

ORIGINAL ARTICLE

## Effect of Whey Beverage Fortified with Vitamin E on Quality of Life in Hemodialysis Patients

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### ABSTRACT

**Background:** Whey protein can improve quality of life and vitamin E can reduce oxidative stress. Due to the reduced quality of life in hemodialysis patients, this study was conducted to evaluate the effect of whey beverage fortified with vitamin E on quality of life in hemodialysis patients.

**Methods:** Ninety two 17 to 65 years old patients who were on hemodialysis were randomly assigned to four groups of (i) 1 receiving whey beverage fortified with vitamin E, (ii) 2 receiving whey beverage, (iii) 3 receiving vitamin E, and (iv) 4 as the control group receiving no intervention. SF-12 questionnaire was used for assessing quality of life in the participants.

**Results:** Bodily pain score improved significantly in group 3 while, a significant decline was seen for bodily pain in control group. An improvement was seen in groups 1 and 2. Physical health showed a significant improvement in group 1. Considering social functioning scores, improvement in whey beverage and vitamin E groups was seen. An improvement of quality of life in whey beverage fortified with vitamin E was noticed.

**Conclusion:** Whey protein and vitamin E were shown to reduce oxidative stress and their effect on neurotransmitters in brain such as serotonin and dopamine leads to improvement in quality of life in hemodialysis patients. Doing longer studies with questionnaires such as SF-36, may help precise investigation of whey protein and vitamin E effects on quality of life of hemodialysis patients.

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### Introduction

Diseases can affect the patient's health status and quality of life by physical, social, economic, and

many other factors. Damages due to renal diseases cause various problems and disorders resulting into chronic and progressive diseases of heart and other

organs. Hemodialysis might disrupt all aspects of a personal life and creates several limitations for the patient. Low quality of life in hemodialysis patients, is an effective factor in incidence of cardiovascular diseases and other outcomes such as hospitalization and death. Renal transplantation is used for chronic advanced renal failure treatment, while medical expenses affects the patient's life, too (1).

Since the purpose of treatment of patients with renal failure is not only the survival, but also is the improvement of the patient's quality of life, physiological parameters, laboratory results, patient satisfaction, and their sentiment about their health and performance. Evaluating quality of life helps to take into consideration the fundamental problems of patients and the treatment approaches to be revised. Existence of high morbidity, anemia, fatigue, sleep disorders, and low renal function are important factors in low quality of life in patients undergoing maintenance hemodialysis. One of the most important factors affecting the quality of life of hemodialysis patients is economical problems that hinder the precise observance of diet or providing required medications. Whey protein is effective in improving quality of life (2). This protein has tryptophan amino acid that plays an important role in increasing the tryptophan and serotonin levels in brain (as an anti-depressant and anti-stress agent) and helps to improve mental health (3). Serotonin as a brain peptide that has abundant receptors in the central nervous system, regulates many physiological, psychological, and behavioral functions (such as behavior, mood, sleep, appetite, and sexual function).

Therefore, any increase in serotonin helps to improve people's mental status.  $\alpha$ -lactalbumin that is one of the components of whey protein, is rich for tryptophan and is effective in increasing the levels of this amino acid in blood and brain serotonin.

In addition, vitamin E by reducing oxidative stress is associated with increasing levels of dopamine (through activation of tyrosine hydroxylase) (4) that can be effective in improving the mental status. As we know, dopamine as a brain neurotransmitter, improves social functioning and self-confidence, too (5).

Vitamin E supplements, while reducing the levels of malondialdehyde as an oxidative marker can help to improve the quality of life, too (6). Due to the reduced quality of life in hemodialysis patients and the effects of whey protein and vitamin E on quality of life improvement, this study aimed to investigate the effect of whey beverage fortified with vitamin E on hemodialysis patients' quality

of life.

## Materials and Methods

Eligible participants were those on stable hemodialysis for at least three months without any acute illness, infection or hospitalization and those who were 17 to 65 years old. We excluded the patients receiving multivitamins, proteins, amino acids or any nutritional supplements except for folic acid within three months prior to the study. All of the patients were on hemodialysis 2-3 times a week for at least three months. They were dialyzed by low-flux dialyzer with polysulfone/polyamide membranes, reverse osmosis, purified water and bicarbonate-containing dialysis solution. This randomized controlled trial was reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences, Iran and was conformed to the Declaration of Helsinki and Good Practice Guidelines. Eligible participants signed the informed consent to participate in this study.

Ninety two stable hemodialysis patients were eligible to participate in the study and were randomly assigned to 4 groups of (i) Group 1 who received 3 bottles of fermented whey beverage fortified with vitamin E per week for 8 weeks (each bottle contained 220 ml of 15 g WPC+600IU vitamin E, all-rac- $\alpha$ -tocopherol; substituted the animal protein in the diet), (ii) Group 2 received 3 bottles of fermented whey beverage per week for 8 weeks (each bottle contained 220 ml of 15 g WPC: substituted the animal protein in the diet), (iii) Group 3 received three capsules of vitamin E per week in the form of all-rac- $\alpha$ -tocopherol for 8 weeks (600 IU vitamin E), and (iv) Group 4 as the control group received no intervention (receiving usual care including drug assessment, routine biochemical and laboratory assessments, nutrition consult, and preventing some complications such as anemia by routine controls).

Randomization was done using random allocation software to randomize the patients by blocked randomization with a fixed block size of 4. Ramak dairy company processed the beverages in prepackaged bottles numbered for each patient based on the randomization sequence (7). For assessing the patients' compliance, they were visited on each dialysis session. They were asked to drink the beverages with their meals after the dialysis sessions or at home (for those who were dialyzed twice per week). The same was done for those receiving the vitamin E capsules. Patients' quality of life was assessed at the beginning and at the end of the study phase. SF-12 questionnaire was used

for assessing quality of life in the participants. The validated Iranian version of SF-12 questionnaire was used to assess health-related quality of life in these patients (8). SF-12 questionnaire was the short form of SF-36 questionnaire that was shorter and included only one third of the SF-36 questionnaire. This questionnaire contained 12 items (questions) and 8 scales including physical functioning (PF), role limitations due to physical health (RP), general health (GH), bodily pain (BP), social functioning (SF), vitality (VT), mental health (MH) and role limitation due to emotional health (RE). Finally, these scales were computed into two summary components of PCS-12 and MCS-12 (9, 10). The main researcher informed the patients about all questions of SF-12. Data was analyzed using SPSS software (Statistical package for the Social Sciences, version 16, SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the normality of distribution.

Paired-t test was used for analyzing changes in each group during the treatment phase for the normally distributed data, and for the skewed data Wilcoxon's signed-rank test was used. We compared the changes in study parameters among the 4 groups using an analysis of covariance (ANCOVA) model with treatment as the main effect and the baseline parameters as covariates. Bonferroni post-hoc test was done to examine pairwise differences between the groups to adequately adjust for multiple comparisons. A *p* value of <0.05 was considered statistically significant.

## Results

Demographic characteristics and causes of renal disease are presented in Table 1. Regarding the patients' quality of life, after evaluating the changes of bodily pain scores in each group during the study period, it was demonstrated that bodily pain score improved significantly in the group receiving vitamin E ( $p=0.003$ ) (Table 2).

A significant decline was visible for the quality of life in terms of bodily pain in the control group during the two months period ( $p<0.001$ ) (Table 3). An improvement that was seen during the two-month period in groups receiving whey beverage fortified with vitamin E and whey beverage alone was not significant (Table 4). There were no significant differences in terms of changes in bodily pain scores between all groups (Table 5). Regarding the results of RP index in the studied groups during the 2 months period, a significant improvement was noted in consumers receiving whey beverage fortified with vitamin E ( $p=0.008$ ) (Table 4) and the increase for whey beverage group was significant ( $p=0.013$ ) (Table 5), even the change in other groups during this period was not statistically significant (Tables 2 and 3). The comparison between the four groups showed no significant difference (Table 6). Considering the social functioning scores, rating changes showed a significant improvement in whey beverage group ( $p=0.012$ ) (Table 4), while a significant improvement was observed in the group receiving vitamin E during the two month period ( $p=0.007$ ), too (Table 2).

**Table 1:** Demographic characteristics of the study population

Parameters	Group Whey protein fortified with vitamin E (n=23)	Whey protein (n=23)	Vitamin E (n=23)	Control (n=23)	<i>p</i> -value
Year (age)	56±9.1	57±9.6	58±8.7	55±6.5	-
Gender: Male (Female)	14 (9)	10 (13)	13 (10)	10 (13)	-
Underlying cause of Diabetes	8 (34.8%)	9 (39.1%)	10 (43.5%)	10 (43.5%)	-
Hypertension	9 (39.1%)	8 (34.8%)	10 (43.5%)	7 (30.4%)	-
Kidney stone	0	0	0	1 (4.3)	-
Cyst	0	3 (13%)	0	1 (4.3%)	-
Pyelonephritis	1 (4.3%)	0	1 (4.3%)	0	-
Glomerulonephritis	0	2 (8.7)	0	0	-
Lupus	1 (4.3%)	0	0	0	-
Other causes	4 (17.4%)	1 (4.3%)	2 (8.7%)	4 (17.4%)	-
Unknown causes	0	0	0	0	-
BUN* (mmol/l)	122.28±43.63	120.25±3.14	112.23±48.77	122.52±13.87	0.741
Creatinine* (mg/dl)	8.7±2.3	8.3±2.1	7.9±0.3	8.1±3.1	0.796
KT/V*	1.0±25.29	1.0±23.24	1.0±33.27	1.0±34.24	0.074
Weight (Kg)*	61.12±9.61	64.13±83.1	61.12±13.4	60.11±76.89	0.653
Body mass (kg/m <sup>2</sup> )* index	22.3±82.85	24.4±37.17	22.4±61.4	22.3±43.52	0.336

\*Mean±standard deviation for comparison of baseline between four groups, ANOVA was used for normal data. #to compare baseline mean between four groups, the Kruskal-Wallis test was used for data with non-normal distribution. BUN: Blood Urea Nitrogen; KT/V: Clearance Time Volume

**Table 2:** The comparison of quality of life indicators (SF-12) in group using vitamin E before and after the intervention

Indicators	Groups	Before intervention	After intervention	* <i>p</i> -value
		Mean±SD	Mean±SD	
Physical functioning		32.60±32.30	45.40±30.51	0.166
Bodily pain		54.35±26.81	73.86±29.35	*0.003
Role limitations due to physical health		39.13±23.63	42.50±22.34	0.27
General health		39.13±22.39	47.73±20.28	0.134
Vitality		45.65±27.85	51.14±23.75	0.31
Social functioning		42.39±12.19	52.27±15.25	*0.007
Role limitation due to emotional health		54.35±23.42	57.95±26.03	0.33
Mental health		54.35±23.41	57.38±14.26	0.43

\*Significant for *p*-value<0.05 (Comparison of base and the two-month parameters by Paired t-test for normal data and Wilcoxon signed rank test for data with non-normal distribution (All the data had non-normal distribution, logarithmic correction only was conducted for analysis of parametric test).

**Table 3:** The comparison of quality of life indicators (SF-12) in control group before and after the intervention

Indicators	Groups	Before intervention	After intervention	* <i>p</i> -value
		Mean±SD	Mean±SD	
Physical functioning		32.60±32.30	45.4±30.51	0.166
Bodily pain		54.35±26.81	73.86±29.35	*0.003
Role limitations due to physical health		39.13±23.63	42.05±22.34	0.27
General health		39.13±22.39	47.73±20.28	0.134
Vitality		45.65±27.85	51.14±23.75	0.31
Social functioning		42.39±19.12	52.27±15.25	*0.007
Role limitation due to emotional health		54.35±23.42	57.95±26.03	0.33
Mental health		54.35±23.41	57.38±14.26	0.43

\*Significant for *p*-value<0.05 (Comparison of base and two-month parameters by Paired t-test for normal data and Wilcoxon signed rank test for data with non-normal distribution (All the data had non-normal distribution, logarithmic correction only was conducted for analysis of parametric test).

The improvement in quality of life in the group receiving whey beverage fortified with vitamin E and the decline in the control group in the social functioning score were not statistically significant (Tables 4). A significant difference was noted between groups during intervention in terms of social functioning score (*p*=0.007), (Table 5). The differences among groups regarding social functioning score are related to the differences between whey beverage group with control group and vitamin E group with control group (Table 5).

After analyzing the scores of PF, GH, MH, VT and RE aspects, comparison of preliminary and final results demonstrated that the changes were not significant in none of the groups during the study (Tables 2-4).

In the field of intended aspects, there was no significant difference between the changes of these aspects between groups (Table 5).

## Discussion

Regarding the findings of this study according

to the questionnaire, a statistically significant improvement was seen for RP between whey beverage fortified with vitamin E, whey beverage groups that these changes were not different from other groups. While an improvement for BP aspect in the vitamin E group and a decline in control group were seen. However, in whey beverage groups, the beverages increased BP scores, but this was not statistically significant. It can be stated that the consumed beverages prevented BP reduction in the studied groups. But the changes in physical aspects of quality of life among the groups were not statistically significant that may be due to the short duration of study and also the small sample size.

The results of mental health variables for quality of life questionnaire including VT, RE, MH, and SF showed that only for SF aspect, significant improvements were visible for whey beverage and vitamin E groups. While the decline seen in the control group and the enhancement in the whey beverage fortified with vitamin E group were not statistically significant. But it may be proposed

**Table 4:** The comparison of quality of life indicators (SF-12) in control group before and after the intervention and The comparison of quality of life indicators (SF-12) in group using whey beverage fortified with vitamin E before and after the intervention

Groups	Variables	Before intervention	After intervention	*p-value
		Mean±SD	Mean±SD	
Group 1	Physical functioning	45.60±30.70	42.05±33.97	0.9
	Bodily pain	57.95±19.49	70.45±25.16	0.061
	Role limitations due to physical health	30.43±21.26	43.18±15.70	*0.008
	General health	36.90±16.60	40.90±21.19	0.357
	Vitality	45.60±16.26	48.86±18.05	0.285
	Social functioning	48.9±15.95	52.27±13.16	0.157
	Role limitation due to emotional health	54.35±23.41	50±13.36	0.635
	Mental health	53.26±22.99	60.79±11.76	0.063
Group 2	Physical functioning	40.22±25.82	38.10±41.54	0.67
	Bodily pain	55.43±23.78	67.86±32.70	0.199
	Role limitations due to physical health	33.70±22.11	52.38±23.59	*0.013
	General health	32.60±19.12	45.24±23.20	0.059
	Vitality	48.90±19.18	52.38±30.52	0.949
	Social functioning	44.57±19.8	59.52±14.70	*0.012
	Role limitation due to emotional health	61.90±23.68	61.90±26.94	0.793
	Mental health	61.95±23.68	61.31±19.73	0.578

Group 1: whey beverage fortified with vitamin E; Group 2: whey beverage; †Significant for p-value<0.05 (Comparison of base and two-month parameters by Paired t-test for normal data and Wilcoxon signed rank test for data with non-normal distribution (All the data had non-normal distribution, logarithmic correction only was conducted for analysis of parametric test))

**Table 5:** Comparison of quality of life aspects based on SF-12 questionnaire during two-month period

Different aspects	#Between groups P	*P comparison of the groups
Physical functioning	0.177	Not significant
Bodily pain	0.090	Not significant
Role limitations due to physical health	0.055	Not significant
General health	0.169	Not significant
Vitality	0.412	Not significant
Social functioning	0.007	Groups 2:4: 0.002 <sup>‡</sup> Groups 3:4: 0.004
Role limitation due to emotional health	0.816	Not significant
Mental health	0.412	Not significant

#In order to compare groups, ANOVA test and Kruskal-Wallis test were used for normal data and data with non-normal distribution respectively (All the data had non-normal distribution, logarithmic correction only was conducted for analysis of parametric test). \*Obtained data from Bonferroni post-hoc (For detection of difference between two groups). ‡ Group 1: Whey beverage fortified with vitamin E, Group 2: Whey beverage, Group 3: Vitamin E, Group 4: Control.

that whey beverage fortified with vitamin E could prevent the drop in this aspect of quality of life in hemodialysis patients. On the other hand, SF changes were significantly different among groups, that may be due to differences between vitamin E and the control and between the whey beverage and the control groups.

For VT and GH, increases were noted in the experimental groups and decreases in the control group, but these were not statistically significant during two months period. We can assert that the dose of vitamin or whey vitamin ingested were

not enough to make more improvements in these variables and only can prevent their reductions or reduction in patients' quality of life. So, it may possible to achieve better results in studies with higher doses or longer durations.

Since there is no similar study that has been done in this regard, the present study is unique in terms of evaluating the effects of whey protein and vitamin E on hemodialysis patients' quality of life based on the SF-12 questionnaire.

Dialysis is associated with a drop in quality of life due to several reasons such as anemia and

fatigue. Various mental, social, and economical stresses lead to a drop in patient's quality of life as well (11). Quality of life in patients was affected by different factors which is associated with symptoms such as increased dependence on others, low self-esteem, feeling of loneliness, etc (12). In this study, some evidences of improved quality of life were observed in terms of social functioning in whey beverage and vitamin E groups. These findings have been aligned with results of a case report study in a cancer patient treated with whey protein and testosterone, while, consumption of whey protein helped to improvement of the patients' quality of life during the chemotherapy in three periods of 21 days (based on a quality of life questionnaire) (13). In assessment of the use of high-calorie diets containing whey protein in patients with respiratory congestion, an improvement was reported in quality of life of whey protein consumers in terms of mental health (14). Moreover, in another study evaluating the effect of vitamins C and E supplements in patients undergoing hemodialysis with restless leg syndrome (RLS), antioxidants helped to improve the quality of life in these patients (4).

Whey protein was previously shown to be effective in improving the quality of life (2). This protein plays an important role in increasing the tryptophan and serotonin levels in brain (as an anti-depressant and anti-stress agent) and helps to improve mental health because of its tryptophan content as an important amino acid (3). This effect of whey protein, justifies the results of whey protein groups.

Serotonin as a brain peptide that has abundant receptors in the central nervous system, regulates many physiological, psychological, and behavioral functions (such as behavior, mood, sleep, appetite, and sexual function). Therefore, any increase in serotonin helps to improve people's mental status (3). Alpha-lac to albumin that is one the important components of whey protein, also is a rich source of tryptophan and is effective in increasing the levels of this amino acid in blood and hence increasing brain serotonin (3). In addition, vitamin E is associated with increasing levels of dopamine (through activation of tyrosine hydroxylase) that can be effective in improving the mental status (4). As we know, dopamine as a brain neurotransmitter, improves social functioning and self-confidence (5). In other words, vitamin E supplement, while reducing the levels of malondialdehyde as an oxidative marker can help to improve the quality of life, too (6). Thus, the observed effect in improving the quality of life in social functioning in our group receiving vitamin E is rationally justifiable based on the mentioned

effects.

Whey protein and vitamin E were shown to reduce oxidative stress and can affect some neurotransmitters in brain such as serotonin

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### Conflict of Interest

None declared.

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