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Original article

Efficacy of DPMAS combined with PE in improving survival outcomes of patients with acute hepatitis E-induced liver failure: A retrospective cohort analysis

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ABSTRACT

Background and aims: Acute hepatitis E can progress to liver failure with high mortality and limited treatment options. This study aimed to evaluate the clinical efficacy and safety of the Double Plasma Molecular Adsorption System (DPMAS) combined with plasma exchange (PE) in individuals with acute hepatitis E-induced liver failure.
Methods: A retrospective analysis was performed on hospitalized patients with acute hepatitis E-induced liver failure admitted from January 2011 to December 2023. Ninety-three patients were enrolled and assigned to either a control group ($n = 36$), receiving standard medical therapy, or a treatment group ($n = 57$), receiving artificial liver support therapy with DPMAS combined with PE. Liver function parameters, coagulation indices, Model for End-Stage Liver Disease (MELD) scores, and survival rates were compared. Adverse reactions in the treatment group were recorded and evaluated.
Results: The treatment group demonstrated significantly greater improvement in liver function and coagulation parameters than the control group. MELD score reduction was more pronounced in the treatment group (-6.78 ± 2.45 vs. -2.59 ± 1.98, $p < 0.001$). The 6-month survival rate was also higher (87.7% vs. 80.5%, $p = 0.038$). Cox regression identified age $\geq$60 years (HR = 2.15), liver cirrhosis (HR = 2.41), infection (HR = 3.15), hepatic encephalopathy (HR = 2.87), ascites (HR = 1.94), and international normalized ratio (INR) $\geq$1.5 (HR = 2.54) as independent risk factors for poor prognosis, while higher serum albumin level (HR = 0.49) and DPMAS combined with PE (HR = 0.47) were protective. A total of eight adverse reactions were mild and infrequent, including transient hypotension (5.3%) and mild allergic reactions (8.8%), and resolved with symptomatic treatment without interrupting therapy.
Conclusion: DPMAS combined with PE is a safe and effective therapeutic modality for acute hepatitis E-induced liver failure, improving liver function, reducing MELD scores, and enhancing survival outcomes. MELD score may serve as a valuable tool to guide treatment stratification and predict prognosis.

1. Introduction

Hepatitis E virus (HEV) is a non-enveloped, positive-sense RNA virus taxonomically classified within the genus *Hepevirus* of the family Hepeviridae. Among the eight recognized genotypes, genotypes 1–4 account for the majority of human infections.[1] HEV is primarily transmitted through the fecal–oral route, with contaminated water and undercooked meat products serving as major infectious sources. The virus remains endemic in many developing regions because of inadequate sanitation. Serological surveys indicate that the global

Abbreviations: HEV, Hepatitis E virus; ALF, acute liver failure; TBil, total bilirubin; INR, international normalized ratio; DPMAS, Double Plasma Molecular Adsorption System; PE, plasma exchange; DBil, direct bilirubin; ALT, alanine aminotransferase; ALB, albumin; MELD, Model for End-Stage Liver Disease; IQR, interquartile range; HR, hazard ratios.

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seroprevalence of prior HEV infection ranges from 8% to 20%,[2,3] and HEV is estimated to cause approximately 20 million infections annually, resulting in 3.3 million symptomatic cases and around 70,000 deaths worldwide.[4] Although most HEV infections are self-limiting and resolve within 6–8 weeks, a subset of cases may progress to acute liver failure (ALF), which carries high mortality and poor prognosis.[5]

Management of ALF includes treating the underlying cause, conventional supportive medical therapy, artificial liver support systems, and liver transplantation. Liver transplantation provides the most favorable survival outcomes with rates approaching 75%, but it is limited by donor shortages and high financial burden.[6] Furthermore, when offered as salvage therapy, overall post-transplant survival declines to approximately 55%.[7,8] Despite advances in supportive care, no significant breakthroughs in ALF treatment have emerged in recent years.

Artificial liver support systems are designed to temporarily replace essential liver functions through extracorporeal mechanical, physicochemical, and biological mechanisms. These systems can remove bilirubin, bile acids, endotoxins, and other hepatotoxic substances, while supplementing deficient proteins and coagulation factors. They may also modulate immune responses and reduce systemic inflammation.[9,10] However, the clinical efficacy and safety of artificial liver support for hepatitis E-induced liver failure remain insufficiently defined as a result of limited available evidence.

This study aimed to evaluate the clinical efficacy and safety of artificial liver support therapy in patients with acute hepatitis E-induced liver failure, with emphasis on improvements in liver function and survival outcomes, in order to provide clinically relevant guidance for therapeutic decision-making.

2. Materials and methods

A total of 102 patients with acute hepatitis E-induced liver failure were hospitalized at our institution between January 2011 and December 2023. The diagnosis of acute hepatitis E was based on the *Diagnosis and Treatment Standards for Hepatitis E Virus*, and liver failure was defined according to the *Diagnosis and Treatment Guidelines for Liver Failure (2018 Edition)*. Liver failure criteria included serum total bilirubin (TBil) ≥10 times the upper limit of normal (ULN) or an increase of ≥17.1 μmol/L per day, and prothrombin activity (PTA) ≤40% or international normalized ratio (INR) ≥1.5. Inclusion criteria were age ≥18 years and confirmed acute hepatitis E with liver failure. Exclusion criteria included disease duration >6 months, severe cardiovascular, respiratory, urinary, or hematologic comorbidities, presence of malignant tumors, and pregnancy or lactation.

A total of 102 patients were initially enrolled in the study. After excluding 9 patients with severe comorbidities, 93 patients were included in the final analysis and assigned to either a control group ($n = 36$), receiving standard medical therapy alone, or a treatment group ($n = 57$), receiving standard therapy plus DPMAS combined with PE, according to the therapeutic regimen administered during hospitalization. Standard medical therapy consisted of comprehensive management including bed rest, hepatoprotective treatment, enzyme reduction, jaundice control, ammonia-lowering therapy, nutritional support, and prevention of complications. In the treatment group, artificial liver support therapy involved DPMAS combined with PE using 800–1000 mL of plasma. The system included a blood purifier (Braun Diapact CRRT), plasma separator (OP–08W), hemoperfusion cartridge (HA330-II), and plasma bilirubin adsorber (BS330). The blood flow rate was maintained at 120–150 mL/min with a plasma separation ratio of 20%–30%. Each session lasted 2.5–3.5 h and was administered 2–3 times per week.

Laboratory indicators monitored included liver function tests (TBil, direct bilirubin [DBil], alanine aminotransferase [ALT], aspartate aminotransferase [AST], albumin [ALB]), coagulation parameters (INR), complete blood count, and blood ammonia. Clinical symptoms such as fatigue, poor appetite, abdominal distension, and jaundice were evaluated, along with complications including infection, hepatic encephalopathy, and ascites. Model for End-Stage Liver Disease (MELD) scores were calculated, and all patients underwent a 6-month follow-up to assess survival outcomes.

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± SD (standard deviation) or median (interquartile range [IQR]), as appropriate, and categorical variables as number (percentage). Continuous variables were compared using the Student *t*-test or Mann–Whitney U test. Categorical variables were compared using the corrected chi-square test. Survival curves were generated using the Kaplan–Meier method, and the Cox proportional hazards model was used to identify risk factors associated with prognosis. Intergroup survival differences were evaluated using the log-rank test, with a significance threshold of $p < 0.05$.

3. Results

3.1. Baseline characteristics

There were no statistically significant differences between the two groups in terms of gender ($p = 0.949$), serum creatinine (CRE, $p = 0.834$), incidence of ascites ($p = 0.274$), or presence of liver cirrhosis ($p = 0.317$) (all $p > 0.25$). These findings indicate strong baseline comparability with respect to demographic characteristics, renal function, and liver-related complications. In contrast, significant differences were observed in ALT, TBil, and DBIL (all $p < 0.01$). Additionally, age ($p = 0.057$), INR ($p = 0.080$), infection ($p = 0.088$), and hepatic encephalopathy ($p = 0.090$) demonstrated trends toward marginal significance ($0.05 < p < 0.10$), likely reflecting the limited sample size and reduced statistical power. Therefore, these variables were incorporated as covariates in subsequent multivariate analyses to account for potential confounding effects (Table 1).

3.2. MELD score analysis

Baseline MELD scores did not differ significantly between the control and treatment groups: 22.45 ± 4.32 vs. 23.12 ± 4.15, $p = 0.405$, confirming the absence of major pretreatment imbalance. After treatment, MELD scores significantly decreased in both groups, although the reduction was more substantial in the treatment group (16.34 ± 4.78 vs.19.86 ± 5.24, $p < 0.001$). The mean change in MELD score further supported this finding, with a reduction of −6.78 ± 2.45 in the treatment group compared with −2.59 ± 1.98 in the control group ($p < 0.001$). The results demonstrate superior improvement in liver functional reserve and short-term mortality risk following DPMAS combined with PE. Intragroup comparisons revealed significant improvement in the control group ($p = 0.024$) and a highly significant improvement in the treatment group ($p < 0.001$), indicating that the combined regimen achieved a more pronounced and clinically meaningful effect (Table 2)

3.3. Survival analysis

During the 6-month follow-up period, survival rates showed a gradual decline in both groups; however, the treatment group consistently demonstrated significantly higher survival rates than the control group at all predefined assessment time points (30, 90, and 180 days). Kaplan–Meier survival curves indicated that the survival trajectory of the treatment group remained above that of the control group throughout follow-up, and the log-rank test confirmed a significant intergroup difference ($p = 0.038$) (Fig. 1).

Cox proportional hazards regression analysis was performed to identify factors influencing patient survival, with results expressed as hazard ratios (HRs), 95% confidence intervals (CIs), and *p*-values. Five categories of prognostic determinants were identified. Among

Table 1
Baseline demographic and clinical characteristics of patients.

Characteristics	Control Group ($n = 36$)	Treatment Group ($n = 57$)	p
Age, years	52.17 ± 11.75	56.84 ± 10.68	0.057
Male, *n* (%)	33 (91.7)	52 (91.2)	0.949
Laboratory biochemical variables			
Albumin, g/L	29.78 ± 3.92	31.12 ± 3.76	0.102
ALT, U/L	305.00 (93.25,607.75)	72.00 (41.00,146.00)	<0.001
AST, U/L	183.00 (88.25,471.50)	89.00 (60.00,150.00)	0.002
TBil, μmol/L	296.10 (226.18,370.65)	441.80 (368.21,540.02)	<0.001
DBil, μmol/L	223.85 (159.70,267.65)	320.50 (257.70,388.02)	<0.001
CRE, μmol/L	86.50 (78.50,98.50)	86.00 (75.00,107.00)	0.834
INR	1.57 (1.31,1.81)	1.41 (1.21,1.71)	0.080
Complications, *n* (%)			
Ascites	26 (72.2)	41 (71.9)	0.274
Infection	17 (47.2)	28 (49.1)	0.088
Hepatic encephalopathy	9 (25.0)	14 (24.5)	0.090
Liver cirrhosis	17 (47.2)	22 (38.5)	0.317

Age and albumin are expressed as mean ± standard deviation (SD). Male sex, ascites, infection, hepatic encephalopathy, and liver cirrhosis are presented as number (percentage). Other continuous variables are expressed as medians (interquartile range [IQR]). TBil, total bilirubin; DBil, direct bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; CRE, creatine.

Table 2
Changes in MELD scores before and after treatment.

Time Point	Control Group ($n = 36$)	Treatment Group ($n = 57$)	p
Baseline	22.45 ± 4.32	23.12 ± 4.15	0.405
After treatment	19.86 ± 5.24	16.34 ± 4.78	<0.001
Mean change	−2.59 ± 1.98	−6.78 ± 2.45	<0.001
p (within group)	0.024	<0.001	

Data are presented as mean ± standard deviation (SD). Intergroup comparisons were performed using the Student *t*-test, and intragroup comparisons were assessed using the paired *t*-test.
MELD: Model for End-Stage Liver Disease.

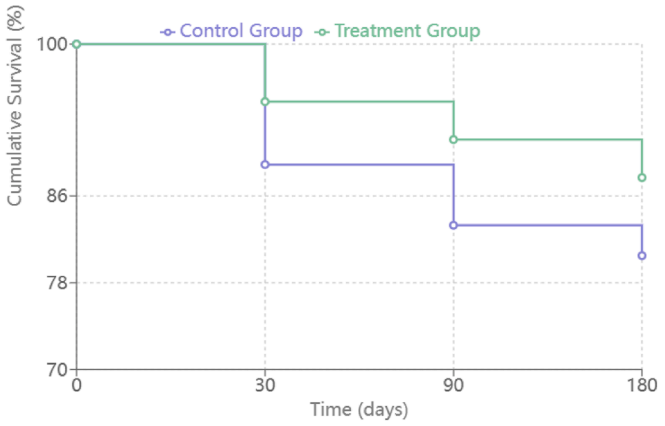

Fig. 1. Kaplan–Meier survival curves.

demographic factors, age ≥60 years significantly increased mortality risk, while male sex was not associated with survival differences. Regarding baseline liver status, the presence of liver cirrhosis was a significant risk factor. Among complications, infection, hepatic encephalopathy, and ascites each significantly increased the risk of death, with infection showing the strongest association. In terms of laboratory indicators, higher serum albumin levels were protective, whereas INR ≥1.5 significantly increased mortality risk. With respect to treatment modality, artificial liver support therapy was independently associated with reduced mortality risk. Taken together, infection and hepatic encephalopathy were the strongest negative prognostic factors, whereas artificial liver support therapy and elevated serum albumin were key protective variables improving survival outcomes (Table 3).

Table 3
Survival analysis and prognostic risk factors.

Variables	Hazard Ratio	95% CI	p
Demographic characteristics			
Age (≥60 years)	2.15	1.24–3.73	0.006
Male sex	1.83	0.92–3.64	0.084
Baseline liver disease			
Liver cirrhosis	2.41	1.38–4.23	0.002
Complications			
Ascites	1.94	1.12–3.36	0.018
Infection	3.15	1.86–5.33	<0.001
Hepatic encephalopathy	2.87	1.65–4.99	<0.001
Laboratory parameters			
ALB	0.49	0.26–0.84	0.016
INR ≥1.5	2.54	1.41–4.96	0.001
Treatment			
Artificial liver support	0.47	0.28–0.82	0.007

Analyses were performed using the Cox proportional hazards regression model.
CI: confidence interval; ALB: albumin; INR: international normalized ratio.

3.4. Hospital stay and treatment response

Analysis of hospital length of stay revealed no statistically significant difference between the treatment and control groups (median 38.0 days [IQR: 26–64] vs. 32.5 days [IQR: 19–46], $p = 0.089$). The distribution of hospital stay duration showed a broader range in the treatment group (7–139 days) compared with the control group (6–81 days). After excluding patients who died during hospitalization or were discharged against medical advice, no significant reduction in hospitalization duration was observed among those who received artificial liver support therapy (Table 4).

Table 4
Length of hospital stay.

Length of Stay	Control Group ($n = 36$)	Treatment Group ($n = 57$)	p
Days, median (IQR)	32.5 (19–46)	38.0 (26–64)	0.089
Range (min–max)	6–81	7–139	–

Data are presented as median (interquartile range [IQR]). p was calculated using the Mann–Whitney U test. Patients who died during hospitalization or were discharged against medical advice were excluded from the analysis.

3.5. Treatment safety and adverse events

Adverse events associated with DPMAS combined with PE treatment were infrequent and mild. Among 57 patients in the treatment group, no grade 3–4 adverse events (based on = CTCAE 5.0 criteria) occurred, and no treatment was discontinued as a result of safety concerns. Documented adverse events included transient hypotension in 3 patients (5.3%) and = mild allergic reactions, primarily urticaria, in 5 patients (=8.8%). All events were fully resolved with symptomatic management, such as fluid resuscitation for hypotension and antihistamines or glucocorticoids for allergic manifestations, without affecting continuation of therapy. The control group ($n = 36$) experienced no adverse events related to standard medical treatment.

4. Discussion

HEV infection constitutes a global public health concern, with the heaviest burden observed in developing regions. China continues to report a relatively high prevalence of HEV infection. A large community-based cohort study demonstrated anti-HEV IgG positivity rates ranging from 20% to 40%, and an annual incidence of new infections in the general population of approximately 1%.[11,12] Although improvements in sanitation have reduced genotype 1 and 2 outbreaks in developing countries including China, sporadic zoonotic infections caused by genotypes 3 and 4 are becoming increasingly common.[13] Multiple outbreak investigations and large-scale cohort studies have demonstrated that most HEV infections remain subclinical, and only a minority of cases result in clinically apparent illness.[11,14] Nevertheless, growing evidence suggests that HEV can lead to chronic infection and may precipitate ALF in vulnerable populations.[15,16]

There are currently no HEV-specific antiviral agents approved for routine clinical use. Accumulating case reports and cellular studies have indicated a potential therapeutic role of sofosbuvir. As an NS5B polymerase inhibitor developed for hepatitis C, sofosbuvir exhibits in vitro inhibitory activity against HEV replication.[17] Case observations have reported reductions in HEV RNA titers in ribavirin-refractory patients treated with sofosbuvir. However, viral relapse or failure to achieve complete viral clearance has also been documented.[18,19]

In the present study, artificial liver support therapy was associated with significantly improved clinical outcomes in patients with acute hepatitis E-induced liver failure. The treatment group exhibited greater improvement in liver function parameters and a higher 6-month survival rate compared with standard medical therapy alone. These findings are consistent with the mechanistic advantages of the DPMAS combined with PE regimen. DPMAS facilitates the efficient removal of bilirubin, inflammatory mediators, and endotoxins through dual-adsorption columns, thereby reducing hepatocellular injury. Concurrently, PE contributes to the replenishment of albumin, which is a proven survival-protective factor, as well as coagulation factors through fresh frozen plasma infusion, enhancing hepatic synthetic function. The combined approach compensates for the limitations of DPMAS alone, which does not supplement essential plasma components, and PE alone, which is less effective in toxin removal. Consequently, it more effectively interrupts the progression from toxin accumulation to hepatocyte impairment and liver function deterioration than conventional therapy. Although inflammatory marker modulation was not directly measured in this study, the clinical improvements observed support the likelihood of enhanced immune regulation contributing to the treatment benefits. Together, these complementary mechanisms provide a biological rationale for the superior therapeutic efficacy observed with DPMAS combined with PE.

The MELD score, originally designed to estimate mortality risk in patients with complications of portal hypertension, has since been validated as a robust prognostic indicator across diverse populations with end-stage liver disease.[20] Consistent with this established role, the present study used MELD scoring to verify baseline comparability between groups and to evaluate therapeutic efficacy. Although both groups demonstrated post-treatment decreases in MELD scores, the magnitude of improvement differed significantly: the treatment group achieved a lower post-treatment MELD score (16.34 ± 4.78) compared with the control group (19.86 ± 5.24), and the mean reduction in MELD score in the treatment group (6.78 ± 2.45) was approximately 2.6 times that observed in the control group (2.59 ± 1.98) ($p < 0.001$). These findings support the clinical utility of dynamic MELD score monitoring not only for mortality prediction but also for early assessment of treatment response and for guiding timely clinical intervention.

The predominance of male patients in this cohort (91.4%) aligns with prior epidemiological reports. International studies have reported male proportions of 64.0%–74.4% among HEV-related liver failure cases, whereas domestic studies in China have reported higher levels ranging from 83.3% to 97.6%.[21-23] This gender disparity may reflect sex-related differences in hormonal regulation, immune response, genetic susceptibility, or behavioral exposures, although the underlying mechanisms remain unclear.

In this study, several independent prognostic determinants of poor survival were identified, including age ≥60 years (HR = 2.15), liver cirrhosis (HR = 2.41), and key complications such as infection (HR = 3.15), hepatic encephalopathy (HR = 2.87), and ascites (HR = 1.94). INR ≥1.5 was also associated with a significantly increased hazard of death (HR = 2.54). Conversely, higher serum albumin levels (HR = 0.49) and receipt of DPMAS combined with PE (HR = 0.47) were protective factors. These results are largely consistent with previously reported risk profiles, although the relative magnitude of each factor varied slightly in this cohort.

The observed improvement in 6-month survival among patients receiving artificial liver support (87.7% vs. 80.5%, $p = 0.038$) highlights the potential utility of DPMAS combined with PE as a bridging strategy to liver transplantation or spontaneous hepatic recovery. Given the high mortality rate associated with ALF, particularly when rapid deterioration occurs, timely initiation of artificial liver support therapy appears crucial and may substantially influence clinical outcomes.[10,24]

With respect to safety, DPMAS combined with PE demonstrated a favorable and manageable adverse reaction profile. Transient hypotension occurred in 3 patients (5.3%), attributable to intravascular volume shifts, and was promptly corrected with fluid administration. Mild allergic reactions, predominantly urticaria, were observed in 5 patients (8.8%) and resolved with antihistamines or low-dose glucocorticoids. No severe adverse reactions occurred and no treatments were discontinued. As expected, no treatment-related adverse reactions were reported in the control group receiving standard medical therapy.

The primary limitation of this study is the relatively small sample size, which affects both the reliability of the findings and the generalizability of the conclusions. First, a limited sample reduces statistical power. Although multivariable regression analysis was applied to adjust for potential confounders, baseline imbalances remained in several variables, including liver function indicators (ALT, TBil, DBil), age, INR, and infection rate. These residual differences may have introduced bias into the evaluation of treatment effects. Second, the small sample size may have reduced the accuracy of the risk factor analysis. Despite the use of Cox proportional hazards regression to identify independent prognostic variables, the hazard ratios and 95% confidence intervals were relatively imprecise. This could result in the omission of additional clinically relevant predictors, such as underlying comorbidities or viral genotypes, or the misestimation of the strength of observed associations. Third, because this was a retrospective, single-center investigation, the limited cohort size further restricts the external validity and hinders extrapolation of the results to broader patient populations.

In addition to sample size constraints, several other limitations warrant consideration. This study did not analyze the effect of different HEV genotypes, such as genotypes 3 and 4, on treatment response. This may restrict the applicability of the results in regions with different genotype distributions. Furthermore, data collection was restricted to

the hospitalization period, which may have led to incomplete characterization of long-term clinical outcomes that are essential for assessing the sustained efficacy of treatment. As with most retrospective analyses, reliance on medical records may also have resulted in incomplete or underestimated reporting of clinical symptoms and complications, potentially affecting the accuracy of symptom-related analyses and the overall study reliability.

Future investigations should incorporate HEV genotyping and immune response evaluation to better elucidate the pathophysiology of hepatitis E-induced liver failure and its responsiveness to artificial liver support therapy. Prospective multicenter studies with larger cohorts are needed, since they would address the current limitations while enabling more standardized data collection, consistent and longer follow-up, and improved assessment of long-term outcomes and late complications. Such multicenter efforts would also provide important external validation of the present findings and facilitate identification of additional prognostic indicators.

5. Conclusion

DPMAS combined with PE represents an effective and safe therapeutic strategy for acute hepatitis E-induced liver failure. This combined approach significantly improves liver function and coagulation parameters, decreases MELD scores, and enhances survival outcomes. Moreover, the prognostic factors identified in this study offer clinically relevant guidance for risk stratification and treatment optimization. While validation through larger prospective multicenter studies remains necessary, the present findings provide strong evidence supporting DPMAS combined with plasma exchange as a beneficial artificial liver support modality for patients with acute hepatitis E-induced liver failure.

CRediT authorship contribution statement

Rujia Tang: Writing – original draft, Data curation. **Yingjie Ji:** Writing – review & editing, Resources. **Hongyu Yao:** Resources, Formal analysis. **Xia Zhou:** Supervision, Methodology, Investigation. **Danni Feng:** Supervision, Methodology. **Eddie C. Cheung:** Writing – review & editing. **Hongling Liu:** Writing – review & editing. **Kaili Wang:** Writing – review & editing, Methodology, Conceptualization.

Informed consent

Written informed consent was obtained from all participants.

Ethics statement

This work is approved by the Ethics Committee of the Fifth Medical Center, PLA General Hospital (Approval No. KY-2025-2-73-1).

Data availability statement

Most of the data presented in this paper is included in the main manuscript, and additional data are available from the corresponding author upon reasonable request.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) do not Generative AI and AI-assisted technologies in the writing process.

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Declaration of competing interest

The authors declare no conflict of interest.

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