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**Research Article** 

# Effects of the Arsoa Fasting Program with Supplemental Eating on Health (A Randomized Intervention Study)

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## Abstract

Metabolic syndrome in middle age is a source of lifestyle-related diseases. As people age, their various functions deteriorate, putting them at high risk for cardiovascular disease, osteoporosis, immunocompromise, frailty, and dementia. In addition to the decline in the quality of life of the elderly, soaring medical costs and the burden of nursing care for hospital visits have become social problems. Fasting is also incorporated into macrobiotics, and by correcting the intestinal tract function, various complaints can be prevented altogether, and people can learn to live in a way that aims to cure and cure illness.

We have been developing a healthy fasting program in the AIIsoa Keio Group, and we studied an attempt to reduce the burden on the body and psychological barriers to participation by employing complementary meals. In this study, 60 participants were randomly divided into three groups: no treatment, fasting plus a complementary meal, and complementary meal only, and were followed continuously for one month after fasting. The fasting-induced decrease in blood glucose and increase in ketones was accompanied by a reduction in TG, changes in fat metabolism, and a transient rise in IL6, which returned to the normal range within one month due to the effects of activated vitamin D3 and minerals provided by the supplemental diet. Fasting resulted in obesity elimination, BMI reduction, blood pressure reduction, and HbA1c reduction; POMS also increased vitality. These effects were not seen in the supplement-only group and may be triggered by fasting.

Keywords: Arsoa Fasting; Supplemental; Health; Intervention

#### **Objectives**

We have found that long-term fasting subjects use ketones as an energy source, and we have observed a decrease in blood glucose and ketone production, as well as changes in physical status, through the Arsoa fasting program [1-5]. We have evaluated changes in intestinal flora, short-chain fatty acids, inflammatory cytokines, and specific microbiota and have found that ketone production is higher in those who become hypoglycemic quickly [6]. Ketones have high transcriptional activity for many genes and also work to protect atherosclerosis and myocardium through their antioxidant and anti-inflammatory properties. Therefore, ketones may play a role in anti-aging and achieving longevity [7-10]. However, it is difficult to fast completely during fasting, as in the case of zazen fasting, due to the psychological burden. Therefore, we attempted to develop a more effective fasting method by including a certain amount of supplementary food.

Fasting is also incorporated into macrobiotic medicine, and by correcting the intestinal tract function, it may be possible to prevent all of these problems at once, making it suitable for people to learn how to live to cure pre-symptomatic diseases. The Arsoa fasting program has improved glucose and lipid metabolisms, resulting in weight loss, bowel movements, and quality of life. This approach has the potential to maintain high patient adherence.

The benefits of improved health in a four-day fasting program are significant for each participant. Participants learn extensively about health through exercise and classroom lectures during the program. In addition to a medical interview, participants must complete a urine collection and body composition assessment, which is a valuable method of evaluation to confirm efficacy and does not require the burden of sample collection. Fasting will naturally lead to a change in the choice of side dishes to healthier, more plant-oriented diets. One disadvantage for the participants is hunger during the study period, but this can be tolerated because "juices" and "Arsoa enzyme solutions" are administered during the program, and complementary meals are provided. The study design is pre- and post-comparative, so it is easy to look at individual results. The health effects of fasting are diverse. Such multifactorial and multi-effectiveness can be easily demonstrated in a pre-post comparative study. We have proposed that a Pre-Post Comparative Study is suitable as a new epidemiological method. The present study attempts to confirm and validate the existing methodology.

# Methods

This study was conducted with members of the general public who applied through the Arsoa Lifestyle Academy and other organizations. Since this was a pilot study no selection of subjects was made except for dementia patients who were unable to communicate. Sixty of them who gave consent to participate were randomly divided into three groups: a fasting group (FS), a supplement group (S), and a no-treatment group (C). The fasting group fasted for four days and three nights at a training facility in Kobuchizawa, while the control and supplement groups lived an everyday life at home. The S group took the same supplements (Arsoa enzymes, Cell energy, and Lyforidin minerals) as the F group, and physical measurements and blood samples were taken at the clinic on designated days.

Questionnaires, body composition assessments, and interviews were conducted at the time of participation and served as baseline

data. The FS group was instructed on diet and exercise therapy at the start and then transitioned to fasting. During the four days, intake, bowel movements, etc., were recorded. At the end of the study and one month later, the same tests as in the initial evaluation were performed.

Efficacy measures included (1) physical condition, weight, blood pressure, and bowel movements as primary endpoints, (2) Secondary measures included blood glucose, ketones, minerals, inflammatory markers, other biochemical indices, and POSM.

During the 4-day/3-night fast, participants consumed 150 ml of enzymes, three bags of Cell Energy V, and five mineral grains at mealtime. (Table 1). The total amount of supplements was 221 kcal for the three meals. Both supplements were created from natural ingredients and contain calories, protein, and carbohydrates (43.5g) due to the Arsoa enzyme; Cell Energy V contains dietary fiber (6.6g), water-soluble vitamins such as vitamin B several to several dozen times more than DRI, and fat-soluble vitamins such as beta carotene several times more than DRI.

Lyforidine minerals include magnesium, calcium, zinc, selenium, vitamin D, potassium, iodine, phosphorus, iron, manganese, and other minerals (Table 1). Roughly one-third to a significant amount of DRI is to be consumed. Tea is freely available during this period.

	Arsoa enzyme/150 ml	Cell energy/3bag, 15g	Mineral/5 tab, 2.0g	DRI2020
Energy	180 kcal	39 kcal	2.1 kcal	B. wt x 80 kcal
Carbohydrate	43.5g	5.4g	0.35 g	
Oligosacchride	3g			
Dietary fiber	0.75g	6.6g		≧21g ≧18g
Protein	1.2g	0.45g	0.05g	B. wt. x 0.8g
Fat	0g	0.24g	0.05g	10g(n6), 2g(n3)
Ash				
Salt	0.06g	0.009 g	0.01g	<6g
Vitamin B1	0.025 mg	45 mg	0.08 mg	1.3, 1.1 (M, F) mg
Vitamin B2	0.025 mg	45 mg	0.0044 mg	1.5, 1.2
Vitamin B6	0.11 mg	45 mg	0.013 mg	1.4, 1.1
Vitamin B12	0	45 ug		2.4, 2.0
Niacin	0.285 mg	90 mg	0.06 mg	14, 11
Panthotenic a.	0.285 mg	45 mg	0.0035 mg	5 mg
Biotin	6.75 ug		0.4 ug	50 ug
Folic acid	16.2 ug	720 ug	0.048 ug	240 ug
Vitamin C	0	600 mg	0.058 mg	100 mg
Vitamin D	0	60 ug	25 ug	8.5 ug
Vitamin E	0.1 mg	15 mg		6 mg
Vitamin A	11.25 ug			900, 700 ug
βcarotene		27.72 mg		<6 mg
Vtamin K3	18.3 ug	45 ug	0.04 ug	150 ug
Са	70.5 mg	6.3 mg	300m g	750, 650 mg
К	402 mg	16.2 mg	1.8 mg	2500 mg

19

# Effects of the Arsoa Fasting Program with Supplemental Eating on Health (A Randomized Intervention Study)

Mg	33.75 mg	2.42 mg	300 mg	370, 270 mg
Р	24 mg	6 mg	1.4 mg	3000 mg
Fe	1.5 mg	0.06 mg	0.89 mg	7.5, 6.5 mg
Mn	0.345 mg	0.03 mg	0.08 mg	11 mg
Zn	0.21 mg	0.03 mg	15 mg	11, 8 mg
Se	0		20 ug	30, 25 ug
Ι	0	0	29 ug	130 ug
Cu	0	0		0.9, 0.7 mg
Мо	0			30, 25 ug
Cr	0			500 ug
Caffein	0	0		

Table 1: Composition of supplements taken at the meal time. DRI is the reference for Japanese.

Participants will meet at noon on the first day for guidance and physical measurements and eat a designated mixed meal starting at dinner. During the fast, participants will have morning and evening InBody body measurements, a urine test using a testape, morning radio exercises, and a walk, carrot juice at 3 p.m. on the second day, a smoothie made with vegetables from an organic farm in the afternoon, and a "dawn meal" of brown rice and miso soup at noon on the fourth day before leaving. During the stay, there will be lectures and discussions on health and practical exercises such as stretching, exercises, and visits to organic farms. The participants recorded their physical condition and what they ate and drank, if any.

Both adverse events (AE) and serious adverse events (SAE) during the fast were assumed to have a clear causal relationship to the intervention (fasting). These include allergic symptoms such as measles and gastrointestinal symptoms such as diarrhea and nausea, which the physician will determine.

### **Analysis methods**

Efficacy measures were evaluated at three time points: baseline, day four at the end of fasting, and one month later, and test results at each time point were compared. Since there were only 20 subjects per group, the analysis was a Pro-Post study, and the results were tested with a paired t-test. If parameters (continuous variables) were not normally distributed, they were compared by Wilcoxon signed-rank test at baseline and at the end of the study. Correlations were evaluated using Spearman's rank correlation coefficient or Pearson's product ratio correlation coefficient, depending on the presence or absence of a normal distribution assumption, and multivariate analysis was also performed. Statistical significant differences were shown by \* (p < 0.05) and \*\* (p < 0.01).

20

#### Results

The physical characteristics of the participants by group are shown below. The participants were in their 50s. The height of the male participants was around 171 cm. and that of female around 160 cm. Body weight was 65-80 kg in males and 60-70 kg in females. The BMI was 25, 26 for men and 23-29 kg/m<sup>2</sup> for women, and fat% was 25% for men and 32-39% for women. (Table 2, Figure 1).

	Control (C)		Supplement (S)		Fasting with Supplement (FS)				
Factor	Pre-Post	t-value	p-value	Pre-Post	t-value	p-value	Pre-Post	t-value	p-value
Body weight	-0.24	-0.997	0.332	-0.44	-2.197	0.041	-2.92	-10.316	.000
Fat volume	-0.36	-1.837	0.082	-0.34	-1.523	0.145	-1.57	-5.778	.000
non-fat volume	0.12	0.446	0.661	-0.11	-0.544	0.593	-1.35	-3.408	0.004
BMI	-0.19	-2.325	0.031	-0.23	-2.969	0.008	-1.07	-9.789	.000
X250HVD	-0.39	-1.439	0.166	1.13	2.027	0.058	3.39	6.354	.000
MCV	-0.62	-2.118	0.048	-0.61	-2.6	0.018	-1.29	-5.862	.000
МСНС	0.27	2.143	0.045	0.16	1.286	0.215	0.45	2.52	0.025
Na	-1.2	-4.06	0.001	-1.37	-3.369	0.003	-3	-7.937	.000

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# Effects of the Arsoa Fasting Program with Supplemental Eating on Health (A Randomized Intervention Study)

									21
Cl	0.9	2.714	0.014	0.58	1.353	0.193	-2.47	-3.954	0.001
TG	-16.6	-0.96	0.349	6.79	0.93	0.365	-60.33	-3.718	0.002
creatinine	0.02	1.966	0.064	0	0.374	0.713	0.05	3.287	0.005
Uric acid	-0.01	-0.052	0.959	-0.04	-0.343	0.735	1.31	5.886	.000
Serum Fe	10.85	1.108	0.282	-1.16	-0.213	0.833	-30.8	-3.778	0.002
Ferritin	-0.53	-0.143	0.888	-4.79	-1.211	0.242	61.71	6.009	.000
Serum Cu	9.5	4.307	.000	9.32	3.638	0.002	22.73	7.474	.000
Dihomo-g-linoleic acid	-8.39	-3.036	0.007	-3.8	-2.059	0.054	-17.69	-5.693	.000
arachidonic acid	-16.58	-2.359	0.029	-15.48	-3.202	0.005	31.19	2.808	0.014
EPA/Aa ratio	-0.01	-0.733	0.473	-0.04	-1.281	0.216	-0.04	-2.353	0.034
EPA/DHA/AA ratio	-0.03	-0.72	.480	-0.02	-0.493	0.628	-0.07	-2.709	0.017
HbA1c	-0.13	-4.626	.000	-0.11	-3.75	0.001	-0.1	-3.24	0.006
TNFa	-0.02	-1.107	0.282	-0.06	-1.661	0.114	0.04	2.361	0.033

 Table 2: Factors showing significant differences by paired t-test between pro- and post values of Control, Supplement and Fasting with

 Supplement group. Shaded area shows significant difference.



Figure 1: Changes of body weight, BMI, and non-fatty tissue weight at the pre- and post fasting points by sex.

For the FS group, changes in the before and after values of each variable were tested with a paired t-test, and those that were ssignificant are shown (Table 3).

Body weight, fat volume, non-fat volume, BMI, and 250HVD (activated vitamin D) showed significant differences, MCV, MCHC,

	Time	С	S	FS
Glucose	Pre	96.0	90.9 ± 9.1	87.3 ± 5.7
	Post	91.3 ± 29.6	92.7 ± 6.7	83.4 ± 8.6*
	1 mos	96.1 ± 11.7	94.3 ± 12.1	85.1 ± 7.3
Glucoalbumin	Pre	13 ± 15.9	13.3 ± 0.9	13.1 ± 0.7
	Post	13 ± 0.9	13.1 ± 0.9*	12.9 ± 0.7*
	1 mos	12.8 ± 0.9*	13.1 ± 0.9	12.7 ± 0.7**
Insulin	Pre	$10.8 \pm 14.8$	$6.6 \pm 4.1$	5.4 ± 2.6
	Post	9.7 ± 7.7	8.4 ± 4.1*	4.2 ± 2.5**
	1 mos	17.2 ± 15.9	12.3 ± 9.6*	6.5 ± 2.6*
Homa-IR	Pre	3.5 ± 7.7	1.5 ± 1.1	1.2 ± 0.6
	Post	2.3 ± 2.1	2 ± 1.0	$0.9 \pm 0.6^{*}$
	1 mos	$4.4 \pm 4.8$	3.1 ± 2.9*	1.3 ± 0.6

Table 3: Changes of glucose metabolism in different groups at the timepoint of pro-, post and one month after the fasting.

Na, Cl, Triglyceride (TG), creatinine, uric acid, serum iron (Fe), Ferritin, serum copper (Cu), dihomo-g-linoleic acid, arachidonic acid (Aa), EPA/Aa ratio, EPA+DHA/AA ratio, HbA1c, and TNF $\alpha$  showed significant changes.

Fasting reduced body weight, BMI, fat mass, and lean body mass in the FS group and continued to do so after one month (Figure 1).

The FS group lost 2.9 kg of body weight, of which 1.57 kg was a reduction in fat and 1.35 kg was a reduction in lean body mass. (Table 2) The decrease in lean body mass may be due to muscle breakdown into amino acids, which were then converted to glucose through the Cori circuit. Creatinine and phosphorus were mildly elevated by fasting. However, serum protein and albumin levels showed that protein synthesis during fasting increased rather than decreased with fasting, and this increase remained after one month of fasting. Ferritin increased from 86.8 mg/dl to 144 mg/dl in response to a decrease in median serum iron from 93 mg/ dl to 72 mg/dl. Mild decreases in other proteins were seen in blood cells, such as MCV, which changed from 92.4% before the fast to 91.3% immediately after the fast and 92.6% after one month.

The decrease in blood glucose and increase in ketones during the fasting period was evident. Still, the intake of supplemental food may have slowed the decline in glucose, and since the lowest blood glucose level was 78 mg/dl, the reduction in glucose and increase in ketones were not as clearly related as in the more severe fasting period (Table 3). At the end of the fast, ketones were above 1.0 mmole/L in eight subjects, with a maximum of 2.6 mM/L. (Table 4).

Glucose tended to decrease, as reflected in glucoalbumin and HbA1c. Insulin and HOMAIR were also lower. (Table 3).

Time	Glucose	B-hydroxy butyrate
Day 1 evening	103.4 ± 12.3	$0.38 \pm 0.23$
Day 2 morning	110.5 ± 14.7	$0.45 \pm 0.45$
Day 2 evening	102.7 ± 8.0	$0.65 \pm 0.36$
Day 3 morning	100.1 ± 10.4	$0.99 \pm 0.72$
Day 3 evening	100.4 ± 7.4	0.85 ± 0.35
Day 4 morning	92.8 ± 12.8	1.14 ± 0.6

 Table 4: Decreasing glucose levels and increasing b-hydroxy butyrate in FS group.

The  $\beta$ -oxidation of fatty acids is necessary for the production of ketones, and the reduction of TG by half in the FS group may be due to the breakdown of fatty acids. The most significant change in dihomo-g-linoleic acid before and after the fast was 41.3 mg/dl before the fast, 26.9 mg/dl after the quick, and recovered to 34.2 mg/dl one month later. After one month, the S group declined from 43.2 mg/dl tto 39.3 mg/dl. (Table 5) EPA went from 39.3 mg/dl to 35.3 mg/dl (median), and DHA went from 108 mg/dl to 110.9 mg/dl. Arachidonic acid increased from 209 mg/dl to 235.6 mg/dl after fasting and recovered to 190.4 mg/dl one month later. In group S, 187.9 mg/dl before, 183 mg/dl after, and 176.2 mg/dl one month later. The differences between groups were significant. EPA/Ara, DHA/Ara, and EPA+DHA/Ara ratio also showed significant differences. (Table 5).

	Time	С	S	FS
Tryglyceride	Pre	$174 \pm 109$	130 ± 81	111 ± 65
	Post	158 ± 83	$138 \pm 74$	51 ± 15**
	1 mos	182 ± 110	163 ± 106	88 ± 36*
EPA	Pre	37.3 ± 16.5	$48.8 \pm 43$	39.8 ± 21
	Post	31.8 ± 15.0	34.9 ± 20.6	35.7 ± 16.5
	1 mos	33.2 ± 19.5	41.1 ± 25.0	36.2 ± 17.5
DHA	Pre	107.6 ± 26.9	$108.5 \pm 42.2$	$108.6 \pm 40$
	Post	97.9 ± 17.4	101.5 ± 34.2	114.0 ± 39.0*
	1 mos	97.9 ± 29.0	107.3 ± 45.3	100.9 ± 27.7*
EPA+DHA/Ara.a	Pre	$0.61 \pm 0.23$	$0.78 \pm 0.27$	$0.68 \pm 0.21$
	Post	$0.58 \pm 0.18$	$0.76 \pm 0.32$	$0.61 \pm 0.17^*$
	1 mos	$0.61 \pm 0.26$	$0.82 \pm 0.42$	$0.70 \pm 0.19$

22

				23
Dihomo-g-linoleic a.	Pre	56.6 ± 22.7	45.0 ± 16.7	44.2 ± 15.7
	Post	48.2 ± 16.7	41.2 ± 12.7	26.5 ± 6.3**
	1 mos	48.7 ± 15.7	42.4 ± 15.4	34.9 ± 13.3*
Arachidonic a.	Pre	252.3 ± 75.7	202.2 ± 56.3	$219.0 \pm 51.3$
	Post	235.8 ± 64.3	186.7 ± 45.8	250.2 ± 64.6**
	1 mos	226.5 ± 56.1	186.3 ± 28.8	$200.8 \pm 46.5$

**Table 5:** Changes of lipid metabolism in different groups at the timepoint of pro-, post and one month after the fasting. Dominance ofw-6 seem to be present than w-3 fatty acids.

There were no significant changes in cholesterol, LDL, oxidized LDL, and HDL.

dl), and Zn (98mg/dl, 104mg/dl, 105mg/dl). Ca and Mg remained stable in all groups and at all times at around 9 mg/dl and 2 mg/dl, respectively. (Table 6).

Mineral changes due to fasting were observed in Na, Cl, Fe (93mg/dl, 72mg/dl, 99mg/dl), Cu (99mg/dl, 119mg/dl, 105mg/

	Time	С	S	FS
Mg	Pre	2.34 ± 0.15	$2.34 \pm 0.16$	2.37 ± 0.10
	Post	$2.23 \pm 0.15$	$2.34 \pm 0.13$	2.39 ± 0.13
	1 mos	$2.19 \pm 0.11$	$2.21 \pm 0.14$	$2.25 \pm 0.18$
Cu	Pre	85.6 ± 16.5	107.6 ± 15.3	102.11 ± 13
	Post	115.1 ± 19.5*	116.9 ± 21.5	124.8 ± 21.1*
	1 mos	103.3 ± 14.6	102.2 ± 10.2	$104.5 \pm 12.2$
Zn	Pre	99.7 ± 15.5	99.2 ± 11.8	$100.5 \pm 14.0$
	Post	93.7 ± 15.3	99.4 ± 12.9	103.0 ± 13.8
	1 mos	93.1 ± 16.2	99.7 ± 14.7	105.2 ± 11.1*
Fe	Pre	95.7 ± 27.3	105.4 ± 25.7	100.1 ± 36.2
	Post	106.5 ± 32.6	$104.3 \pm 33.0$	69.3 ± 20.5**
	1 mos	94.9 ± 29.7	96.5 ± 37.3	97.2 ± 30.8
Ferritin	Pre	109.1 ± 76.7	78.8 ± 60.3	97.1 ± 92.4
	Post	108.5 ± 73.1	73.9 ± 54.6	158.8 ± 124.0**
	1 mos	108.3 ± 67.6	73.4 ± 59.6	99.5 ± 103.1

**Table 6:** Changes of mineral metabolism in different groups at the timepoint of pro-, post and one month after the fasting. Unit is mg/dl.Decreased iron and increased cupper and ferritin after fasting are noteworthy.

We examined whether the liver and kidney were involved in ketone production or inflammation. The relationship between ketone concentrations and ASP and ALP showed a significant positive correlation in both groups (Figure 2).

Changes in inflammatory markers in each group are shown (Figure 3,4). Inflammatory markers such as IL-6 and TNF $\alpha$  were elevated in the fasting group but returned to normal after one month. The median values of changes in inflammatory markers are shown: CRP was 0.069, 0.05, and 0.071 in the C group, 0.036, 0.044, and 0.060 in the FS group, and 0.075, 0.046, and 0.068 in the S group; IL6 was 1.2, 1.12, and 1.5 in the C group and 0.9, 1.3,

and 1.0 in the FS group. TNF $\alpha$  was 0.65, 0.63, and 0.41 in group C, 0.59, 0.65, and 0.39 in group FS, and 0.66, 0.70, and 0.46 in group S. Both FS and S groups showed a decrease after the follow-up period. IL6 and TNF $\alpha$  were significant in the before and after comparisons. The anti-inflammatory 250HVD was 12.7 throughout the period in group C, increased from 14.3, to 17.4, and 22.2 in group FS, and from13.9, to 17.0, and 22.5 in group S, respectively, during the entire period. The fact that the continued to increase even one month after the fasting period in both FS and S groups suggests the overall effect of continued intake of enzymes, vitamins, and minerals.

In the POMS group, V (lively emotion) significantly increased at the end of the fasting period in FS group.







Figure 3: Changes of CRP, IL-6, BUN and 25ohVitamin D by C, S, and FS group.



Figure 4: Graphic abstract of Multifactor-Multieffects of Arsoa Fasting.

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24

#### Discussion

We have found that ketones ( $\beta$ Hydroxy butyrate: bHD) finance the body's ATP production in the low glucose state caused by fasting [1]. We have subsequently demonstrated in the Arsoa fast that a decrease in glucose leads to an increase in ketones [2-6]. Fasting is often used with meditation from a religious standpoint and can range from a few days to longer than a week. Long-term fasting is a life-threatening practice because of the damage to the body caused by weight loss. Arsoa fasting has been oriented toward wellness and is an easy method for the body.

Ketones have been ruled out as a cause of ketoacidosis in the late stages of diabetes. Still, recent research into the physiological effects of bHD has revealed that they are essential for energy production along with glucose [6]. Supplements of ketones were also available and tested in athletes, but again, an administration that ignored glucose and other overall metabolic balances was unsuccessful and discontinued [9]. A low-carbohydrate diet (ketogenic diet) is a surefire way to raise ketones, but the use of SGF2 inhibitors and ketone precursors (1,3 butanediol) have also been investigated [10]. However, ketone metabolism is complex and involves a variety of substances, which may produce different results concerning organ protection. It may be necessary to devise ways to maintain an overall balance.

Cells are equipped with systems that sense changes in extracellular nutritional conditions and alter cellular function to maintain cellular activity in response to starvation. In diabetic kidneys, mTORC1, a signal that detects overnutrition, is found to be abnormally activated, causing tubular cell damage and glomerular damage [10].

This clinical intervention study was designed to comprehensively observe the various reactions in the body during ketone production, with particular attention paid to changes in lipid metabolism, metabolic enzymes, and inflammatory markers in the liver and kidneys related to ketone production.

IL6, CRP, and TNF $\alpha$  increased after fasting and decreased after a month of continuous intake of supplemental food. Ketone concentrations were correlated with AST and ALT, suggesting that inflammatory stimuli from the intestinal tract may be involved [11].

After fasting in an 80 kg man with low 250HVD, low copper, insulin, EPA, DHA, and high and elevated AST, ALT, and CRP for one month, IL6 returned to normal one month later. When FS and S groups showed similar trends, we may consider the effects of enzyme-mix, especially 250hHVD in it.

It is now known that intestinal bacteria are responsible for increased inflammatory cytokine production and that chronic inflammation is associated with cardiovascular disease, proteinenergy malnutrition, and mortality. The gut-brain, gut-kidney, and heart-kidney pathways make up a complex network. A new perspective is required for the development of fasting and diet therapy.

In this study, we focused on the effects of supplementation during fasting. No subjects dropped out after taking "Arsoa enzyme, Cell energy, and Lyforidine mineral" supplements instead of breakfast, lunch, and dinner. Although the amount of energy was about one-tenth that of DRI the vitamins and minerals were sufficient, and there were no health problems. It could be used to treat one's unwell state casually.

Food intervention studies and RCTs are challenging to conduct because of their high cost. This study shows that a Pro-Post study can be conducted relatively inexpensively if well-planned.

We would like to see more and more food intervention studies adopted in dietary therapy to accumulate evidence [12].

## **Conflict of Interest**

All authors does not have any COI to declare.

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