE-related adverse events: Analyzed data indicated a significant increase in the risk of adverse events (by case count) [13, 15, 17, 20, 22, 23, 25] (RD=0.57, 95% CI [0.26, 0.87], P=0.0003) (**Figure 3B**). Consistent with this finding, a significant increase was also observed in the risk of adverse events (by TPE cycle count) [16, 18, 21, 24] (RD=0.13, 95% CI [0.04, 0.22], P=0.004) (**Figure 3C**).

Clinical outcomes [15-17, 23, 25]: A fixed-effects model was used to analyze clinical outcomes (1-year recurrence rate and mortality rate). The results showed a significant increase in the 1-year recurrence risk, while no statistically significant difference was observed in mortality risk (RD=0.07, 95% CI [0.02, 0.11], P=0.004) (**Figure 3D**).

Publication bias of included studies

In the meta-analysis of blood purification for the treatment of autoimmune encephalitis, publication bias was evaluated using funnel plots (visual assessment) and Egger's test (statistical quantification). For key outcomes including efficacy, adverse events (by case count), and clinical outcomes, funnel plots were generated (**Figure 4**). The plots showed approximate symmetry, with included studies evenly distributed around the pooled effect size and converging toward the top of the funnel, indicating a low risk of publication bias. Additionally, Egger's test was conducted: for efficacy, the intercept was 0.25 (95% CI: -0.61 to 1.11, P=0.56); for adverse events, the intercept was -0.32 (95% CI: -1.15 to 0.51, P=0.44); and for clinical outcomes, the intercept was 0.18 (95% CI: -0.72 to 1.08, P=0.69). All *P* values were greater than 0.05, confirming no statistically significant funnel plot asymmetry.

These findings indicate that there is no obvious publication bias in the included studies, thus supporting the reliability of the conclusions. Sensitivity analysis was further performed: after excluding some studies with relatively high heterogeneity, the combined results of these indicators were still consistent with the initial results (**Figure 5**), validating the robustness of the meta-analysis findings.

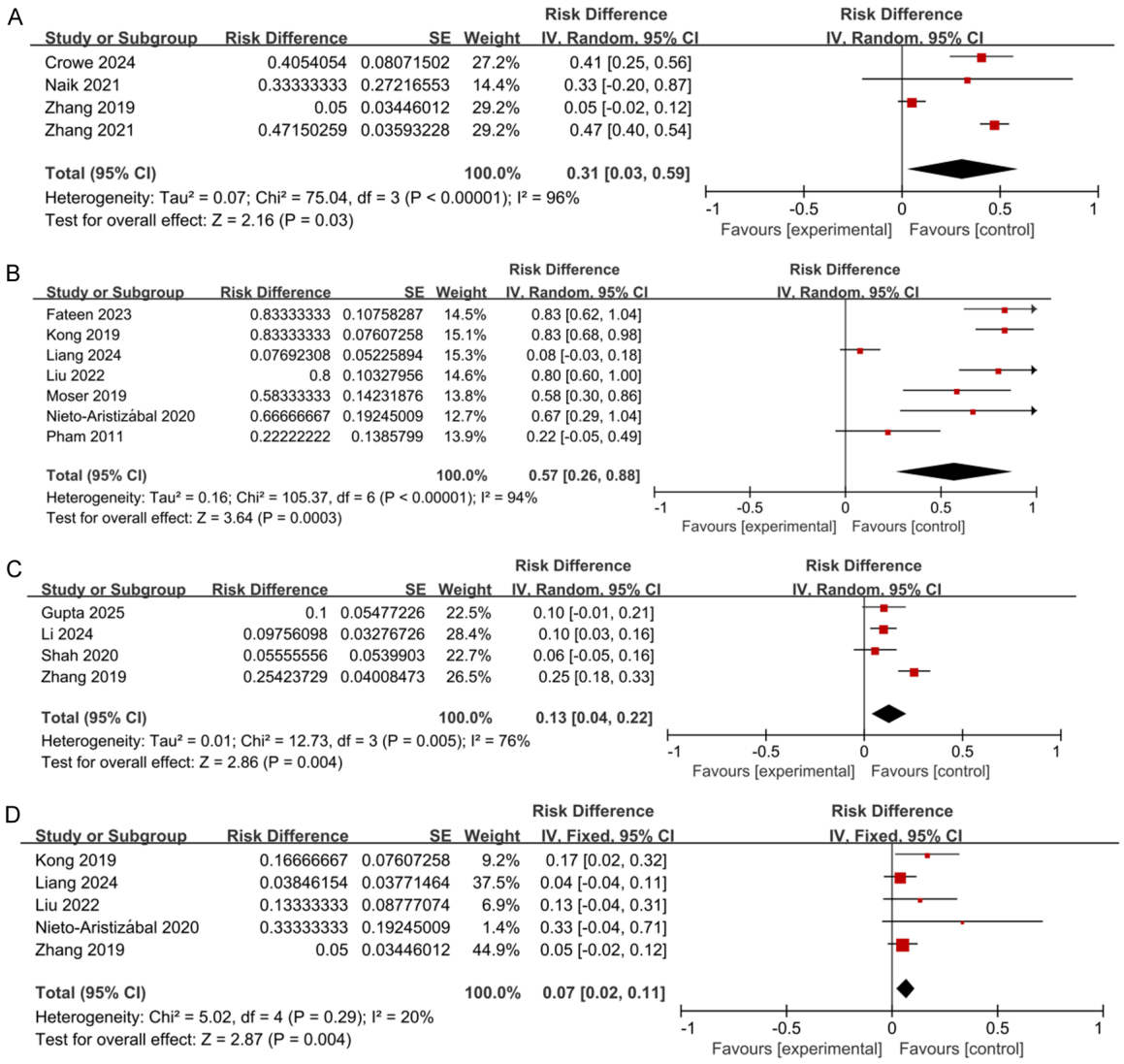

Figure 3. Forest plot of safety. A. TPE-related adverse events; B. Non-TPE-related adverse events (in the number of cases); C. Non-TPE-related adverse events (in the number of TPE cycles); D. Clinical outcomes.

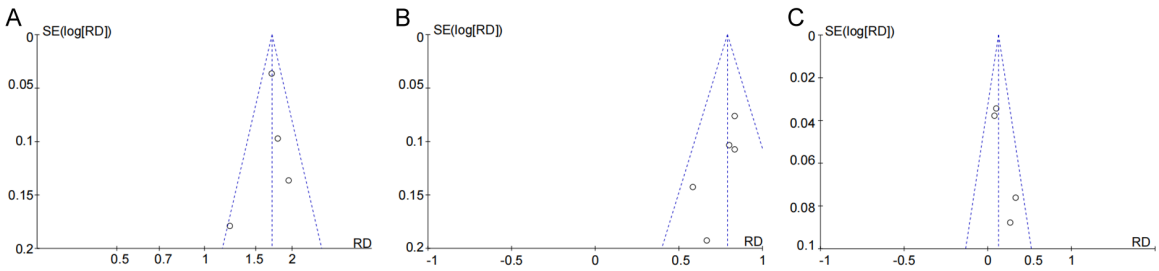

Figure 4. Funnel plot of publication bias. A. Efficacy; B. Adverse event (in the number of cases); C. Clinical outcomes.

Discussion

Blood purification (e.g., TPE) exerts its therapeutic effects by removing circulating autoantibodies, immune complexes, and proinflammatory cytokines. In terms of clinical improvement, the meta-analysis results showed a significant overall effect across most efficacy outcomes,

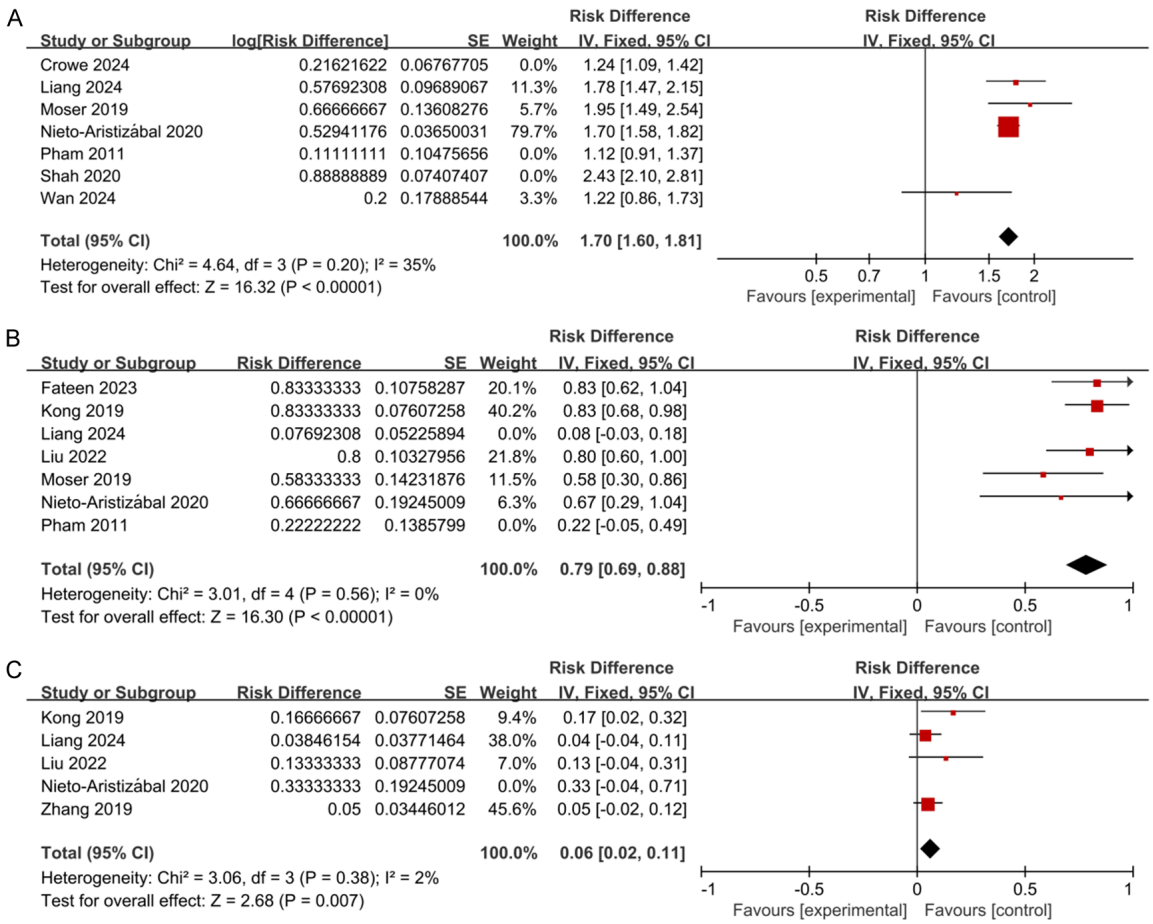

Figure 5. Forest plot for sensitivity analysis (one-by-one exclusion method). A. Efficacy; B. Adverse event (in the number of cases); C. Clinical outcomes.

except for improvements in MRI pathological changes. This suggests that blood purification can regulate immune responses and reduce pathogenic factors contributing to neurological dysfunction. For example, clearance of autoantibodies targeting neuronal antigens may promote the recovery of neuronal function, thereby achieving improvements in clinical symptoms [27].

For MRI pathological changes and mRS score improvement, the direction of effect was stable, indicating that blood purification consistently contributes to reducing intracerebral pathological load and improving functional outcomes. This may be related to the reduction of inflammatory mediators that induce cerebral edema and neuronal damage, as well as the promotion of neuroplasticity by clearing inhibitory factors [28]. When control groups were included, the meta-analysis of clinical improvement showed significant overall effects. The low heterogeneity indicates consistent responses across studies, which may benefit from more standardized comparisons between blood purification and control interventions (such as conventional immunotherapy or supportive care). The underlying mechanism might be that blood purification directly removes pathogenic autoantibodies, thus having an advantage over traditional therapies in rapidly reducing antibody load. For instance, a study by Gao et al. [29] demonstrated that TPE can clear specific autoantibodies associated with autoimmune encephalitis in a short term; compared with the control group, it achieves more rapid improvement in clinical symptoms - a finding consistent with the positive effect of blood purification on clinical improvement reflected by the OR value in this meta-analysis. The meta-analysis showed significant heterogeneity across different models for efficacy out-

comes (clinical improvement, MRI pathological changes, and mRS score improvement) in studies without control groups. This high heterogeneity may stem from the diversity of study populations (e.g., variations in the severity and stage of autoimmune encephalitis) and differences in the blood purification protocols adopted in each study. For instance, the inclusion criteria for autoimmune encephalitis may vary slightly among studies: some included cases had more extensive brain damage and severe conditions, while others focused on mild cases.

The meta-analysis of TPE-related adverse events showed significant overall effects with low heterogeneity. The increased risk of TPE-related adverse events may be associated with the inherent characteristics of the procedure itself. TPE involves plasma separation and replacement, a process that may cause hypotension due to fluctuations in blood volume, allergic reactions triggered by replacement fluids, or complications such as infections related to vascular access. Soares Ferreira Junior et al. [30] noted that manipulation of blood components during TPE can disrupt normal hemostatic and immune balance, thereby increasing the risk of adverse events. The significant RD of TPE-related adverse events in this study is consistent with this view. The consistency of the results suggests that clinicians should be vigilant and closely monitor these potential complications when using TPE for treating autoimmune encephalitis. Among adverse events analyzed by case count (including complications, hypotension, hypersensitivity, and seizures), the risks of complications and seizures were significantly increased, while no statistically significant differences were observed in the risks of hypotension and hypersensitivity. The increased risk of complications may be related to the invasiveness of blood purification procedures, such as access site infections or other iatrogenic complications. Seizures may be induced by rapid changes in the immune environment and electrolyte disturbances during blood purification. When analyzed by treatment cycles, the fixed-effects model showed a significant increase in the risk of hypotension, but heterogeneity persisted. This may be associated with the cumulative impact of multiple TPE cycles on blood volume and hemodynamics. The significant increase in the overall incidence of adverse reactions emphasizes the need to carefully balance the benefits and risks of blood purification when multiple cycles of treatment are required.

Meta-analysis of prognostic outcomes (1-year relapse rate and mortality rate) indicated that blood purification may be associated with an increased risk of relapse, while its association with mortality remains to be further verified. The increased relapse risk might be attributed to the failure of blood purification to completely eliminate pathogenic factors or the rebound activation of the immune system following treatment. A previous study [31] proposed that the immune system may undergo rebound activation after blood purification reduces autoantibody levels, thereby leading to disease recurrence. The relatively stable results of relapse risk in the sensitivity analysis suggest the reliability and consistency of this finding. Future studies are needed to explore targeted relapse prevention strategies, such as combining blood purification with long-term immunomodulatory therapy to maintain immune homeostasis.

This meta-analysis has several limitations: First, there is heterogeneity in the design of the included studies. Differences exist in inclusion criteria, blood purification protocols (type, frequency, duration) across studies - some used TPE alone, while others combined it with other immunotherapies [12] - and these variations may have influenced the results. Second, although sensitivity and publication bias analyses indicated no significant publication bias, small-scale studies with negative results may remain unpublished (i.e., publication bias cannot be completely ruled out). Additionally, the quality of the included studies varies; there is a paucity of randomized controlled trials (RCTs), with all being observational studies, which may introduce selection and confounding biases. Third, the included patient population is mostly from specific regions and medical settings with high homogeneity, potentially restricting the generalizability of the results, as genetic and environmental factors can influence treatment responses [32]. Fourth, most studies have short follow-up periods, making it difficult to assess long-term efficacy and safety; long-term outcomes such as those related to impacts on cognitive function and quality of life have not been fully explored. Future research should focus on three aspects: First, protocol standardization - clarifying inclusion

and exclusion criteria, unifying blood purification types, frequencies, and durations, and developing standardized outcome indicators to improve result comparability through large-scale multicenter RCTs. Second, biomarker exploration - identifying specific biomarkers (e.g., autoantibody subtypes, cytokine profiles) that can predict treatment responses and adverse event risks to enable personalized treatment strategies. Third, combination therapy investigation - exploring the combined use of blood purification with long-term immunomodulators (e.g., immunosuppressants, monoclonal antibodies) to optimize therapeutic effects and reduce relapse risk.

Conclusion

In summary, this meta-analysis provides valuable insights into the efficacy, safety, and prognostic outcomes of blood purification in the treatment of autoimmune encephalitis (AE), albeit with certain limitations. Standardizing treatment protocols, exploring predictive biomarkers, and investigating optimized combination therapies can further enhance its role in the clinical management of AE and improve long-term patient outcomes.

Disclosure of conflict of interest

None.

Address correspondence to: Jie Wei, Department of Neurology, No. 905 Hospital of People's Liberation Army Navy Affiliated to Naval Medical University, No. 1328 Huashan Road, Changning District, Shanghai 200052, China. Tel: +86-021-81819181; E-mail: 13501717467@163.com; Jianhua Zhuang, Department of Neurology, The Second Affiliated Hospital of Naval Medical University (Shanghai Changzheng Hospital), No. 415 Fengyang Road, Huangpu District, Shanghai 200003, China. Tel: +86-021-81885451; E-mail: jianhuazh11@126.com

References

[1] Jha S, Mundlamuri RC, Alladi S, Mahadevan A and Netravathi M. Electroencephalographic outcomes and predictors of epilepsy in autoimmune encephalitis. Seizure 2024; 121: 162-171.

[2] Yang JH, Liu EN, Nguyen L, Dunn-Pirio A and Graves JS. Survival analysis of immunotherapy effects on relapse rate in pediatric and adult autoimmune encephalitis. Neurology 2023; 101: e2300-e2313.

[3] Borko TL, Winters P, Money KM, Sillau S, Eggmann S, Selva S, Ritchie A, Kammeyer R, Owens GP, Bennett JL and Piquet AL. Long-term outcomes in leucine-rich glioma inactivated-1 autoimmune encephalitis and associated biomarkers of inflammation and neuronal and glial injury. Front Neurol 2025; 16: 1583892.

[4] Borko TL, Winters P, Money KM, Sillau S, Eggmann S, Selva S, Ritchie A, Kammeyer R, Owens GP, Bennett JL and Piquet AL. Long-term outcomes in leucine-rich glioma inactivated-1 autoimmune encephalitis and associated biomarkers of inflammation and neuronal and glial injury. Front Neurol 2025; 16: 1583892.

[5] Gu S, Wei D and Yu L. Influencing factors of hypotension during plasma exchange in patients with neuroimmunological diseases: a retrospective cohort study. Cardiovasc Diagn Ther 2025; 15: 414-422.

[6] Macher S, Bsteh G, Höftberger R, Berger T, Rommer P and Zrzavy T. Clinical scales in autoimmune encephalitis-a retrospective monocentric cohort study. Ann Clin Transl Neurol 2023; 10: 1768-1775.

[7] Hartung TJ, Bartels F, Kuchling J, Krohn S, Leidel J, Mantwill M, Wurdack K, Yogeshwar S, Scheel M and Finke C. MRI findings in autoimmune encephalitis. Rev Neurol (Paris) 2024; 180: 895-907.

[8] Thaler FS, Zimmermann L, Kammermeier S, Strippel C, Ringelstein M, Kraft A, Sühs KW, Wickel J, Geis C, Markewitz R, Urbanek C, Sommer C, Doppler K, Penner L, Lewerenz J, Rößling R, Finke C, Prüss H, Melzer N, Wandinger KP, Leypoldt F and Kümpfel T; German Network for Research on Autoimmune Encephalitis (GENERATE). Rituximab treatment and long-term outcome of patients with autoimmune encephalitis: real-world evidence from the GENERATE registry. Neurol Neuroimmunol Neuroinflamm 2021; 8: e1088.

[9] Srivastava A, Elhence P, Singh B, Verma A, Agarwal P, Khetan D, Chaudhary RK, Srivastava A and Prasad N. ABO antibody titer dynamics and optimization in incompatible renal transplants using therapeutic plasma exchange. Cureus 2025; 17: e91015.

[10] Mangioris G, Orozco E, Dubey D, Flanagan EP, Pittock SJ, Zekeridou A and McKeon A. Long-term outcomes in antibody-negative autoimmune encephalitis: a retrospective study. Neurology 2024; 103: S83-S84.

[11] Carra MC, Romandini P and Romandini M. Risk of bias evaluation of cross-sectional studies: adaptation of the Newcastle-Ottawa scale. J Periodontal Res 2025; [Epub ahead of print].

[12] Zhang Y, Huang HJ, Chen WB, Liu G, Liu F and Su YY. Clinical efficacy of plasma exchange in patients with autoimmune encephalitis. Ann Clin Transl Neurol 2021; 8: 763-773.
[13] Moser T, Harutyunyan G, Karamyan A, Otto F, Bacher C, Chroust V, Leitinger M, Novak HF, Trinka E and Sellner J. Therapeutic plasma exchange in multiple sclerosis and autoimmune encephalitis: a comparative study of indication, efficacy and safety. Brain Sci 2019; 9: 267.
[14] Crowe EP, Diaz-Arias LA, Habis R, Vozniak SO, Geocadin RG, Venkatesan A, Tobian AAR, Probasco JC and Bloch EM. Suspected autoimmune encephalitis: a retrospective study of patients referred for therapeutic plasma exchange. J Clin Apher 2024; 39: e22112.
[15] Nieto-Aristizábal I, Vivas ÁJ, Ruiz-Montaño P, Aragón CC, Posso-Osorio I, Quiñones J, Rivillas JA and Tobón GJ. Therapeutic plasma exchange as a treatment for autoimmune neurological disease. Autoimmune Dis 2020; 2020: 3484659.
[16] Zhang Y, Liu G, Jiang M, Chen W and Su Y. Efficacy of therapeutic plasma exchange in patients with severe refractory anti-NMDA receptor encephalitis. Neurotherapeutics 2019; 16: 828-837.
[17] Liang X, Zhang C, Xue J and Zheng Y. Efficacy of double filtration plasmapheresis in the treatment of steroid and/or IVIG unresponsive neuronal surface antibodies associated autoimmune encephalitis. BMC Neurol 2024; 24: 475.
[18] Gupta S, Tiwari AK, Aggarwal G, Bhardwaj G, Pawar S, Goyal V, Garg A and Sehgal J. Effectiveness and safety of therapeutic plasma exchange in neurological disorders; measuring the response to treatment using Modified Rankin Scale-a single-center study. Asian J Transfus Sci 2025; 19: 187-192.
[19] Naik A, Prakash S, Ray GK and Mukherjee S. Variable response to therapeutic plasma exchange in pediatric anti-NMDA receptor encephalitis. Transfus Clin Biol 2021; 28: 287-290.
[20] Fateen T, Sultana N, Sarwar M and Saqlain N. Complications of therapeutic plasma exchange in pediatric patients: an experience at a tertiary care hospital. Pak J Med Sci 2023; 39: 994-998.
[21] Shah YD, Eksambe P, Fomani K, Louie J, Shefali K and Kothare S. Feasibility & safety of plasma exchange in paediatric neuro-immunology: a single center experience. Eur J Paediatr Neurol 2020; 27: 94-97.
[22] Pham HP, Daniel-Johnson JA, Stotler BA, Stephens H and Schwartz J. Therapeutic plasma exchange for the treatment of anti-NMDA receptor encephalitis. J Clin Apher 2011; 26: 320-325.
[23] Kong SS, Chen YJ, Su IC, Lin JJ, Chou IJ, Chou ML, Hung PC, Hsieh MY, Wang YS, Chou CC, Wang HS and Lin KL; CHEESE Study Group. Immunotherapy for anti-NMDA receptor encephalitis: experience from a single center in Taiwan. Pediatr Neonatol 2019; 60: 417-422.
[24] Li J, Huang B, Lao Q, Zou L and Xie K. To analyze the efficacy and safety of plasma exchange in the treatment of anti-NMDA receptor encephalitis. Ther Apher Dial 2024; [Epub ahead of print].
[25] Liu Y, Tian Y, Guo R, Xu X, Zhang M, Li Z, Xiao Y, Cao W, Gao H, Kong D, Du Y, Meng L, Zhang J and Huang X. Anti-NMDA receptor encephalitis: retrospective analysis of 15 cases, literature review, and implications for gynecologists. J Healthc Eng 2022; 2022: 4299791.
[26] Wan W, Pan Y, Chen Y, Bai S, Yao X, Lin Y, Wu J, Ni L, Mei Y, Qiu H, Zhou Y, Hao Y and Guan Y. The effect of double filtration plasmapheresis and corticosteroids on patients with anti-dipeptidyl-peptidase-like protein 6 encephalitis. Ther Apher Dial 2024; 28: 141-151.
[27] Shang H, Shen X, Yu X, Zhang J, Jia Y and Gao F. B-cell targeted therapies in autoimmune encephalitis: mechanisms, clinical applications, and therapeutic potential. Front Immunol 2024; 15: 1368275.
[28] Ergun C and Eskizengin H. Recent updates on blood purification: use of smart polymer materials. J Biomed Mater Res A 2025; 113: e37883.
[29] Gao W, She J, Su L, Jin S, Yang Q, Chen X and Zhu R. Clinical features and immunotherapy outcomes in antibody-negative autoimmune encephalitis: a retrospective case-control study. Front Neurol 2024; 15: 1464165.
[30] Soares Ferreira Junior A, Lessa MPM, Sanborn K, Kuchibhatla M, Karafin MS and Onwuemene OA. In hospitalized patients undergoing therapeutic plasma exchange, major bleeding prevalence depends on the bleeding definition: an analysis of the recipient epidemiology and donor evaluation Study-III. J Clin Apher 2023; 38: 694-702.
[31] Hu SZ, Yuan ZY, Zhang XX, Yu XJ, Ni HY, Sun SJ, Xu T and Zhan HQ. The emerging role of BLyS/APRIL in autoimmune diseases: biological characteristics, functions, and therapeutic potential. J Autoimmun 2024; 149: 103329.
[32] Bieber K, Hundt JE, Yu X, Ehlers M, Petersen F, Karsten CM, Köhl J, Kridin K, Kalies K, Kasprick A, Goletz S, Humrich JY, Manz RA, Künstner A, Hammers CM, Akbarzadeh R, Busch H, Sadik CD, Lange T, Grasshoff H, Hackel AM, Erdmann J, König I, Raasch W, Becker M, Kerstein-Stähle A, Lamprecht P, Riemekasten G, Schmidt E and Ludwig RJ. Autoimmune pre-disease. Autoimmun Rev 2023; 22: 103236.