RESEARCH PAPER

Preliminary study of the applications of *Ganoderma lucidum* in chronic fatigue syndrome

Sukanya Soksawatmakhin and Wijit Boonyahotra

Department of Aging and Rehabilitation, School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University, Chiang Rai, Thailand

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Correspondence
Sukanya Soksawatmakhin
Mae Fah Luang University Hospital
38/11-13 Asoke Place Building
Sukhumvit 21
Bangkok 10110
Thailand

E-mail
dr.sukunyasok@gmail.com

Abstract

Chronic fatigue syndrome (CFS), a group of physical and mental disorders with no medical treatment, can disturb quality of life and daily routine of the sufferers. An extract from a traditional herb, *Ganoderma lucidum*, was applied in this preliminary study on fatigue and quality of life of CFS. A total of 50 volunteers were randomly assigned to receive *G. lucidum* extract or placebo. Each volunteer was asked to respond to SF-12 questionnaires for quality of life and score the levels of fatigue and VAS, before and 4, 8 and 12 weeks after the first dose. Serum cortisol level was measured before and 12 weeks after the first dose. Satisfaction and side effects were also evaluated at the end of the study. In comparison to placebo, a significant increase in quality of life ($p=0.005$) with a decrease in VAS scores ($p=0.010$) of those who received *G. lucidum* extracts was observed 4 weeks after the first dose. An increase in serum cortisol was observed in volunteers who took *G. lucidum* extract for 12 weeks, but not placebo. Satisfaction of volunteers with 12-week G. lucidum extract was significantly higher than those with the placebo group ($p<0.001$) while side effects, diarrhea and nausea, from both groups were not significantly different ($p = 0.785$). It is concluded that *G. lucidum* extract could be potentially effective in the treatment of fatigue and improve quality of life in CFS patients.

Introduction

Chronic fatigue syndrome (CFS) is a group of persistent fatigue symptoms of ailments affecting physically and mentally throughout the body of a person. CFS is characterized by long term fatigue and other specific

symptoms, not less than 6 months in adults and 3 months in children or adolescents. Current incidence of CFS has been reported to be over 200 per 100,000 among worldwide population (Guideline 53, 2007). The majority of the incidence was found among those between 25-45 years old. CFS reduces work capability as well as quality of daily life and well-being of the persons whose physical, mental and social functions can be greatly affected. To date, there is no medical cure for CFS, however, symptomatic palliative treatment may be suggested for supportive care (Guideline 53, 2007).

Lingzhi or reishi mushroom (*Ganoderma lucidum,* family Ganodermataceae) is a well-known traditional Chinese herb for over 2000 years and used as health and longevity promotion in various Asian countries. It is a large, dark mushroom with a glossy exterior and a woody texture. As a medicinal mushroom, its powerful effects have been documented in ancient scripts. Polysaccharides, peptidoglycans and triterpenes are three major physiologically active constituents in *G. lucidum* (Boh *et al*, 2007, Benzie and Wachtel-Galor, 2011). Currently, there is a lack of scientific evidence to indicate the effect of an extract of *G. lucidum* in the treatment of patients with CFS.

Previous studies show that *G. lucidum* extract can be effective as hepatoprotective, anti-hypertensive, hypocholesterolemic, anti-histaminic, anti-tumor, anti-angiogenic with protective effect against free radicals and protective effect on cell damage caused by mutagens (Boh *et al*, 2007). A two-way randomized controlled trial which followed up neurasthenia patients for 8 weeks, compared *G. lucidum* with placebo, using Clinical Global Impression (CGI) and Visual Analog Scale (VAS) suggested a lower fatigue level with clinical improvement (Tang *et al*, 2005). It was demonstrated that *G. lucidum* potentially reduced the severity of chronic fatigue in comparison to placebo (Tang *et al*, 2005).

Abnormalities in patients with fatigue syndrome involve immunoneuroendocrine system related to stress mechanism, thus, chronic physical or mental health of these patients affect the functioning of brain cells and hypothalamus-pituitary-adrenal axis, resulting in a reduction of the central nervous system and hypothalamus in the brain, corticotrophin-releasing hormone and cortisol (Silverman *et al*, 2010). *G. lucidum* also possesses immunomodulation activity via cell-mediated immune system by stimulating interleukin-1, tumor necrosis factor-αlpha, T-lymphocytes, natural Killer cell and humoral immune system related to inflammation. *G. lucidum* extract has been effective in patients with asthma (Web *et al*, 2004). It can help relieve the symptoms of asthma by reducing the amount of white blood cells and serum immunoglobulin E of inflammation of the lower respiratory tract and normalizing serum cortisol of patients with allergic asthma. If *G. lucidum* extract can increase serum cortisol levels, it should be able to promote immune system and hypothalamus-pituitary-adrenal axis, and thus healing. Long history of the use of *G. lucidum* in health promotion with increases in evidence on its effect for health, it is interested to investigate on its possibilities to alleviate the symptoms of CFS.

This study was, thus, intended to investigate the effects of *G. lucidum* extract in CFS patients. The level of fatigue and quality of life of CFS patients as well as satisfaction and

side effects extracts of *G. lucidum* were determined.

Methods

This study was approved by an Institutional Ethical Committee before starting (EC 24/2013). All of the participated volunteers were patients who were diagnosed with chronic fatigue syndrome by physicians.

A total number of 50 volunteers were randomly assigned into 2 groups. A control group (25) received a daily dose of placebo, while an intervention group received a daily dose of 2 g, divided into 0.5 g four times a day, of *G. lucidum* extract. Each volunteer was asked to orally intake the assigned dose before meals and bedtime.

Quality of life assessment: A questionnaire Short Form-12 (SF-12), reported to be used in health survey (Ware et al, 1966), was adopted for quality of life assessment of the volunteers before and 4, 8 and 12 weeks after the first dose. The levels of fatigue were measured using visual analogue scale (VAS) by scoring 0 representing fatigueless up to 100 representing fatigue with exhaustion. Each volunteer was asked to give VAS score before and 4, 8 and 12 weeks after the first dose. Satisfaction and side effects were also evaluated by each volunteer at the end of the study by using a questionnaire.

Cortisol measurement: Blood sample (6 ml) of each volunteer was taken and filled in a lithium heparin tube during 8-10 am for measuring serum cortisol level by electrochemi-luminescence immunoassay (ECLIA) following the instructions and the reference standard of Faculty of Medicine Siriraj Hospital, Mahidol University (Thailand). The serum cortisol levels were measured before and 12 weeks after the first dose.

Statistical analysis: Results from before and after treatments within the same person taking were compared by student pair t-test, while those between groups were analyzed by independent t-test. Results from satisfaction evaluation were analyzed by Mann-Whitney U-test while side effects between groups were compared by Chi-square. Statistical significance was determined at a confidence level of 95%.

Results

Figure 1 shows a significant increase trend in the quality of life within the group of the volunteers who received daily *G.lucidum* extract ($p<0.001$). The quality of life within the group of those who received daily placebo for the whole duration of study did not show any significant changes ($p<0.001$). Comparison between groups of the 2 groups, a significant change in quality of life was obtained ($p = 0.016$).

Averaged VAS scores obtained from the volunteers who received daily placebo did not significantly change over the 12 weeks of study ($p<0.01$) while those obtained *G. lucidum* extract showed a significant reduc-tion trend ($p=0.002$), as shown in Figure 2. The overall results of VAS scores among the treatment and control groups were significantly different ($p < 0.001$), suggesting the effect of *G. lucidum* extract on fatigue reduction in CFS volunteers.

Averaged serum cortisol level, measured 12 weeks after the first dose, was shown to be slightly decreased in the placebo group ($p = 0.039$). On the other hands, serum cortisol levels of CFS volunteers who

were treated for 12 weeks with *G. lucidum* extract were increased up to 1.5 times from the baseline measurement ($p < 0.001$) as the results shown in Figure 3. *G. lucidum* extract might have promoted serum cortisol. Further studies are required to investigate its mechanism.

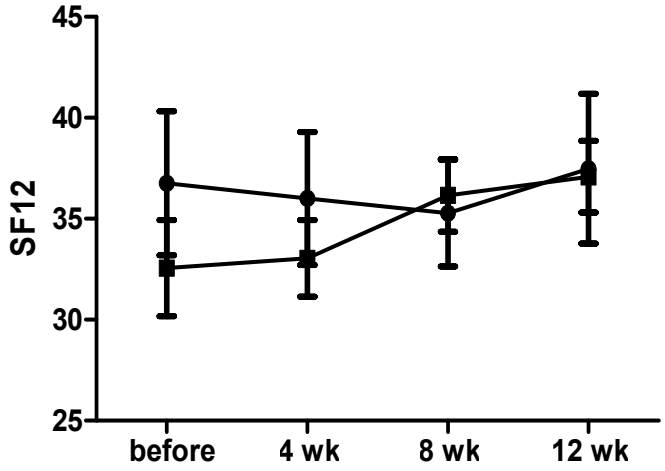

Figure 1 Changes of averaged scores of quality of life assessed by the CFS volunteers receiving daily placebo (●) and *G.lucidum* extract (■) using SF-12 (overall $p = 0.016$ between groups)

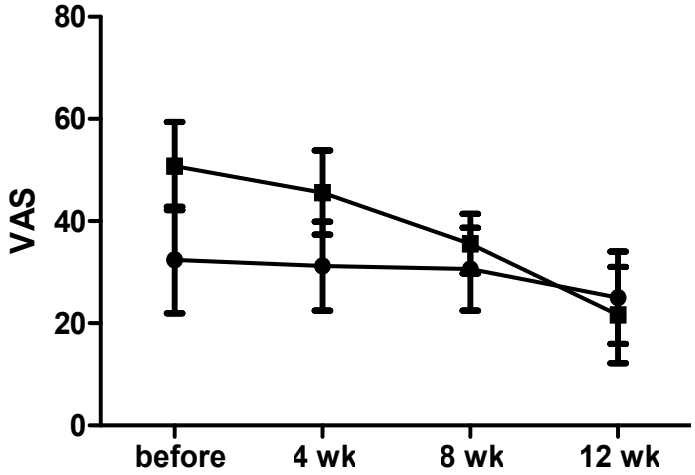

Figure 2 Average VAS scores obtained from CFS volunteers receiving daily placebo (●) and *G. lucidum* extract (■) (overall $p < 0.001$ between groups)

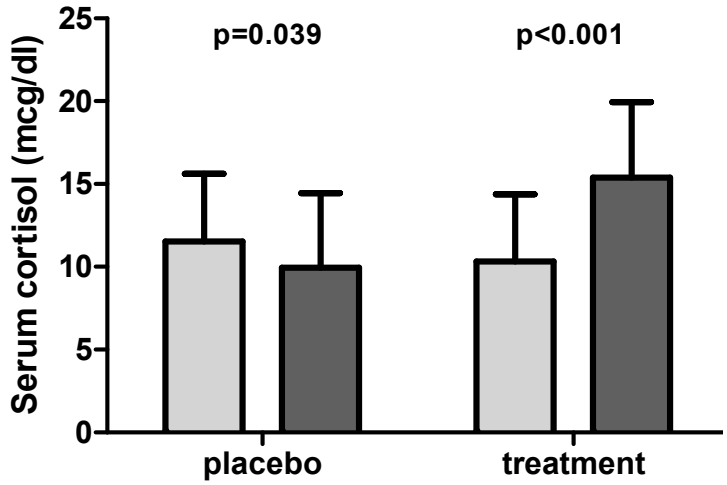

Figure 3 Average serum cortisol levels of CFS volunteers receiving daily placebo and *G. lucidum* extract (treatment) before (light grey columns) and 12 weeks after the first dose (dark grey columns).

Table 1 Satisfaction scores of the volunteers after orally taken the placebo or G.lucidum extracts for 12 weeks

Group	No. volunteers (%) with satisfaction score*					Mean ±SD	Median (Min-Max)	p-value**
	1	2	3	4	5			
Placebo	0	6(24)	15(60)	4(16)	-	2.9±0.6	3(2-4)	<0.001
G.lucidum	0	0	6(24)	17(68)	2(8)	3.8±0.6	4(3-5)	

*satisfaction rating score: 1 = worst, 2 = worse, 3 = not satisfied, 4 = satisfied, 5 = highly satisfied; **Mann-Whitney U test

Table 2 Side effects of the placebo or *G. lucidum* extract reported by CFS volunteers after12 weeks consumption

	Placebo	*G.lucidum*	p-value*
None	18 (72%)	17 (68%)	0.758
Reported Side Effect	7 (28%)	8 (32%)	

*Chi-Square test

Satisfaction scores evaluated by the CFS volunteers who consumed the placebo of *G.lucidum* were shown in Table 1. Overall, the number of CFS volunteers who treated with *G. lucidum* extract for 12 weeks gave higher satisfaction scores than the placebo group. Satisfaction scores on the efficacy of *G. lucidum* extract assessed by 68-70% of the volunteers who consumed the extract were averaged to be 3.84 ± 0.6, with 24% showed non-satisfaction rating. There was no volunteer in *G. lucidum* group who rated worse or less. In comparison to the placebo group with an average overall score of 2.92 and 16% indicated satisfaction. 60% of the placebo group indicated non-

satisfaction and 24% worse. *G. lucidum* extract obtained significantly higher satisfaction rating than the placebo ($p < 0.001$).

Most of the side effects reported by the volunteers from both groups were diarrhea and nausea. There were 28% of the volunteers in the placebo group with side effects while 32% from the *G.lucidum* group, as shown in Table 2. However, this difference was shown to be insignificant ($p = 0.758$).

Conclusion

G. lucidum extracted by aqueous method has been shown in this study to improve quality of life of CFS patients, compared to the placebo which was prepared using the same method. The use of SF-12 questionnaire is found to be appropriate as it is a gold standard method for evaluation of quality of life related to health survey which implies that it is suitable for ailment conditions (Ware *et al*, 1966). VAS score is a subjective measurement of fatigue levels which were defined into numeric levels for better comparison (Lee *et al, 1991).*

At the beginning of the study, i.e. before the first dose, higher average VAS scores (Figure 2) may lower the quality of life (Figure 1) of the treatment group when compared to the control group. This indicates that the data match well and confirm that *G.lucidum* extract reduced fatigue and improved quality of life in CFS volunteers. Results obtained from analysis of serum cortisol levels complemented the previously described data on fatigue reduction and quality of life improvement of *G. lucidum*. Serum cortisol is important as it is an essential index for measuring the improvement of CFS. Serum cortisol after 12 weeks of *G. lucidum* treatment increased to nearly normal level of normal population (Figure 3) which implies that the *G. lucidum* extract could be potentially effective in the treatment of fatigue and improve quality of life in chronic fatigue syndrome patients. Satisfaction on the use of this extract in CFS patients was found to be high while side effects were not severe and not obvious. *G. lucidum* extract is a promising remedy for CSF patients, however, further studies are needed for thorough therapeutic confirmation.

In conclusion, the extracts from *G. lucidum* were effective in the treatment of chronic fatigue syndrome patients by helping reduce fatigue and improve quality of life. The patients were satisfied with the treatment in which side effects were not obvious.

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