BMC Anesthesiology

RESEARCH

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Fospropofol disodium versus Propofol for deep sedation in critically ill patients: a randomized pilot study

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Abstract

Background Fospropofol disodium is comparable to propofol in maintaining mild-to-moderate sedation for mechanically ventilated patients in intensive care unit (ICU). However, its efficacy for deep sedation remains unclear. Therefore, we conducted a randomized-controlled trial comparing the efficacy and safety of fospropofol disodium with propofol for deep sedation of mechanically ventilated patients in ICU.

Methods In this randomized pilot study, critically ill adult patients requiring deep sedation were randomized to receive fospropofol disodium or propofol. The study drug was titrated to maintain a Richmond Agitation-Sedation Scale score (RASS) of−5 or−4. Narcotrend Index (NI) value was monitored during the whole study period. The primary outcome was the percentage of time in the target sedation range without rescue sedation. The secondary outcomes were successful extubation, ventilator-free days at day 7, ventilator-free days at day 28, 28-day all-cause mortality and adverse events.

Results Thirty patients were included in each group. The fospropofol disodium infusion lasted for 47.50 (IQR 31.75 to 48.00) hours at a dose of 8.19 ± 2.36 mg/kg/h, while propofol infusion for 48.00 (IQR 30.88 to 48.00) hours at 2.73 ± 0.83 mg/kg/h. The proportion of time within the target RASS range without rescue sedation was 96.78%±0.07% in the fospropofol group and 98.43%±0.04% in the propofol group ($p = 0.273$). A total of 39 patients experienced adverse events, with 19 in the fospropofol group and 20 in the propofol group. The most common adverse event was hypotension, with 18 patients (60.0%) in each group. No significant differences were observed in successful extubation, ventilator-free days at day 7, ventilator-free days at day 28, or 28-day all-cause mortality.

Conclusions In this open-label trial, fospropofol disodium achieved deep sedation at a rate comparable to propofol. For mechanically ventilated ICU patients, fospropofol disodium may offer a safe and effective sedation option. Larger multicenter trials are needed to confirm these findings.

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Trial registration The trial was registered on ClinicalTrials.gov on May 12, 2023, with the identifer NCT05870514.
Keywords Deep sedation, Fospropofol disodium, Propofol, Richmond agitation-sedation scale, Narcotrend index

Introduction

Sedation plays a vital role in the management of most patients undergoing mechanical ventilation in the intensive care unit (ICU) [1, 2]. And the therapeutic concept of sedation in ICU is gradually changing. While clinical practice guidelines advocated for a minimal sedation approach for adult patients on mechanical ventilation [3, 4], patients with severe acute respiratory distress syndrome (ARDS) of unstable hemodynamics are usually exceptions [2, 5]. A multinational study of general ICU patients receiving mechanical ventilation for less than 12 h before enrollment, approximately 50–60% of patients were deeply sedated for the first 48 h [6].

Propofol is one of the most commonly used intravenous sedative in the ICU. However, its clinical formulations are associated with side-effects, including injection-site pain, risk of bacterial contamination, and pancreatitis linked to high lipid intake [7]. Fospropofol disodium, a water-soluble prodrug of propofol, was developed to circumvent the disadvantages of propofol [8]. After intravenous injection, it is metabolized by alkaline phosphatase into active propofol [9, 10]. Compared to propofol, fospropofol disodium exhibits a slower onset of action (3–13 min), which may contribute to a more stable hemodynamic profile due to the gradual release of propofol [9, 11–13]. For critically ill patients with hemodynamic instability requiring prolonged sedation without an urgent need for rapid onset, fospropofol disodium may be preferable to propofol.

Our prior research demonstrated that fospropofol disodium is comparable to propofol for maintaining mild-to-moderate sedation in mechanically ventilated ICU patients [14]. However, to our knowledge, no studies have yet explored its application for deep sedation in this population. The objective of this study was to conduct a preliminary comparison of the efficacy and safety of fospropofol disodium versus propofol for deep sedation in mechanically ventilated ICU patients.

Methods

Study design

This was a single-center, single-blinded, propofol-controlled, randomised trial. The trial was approved by the the Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, reference number 2023–0337 on 9 May 2023. Legal representatives of all the patients provided informed consent prior to participation. The trial was registered on clinicaltrials.gov (No. NCT05870514) May 12, 2023, prior to enrollment. The study adhered to CONSORT guidelines.

Drug formulations

Fospropofol disodium for injection (Yichang Humanwell Pharmaceutical Co., Ltd., Hubei, P. R.China) is a sterile, white, lyophilized powder for intravenous administration after being reconstitution with normal saline to a clear and colourless solution. Propofol (Fresenius Kabi China Co., Ltd.) is a pre-filled white uniform milky liquid for direct use.

Participants

Patients were recruited from May 2023 to January 2024 at the general ICU of Union Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China. Patients aged between 18 and 80 years who were intubated within 96 h and expected to still require invasive ventilation and deep sedation for more than 8 h were considered eligible. And deep sedation is defined as maintaining a target sedation score of–5 and–4 on the Richmond Agitation-Sedation Scale (RASS).

The exclusion criteria included previous inclusion into this study or another interventional study within the previous three months, a body mass index (BMI) < 18 or > 30 kg/m^2, pregnancy or lactatation, contraindication or allergy to study drugs, the state of tracheotomy, general anesthesia expected within 8 h, myasthenia gravis, acute severe neurological disorder and any other condition interfering with RASS assessment, moribund state, extracorporeal membrane oxygenation support, chronic kidney disease with glomerular filtration rate (GFR) < 60 ml/min/1.73m^2, acute hepatitis or severe hepatic dysfunction, unstable angina or acute myocardial infarction, left ventricular ejection fraction less than 30%, heart rate less than 50 beats/min or second or third degree heart block without a pacemaker and alcohol or drug abuse.

Randomization

Randomisation was performed using a computer-generated random number sequence with concealed allocation. Eligible patients were randomly assigned to either group with a 1:1 ratio. The allocation was unblinded to investigators in view of the obvious difference in appearance between fospropofol disodium and propofol.

Intervention

The degree of sedation was measured using RASS, while concurrently, the Narcotrend Index (NI) value was continuously monitored using Narcotrend-Compact.

(MT MonitorTechnik, Germany)(Supplemental Table 1).

The titration of fospropofol disodium or propofol, as shown in Supplemental Fig. 1, was adjusted at the discretion of the treating investigators/clinicians based on the patient's condition and targeted sedation depth. All analgesics and sedatives were discontinued prior to study, and remifentanil was administered initially at a dosage of 6.0 μg/kg/h and then titrated (maximum of 9.0 μg/kg/h) as needed to maintain a Critical care Pain Observation Tool score between 0 and 2. Patients allocated to the fospropofol disodium group were given fospropofol disodium at an initial rate of 10.0 mg/kg/h, and then adjusted (maximum of 20 mg/kg/h) to maintain a RASS score of–4 or–5 and an NI between 13 and 64. Patients allocated to the propofol group were given propofol at an initial rate of 3.0 mg/kg/h, and then adjusted (maximum of 12.0 mg/kg/h) to maintain a RASS score of–4 or–5 and an NI between 13 and 64. If the two indices were contradictory, priority was given to the RASS score. If the maximum doses of the study drugs were still insufficient to maintain deep sedation, midazolam was given to rescue sedation. Two investigators continuously monitored the sedation level, including RASS score and NI values, and then adjusted the study drugs as needed. The RASS score and NI value were recorded every 2 h until one the following occurred first: 48 h after inclusion, discharge from the ICU, death, no need for deep sedation, need for surgery under general anesthesia or requested discontinuaton by attending physicians or investigators. If a patient still needed sedation, sedatives were administered at the discretion of attending physicians. Patients were followed up for 28 days after inclusion.

Other treatments and monitoring followed routine practice of our ICU. All investigators receive unified training, including RASS evaluation, titration of study drugs, and the use of Narcotrend-Compact M.

Primary outcome and secondary outcome

The primary outcome was the percentage of time in the target sedation range without rescue sedation (defined as the percentage of the RASS evaluations in the target sedation range). The Secondary outcomes included ventilator-free hours within 7 days, ventilator-free hours within 28 days, successful extubation, length of ICU stay within 28 days, 28-day all-cause mortality and adverse events.

Safety evaluation

Safety was assessed based on the treatment of adverse events, physical exams, clinical lab tests, vital sign monitoring, and ECG assessments. Adverse events mainly focused on compromised hemodynamics, including hypotension, and bradycardia. Moreover, we also assessed the incidence of propofol infusion syndrome, and hypertriglyceridemia.

Hypotension was defined as a decrease of mean arterial pressure (MAP) greater than 20% from baseline, or a MAP below 60 mmHg; bradycardia was defined as a decrease of heart rate (HR) greater than 20% from baseline or less than 50 beats per minute; propofol infusion syndrome was defined as one or more of otherwise unexplained metabolic acidosis, rhabdomyolysis, or ECG changes, with or without acute kidney injury, hyperkalaemia, lipidaemia, cardiac failure, fever, elevated liver enzymes or raised lactate when critically ill patients receive propofol infusions, typically either high dose (>5 mg/kg/h) or of long duration (>48 h) [15]. And blood samples were taken before and after medication for all patients to test serum triglyceride concentration. Hypertriglyceridemia included mild, moderate and severe hypertriglyceridemia with the diagnostic criteria of serum triglyceride concentration between 1.7 and 2.3 mmol/L, between 2.3 and 11.2 mmol/L and above 11.2 mmol/L, respectively [16].

Statistical analysis

The sample size of this pilot study was not planned for an efficacy analysis but rather to obtain an estimate of the effect size and variance for a further definitive study. 30 patients for each of the two groups were planned. For continuous variables, data were summarized as mean with standard deviation (SD) or median with interquartile range (IQR) and analyzed using the Student's t test or the Mann-Whitney U test. For categorical variables, data were summarized as count (percentage) and analyzed using the chi-square test or the Fisher exact test. Mortality over time was assessed using Kaplan-Meier analysis and the log-rank test. Statistical analyses were performed using SPSS 25.0 software (IBM SPSS Statistics, Armonk, NY) and GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA). A two-side p value < 0.05 was considered statistically significant.

Results

Enrollment and baseline characteristics

A total of 744 patients were screened and 60 patients were enrolled with 30 patients randomized to each group (Fig. 1). Patient demographics and baseline characteristics of the patients were similar between the 2 groups (Table 1 and Supplemental Table 2).

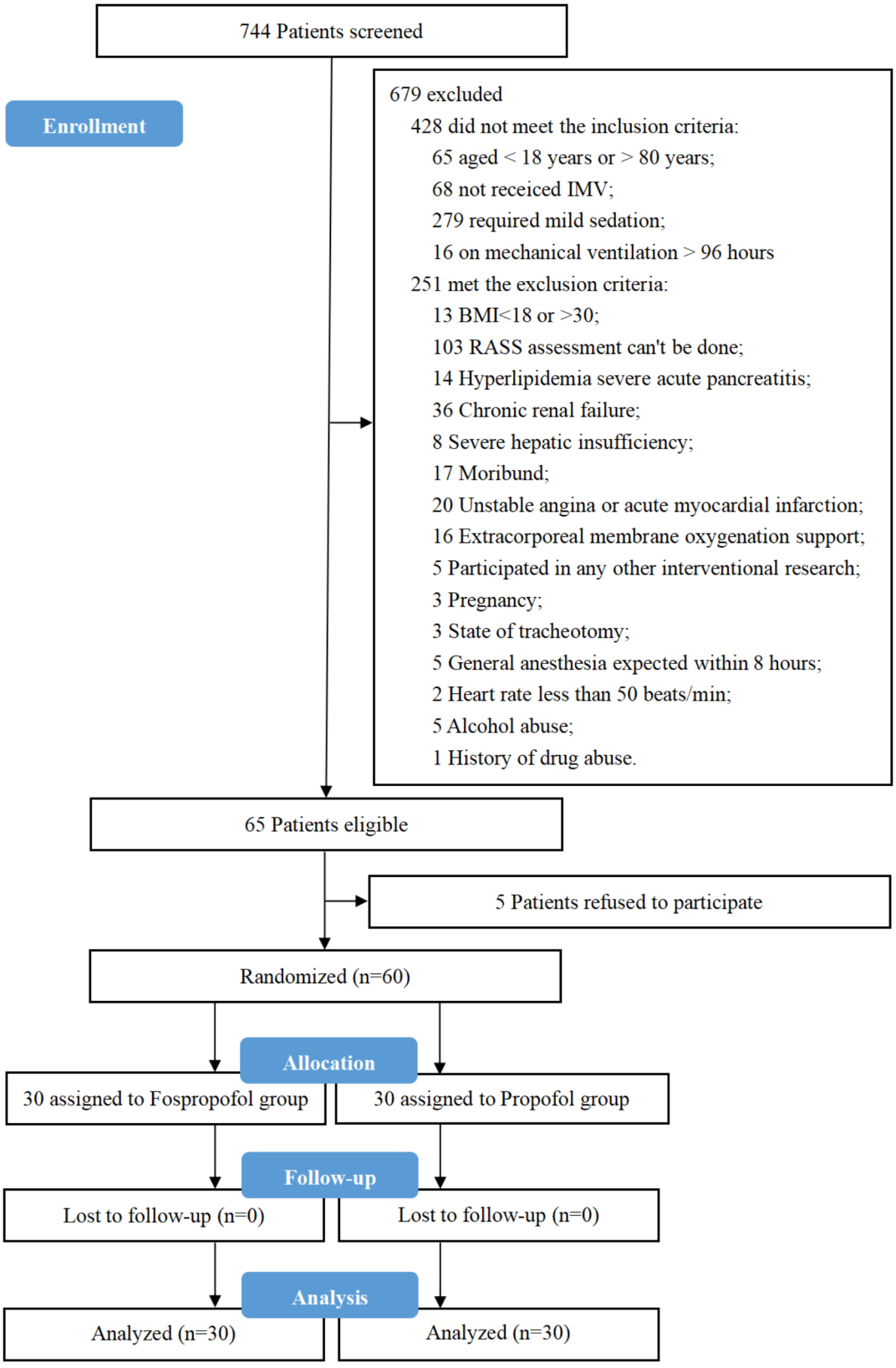


Fig. 1 Consort flow diagram

Table 1 Baseline demographics and clinical characteristics of study population

	Total (*n* = 60)	Fospropofol (*n* = 30)	Propofol (*n* = 30)	*P* value
Age, years	65.50 (54.25 to 70.25)	60.00 (52.75 to 67.75)	69.00 (61.00 to 74.75)	0.081
Male	42 (70.0)	18 (60.0)	24 (80.0)	0.159
Height, cm	165.05 ± 7.91	163.86 ± 8.27	166.20 ± 7.49	0.260
Weight, kg	60.00 (55.00 to 70.00)	57.50 (54.00 to 68.75)	60.00 (58.50 to 69.50)	0.145
BMI, kg/m^2	22.57 ± 3.10	22.30 ± 3.42	22.83 ± 2.80	0.510
APACHE II score	17.02 ± 4.46	16.87 ± 4.32	17.17 ± 4.67	0.797
SOFA score	7.90 ± 2.87	8.20 ± 2.98	7.60 ± 2.97	0.423
RASS score at enrollment	-4.60 ± 0.56	-4.67 ± 0.55	-4.53 ± 0.57	0.360
Narcotrend index values at enrollment	31.73 ± 11.71	33.07 ± 13.72	30.40 ± 9.32	0.382
Type of admission				
Medical	50 (83.3)	24 (80.0)	26 (86.7)	0.729
Surgical	10 (16.7)	6 (20.0)	4 (13.3)	0.729
Medical history				
Hypertension	14 (23.3)	6 (20.0)	8 (26.7)	0.760
Diabetes mellitus	8 (13.3)	5 (16.7)	3 (10.0)	0.704
Coronary artery disease	6 (10.0)	3 (10.0)	3 (10.0)	> 0.999
Chronic liver disease	2 (3.3)	1 (3.3)	1 (3.3)	> 0.999
COPD	2 (3.3)	1 (3.3)	1 (3.3)	> 0.999
Cancer	26 (43.3)	10 (33.3)	16 (53.3)	0.193
Other	9 (15.0)	4 (13.3)	5 (16.7)	> 0.999
Sedative before randomization				
Propofol	26 (43.3)	9 (30.0)	17 (56.7)	0.068
Remimazolam besylate	25 (41.7)	12 (40.0)	13 (43.3)	> 0.999
Dexmedetomidine	5 (8.3)	3 (10.0)	2 (6.7)	> 0.999
Midazolam	11 (18.3)	8 (26.7)	3 (10.0)	0.182
Fospropofol	3 (5.0)	3 (10.0)	0 (0.0)	0.236
Reasons for deep sedation				
ARDS	48 (80.0)	25 (83.3)	23 (76.7)	0.747
Severe pneumonia	6 (10.0)	2 (6.7)	4 (13.3)	0.671
Sepsis shock	9 (15.0)	5 (16.7)	4 (13.3)	> 0.999
Multiple rib fractures	1 (1.7)	0 (0.0)	1 (3.3)	> 0.999
Sepsis at enrollment	47 (78.3)	23 (76.7)	24 (80.0)	> 0.999
Hypertriglyceridemia at enrollment	10 (16.7)	5 (16.7)	5 (16.7)	> 0.999
Prone position	25 (41.7)	11 (36.7)	14 (46.7)	0.600
Duration of MV before randomization, h	19.50 (9.75 to 26.25)	19.50 (9.25 to 43.50)	19.50 (10.00 to 23.50)	0.459

Data are number (%), mean ± standard deviation or median (interquartile range)

Abbreviations: BMI, body mass index; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; COPD, chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; RASS, Richmond Agitation and Sedation Scale

Table 2 Details of study drug administered

	Fospropofol (*n* = 30)	Propofol (*n* = 30)	*P* value
Study drug			
Duration of study drug infusion, h	47.50 (31.75 to 48.00)	48.00 (30.88 to 48.00)	0.771
Dose of study drug, mg/kg/h	8.19 ± 2.36	2.73 ± 0.83	-
The reason for the discontinuation of drug			
48 h after inclusion	17 (56.7)	18 (60.0)	> 0.999
Being discharged from ICU	0 (0.0)	1 (3.3)	> 0.999
The need for an operation under general anesthesia	4 (13.3)	2 (6.7)	0.667
No need for deep sedation	9 (30.0)	9 (30.0)	> 0.999
Dose of remifentanil, μg/kg/h	5.94 ± 0.29	6.01 ± 0.20	0.321
Midazolam for rescue sedation	1 (3.3)	0 (0.0)	> 0.999
Duration of norepinephrine infusion, h	29.25 (12.75 to 46.75)	41.50 (7.50 to 48.00)	0.619
Maximal dose of norepinephrine from nursing charts, μg/kg/h	0.28 (0.06 to 0.96)	0.33 (0.08 to 0.88)	0.458

Data are number (%), mean ± standard deviation or median (interquartile range)

ICU, intensive care unit

Study drug administration

The reasons for discontinuation of the study drug were not different between the two groups of patients. In the fospropofol disodium group, one patient used midazolam for rescue sedation for 12 h, while no patient in the propofol group required rescue sedation. The median duration of the fospropofol disodium infusion was 47.50 (IQR 31.75 to 48.00) hours and of propofol infusion 48.00 (IQR 30.88 to 48.00) hours ($p = 0.771$). The dose of fospropofol disodium was 8.19 ± 2.36 mg/kg/h and of propofol 2.73 ± 0.83 mg/kg/h (Table 2).

Efficacy

The percentages of time in the target RASS without rescue sedation were similar in both groups, 96.78%±0.07% in the fospropofol group and 98.43%±0.04% in the propofol group, $p = 0.273$ (Table 3). The infusion of fospropofol disodium and propofol yielded a total of 614 and 601 RASS evaluations, respectively. 595 (96.91%) of the observations in the fospropofol group fell into the target RASS range and 590 (98.17%) in the propofol group (Fig. 2). During the intervention period, the RASS score was–4.68 ± 0.40 with an NI value was 30.32 ± 8.84 in the fospropofol group and the RASS score was–4.72 ± 0.34 with an NI value of 29.21 ± 7.67 in the propofol group. And the sequential mean RASS scores and NI values in the two groups are shown in Supplemental Figs. 2 and 3. The majority of NI values fell into stages D and E, and most of the time there was a good alignment between NI values and RASS scores. The distribution of RASS scores and NI value was shown in Fig. 3.

Table 3 Outcomes

	Fospropofol (*n* = 30)	Propofol (*n* = 30)	*P* value
Primary Outcome			
Percentage of time with a RASS score of -4 or -5 without rescue sedation, %	96.78 ± 0.07	98.43 ± 0.04	0.273
Secondary Outcomes			
Successful extubation	10 (33.3)	11 (36.7)	> 0.999
Ventilator-free hours within 7 days, h	0.00 (0.00 to 36.75)	0.00 (0.00 to 30.25)	0.936
Ventilator-free hours within 28 days, h	58.50 (0.00 to 486.00)	76.50 (0.00 to 480.00)	0.963
Length of ICU stay within 28 days, days	5.50 (4.00 to 11.50)	10.00 (5.75 to 17.75)	0.091
28-day all-cause mortality	13 (43.3)	12 (40.0)	> 0.999
Safety Outcomes			
Hypotension	18 (60.0)	18 (60.0)	> 0.999
Bradycardia	2 (6.7)	0 (0.0)	0.472
Propofol infusion syndrome	0 (0.0)	0 (0.0)	-
Triglyceride at discontinuation of study drug, mmol/l	1.56 (1.01 to 1.88)	1.91 (1.47 to 2.60)	0.056
Increase of triglyceride¶, mmol/l	0.18 (-0.12 to- 0.44)	0.69 (0.07 to 0.96)	0.027
Hypertriglyceridemia at discontinuation of study drug§	6 (20.0)	13 (43.3)	0.052
Mild hypertriglyceridemia	2 (6.7)	5 (16.7)	0.424
Moderate hypertriglyceridemia	4 (13.3)	8 (26.7)	0.197
Severe hypertriglyceridemia	0 (0.0)	0 (0.0)	-

Data are number (%), mean ± standard deviation or median (interquartile range)

ICU, intensive care unit; RASS, Richmond Agitation and Sedation Scale

¶,Increase of triglyceride was defined as the difference between the triglyceride at discontinuation of study drug and the baseline triglyceride

§, The diagnostic criteria of serum triglyceride concentration for mild, moderate and severe hypertriglyceridemia are between 1.7 to 2.3 mmol/L, between 2.3 to 11.2 mmol/L and above 11.2 mmol/L, respectively

In terms of ventilator-free hours within 7 days, ventilator-free hours within 28 days, successful extubation, length of ICU stay within 28 days and 28-day all-cause mortality, there were no significant differences between the groups (Table 3; Fig. 4).

Safety

At least one adverse event was identified in 39 (65.0%) cases, including 19 (63.3%) in the fospropofol disodium group and 20 (66.7%) in the propofol group. Since some patients experienced multiple adverse events, the total number of adverse event episodes may exceed the number of affected individuals. The most common adverse event was hypotension, with 18 cases (60.0%) in both groups (Table 3). There were no differences in the duration and dosage of vasopressors between the two groups (Table 2). Tadycardia occurred in two patients in the fospropofol disodium group and none in the propofol group. The sequential mean heart rate and mean arterial pressure were presented in Supplemental Figs. 4 and 5.

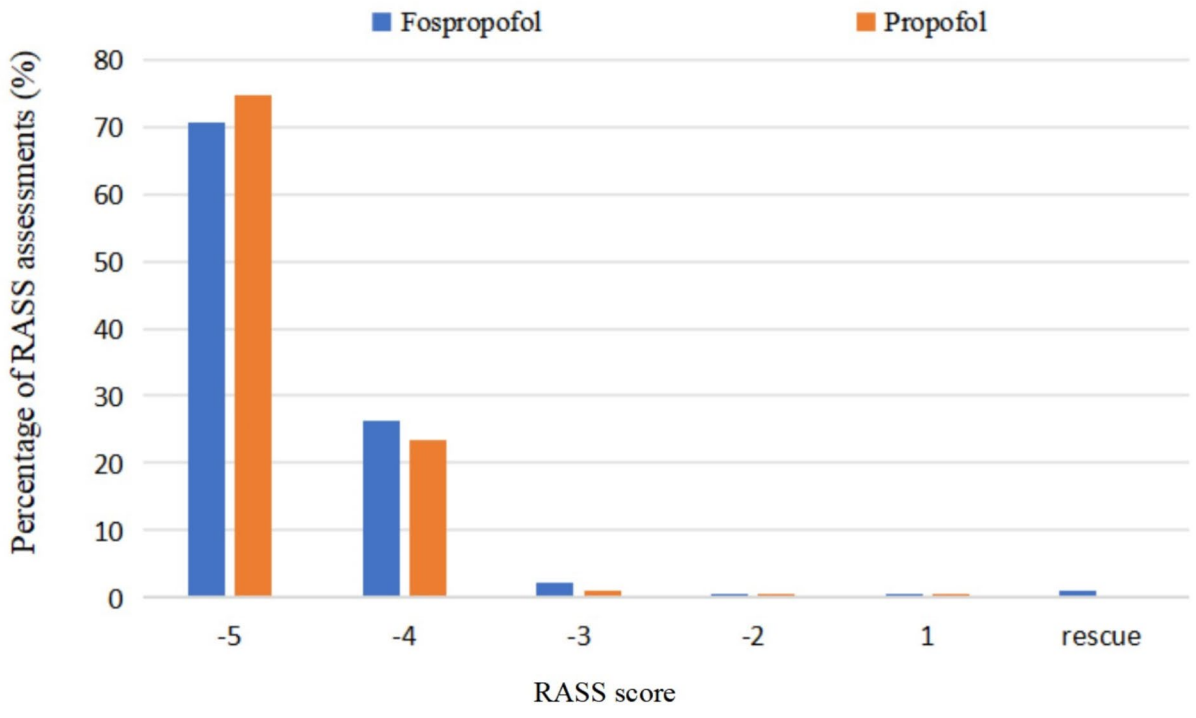
The triglyceride concentration at discontinuation was significantly higher in the propofol group than in the fospropofol disodium group, however, there was no statistically significant difference in the incidence of hypertriglyceridemia between the two groups (Table 3). No patients experienced propofol infusion syndrome, and there were no patients who withdrew from the study due to the occurrence of serious adverse events.

Discussion

In this study, we found that both fospropofol disodium and propofol could provide adequate sedation for mechanically ventilated patients requiring deep sedation in the ICU. And the percentage of patients in both groups who did not require rescue sedation with midazolam for deep sedation was comparable.

Fospropofol disodium undergoes rapid and complete conversion by alkaline phosphatase on endothelial cell surfaces, yielding propofol, formaldehyde, and phosphate in equimolar proportions [17]. Fospropofol disodium for injection has a molecular weight of 350.26, compared to propofol's 178.3. Assuming 100% conversion of fospropofol disodium to propofol, one would anticipate that 1.96 times the amount of fospropofol disodium would be required to produce equivalent sedation. However, our recent study found that incomplete conversion of fospropofol disodium to propofol may be possible [14]. For mechanically ventilated patients in the ICU requiring mild to moderate sedation, the dosage of fospropofol disodium was needed to be increased to 2.2 times that of propofol to achieve an equivalent sedative effect. Fechner J et al. reported that the infusion dose of fospropofol disodium was 2.58 times that of propofol for total intravenous anesthesia in coronary artery bypass graft surgery [10]. In this study, the infusion dose of fospropofol disodium (8.19 mg/kg/h) was 3 times that of propofol infusion dose (2.73 mg/kg/h) to achieve deep sedation, further indicating the potential incomplete conversion from fospropofol disodium to propofol, and this phenomenon may become more pronounced with increasing drug doses. The infusion dose of propofol in this study is comparable to the propofol dose reported in another study of deep sedation in the ICU [18].

Sedation levels in ICU patients are typically assessed using subjective scoring systems, such as the RASS. The subjective scoring systems assesses the depth of sedation based on the patient's response to sound and physical stimuli [3]. However, for ICU patients in deep sedation, it is challenging to further differentiate whether oversedation has occurred [19]. The Narcotrend monitor provides continuous, quantified, and objective monitoring of sedation status in critically ill patients [20]. Therefore, in this study, we employed both RASS score and NI value to assess the depth of sedation in patients. Similar to the



No. of RASS						
Fospropofol	433	162	14	3	2	6
Propofol	449	141	6	4	1	0

Fig. 2 Percentage of RASS assessments. RASS, Richmond Agitation Sedation Scale

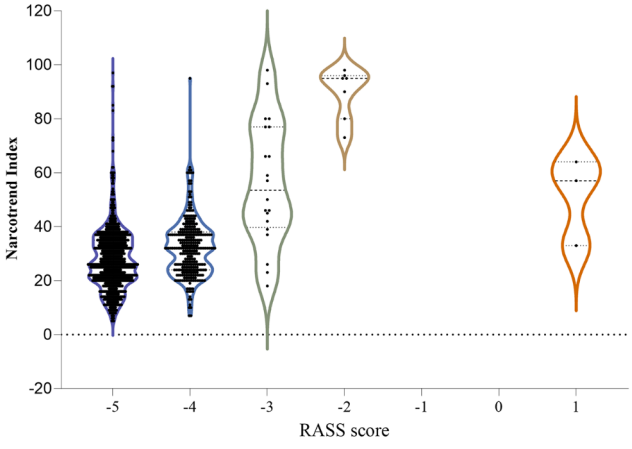
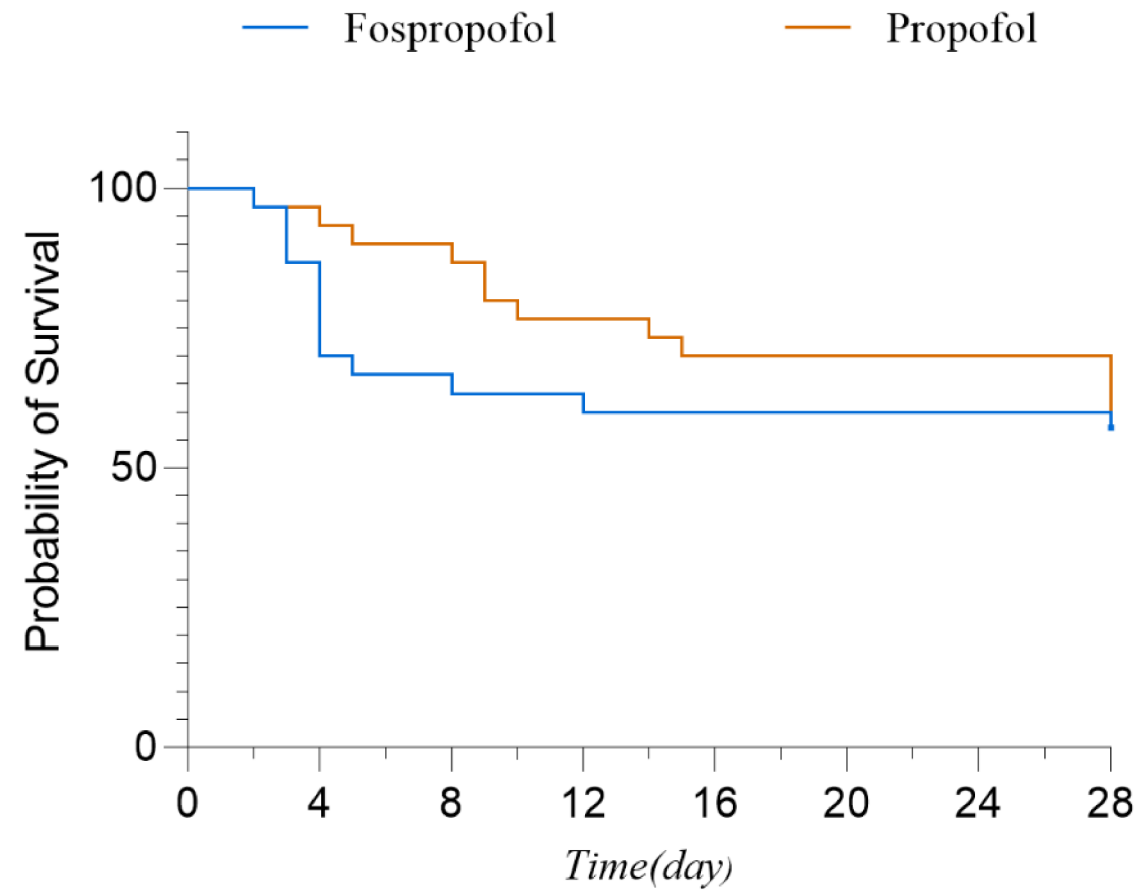


Fig. 3 Narcotrend Index values for each RASS scores. RASS, Richmond Agitation Sedation Scale

Bispectral Index (BIS), NI is influenced by various factors, with electromyographic interference affecting the accuracy of NI values [21]. With the exception of a few numerical deviations that may be influenced by external factors, our results demonstrate a good overall consistency between RASS scores and NI values in most cases.

Fospropofol disodium, as a propofol prodrug, primarily demonstrates advantages in its water solubility and low lipid properties [22], which are particularly crucial for patients with dyslipidemia or in regions without suitable storage conditions for ester-based drugs. This study focused on the changes in blood lipids before and after medication for all patients. We observed that the increase in triglycerides after medication in the propofol group was significantly higher than that in the sodium phosphinate group, which is consistent with previous reports [23, 24]. However, there was no statistically significant difference between the two groups in the incidence of hyperlipidemia ($p = 0.052$). This issue warrants attention, and we will continue to monitor this issue in future large-scale studies.

Respiratory and circulatory depression are common concerns with sedation, especially in mechanically ventilated ICU patients requiring deep sedation [25, 26]. Given that all patients were under deep sedation and mechanical ventilation, the issue of respiratory depression could not be observed. Hypotension was the most common adverse event, but the blood pressure of all patients can be maintained at a relatively stable level after vasopressors, with no significant difference of the duration and



No. of patients at risk

Fospropofol	30	26	20	18	18	18	18	17
Propofol	30	28	26	23	21	21	21	18

Fig. 4 Kaplan-Meier Estimates of Survival (log-rank test $p = 0.542$)

dosage of vasopressors between groups. Two patients in the fospropofol disodium group experienced bradycardia, compared to none in the propofol group. Overall, patients remained hemodynamically stable, with no significant changes in heart rate or mean arterial pressure during the medication period.

A further concern with ICU sedation is the development of delirium, as it can greatly elevate the risk of mortality in ICU patients and extend their length of stay [27]. We conducted the evaluation when each patient reached his or her endpoint of intervention according to the Intensive Care Delirium Screening Checklist. Unfortunately, at this point, most patients remained sedated, making delirium assessment impractical. As a result, we did not proceed with evaluating delirium, which clearly calls for further studies in the near future.

This study has other several limitations that should be acknowledged. First, the small sample size may limit the statistical power and generalizability of our findings, making it insufficient for detecting rare adverse events. Second, as a single-center study, our results may not be broadly applicable to other clinical settings, where variations in patient populations, sedation protocols, and healthcare practices could influence outcomes. Third, the lack of blinding for investigators introduces the possibility of assessment bias, particularly in subjective measures such as RASS scoring. Additionally, the duration of drug infusion in the study was relatively short. The cut-off at 48 h was based on a multinational study, which found that approximately 50–60% of patients with deeply sedated turned to mild sedation after 48 h [6]. Further research is needed to assess the efficacy and safety of fospropofol disodium for prolonged deep sedation. A larger cohort would be necessary to confirm the observed trends and detect potential differences in sedation efficacy and safety outcomes.

Conclusions

In this open-label trial, fospropofol disodium achieved deep sedation at a rate comparable to propofol. For mechanically ventilated ICU patients, it may offer a safe and effective sedation option. However, larger-scale, multicenter trials with improved blinding, alternative sedation endpoints, and extended infusion durations are needed to validate these findings. Future studies should also examine the long-term safety profile and the potential influence of adjunctive medications. These considerations will be essential for optimizing sedation protocols in critically ill patients.

Abbreviations

RASS	Richmond Agitation-Sedation Scale score
NI	Narcotrend Index
ICU	Intensive care unit
ARDS	Acute respiratory distress syndrome
BMI	Body mass index
GFR	Glomerular filtration rate
MAP	Mean arterial pressure
HR	Heart rate
BIS	Bispectral Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-03025-x.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

We gratefully acknowledge all the physicians and nurses for their dedication to patient care and their support of this study.

Author contributions

Xiaobo Yang and You Shang supervised the study and revised the manuscript. Xuehui Gao, Xiaobo Yang and You Shang conceived and designed the study. Xuehui Gao and Hongling Zhang interpreted the data. Xuehui Gao and Chenggang Gao drafted the manuscript. Xuehui Gao, Chenggang Gao, Xiangzhi Fang and Lehao Ren recruited patients and performed the study. Xuehui Gao, Xiangzhi Fang, Lehao Ren, Yun Tang, Yin Yuan, Hong Qi, Huaqing Shu and Xiaojing Zou acquired the data. All authors made substantial contributions to study conception and design, data acquisition, data analysis and interpretation and drafting, revising or critically reviewing the article.

Funding

No funding.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All patients or their legally authorized representatives provided written informed consent. The study was approved by the Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, reference number 2023–0337. The trial was registered on clinicaltrials.gov (No. NCT05870514) May 12, 2023, prior to enrollment. All procedures involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, as well as the 1964 Helsinki Declaration and subsequent amendments or comparable ethical standards.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 29 November 2024 / Accepted: 25 March 2025
Published online: 10 April 2025

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