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The Efficacy of Channa Striata Extract Administration in Improving Albumin and Creatinine Levels in Sepsis Patients in the Intensive Care Unit

Mathilda Panggabean[1], Andriamuri Primaputra Lubis[1], Rr. Sinta Irina[1], Rina Amelia[2]

[1]Study program of Anesthesiology and Intensive Care,Faculty of Medicine, Universitas Sumatera Utara, Indonesia
[2]Department of Community Medicine, Faculty of Medicine, Universitas Sumatera Utara, Indonesia

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Corresponding Author:
Andriamuri Primaputra Lubis
andriamuri@usu.ac.id

ABSTRACT

Albumin levels in the blood are an indicator for assessing the severity of sepsis. In sepsis patients, administering albumin extract from Channa striata has better potential to replace Human Albumin by 20%. This study aims to determine the role of Channa striata extract (CSE) in improving albumin and creatinine in sepsis patients. This research is a quasi-experimental research with a pre-post-test design. Sepsis patients who meet the inclusion and exclusion criteria and sign the informed consent form will be divided into treatment and control groups. Both groups received the same therapy protocol, except for the treatment group, which willbe given CSE at a dose of 5gr, three times a day, for five days. Albumin, creatinine, and SOFA score measurements will betaken before the treatment and on the 7th day. All data will betabulated and analyzed using statistical software. This study consisted of 2 groups, with a sample size of 20 patients for each group. It was found that the mean age of the research sample was 56.1 + 11.8 years. In the treatment group, there wasno decrease in albumin levels before and after (2.76 + 0.41 to 2.76 + 0.40), p=0.952. There was no significant difference in assessing creatinine levels before and after treatment, p>0.05. There was an increase in SOFA score before and after treatment in both groups, p<0.05. Channa striata extract is clinically significant for improving the condition ofsepsis patients in the ICU.

1. Introduction

Early recognition and appropriate treatment in the first hours after sepsis diagnosis improves patient outcomes. The Surviving Sepsis Campaign (SSC) 2021 recommends injecting albumin in older patients with sepsis or septic shock receiving large amounts of crystalloids. Sepsis is related to increased vascular permeability pressure and capillary leakage, leading to intravascular to extravascular outflow of albumin, decreased synthesis, and increased albumin catabolism. The amount of capillary leakage that is affected by capillary permeability is a response from cytokines such as tumor necrosis factor-alpha (TNF-α), Interleukin-6 (IL-6), chemokines, as well as the action of prostaglandins and other components as endotoxins from gram-negative bacteria (Gounden et al., 2018). In addition, serum lactate examination is performed to assess the success of resuscitation, as well as signs of hypoxia and tissue failure occur in sepsis, but it is not possible to accurately determine tissue perfusion (Li et al., 2022; Rhodes et al., 2017).

The level of serum albumin is one of the indicators for assessing the degree of severity of sepsis. Albumin has physiological functions such as inhibition of platelet aggregation, antioxidant, endothelial stabilization, anti-inflammatory, and as an essential molecular carrier in physiology and pharmacology. Hypoalbuminemia is associated with poor prognosis in several acute and chronic diseases. From a cohort study of 237 pediatric patients with sepsis, mortality in patients with hypoalbuminemia ranged from 19.9%, while mortality in patients with normal albumin levels ranged from 2.9% ($p<0.001$) (Liu et al., 2023; Qian & Liu, 2012). Administration of albumin in sepsis patients aims to maintain oncotic pressure and circulatory volume and improve the status of hypoalbuminemia. Hypoalbuminemia is associated with an increased risk of acute kidney injury (AKI), and in some cases, albumin administration can prevent AKI. The Italian Albumin Outcomes in Sepsis (ALBIOS) also showed that patients with sepsis who received 20% human albumin had a lower risk of hypoalbuminemia. Several studies suggest using striped snakehead fish extract, *Channa striata* extract, as a substitute for 20% human albumin. Research by Permana (2022) found that the albumin in the striped snakehead extract was not significantly different from human albumin in sepsis patients, so the striped snakehead fish extract is more cost-effective for treatment.

The study found that the administration of striped snakehead fish extract was more effective in stabilizing endothelial nitric oxide synthase (eNOS) levels in sepsis patients than administering 20% human albumin and stabilizing neutrophil levels. Another study conducted by Putranto et al. (2023); and Isamahendra et al. (2023) showed that theadministration of striped snakehead fish extract increased the level of serum albumin and decreased the high levels of C-reactive protein (HS-CRP) in patients with end-stage renal disease (ESRD) in sepsis patients, striped snakehead albumin extract is more effective than administration of 20% human albumin. In addition to being less expensive than parenteral albumin, striped snakehead fish extract is as effective as parenteral albumin in preventing thrombocytopenia in sepsis patients. Currently, there are not enough studies discussing the effectiveness of using *Channa striata* extract as an albumin supplement in sepsis patients, so further evaluation is needed (Hu et al., 2021; Putranto et al., 2023). This study aims to determine the role of *Channa striata* extract (CSE) in improving albumin and creatinine in sepsis patients.

2. Methods

2.1. Study Design

This study is a quasi-experimental study with a pre-post-test design. It aims to determine the comparative efficacy of using *Channa striata* extract as an enteral supplement against albumin and creatinine repair in sepsis patients in the ICU of Central General Hospital H. Adam Malik.

2.2. Research Population and Sample

The study population is sepsis patients in the ICU of H. Adam Malik General Hospital. The study sample comprised patients who met the inclusion and exclusion criteria. The sample was 40 people. The sampling technique is carried out using the consecutivesampling method, where the subjects involved in this study meet the inclusion and exclusion criteria and are included until the entire number of samples is met. The inclusioncriteria were patients with a diagnosis of sepsis made within 24 hours of treatment and hospitalization in the ICU, using a ventilator, albumin levels of 2.5–3.5 mg/dl, ages 18–65, and a BMI of 18.5-24.9 kg/m2. The exclusive criteria are patients with chronic renal failure, malnutrition with a BMI <18.5 kg/m2, being unable to receive enteral nutrition (stressulcers, patients with TPN), having been given albumin supplements before, and allergies.

2.3. Research Procedure

The study was conducted in July–September 2023. After obtaining approval from the Faculty of Medicine Ethics Committee, Universitas Sumatera Utara, and RSUP H. Adam Malik Medan, researchers took samples by taking all sepsis patients treated in the RSUP H. Adam Malik ICU. Identification of research subjects according to the inclusion and exclusion criteria set. After that, informed consent is obtained by explaining the objectives, procedures, benefits, and potential risks of this study, if the patient or family is willing to participate, it will be documented by signing the research approval form.

The subjects were sepsis patients who were enforced using SIRS criteria and SOFA scores, then randomly divided into two groups, namely Group A, who received *Channa striata* treatment, and Group B, which was a control. On the first day of ICU treatment, a complete laboratory examination of blood, albumin, lactate, procalcitonin, kidney, and liver function was conducted. SOFA scores were re-evaluated in both groups. In Group A, the intervention of *Channa striata* extract (Onoiwa®) 3 x 5 gr/day was given enterally (NGT) and nutritional therapy according to the daily needs of patients for five days, and Group B received nutritional therapy according to the daily needs of patients for five days. The patient'sdaily nutritional needs are determined based on calculations by the nutrition specialist at AdamMalik General Hospital. On the 7th day, a complete re-examination of blood, albumin levels,kidney function, and liver function was conducted, and SOFA scores were re-assessed in bothgroups. Recording and calculation of differences in albumin and creatinine levels before and after the intervention in the sample were carried out.

2.4. Statistical Analysis

After all the necessary data is collected, it is tabulated into the master table using the software, and the data is processed using SPSS. An analysis was conducted to see the characteristics and distribution of the subjects. Numerical data is displayed as the average value (standard deviation), and then a normality test is performed with the Shapiro-Wilk test. Bivariate analysis between groups receiving *Channa striata* and not getting *Channa striata* was performed using the independent T-test for parametric data and the Mann-Whitney test for non-parametric data. The result is that $p < 0.05$ indicates a significant difference. To analyze the pre- and post-administration of *Channa striata* using the dependentT test for parametric data and the Wilcoxon test for non-parametric data. With results, a valueof $p<0.05$ indicates a significant difference.

3. Results and Discussion

3.1. Results

3.1.1. Descriptive Data Analysis Results

This study consisted of 2 groups: the treatment group (*Channa striata*) and a control group, with a sample of 20 patients for each group. Table 1 shows the essential characteristics of the research sample.

Table 1 Basic demographics and clinical characteristics of patients

Variable	Total (n=40)	Treatment (n=20)	Control (n=20)	P-value*
Age (years)	56.1 + 11.8	55.6 + 13.5	56.6 + 10.2	0.100
Sex (n,%)				
• Male	19 (47.5)	11 (55)	8 (40)	
• Female	21 (52.5)	9 (45)	12 (60)	
BMI (kg/mg2)	22.6 + 1.6	22.5 + 1.7	22.7 + 1.5	0.085
Albumin (gr/dL)	2.77 + 0.39	2.76 + 0.41	2.78 + 0.38	0.816
Creatinin (mg/dL)	1.70 + 1.15	1.32 + 0.86	2.02 + 1.31	0,052
SOFA Score	9.65 + 1.65	9.3 + 1.6	10.0 + 1.6	0.078
Result (n%)				
• Changing ward	17 (42.5)	10 (50)	7 (35)	
• Mortality	23 (57.5)	10 (50)	13 (65)	
Length of stay (days)	10 (8-28)	11 (8-28)	10 (8-16)	0.001

*) Shapiro-wilk

3.1.2. Comparison of Albumin Levels Results

Both groups assessed and compared albumin levels before and after treatment. Albumin was assessed before and after the supplementation of *Channa striata*.The results of comparing the two groups are displayed in Table 2.

Table 2 Comparison of albumin levels in both groups

Variable	Pre	Post	Mean Difference	P-value
Treatment (gr/dL)	2.76 $\pm$ 0.41	2.76 $\pm$ 0.40	0.002 $\pm$ 0.18	0.952[b]
Control (gr/dL)	2.78 $\pm$ 0.38	2.56 $\pm$ 0.37	0.21 $\pm$ 0.23	0.001[b]
P-value	0.890[a]	0.113[a]		

[a)] T-independent test [b)]T-dependent test

With a p-value>0.05, there was no statistically significant difference in albumin levels; treatment groups were compared to controls before and after treatment. From the table,we also obtained changes in albumin levels after and before treatment in both groups. In the treatment group, there is no significant change in albumin values, with a mean difference of 0.002 $\pm$ 0.18, and the value of p = 0.952 did not show a significant difference between beforeand after the treatment. Meanwhile, in the control group, levels decreased before and after treatment; the mean difference is 0.21 $\pm$ 0.23. With a value of p = 0.001, a statistically significant reduction in albumin levels was obtained in the control group.

3.2. Discussion

Previous studies have reported that *Channa striata* (CS) albumin extract has anti-inflammatory and antioxidant effects and can stabilize PAI-1 levels in sepsis patients becauseit also contains chitosan and glutathione (Hu et al., 2021; Putranto et al., 2023). In assessing serum albumin levels, it was found that the group receiving CS extract supplementation did not experience a decrease in albumin levels after treatment (2.76 + 0.41 versus 2.76 + 0.40) compared to controls, who experienced a statistically significant decrease (2.78 + 0.38 gr/dl to 2.56 + 0.37). According to previous studies, CS extract increased serum albumin levels in ESRD patients (Putranto et al., 2023). Meanwhile, the use of CS extract in other critical diseases (e.g., stroke) may increase albumin levels after CS supplementation (Kasim et al., 2017). In this study, patients with sepsis received CS supplements for five days (Permana et al., 2023). In another study, five-day CS supplementation accelerated healing processes and wound inflammation after the surgery. Supplementing seven days also helps woundhealing (Suryanti et al., 2020). In addition, another study reported that CS supplementation for five days increased albumin and accelerated wound healing aftersurgery (Parliastina & Parliastina, 2018). These studies proved that CS supplementationfor five days increased albumin production. The increase in albumin is caused by the high content of amino acids needed in the process of albumin synthesis in CS extract. In another study conducted, the extract was shown to accelerate the wound healing process and have antinociceptive, anti-inflammatory, and antioxidant activities by increasingIGF-1 levels, which in turn will increase albumin levels (Kwan et al., 2020; Mustafa et al., 2013; Putranto et al., 2023; Siddaiah et al., 2022). It contributes to maintaining muscle mass, anti-inflammatory, antioxidants, and preventing apoptosis (Ma'rufi et al., 2019; Mulyana et al., 2017). In other studies by Permana (2022), a study was conducted in sepsis patients where acomparison was made between administering CS and 20% human albumin for two days. It turnedout that there was no significant difference between the two in stabilizing PAI-1 in sepsis patients (p = 0,503). In addition, platelet differences between the CS group and human albuminwere not significant differences (p = 0.187) (Permana et al., 2023) then conducted a follow-up study in 2023 with the same treatment group with administration for two days to see the effecton syndecan-1. It was found that there was a decrease in syndecan-1 in the CS group (p = 0.013) and human albumin (p = 0.027), so it was concluded that there was no significant difference between the two. This study shows that CS supplementation for five days is sufficientand may indicate increased albumin production.

In the control group, which only received enteral nutrition, there was a decrease inserum albumin levels. Several potential mechanisms could explain this phenomenon. First, sepsis increases inflammation of all types, damages the endothelium of blood vessels, and increases capillary permeability. Therefore, when albumin breaks down in blood vessels, albumin levels in the blood decrease, and the risk of adverse effects increases; furthermore, elevated cytokine levels can affect gene expression and albumin catabolism and reduce plasmaalbumin levels. Secondly, in the body, albumin is produced in the liver, and liver function is impaired in sepsis, resulting in low albumin levels. In addition, when septicemia occurs, the function of the stomach is often disturbed, which affects the absorption of nutrients and leadsto food deficiency. The amino acid content in CS extract can supply the amino acid needsneeded to increase albumin production (Putranto et al., 2023).

Assessment of creatinine levels showed a non-significant decrease in serum creatinine levels in both treatment groups. This is in line with the study of Thamrin and Rusman (2021), who found that the administration of CS extract in patients undergoing radiotherapy had no significant effect on changes in albumin, urea, and creatinine. Another study found no significant difference between administering human albumin and CS albumin to sepsispatients in intensive care units because CS extracts are considered reliable and cost-effectivefor patients (Permana et al., 2023). This is due to Branched Chain Amino Acids (BCAA) content and the ketogenic amino acids

contained in CS, which can prevent impaired kidney function characterized by increased creatinine levels (Palupi et al., 2015).

In this study, there was an increase in SOFA scores before and after treatment in both treatment groups, increasing in the treatment group (9.3 $\pm$ 1.6 to 11.6 $\pm$ 2.4), $p<0.001$, and also increasing in the control group (10.0 $\pm$ 1.6 to 11.7 $\pm$ 3.7), $p=0.034$. Retracted (2023) found intheir study that the mean SOFA score of patients with severe sepsis was 9.15±2.46, $p<0.001$. The results of this study were inversely proportional to the study conducted by Utariani et al.(2017), who found a decrease in SOFA scores after albumin infusion, which was also associated with a decrease in mortality. The results of the study can occur because sepsis develops rapidly, so it can turn into severe sepsis or septic shock, with mortality rates reaching.
50%. From other studies, it is said that a score greater than 7 has a relative risk (RR) of 3.9 ($p=0.024$), so a higher SOFA score is associated with an increased risk of death (Iskandar& Siska, 2020).

Finally, we assess the mortality rate as an outcome of this study. It is known that the mortality rate in the group that received the CS extract was lower than that of the controls. Chou et al. (2009) analyzed 143 patients with sepsis due to secondary peritonitis and found that albumin administration can reduce the 28-day mortality rate in patients with albumin levels <20 g/L. It is known that albumin levels are associated with both short-term and long-term outcomes in sepsis. A nonlinear relationship was found between albumin and clinical outcomes, with 28 days, 60 days, 180 days, and one year for albumin levels ≤ 2.6 g/dL and for each 1 g/dL increase in albumin levels. The risk of later death was reduced, respectively 59%,62%, 65%, and 62%. There are no published studies yet on the effect of CS extract on the length of hospital stay in patients with sepsis. A study by Rosyidi et al. (2019) on the impactof CS on albumin levels in patients after neurosurgical surgery states that serum albumin canbe used as a predictor of mortality and length of hospital stay. Published by Farouk Musa andJia Min (2022), the effect of CS as a mediator to promote wound healing states that the hospital stay is shortened by promoting the healing process. CS extracts have been shown to promote wound healing and wound epithelialization processes. Accelerated wound healing while minimizing wound infection reduces hospital length of stay and treatment costs.

4. Conclusion

The use of *Channa striata* extract is clinically significant for improving the conditionof sepsis patients in the ICU; it can be seen based on no decrease in albumin levels and decreased creatinine levels. The mean albumin levels in *Channa striata* extract administration did not decrease significantly compared to the mean albumin levels of controls, which decreased significantly. There was a statistically insignificant decrease in creatinine levels inboth groups before and after treatment. There was a significant improvement in SOFA scoresbefore and after both treatment groups ($p<0.05$), but no significant difference in the comparison between groups at the time before and after treatment ($p>0.05$). In this study, thereare limitations. First, there was no assessment of the relationship between albumin and creatinine levels and sample mortality. Second, the condition of patients who come to Adam Malik General Hospital as patients with severe conditions can be seen based on the SOFA score, so the initial condition of patients who come can cause difficulty in the recovery process. However, it is necessary to do further research on these variables and comparethe effects of CS albumin given enterally and parenterally.

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