

# Comparison of freeze-dried snakehead fish albumin extract and intravenous albumin in treating patients with hypoalbuminemia

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## ABSTRACT

**Objective:** This study aims to determine the effectiveness of snakehead fish freeze-dried albumin extract (VipAlbumin® Plus) in increasing the albumin level of hypoalbuminemia patients. **Materials and Methods:** A total of 58 patients were divided into four groups, K1 (were given intravenous albumin 20 gram/vial daily for 3 days) K2, K3, and K4 (were given different doses of VipAlbumin® Plus orally, 20, 30, or 40 g for 3 days). Two to four doses of VipAlbumin® Plus were administered per day as needed in each group. The albumin level was measured a day before and during the albumin treatments. The data were analyzed statistically. **Results:** The results showed that the albumin levels increased after the 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> days of treatment in all treatments. **Conclusion:** There were no significant differences between VipAlbumin® Plus at each tested dose and human albumin 20% in terms of their ability to increase the albumin level of hypoalbuminemia patients.

**KEY WORDS:** Freeze-dried, Human albumin, Hypoalbuminemia, Intravenous, Snakehead fish albumin

## INTRODUCTION

There are several ways to increase the albumin level of patients with hypoalbuminemia such as parenteral and peroral albumin supplementation. One of the common ways to supplement albumin orally is consumption of egg whites. Albumin capsules are also known as a less expensive yet effective way to increase albumin levels. Chairudin<sup>[1]</sup> shows that albumin capsule supplementation increases the albumin level of patients with preeclampsia and is much less expensive than albumin infusion. Likewise, the addition of more fish to the diet is also used, as it is rich in protein; in this region, snakehead fish (*Ophiocephalus striatus*) are commonly consumed for this purpose, often through a processed extract.<sup>[2]</sup>

A study has shown that snakehead fish extract is more effective than egg white in increasing the albumin level of patients suffering from burns.<sup>[3]</sup> In addition,

albumin extract from snakehead fish was effective in increasing the albumin level. However, peroral albumin supplementation should not be effective in patients with digestive problems since albumin absorption is affected. Despite these absorption problems, capsules containing freeze-dried albumin extract have given a solution to hypoalbuminemia patients with digestive problems.<sup>[4]</sup>

For instance, severe malnutrition was found in 17% and medium malnutrition in 77% of patients in a study of African hospitals in 1997. In general, the prevalence of malnutrition is around 30–50%. In Australia, in a study of 351 patients in public hospitals, 45% were found to have low hemoglobin, 35% hypoalbuminemia, and 24% were underweight. In a study in 13 hospitals in America, 90% of patients were malnourished and 70% were underweight and suffer from hypoalbuminemia with albumin level 0.5 g/dL.<sup>[3]</sup>

The aim of this study is to investigate the effectiveness of VipAlbumin® Plus produced through a freeze-drying method in increasing the albumin level of patients with hypoalbuminemia in public hospital of Dr. Moewardi Surakarta, which may have increased

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absorbability and, moreover, can be an alternative, less expensive way to increase albumin levels.

## MATERIALS AND METHODS

### Research Subject

This study was conducted in the Dr. Moewardi Surakarta public hospital in January 2014. In a preliminary study, eight of 15 (56%) patients in the emergency room (ER) unit were found with hypoalbuminemia. The number of patients with hypoalbuminemia was 51.6% in the other units of the hospital in February 2014.

### Experimental Design

The study was designed as an experimental study with a single-blind randomized controlled trial design, which was focused on the ER unit. Patients were selected based on several inclusion and exclusion criteria. The inclusion criteria were as follows: The patients should be hospitalized in ER, adult either man or woman aged 18–60 years old, albumin level <2.8 g/dL, able to perform peroral liquid diet, and willing to participate in this study and also follow the procedure. The exclusion criteria were as follows: Patients were allergic to snakehead fish, suffering from certain diseases (hepatic cirrhosis, renal disease, and burns), and were already treated with albumin for a week before the study and pregnant. Moreover, there were also drop out criteria such as the subject is under intervention and retreat from the study or recalled the informed consent, the subject did not follow the protocol, and the subject faces serious unforeseen side effects using the product.

### Treatment

A total of 58 patients were divided into four treatment groups. 14 patients in control group (K1) were given intravenous albumin 20 g/vial daily for 3 days. 14 patients in the second group (K2) were given VipAlbumin® Plus orally twice a day 10 g/sachet for 3 days. 15 patients in the third group (K3) were given VipAlbumin® Plus orally 3 times a day 10 g/sachet for 3 days. 15 patients in the fourth group (K4) were given VipAlbumin® Plus orally 4 times a day, 10 g/sachet for

3 days. In addition, the measurement of albumin level was done a day before (T1) and during the albumin treatment (T2, T3, and T4). The obtained data were analyzed statistically.

## RESULTS AND DISCUSSION

### The Basic Characteristics of the Subjects

As can be seen in Table 1, the subjects were 53.6% of female, 46.4% of male ( $P = 0.835$ ). The proportion of men and women was attempted to be balanced between K1, K2, K3, and K4. Moreover, the majority of subjects were categorized as normal weight (71.4%), while 12.5% of them were overweight ( $P = 0.163$ ). Likewise, there were no significant differences among the groups in their nutrition status and range of age. In general, subjects were aged about  $43.64 + 9.621$  years old on average, specifically  $43.64 + 9.621$  years old for K1,  $46.64 + 11.453$  years old for K2,  $40.36 + 12.592$  for K3, and  $40.64 + 11.738$  years old for K4 ( $P = 0.430$ ). In brief, there were no significant differences in the characteristics of subjects in this study.

### The Comparison of VipAlbumin® Plus and Human Albumin 20% in Their Effectiveness to Increase Albumin Levels of Hypoalbuminemia Patients

Hypoalbuminemia is a condition related to an abnormally low level of albumin in the bloodstream; under normal conditions, the albumin level is about 3.5–5.0 g/dL. There are several factors that can cause the blood albumin level to drop such as a decrease in protein synthesis, the increase of catabolism rate, and other conditions such as nephrotic syndrome, burn, and bleeding. This can be also caused by malnutrition, systemic diseases, severity, or hypermetabolism induced by infection, medical treatment, or surgery. High-protein foods are believed as the effective remedies to increase and maintain the albumin level as they prevent the albumin loss.<sup>[2]</sup>

As seen in Table 2, the albumin levels of each group were equal on the day before treatment (T1) ( $P = 0.636$ ). The levels of albumin were  $2.36 \pm 0.285$  g/dL,  $2.49 \pm 0.234$  g/dL,  $2.40 \pm 0.299$  g/dL, and  $2.39 \pm 0.320$  g/dL for K1, K2, K3, and K4, respectively. It is notable

**Table 1: The subject classification based on the basic characteristics**

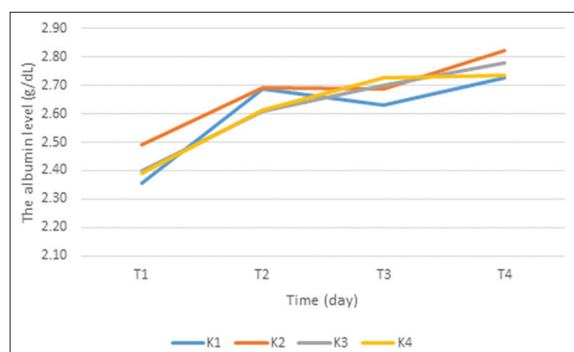
Characteristic	Groups				Total	P
	K1 (%)	K2 (%)	K3 (%)	K4 (%)		
Sex*						0.835
Woman	9 (64.3)	7 (50.0)	7 (50.0)	7 (50.0)	30 (53.6)	
Man	5 (35.7)	7 (50.0)	7 (50.0)	7 (50.0)	26 (46.4)	
IMT**						0.163
Underweight	2 (14.3)	4 (28.6)	1 (7.1)	2 (14.3)	9 (16.1)	
Normoweight	12 (85.7)	9 (64.3)	9 (64.3)	10 (71.4)	40 (71.4)	
Overweight	0 (0)	1 (7.1)	4 (28.6)	2 (14.3)	7 (12.5)	
Age***	$43.64+9.621$	$46.64+11.453$	$40.36+12.592$	$40.64+11.738$	$42.82+11.383$	0.430

\*Chi-square test (nominal scale data category), \*\*Kruskal–Wallis test (ordinal scale data category), \*\*\*One-way ANOVA test (normal-distributed numerical data) IMT

**Table 2: The effectiveness of VipAlbumin® Plus in different doses in increasing the albumin level**

Albumin	K1	K2	K3	K4	P
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
T1*	2.36±0.285	2.49±0.234	2.40±0.299	2.39±0.320	0.636
T2**	2.69±0.348	2.69±0.518	2.61±0.450	2.61±0.241	0.910
T3*	2.63±0.528	2.69±0.442	2.70±0.528	2.73±0.315	0.918
T4**	2.73±0.495	2.82±0.404	2.78±0.565	2.74±0.295	0.944
<b>Albumin interval</b>					
T2-T1**	0.33±0.284	0.20±0.619	0.21±0.421	0.22±0.336	0.847
T3-T1*	0.27±0.439	0.19±0.548	0.30±0.480	0.34±0.478	0.788
T4-T1*	0.37±0.395	0.33±0.448	0.38±0.482	0.34±0.399	0.976

\*Kruskal–Wallis test (data are not normally distributed), \*\* One-way ANOVA test (data are normally distributed), SD: Standard deviation



**Figure 1:** The increase of albumin level for K1, K2, K3, and K4 groups

that the same pattern can be seen in the days after treatment in which the albumin levels were not significantly different between treatments, with  $P = 0.910$ ,  $P = 0.918$ , and  $P = 0.944$ , for T2, T3, and T4, respectively. The albumin for each day stayed at the same level for every treatment. In other words, there were no significant increases in the albumin level after the initial administration of treatment. This can be clearly seen on the intervals of albumin level after treatment with its level in the day before treatment, which  $P = 0.847$ ,  $0.788$ , and  $0.976$  for T2-T1, T3-T1, and T4-T1, respectively [Figure 1].

Many studies have found that peroral albumin supplementation in the form of a capsule was effective in increasing the albumin level of patients with hypoalbuminemia. This method is considerably cheaper than albumin infusion for the treatment of preeclampsia patient.<sup>[1]</sup> This method not only cuts the medication budget but also accelerates the recovery process since it needs a faster time to help the patients fully recovered.<sup>[4]</sup> On the other hand, the outcome of peroral albumin supplementation cannot be achieved by patients with digestive problems. The freeze-drying technique, however, has allowed such patients to have the same opportunity for peroral supplementation.

Overall, the highest interval was achieved by K1 with an increase of  $0.33$  g/dL over baseline (T2-T1) in blood albumin level after the 1<sup>st</sup> day of treatment which slightly dropped into  $0.27$  g/dL over baseline (T3-T1) on the 2<sup>nd</sup> day and rose again to  $0.37$  g/dL

over baseline on the past day of treatment (T4-T1). Moreover, the highest interval among all days was seen on the 3<sup>rd</sup> day of treatment in the K3 group, which was  $0.39$  g/dL. On the other hand, K2 contributed the lowest interval for each day of treatment, which is  $0.20$  g/dL,  $0.19$  g/dL, and  $0.32$  g/dL for T2-T1, T3-T1, and T4-T1, respectively.

While the increases of the albumin level were considerably similar for all treatments at each dose, the supplementation of snakehead fish albumin extract twice a day (K2) performed the weakest induction for the increasing of albumin in the patient's body. This supplementation performed better as the capsule intake frequency increased. On the other side, intravenous albumin (K1) had the highest level of albumin in the 1<sup>st</sup> day of treatment.

The supplementation with VipAlbumin® Plus increases the albumin level of patients with hypoalbuminemia gradually since the dose is spread out overtime. However, human albumin 20% infusion increased albumin level significantly only on the 1<sup>st</sup> day of treatment and plateaued to a similar level on subsequent days. VipAlbumin® Plus treatments were the same as human albumin 20% effectiveness in increasing the albumin level and maintaining the acid-base condition of patients with hypoalbuminemia.

The level of albumin is maintained through the rates of its synthesis, degradation, and distribution to intravascular also extravascular compartments. The liver is the main organ that produces albumin with synthesis rate around  $12$ – $25$  g/day. There are only  $20$ – $30\%$  hepatocyte cells that actively produce albumin under normal conditions. This rate is defined by the body condition and the nutritional situation of patients. Albumin can only be optimally produced under optimal osmotic pressures, hormonal conditions, and nutritional situation. The colloidal osmotic pressure of interstitial liquid surrounding the hepatocyte cells is an important regulator of albumin synthesis.<sup>[5]</sup>

Albumin degradation in adult human weighing  $70$  kg is normally around  $14$  g/day or  $5\%$  of the whole amount of protein metabolism for a day. For instance, around

40–60% of the degradation is performed by muscles and skin. Degradation also occurs in the heart (15%), kidney (10%), and the rest of it (10%) infiltrates into the digestive tract through the stomach wall. The final product of albumin degradation is free amino acids. Normally, this product will be excreted from the body through the urinary tract with a total amount of about 10–20 mg/day; some of the free amino acids are reabsorbed by the glomerulus membrane.<sup>[6]</sup>

In addition, the albumin level decreases on several conditions such as albumin synthesis dysfunction (liver disease, alcoholism, malabsorption, starvation, and chronic diseases), albumin loss (nephrotic syndrome and burns), and malnutrition as the imbalance ratio of albumin and globulin (chronic inflammation, collagenic diseases, and severe infection). On the other hand, there are also factors that increase the albumin level, namely albumin infusion and dehydration (the increase of hemoglobin and hematocrit level).<sup>[6]</sup>

The production of albumin extract through freeze-drying method is considerably more stable than its production through heating process or pasteurization. Specifically, the materials will be frozen first before they are dried. Freezing process is performed under vacuum conditions followed by sublimation of the remaining water present in the drying process.<sup>[7,8]</sup> The VipAlbumin® Plus is also made with combinations of fruit to facilitate the patients with capsule intolerance and intake by children.

## CONCLUSION

There were no significant differences between snakehead fish albumin extract (VipAlbumin® Plus) supplementation and human albumin 20% infusion; both treatments were effective in increasing albumin levels in our sample of patients with hypoalbuminemia.

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## ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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