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Study of the effect of nutrition interventions on the recovery of fatigue: a placebo-controlled, randomized, double-blinded cross-over trial.

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Abstract

Objectives: To investigate the effects of multivital supplement on physical overtraining young males who were on ordinary Chinese diet, and the suitable time of using mulvital on young males to dispel fatigue.

Methods: 240 young male volunteers after thousand meters running were randomly divided into group A (mulvital was first given, then placebo) and group B (placebo was first given, then mulvital). Medical history, physical examination, the Fatigue Assessment Scale, as well as hormone axises and cellular immune parameters were evaluated after high-intensity training program.

Results: The recovery of pituitary-adrenal axis and immune system of the mulvital group were significantly better than the placebo group (P<0.05). There was no significant difference of the pituitary-gonadal axis and fatigue scale score between two groups were observed. The pituitary-thyroid axis and symptom check list score of the medication group were significantly better than the placebo group after the intervention using the mulvital (P<0.05).

Conclusions: Our research confirmed that the use of mulvital is beneficial for the recovery of pituitary-adrenal function, pituitary thyroid function, immune function, and psychological status. The earlier application of mulvital is better for the recovery.

Keywords: Mulvital, Endocrine Hormone, Immune Indexes, Nutrition interventions.

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Introduction

With the faster pace of life, overtraining has gradually become a major conundrum in most young people. Overtraining syndrome, which is presented as persistent performance incompetence, high fatigue ratings, altered mood state, increased risk of infections, and reproductive dysfunction, could be caused by both physical and psychological stresses. [1] Other researches have already shown that high-intensity would cause immunosuppression and inflammatory reaction. [2,3] Moreover, it has been reported that overtraining could affect the balance of redox system, which leaded to production of oxidative stress [4]. Besides, overtraining could also decrease the adrenal sensitivity to ACTH (cortisol release) and increase the pituitary sensitivity to GHRH (GH release), which in turn cause a counter-regulatory shift to a more serious endocrine imbalance [5].

The American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine recommended that the use of vitamin and mineral supplement in recommended daily intake was benefit for those people who were at increased risk of nutrient depletion [6]. However the effect and suitable timing of mulvital supplement on young males was still unknown. In this study, we have performed a placebo-controlled, randomized, double-blinded cross-over trial to investigate the effects of mulvital supplement on physical overtraining young males who were on ordinary Chinese diet, and the suitable time of using mulvital on young males to dispel fatigue.

Material and Method

Subjects

Two hundred and forty young volunteers, who undertook after thousand meters running exercise and were on ordinary Chinese diet, were enrolled in this study. All subjects were male; the age was from 18 to 24 years with average of 20.11 ± 2.24 years old. All subjects were screened for contraindicating health problems or pharmaceutical use and were cleared for unrestricted physical activity by a physician. The experimental protocol was approved by the Chinese PLA General Hospital's Ethical Committee, and all subjects gave written informed consent.

Drug intervention

Mulvital and placebo were provided by Nutrition Department of the Chinese PLA General Hospital. Every mulvital pill consisted of vitamin D 2.5 μg, vitamin E 8.7 mg, vitamin B1 0.5 mg, vitamin B2 0.5 mg, vitamin B6 0.5 mg, vitamin C 150 mg, folate μg, calcium 200 mg, iron 3 mg, zinc 3 mg, and selenium 12.5 mg. The pills were taken two times a day, in the morning and in the evening, 2 pills for each time. The process was supervised by experimenter to ensure the medication rate.

Experimental design

Medical history, physical examination, Symptom Checklist-90 (SCL-90), the Fatigue Assessment Scale, the blood and urine sample were detected after high-intensity training program. All subjects were then randomly divided into two groups (A and B), and double blind method was performed. Group A were given mulvital, while group B received placebo for 1 week. All inspection items were performed after the first week. Then, mulvital and placebo were cross over in group A and group B in the second week. Inspection item were performed again after that.

Examination

Physical examination (height, weight, blood pressure, heart rate) was performed.

Blood samples were collected from subjects under fasting and proportion of $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, B cell, NK cell subsets were determined by flow cytometer (Beckman Coulter, US). At 8:00 a.m., 15 mL of blood was drawn from the antecubital vein of subjects after a 12-hour fast and collected into sterile vacuum tubes. Once blood was collected, these tubes were immediately placed on ice and later centrifuged at 3000 rpm at room temperature for 10 min, and then the sera were transferred into cryo-freeze tubes and stored frozen at -80 Celsius degree. Levels of Adrenocorticotropin (ACTH), Testosterone (T), Cortisol (F), Thyrotropic hormone (TSH), 3,5,3-triiiodothyronine (TT3), Thyroxine (TT4), Free 3,5,3-triiiodothyronine (FT3), and Free Thyroxine (FT4) were determined in plasma by IMMULITE2000. At 9:00 a.m. on the same day, urine samples were also collected from subjects after a 12-hout fast. Urine samples were evaluated for urine free cortisol (UFC), Luteinizing hormone (LH) and Estradiol (E2).

We used SCL-90 to measure psychological symptoms. The Chinese version of SCL-90 has been validated and widely used in China. Each of the items is rated on a five-point scale of distress ranging from ‘‘not at all’’ (1) to ‘‘extremely’’ (5). The nine primary symptom dimensions were labelled as: somatization, obsessive-compulsive behaviour, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.

The questionnaire of Fatigue Assessment Scale consisted of 25 items, 5 factors scale, with 1-5 points. Higher scores indicated the degree of fatigue was more obvious.

Statistical analysis

All statistical analyses were performed by using SPSS (version 13.0; SPSS Inc., Chicago, IL, USA). All data were presented as means ± SD, and for all tests, the statistical significance was set at $P<0.05$. Compared t-test and ANOVA were used to determine whether there were significant differences.

Results

Comparison of general condition before and after mulvital intervention

As shown in Table 1 and 2, heart rate of the two groups after the first week, second week were significantly slower compared with the heart rate post exercise. Moreover, in ANOVA test, sequence of P value was 0.019, which indicated that the heart rate recovery was faster in the cases who received mulvital intervention earlier (Group A).

Table 1. *Comparison of general condition, adrenocortical function, gonadal function, thyroid function, immune function, fatigue assessment scale and symptom checklist-90 between the two groups before and after medical intervention.*

	Group A			Group B		
	After training	Mulvital (first week)	Placebo (second week)	After training	Placebo (first week)	Mulvital (second week)
Height (cm)	171.91 ± 4.80	171.91 ± 4.80	172.51 ± 4.67	172.62 ± 4.85	172.03 ± 4.32	172.57 ± 6.05
Weight (kg)	63.87 ± 6.56	63.46 ± 6.66	65.69 ± 10.96$^{*\Delta}$	63.94 ± 7.51	63.85 ± 7.36	64.49 ± 9.19
Systolic blood pressure (mmHg)	109.53 ± 11.25	112.30 ± 8.11	114.75 ± 5.57*	110.52 ± 10.83	113.83 ± 7.87	114.75 ± 6.26*
Diastolic blood pressure (mmHg)	71.91 ± 9.10	73.73 ± 6.42	74.75 ± 6.17*	72.87 ± 8.14	73.59 ± 6.97	74.9 5 ± 6.26*
Heart rate (bpm)	75.43 ± 9.62	70.03 ± 5.38*	71.95 ± 5.72*	75.96 ± 7.26	71.13 ± 3.75*	73.25 ± 5.37*
ACTH (pmol/L)	6.30 ± 3.28	7.09 ± 5.43*	8.67 ± 4.20 $^{*\Delta}$	5.95 ± 3.48	6.42 ± 3.39	7.36 ± 4.47$^{*\Delta}$
F (nmol/L)	302.05 ± 83.32	359.56 ± 101.7*	379.7 ± 112.77$^{*\Delta}$	263.39 ± 80.79	287.62 ± 73.21*	363.32 ± 70.08$^{*\Delta}$

UFC (nmol/24h)	381.75 ± 110.93	426.59 ± 109.93*	438.63 ± 0.95*	365.62 ± 120.80	390.62 ± 105.82*	421.38 ± 0.74*Δ
LH (mIU/L)	3.37 ± 1.94	3.55 ± 1.74	3.88 ± 1.55*	3.52 ± 3.77	3.79 ± 3.41	4.03 ± 3.50*
T (nmol/L)	19.90 ± 5.98	21.26 ± 5.60*	21.00 ± 5.63*	18.65 ± 5.87	21.59 ± 5.10*	20.16 ± 5.21*Δ
E2 (pmol/L)	115.8 ± 78.4	156.3 ± 55.6*	130.81 ± 37.00*Δ	108.24 ± 39.02	151.69 ± 34.91*	123.57 ± 38.58*Δ
TSH (mU/L)	2.29 ± 1.07	2.36 ± 1.15	2.13 ± 1.19*	2.24 ± 1.56	2.72 ± 3.51	2.65 ± 1.58
TT3 (nmol/L)	2.55 ± 0.41	2.29 ± 0.48*	2.05 ± 0.41 *Δ	2.89 ± 1.77	2.17 ± 0.33*	2.06 ± 0.27 *
TT4 (nmol/L)	95.75 ± 17.49	100.96 ± 21.46*	99.85 ± 16.70*Δ	93.74 ± 13.44	99.36 ± 15.44*	98.50 ± 14.14*Δ
FT3 (pmol/L)	5.76 ± 0.98	5.70 ± 0.59*	5.66 ± 0.69	6.05 ± 4.19	5.90 ± 0.43*	5.55 ± 0.43
FT4 (pmol/L)	17.46 ± 2.71	16.15 ± 2.14*	15.59 ± 1.93*Δ	16.69 ± 1.96	15.64 ± 1.70*	15.37 ± 1.95*Δ
CD3+	0.58 ± 0.10	0.56 ± 0.10*	0.61 ± 0.09*Δ	0.56 ± 0.10	0.52 ± 0.10*	0.59 ± 0.09*Δ
CD4+	0.26 ± 0.06	0.25 ± 0.06*	0.29 ± 0.06*Δ	0.25 ± 0.60	0.24 ± 0.06	0.27 ± 0.07*Δ
CD8+	0.28 ± 0.08	0.28 ± 0.08	0.28 ± 0.08	0.28 ± 0.09	0.26 ± 0.09	0.28 ± 0.08Δ
CD4+/CD8+	1.02 ± 0.40	0.99 ± 0.39	1.11 ± 0.40*Δ	1.00 ± 0.44	1.03 ± 0.46	1.06 ± 0.42
B	0.11 ± 0.04	0.12 ± 0.06	0.10 ± 0.03	0.11 ± 0.04	0.11 ± 0.04	0.11 ± 0.04
NK	0.30 ± 0.11	0.28 ± 0.10*	0.24 ± 0.10*Δ	0.31 ± 0.12	0.32 ± 0.15	0.25 ± 0.09*Δ
Sleepiness score	9.53 ± 3.41	8.52 ± 3.64*	7.56 ± 2.88*Δ	9.09 ± 3.64	7.89 ± 3.54*	7.19 ± 2.87*Δ
Emotional anxiety score	7.97 ± 3.14	7.63 ± 3.63*	6.64 ± 2.648*Δ	7.99 ± 2.59	6.82 ± 2.69	6.12 ± 2.078*Δ
Unpleasant fraction	8.04 ± 3.24	7.36 ± 3.12	6.59 ± 2.63*	8.00 ± 3.08	6.96 ± 2.55	6.44 ± 2.27*Δ
Burnout score	8.95 ± 2.93	8.68 ± 3.17*	7.93 ± 2.46*Δ	9.56 ± 2.84	7.94 ± 2.92	7.55 ± 2.41*
Visual fatigue fraction	8.20 ± 3.47	7.65 ± 3.45*	6.85 ± 2.83*Δ	8.45 ± 3.41	7.36 ± 3.44	6.23 ± 2.42*
Total score	127.57 ± 33.01	116.65 ± 30.37*	106.73 ± 26.05*Δ	134.77 ± 41.57	126.42 ± 43.82*	118.38 ± 41.42*Δ
Somatic score	1.48 ± 0.50	1.34 ± 0.43*	1.23 ± 0.394*Δ	1.63 ± 0.55	1.42 ± 0.52*	1.41 ± 0.54*Δ
Forced score	1.48 ± 0.50	1.34 ± 0.43*	1.23 ± 0.39*Δ	1.60 ± 0.53	1.49 ± 0.54*	1.41 ± 0.54*Δ
Interpersonal sensitivity score	1.51 ± 0.5	1.37 ± 0.49*	1.22 ± 0.41*Δ	1.62 ± 0.59	1.46 ± 0.59*	1.37 ± 0.55*Δ
Depression score	1.39 ± 0.45	1.27 ± 0.37*	1.19 ± 0.36*Δ	1.45 ± 0.52	1.37 ± 0.53	1.31 ± 0.53*Δ
Anxiety score	1.29 ± 0.36	1.19 ± 0.30*	1.13 ± 0.27	1.36 ± 0.49	1.33 ± 0.52*	1.26 ± 0.47*Δ
Hostility score	1.54 ± 0.54	1.43 ± 0.48*	1.19 ± 0.30*Δ	1.65 ± 0.67	1.54 ± 0.67*	1.39 ± 0.58*Δ
Terror score	1.17 ± 0.27	1.12 ± 0.24*	1.07 ± 0.20*Δ	1.24 ± 0.40	1.18 ± 0.38*	1.18 ± 0.41*Δ
Paranoid score	1.42 ± 0.52	1.29 ± 0.45*	1.20 ± 0.45*Δ	1.52 ± 0.56	1.42 ± 0.60*	1.28 ± 0.50*Δ
Psychotic score	1.36 ± 0.39	1.24 ± 0.37*	1.12 ± 0.31*Δ	1.43 ± 0.52	1.36 ± 0.52*	1.26 ± 0.47*Δ
Other	1.40 ± 0.40	1.34 ± 0.37*	1.19 ± 0.23*Δ	1.45 ± 0.44	1.39 ± 0.47	1.26 ± 0.44*

*Compare with after training subgroup, P<0.05; ΔCompared with first week, P<0.05.

Table 2. *Physical examination analyzed by ANOVA test.*

		Cross	
		F value	**P value**
Height	Group A *vs.* Group B	1.17	0.2808
	Mulvital *vs.* placebo	1.6	0.2069
Weight	Group A *vs.* Group B	0.13	0.7238
	Mulvital *vs.* placebo	2.09	0.1502
Systolic blood pressure	Group A *vs.* Group B	1.32	0.2509
	Mulvital *vs.* placebo	1.57	0.2113
Diastolic blood pressure	Group A *vs.* Group B	0	0.9734
	Mulvital *vs.* placebo	0.08	0.7794
Heart rate	Group A *vs.* Group B	5.53	0.0195

	Mulvital *vs.* placebo	0	0.96

Comparison of adrenocortical function between two groups before and after mulvital intervention

As shown in Table 1 and 3, P value of ANOVA test for ACTH between different medication time was 0.3532, between mulvital group and placebo group was 0.0001, which meant the recovery of ACTH in mulvital group was better than placebo group, but the different intervention time had no effect on the results. ANOVA test for F showed that, the recovery in mulvital group was better than placebo group (P=0.042), and earlier use of mulvital had also better effect than later use (P=0.000). Analysis of UFC had similar results as ACTH. Mulvital group was better than placebo group, but group A had no difference compared with group B. All these results showed that the recovery of adrenocortical function in mulvital group was significantly better than placebo group. Moreover, earlier use of mulvital had better effect than the later use.

Table 3. *Adrenocortical function, gonadal function, thyroid function, immune function analyzed by ANOVA test.*

		Cross	
		F value	**P value**
ACTH	Group A *vs.* Group B	15.24	0.3532
	Mulvital *vs.* placebo	0.87	0.0001
F	Group A *vs.* Group B	67.16	0
	Mulvital *vs.* placebo	4.22	0.0412
UFC	Group A *vs.* Group B	3.21	0.0745
	Mulvital *vs.* placebo	10.9	0.0012
LH	Group A *vs.* Group B	1	0.319
	Mulvital *vs.* placebo	0.97	0.3246
T	Group A *vs.* Group B	0.12	0.7257
	Mulvital *vs.* placebo	3.45	0.0648
E2	Group A *vs.* Group B	1.06	0.3054
	Mulvital *vs.* placebo	0.99	0.3215
FT3	Group A *vs.* Group B	0.17	0.6764
	Mulvital *vs.* placebo	1.56	0.2134
FT4	Group A *vs.* Group B	3.61	0.0587
	Mulvital *vs.* placebo	6.52	0.0114
TSH	Group A *vs.* Group B	0.94	0.3338
	Mulvital *vs.* placebo	1.24	0.2661
TT3	Group A *vs.* Group B	1.43	0.2334
	Mulvital *vs.* placebo	8.63	0.0037
TT4	Group A *vs.* Group B	0.45	0.503
	Mulvital *vs.* placebo	0.09	0.7646
CD3	Group A *vs.* Group B	5.77	0.0171
	Mulvital *vs.* placebo	5.67	0.0185
CD4	Group A *vs.* Group B	5.56	0.0192
	Mulvital *vs.* placebo	0.11	0.7433
CD8	Group A *vs.* Group B	1.03	0.3109
	Mulvital *vs.* placebo	40.39	0
CD4/CD8	Group A *vs.* Group B	0	0.9825
	Mulvital *vs.* placebo	6.47	0.0119
B	Group A *vs.* Group B	0.19	0.6619
	Mulvital *vs.* placebo	1	0.3189
NK	Group A *vs.* Group B	4.15	0.0428
	Mulvital *vs.* placebo	11.35	0.001

Comparison of gonadal function between two groups before and after mulvital intervention

There were no difference of LH, T and E2 between mulvital group and placebo group. (P=0.3246, 0.0648, 0.3215) (Table 1 and 3) The different intervention time had also no effect on the results. (P=0.3190, 0.7257, 0.3054) It meant that mulvital intervention had no effect on the recovery of pituitary-gonadal function.

Comparison of thyroid function between two groups before and after mulvital intervention

There were no differences of TSH and TT4 between mulvital group and placebo group or group A and group B (Table 1 and 3). However, the recovery of TT3 and FT4 was significantly better in mulvital group than placebo group. But the order of the drug intake had no influence on the results. The recovery of thyroid function of mulvital was better than placebo group in total and he different intervention time had also no effect on the final results, which meant mulvital was beneficial to pituitary thyroid function's recovery.

Comparison of immune function between the two groups before and after the mulvital intervention

As shown in Table 1 and 3, P value of ANOVA test for $CD3^+$ between different medication times was 0.0171, between different treatment was 0.0185, which meant the recovery of $CD3^+$ in mulvital group was better than placebo group, and the earlier use of mulvital had also better effect than the later use. The recovery of $CD8^+$, $CD4^+/CD8^+$ and NK cells in mulvital was also better than placebo group. However there was no difference of the B lymphocyte recovery between the two groups. These results showed that mulvital treatment was beneficial to the recovery of immune function after high-intensity training.

Comparison of Fatigue Assessment Scale between two groups before and after mulvital intervention

Emotional anxiety score and visual fatigue fraction were significantly lower in mulvital group than placebo group. Early use of mulvital has better effect on visual fatigue fraction than later use. There were no significant differences of sleepiness score, unpleasant fraction and burnout score between the groups (Table 1 and 4).

Table 4. *Fatigue Assessment Scale and psychological assessment cross design analyzed by ANOVA test.*

		Cross	
		F value	**P value**
Sleepiness score	Group A *vs.* Group B	1.72	0.1911
	Mulvital *vs.* placebo	0.76	0.3853
Emotional anxiety score	Group A *vs.* Group B	1.52	0.2197
	Mulvital *vs.* placebo	3.95	0.0481
Unpleasant fraction	Group A *vs.* Group B	0.87	0.3528
	Mulvital *vs.* placebo	0.8	0.3718
Burnout score	Group A *vs.* Group B	2.99	0.0853
	Mulvital *vs.* placebo	2	0.1595
Visual fatigue fraction	Group A *vs.* Group B	1.45	0.2303
	Mulvital *vs.* placebo	0.87	0.3513
Total score	Group A *vs.* Group B	5.6	0.8915
	Mulvital *vs.* placebo	11.25	0.0187
Somatic score	Group A *vs.* Group B	3.51	0.9148
	Mulvital *vs.* placebo	7.13	0.0622
Forced score	Group A *vs.* Group B	0.01	0.9315
	Mulvital *vs.* placebo	7.21	0.0078
Interpersonal sensitivity score	Group A *vs.* Group B	3.51	0.3519
	Mulvital *vs.* placebo	7.16	0.0622
Depression score	Group A *vs.* Group B	0	0.9588
	Mulvital *vs.* placebo	3.76	0.0537
Anxiety score	Group A *vs.* Group B	0.94	0.3331
	Mulvital *vs.* placebo	7.67	0.0061
Hostility score	Group A *vs.* Group B	1.62	0.204
	Mulvital *vs.* placebo	5.74	0.0174
terror score	Group A *vs.* Group B	1.18	0.2785
	Mulvital *vs.* placebo	4.11	0.0439
Paranoid score	Group A *vs.* Group B	3.36	0.0679
	Mulvital *vs.* placebo	1.7	0.194
Psychotic score	Group A *vs.* Group B	0.1	0.7539
	Mulvital *vs.* placebo	6.31	0.0127
Other	Group A *vs.* Group B	2.13	0.1455
	Mulvital *vs.* placebo	0.26	0.6075

Comparison of psychological assessment between the two groups before and after the mulvital intervention

The total score of Symptom Checklist-90 (SCL-90) showed that, the symptoms improvement in mulvital group was significantly better than placebo group and the intervention time of use of mulvital had no effect. There was significantly improvement in forced score, anxiety score, hostility score and terror score of mulvital group. (Table 1 and 4)

Discussion

Though the potential mechanism of overtraining syndromes are still unknown, it is well believed that the increase of fatigue and stress have direct effect on human's immune and neuroendocrine systems which could then lead to psychological disorders.[7] With the similar results of previous research, our current study indicated that high-intensity training was associated with the increase stress of organism function and psychological status, such as depression anxiety hostility and so on.[8] However, former researches on multiple vitamins or minerals have not proven their effectiveness on the recovery of fatigue. Moreover, a major part of these studies was performed on professional athletes who might already be adapted to high-intensive training and have specifically prepared adequate diet.[8] In this study, we have investigated the effects of mulvital on immune, neuroendocrine systems and psychological status of young male volunteers, whose diet was provided with enough energy and body weight had not been influenced throughout this study. There was abundance of studies about the consequences of the lack of vitamin. It was reported that dietary insufficiency would lead to immunological dysfunction.[9] Correspondingly, the body's recovery would be prolonged,[10,11] even followed with psychological disorders.[12] Previous studies found that the effect of single nutrients supplement was not obvious, thus comprehensive supplementation of multiple micronutrients aroused scholar's attention.[13] Therefore, the appropriate nutrient supplement, especially Zn^{2+}, Fe^{2+} and Mg^{2+} and other micronutrients, is beneficial for restoration of physical strength.

High-intensity activity caused different degrees of change in internal micronutrients, especially the lack of Zn^{2+}, Fe^{2+} and Mg^{2+}. Therefore, during high-intensity training, through the proper supplement of beneficial micronutrients, especially Zn^{2+}, Fe^{2+} and Mg^{2+}, could promote the fatigue recovery.

Ca^{2+} could reduce the permeability of capillary and cell membranes, activate muscle protein, promote muscle contractions, keep the normal neuromuscular excitability, regulate myocardial contractility, participate in the coagulation process and so on.[14] When Ca^{2+} deficiency happened, muscle was prone to spasm, which would cause muscle

twitching and osteoporosis, affect the coagulation. The relationship between Ca^{2+} and exercise-induced fatigue is becoming a new hot spot of sports medicine, military medicine and worthy of further study.[9] Fe^{2+} is a hematopoietic elements, which functions physiologically mainly as a component of haemoglobin, myoglobin and cytochrome to participate in oxygen transporting and tissue respiration process in vivo. Fe^{2+} plays a key role in the transport of oxygen and electron. After high-intensity training, increased release of Fe^{2+} by sweat and kidney causes negative balance, which leads to the lack of Fe^{2+} in serum and promotes exercise anaemia. Severe Fe^{2+} deficiency causes the reduction of the activity of monoamine oxidase in brain tissue and induces 5-serotonin metabolism disorder, excitatory neurotransmitter accumulation, exercise capacity loss.[15] Zn^{2+} is an essential component of 80 kinds of enzyme or activator in vivo. The zinc containing carbonic anhydrase, lactate dehydrogenase and insulin are associated with energy metabolism enzymes and hormones. The lack of Zn^{2+} directly affects the exercise ability. Zn^{2+} plays an important role on growth development, cell replication, tissue repair and so on. At the same time, Zn^{2+} also plays a major role in development of cognition, central nervous system, immune system and maintenance of host defence.[16] There are more than 30 kinds of proteins and enzymes contain Cu^{2+} in human body. Cu^{2+} is a necessary component of tyrosinase, ascorbic acid oxidase, and cytochrome oxidase and so on. Cu^{2+} is also involved in hematopoiesis and copper deficiency can cause hypochromic and microcytic anemia, even affect the synthesis of norepinephrine, adrenal cortical hormone and progesterone.[17,18] By scavenging superoxide produced by immune cell metabolism, vitamin E can protect the cell membrane from oxidative damage, maintenance of integrity and stability of cells and organelles, ensure the normal function of cells and immunization and generate a normal immune response.[19] Vitamin B1, B2 and vitamin C contribute to the eliminate of accumulation produced in metabolic. Vitamin C have obvious complement role in against free radical toxicity. It can also protect other biological antioxidants restore them to the reduced form. Therefore, vitamin C plays an important role on the protection of DNA protein and membrane structures against free radicals damage, which are the theoretical basis for vitamin C's antioxidant and anti-fatigue effect.

Based on these studies, mulvital intervention systems were utilized in the present study to provide young volunteer with desirable nutrition to recover from overtraining syndrome caused by high-intensity training.

The results of this study demonstrated that the recovery of pituitary-adrenal function in medication group was obviously better than placebo group and the earlier use of mulvital had better effect than later use. The recovery of thyroid function, immune function, fatigue scale score and psychological recovery was also better in mulvital group. However, there was no difference between the two administration orders.

In conclusion, our research confirmed that the use of mulvital is beneficial for the recovery of pituitary-adrenal function, pituitary thyroid function, immune function, and psychological status.

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