Effects of Ganoderma Lucidum on Palliative Cares In Oral Squamous Cell Carcinoma (Oscc) Patients: An Evidence of Excellent Postoperative Support for Cancer Patients

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Abstract: Patients with oral squamous cell carcinoma (OSCC) respond to treatment modalities such as surgery and radiochemotherapy. Clinicians are, however, continuously testing other treatment combinations to see if they can improve the therapeutic results, lessen side effects or increase quality of life in cancer survivors. The aim of this study was to investigate the effectiveness of prescription of Ganoderma lucidum powder and/or extract on OSCC patients undergoing radiochemotherapy treatment following surgical removal of primary cancerous tissues. After surgery, G. lucidum was prescribed in three forms: G. lucidum powder capsule (500 mg/capsule), brushing teeth with dental paste (containing 0.5% extract) and drinking tea (containing 0.2% extract) thrice daily for three months. Then, the status of the OSCC patients was evaluated and compared against a placebo in terms of body weight gain, BMI, conditions of appetite, tolerability to radiotherapy, Karnofsky score and visual analog scale. Also, the levels of blood hemoglobin, urea, creatinine, total protein, albumin, and globulin, AST, ALT, ALP, TNFα, LPO and P53 were measured to assess the effect of this mushroom. Body weight, BMI, and the levels of Hb, creatinine, urea, glucose, AST, ALT, ALP, total protein, albumin, globulin, TNF-α, p53 were also significantly ameliorated in the G. lucidum-prescribed patients, when compared to those of the placebo-prescribed OSCC patients. The appearance of OSCC patients, appetite, Karnofsky score, visual analog scale and tolerability to radiochemotherapy were clinically improved. Our results, thus, support that G. lucidum, which has been used for antitumor effects since ancient times, has potential benefits in the palliative form of treatment for OSCC patients.

Keywords: Squamous Cell Carcinoma, Palliative Treatment, G. lucidum, LPO, TNFα

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I. Introduction

Oral cancer is one of the most prevailing neoplasms responsible for head and neck cancer, and approximately 90% of oral cancers are squamous cell carcinoma (OSCC) that appears on the buccal mucosa, lip, lateral part of the tongue, palate, vestibule and floor of the mouth as a lump or ulcer having white, red, or mixed white and red in color [1-3]. As the survival period of OSCC patients is mostly ~ 5 years, post-surgical palliative cares might, therefore, be important for the patients. OSCC is particularly common among elderly people in developing countries like Bangladesh. It, for instance, accounts for about 25% of all the malignancies in developing countries.

In Bangladesh more than 7000 people are diagnosed each year with OSCC and 6.6 % of the people diagnosed [4] die of it. The percentage of incidence and mortality rate are increasing every year. G. lucidum, also known as Reishi (in Japanese) or Lingzhi (in Chinese), is a traditional Chinese medicinal mushroom that has been used for centuries. G. lucidum has been reported to reduce cancers in murine lymphocytic leukemia and Lewis lung carcinoma [5], murine sarcoma [6], human hepatoma HepG2 [7], human bladder cells [8], human small-cell lung carcinoma [9] and uroepithelial cancer [10]. Gao et al. (2003a, 2003b) [11,12] reported that cancer patients supplemented with 1.8 gm G. lucidum capsules for 12-weeks had increased immunological response and Karnofsky scores (an indicator of the quality of life). Oka et al. (2010) [13] showed that mycelial extract of G. lucidum suppressed the development of colorectal adenomas in the cancer patients. These studies thus shed lights on the ameliorative effects of G. lucidum on cancers. The objective of the present study was thus to
examine and evaluate the medicinal effects of G. lucidum on the palliative treatment process of oral squamous cell carcinoma (OSCC) in human patients and biochemical parameters to assess prognosis the state of the health at postoperative stage.

II. Materials And Methods

2.1 Collection of G. lucidum

*G. lucidum* mushroom was collected from National Mushroom Development and Extension Centre (NAMDEC), Savar, Dhaka-1342, Bangladesh. The dried fruiting bodies of *G. lucidum* mushroom were ground, and finely pulverized by a mechanical grinder. The powder was used in the preparation of capsules, while the extract of the powder was used to admix with dental paste and drinking tea. The ordinary dental paste was collected from a local dental paste manufacturing company (Oral Health Care Bangladesh, Ltd.). It was admixed homogeneously with *G. lucidum* extract (0.5%) in the laboratory and packed into tubes. Ordinary paste without *G. lucidum* extract was used as a placebo. Ordinary tea was collected from local market and it was sprayed, and admixed with *G. lucidum* extract (0.2%) homogeneously. Each mushroom capsule weighing 500 milligram (mg) was prepared by pouring 500 mg pulverized mushroom powder into a capsule shell. For preparation of placebo capsules, dried good quality *Plantago psyllium* (Isabgul) husk was poured into the same type of capsule shell, so that mushroom capsule and placebo capsules were same to look at. The capsulation procedure was done with the help of Bangladesh Herbal & Nutrition Research Ltd., Savar, Dhaka-1342, Bangladesh. Prepared capsules were stored in a cool and dry place, avoiding light. The study protocol and all procedures were reviewed and approved by the Institutional Review Board of Jahangirnagar University, Savar, Dhaka, as well as by the Dental Unit, Dhaka Medical College, Dhaka. Subjects with oral squamous cell carcinoma (OSCC) participating in this study were aged from 30 to 50 years.

2.2 Human subjects (OSCC patients)

All participants were explained about the study and were selected after getting their written consent. The detail history was taken from each subject, which included age, sex, occupation, educational history, marital status, family history, disease history with medicine.

Patients having acute illness, as well as known chronic diseases like hypertension, diabetes, chronic kidney disease, hepatitis were excluded from the study. A total of 53 subjects was selected for the study. They were divided into two groups: OSCC patients with *G. lucidum* group comprised of 28 subjects, and OSCC patients with placebo group consisted of 25 subjects. The placebo or the *G. lucidum*-treated group received the regimen for 90 days after surgical removal of the cancerous tissues from the primary sites. A questionnaire was filled up for every participant in the study. Height and body weight of the subjects were taken with light cloths without shoes. Then, body mass index (BMI) of the subjects was calculated (BMI = Weight in Kg/Height in m²). Both systolic and diastolic blood pressure (BP) of the patients was measured using a sphygmomanometer.
by trained persons, and blood samples were collected for biochemical analyses. Data were collected at baseline (day 0) and at the end of 90 days.

2.3 Evaluation of condition of appetite

After the surgical removal of cancerous tissues from the primary sites, patients were fed by nasogastric feeding tube for up to three consecutive days. When the oral feeding was started after nasogastric feeding with semi-solid food, the patients were inquired about their conditions of appetite. Their response was always recorded, as described previously [14]. The question was focused on mainly whether the amount and frequencies of meals taken were decreased or increased and/or was the same as before. After their discharge from the hospital, one of the members of our research team recorded the conditions of appetite. When the patients were re-examined at the hospital for a follow-up, the data were recorded again. In this way, the condition of appetite was evaluated through the history of ‘intake amount’ of the meals and/or frequencies of meals etc.

2.4 Evaluation of tolerability to radiochemotherapy

Poor treatment tolerability is defined as any instance of an interruption to or breaks from treatment, or early cessation of radiation treatment for any cause, including side effects. There were a number of adverse effects after the start of radiochemotherapy. These are nausea and vomiting, irritability, generalized weakness, lassitude, oral thrush and candidacies, skin rash and inability of deglutition. When the course of radiochemotherapy started in our study, the physical and mental condition of every patient was recorded by asking the patient whether he/she had any of the side effects mentioned above. The normal oral examination was also done and recorded. All these data were finally processed. The effect of G. lucidum on the tolerability was thus evaluated by recording the treatment-related events.

2.5 Evaluation of improvement of body activity by Karnofsky scale

We wanted to observe the overall effects of the G. lucidum on the generalized body activities of the patients. So, we made the Karnofsky score to sort out any of their body-function impairments [15]. We monitored the patients from the very early days of their treatment until the end of it. We took history, compared it by physical examination, and recorded it. The Karnofsky scale comprises of integers from ‘0’, which implies dead, to ‘100’, which implies ‘no symptoms’ of the disease. The lower the Karnofsky score is, the worse is the survival for most of the serious illnesses. Finally, we processed all data and assigned them a percentage value.

2.6 Prognostic parameters by visual analog scale (VAS)

The effect of G. lucidum treatment on prognostic parameters was evaluated by means of visual analog scale. The procedure of ‘visual analog scale’ is done by measuring the intensity of the disease state of the OSCC patients after three months of treatment. In this assessment, the lower the score is, the higher the efficiency of treatment is. It is a psychometric response scale [16]. Furthermore, the serum biomarkers were accepted as a valuable tool for diagnosis and prognosis in different kind of tumors [17-19]. Therefore, the levels of blood Hb, urea, creatinine, AST, ALT, ALP, albumin, globulin and total protein were determined to examine whether these parameters have any prognostic values in the OSCC patients.

2.7 Analytic procedures

Plasma samples were analyzed for blood hemoglobin (Hb), glucose, AST, ALT, ALP, creatinine, urea, albumin, globulin, by commercially available standard reagent kits. The effects of G. lucidum on blood parameters were evaluated by comparing the values obtained after 90-days of prescription with those obtained at day 0. Plasma LPO of the OSCC patients was measured by ELISA according to the methods of Hashimoto et al. ((2001) [20]. The levels of TNFα in the plasma were measured as previously described from this laboratory [21]. The levels of plasma p53 were determined by following the methods of Rossner et al. (2002) [22]. Briefly, the multi-well plate was coated with 50 μl plasma in 0.1 M sodium bicarbonate (pH 9.6) and incubated at 4°C overnight and then blocked with 1% BSA in Tris-buffered saline (TBS). After a wash on the next day, the primary rabbit anti-TNFα and anti-rabbit p53 antibodies (Santa Cruz Biotechnology, CA, USA) at 1:1000 dilutions, were incubated in the plate for overnight at 4°C. After blocking, horseradish peroxidase-coupled anti-rabbit IgG (Biosource International, Inc., Camarillo, CA, USA) was used as the secondary antibody; it was incubated for 2h at room temperature before adding the tetramethylbenzidine substrate to develop color. The reaction was stopped by adding 0.1N HCl. Wells coated with only 0.1M carbonate buffer (pH 9.6) were used as blank. The plates were analyzed by a multiwell plate reader (Erba Lisascan II, Mannheim, Germany) at 450 nm. The relative concentrations of plasma TNFα/p53 in the OSCC patients at day or at day90 were calculated by considering the absorbance of the age-matched subjects’ as 100%. Finally, all absorbance values were normalized to per ml of plasma.
2.8 Histology

Histological sections with 4 µm thickness were prepared from paraffinized blocks and stained with hematoxylin and eosin (HE). The slides were evaluated by using an optical microscope (Eclipse 200, Nikon, Japan) according to histopathologic grading systems.

III. Statistical Analysis

Data are expressed as mean ± standard error of mean (SE). Data were analyzed using Student’s t-test for determining the significant changes over control values. One-way ANOVA also was used when it was necessary to compare the values among three groups. P < 0.05 was considered to be significant.

IV. Results

4.1 Baseline characteristics of the OSCC patients

During baseline of the study, the age, height, weight and body mass index (BMI) were not significantly different between *G. lucidum*-treated and the placebo group (Table 1). The percent of males and females between the groups were different.

Table 1. Anthropometry of the OSCC patients in each group.

<table>
<thead>
<tr>
<th></th>
<th>Oral Small Cell Carcinoma (OSCC) patients</th>
<th>Placebo control (25)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>G. lucidum</em>-prescribed (28)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>54.0 %</td>
<td>64.0 %</td>
</tr>
<tr>
<td>Female</td>
<td>46.0 %</td>
<td>36.0 %</td>
</tr>
<tr>
<td>Age (y)</td>
<td>46 ± 1.93</td>
<td>44.9 ± 1.12</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.56 ± 0.008</td>
<td>1.54 ± 0.009</td>
</tr>
<tr>
<td>Weight</td>
<td>50.08 ± 1.25</td>
<td>51.56 ± 1.26</td>
</tr>
<tr>
<td>BMI (Kg/m2)</td>
<td>20.57 ± 0.36</td>
<td>21.74 ± 0.40</td>
</tr>
</tbody>
</table>

Results are expressed as mean ±SE. y = age in years, m= meter in height

4.2 Oxidative stress, TNFα and p53 antigen at the baseline (at day0) of the study

The levels of lipid peroxide (LPO) (Fig 2A) and TNFα (Fig 2B) were significantly higher in the cancerous tissues of the OSCC patients, when compared to those of the age-matched normal noncancerous control subjects. Concurrently, the levels of p53 increased in the plasma of the OSCC patients (Fig 2C).

Figure 2. The levels of lipid peroxide (LPO) (A) and TNFα (B) in the cancerous tissues, and the plasma levels of p53 antigens (C) were higher in the OSCC patients (n = 30-36), as compared to those of the age-matched control subjects (n=8). Results are mean ± SE. Bars with different alphabets are significantly different at P<0.05 (unpaired student’s t-test).

4.3 Histological Analysis

We examined the differentiation status of the cancerous tissues of the OSCC patients. Three types of characteristics were observed: Well differentiated squamous cell carcinoma (W-d-SCC) (Fig 3A): Slide showed epithelial proliferation and invasion to the underlying stromal tissues by strands and islands of dysplastic cells. The sub-epithelial connective tissue infiltrated heavily with inflammatory cells created a large circular hyaline structure referred to as epithelial pearl. There was keratin formation with well differentiated architecture of cells.

Moderately differentiated squamous cell carcinoma (M-d-SCC) (Fig 3B): Slide showed moderate epithelial proliferation and extension to the underlying stromal tissue. The cellular architecture was somewhat maintained and there was infiltration of inflammatory cells. There were less keratin formation and cell nests. Poorly differentiated squamous cell carcinoma (Pd-SCC) (Fig 3C): Slide showed a scantly cell nest of epithelium and poor architecture of cells. Stromal tissue was infiltrated with large sized inflammatory cells. There was...
hyperchromatism with lots of mitosis, and giant tumor cells. There was no formation of keratin with void epithelial pearl. Histological investigations by microscope clearly manifested oral squamous cell carcinoma among the patients of our investigation.

Figure 3. Histological sections with 4 µm thickness were prepared from paraffinized blocks and stained with hematoxylin and eosin (HE). The slides were evaluated by using an optical microscope (Eclipse 200, Nikon, Japan) according to histopathologic grading systems. Different grades of OSCC showed a difference in grades/patterns of staining. Three types of characteristics were observed. A. Widely differentiated squamous cell carcinoma (Wd-OSCC) predominantly showed epithelial proliferation and invasion to the underlying stromal tissues by strands and islands of dysplastic cells, while staining was predominantly patchy, diffused, infiltrated (by inflammatory cells), less keratinized in moderately differentiated squamous cell carcinoma (Md-SCC) (B). Stromal tissue was infiltrated with large sized inflammatory cells and there was hyperchromatism with lots of mitosis and giant tumor cells. Here, slide also showed a scanty cell nest of epithelium and poor architecture of cells (Pd-OSCC) (C).

4.4 Effects of G. lucidum prescription on BW and BMI

The body weight (BW) and BMI before and after three months of treatment with G. lucidum are shown in Table 2. Both BW and BMI increased significantly after treatment with G. lucidum. However, these parameters did not change significantly in the placebo-treated OSCC patients.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weight (kg)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>G. lucidum</td>
<td>50.08±1.25</td>
<td>54.78±1.22</td>
</tr>
<tr>
<td>Placebo</td>
<td>51.56±1.26</td>
<td>52.16±1.28</td>
</tr>
</tbody>
</table>

Results are mean±SE. Data were subjected to student’s paired t-test. Means were significantly different at p < 0.05.

4.5 Effect of G. lucidum on the appetite and tolerability to radiochemotherapy of the OSCC patients

The condition of appetite was significantly higher (68.73%) in the OSCC patients who received G. lucidum after surgery, when compared to that of the placebo-receiving patients (57.62%) (Fig 4A). About 30% of the patients receiving placebo did not have any change in appetite, while 22% of patients receiving G. lucidum did not show any effect on appetite. 8.8% of the total patients receiving G. lucidum had decreased appetite, while the decrease in appetite was reported in 12.7% of the placebo-taking patients.
G. lucidum benefits palliative care in postoperative OSCC patients

The effect of G. lucidum treatment on the tolerability (the ability of the patients to withstand the curse made by radiochemotherapy) is shown in Fig 4B. More than eighty percent (81.24%) of OSSC patients from G. lucidum-prescribed group had well tolerated the radiotherapy procedures, while about 69% of the placebo taking OSSC patients well tolerated the radiotherapy procedures post-surgically.

4.6 Effect of G. lucidum on the improvement of body activity (Karnofsky score)

The effect of G. lucidum on the Karnofsky score is shown in Fig 5. Karnofsky score was 73.2±2.31 for the G. lucidum-prescribed patients, while it was 62.1±2.12 in the placebo-prescribed patients. Thus, the data revealed that the Karnofsky score was higher (P = 0.014) in the OSCC patients receiving G. lucidum (Fig 5A). In other words, the degree of ‘wellness’ was significantly augmented in the G. lucidum-prescribed patients.

Representative female patients of our investigation are shown in the Fig 5B1, 5B2, after 1 and 3 months of G. lucidum treatment, respectively.

4.7 Effect of G. lucidum treatment on prognostic parameters for OSCC patients

The mean visual analog scale was 4.07 for the G. lucidum receiving group and 5.32 for the placebo group. The score was significantly better for the G. lucidum-prescribed subjects (Fig 6B). The disease state of the patients during visual analog score determination is shown in the Fig 6C and 6D as representative pictures.
G. lucidum benefits palliative care in postoperative OSCC patients

4.8 Effect of G. lucidum on serum albumin

The levels of both serum albumin (Fig 7A) and globulin (Fig 7B) increased, however, significantly only the later, in the G. lucidum-prescribed OSCC patients. The levels of total protein (albumin plus globulin) significantly in the higher in the OSCC patients taking the G. lucidum, however, not in the placebo-treated subjects (Fig 7C).

4.9 Effect of G. lucidum on blood hemoglobin (Hb), urea, and serum creatinine, ALT, AST and ALP

The levels of Hb significantly increased after three-months of treatment with G. lucidum (Fig 8A). In contrast, the Hb levels decreased slightly, though not significantly, in the placebo-treated patients. After three months of treatment with G. lucidum, the levels of blood urea, serum creatinine, ALT and AST enzyme activities decreased significantly (P<0.05) (Fig 8B,8C,8D), while the levels of serum ALP enzymes were not altered in the G. lucidum-treated patients. On the other hand, the levels of serum urea, creatinine, and ALT, AST and ALP enzyme activities increased but not significantly in the placebo group. However, only the levels of ALP enzyme activities increased significantly in the placebo-treated patients (Fig 8F). The fasting blood sugar levels were not altered either in the G. lucidum-or in the placebo-treated patients (data not shown).
Figure 8. The levels of hemoglobin (A), serum urea (B), serum creatinine (C), ALT (D), AST (E) and serum ALP (F) before and after treatment of G. lucidum and placebo for three months.

4.10. Effect of G. lucidum prescription on blood oxidative stress (lipid peroxide (LPO))

The levels of LPO in the plasma of the OSCC patients receiving G. lucidum for three months decreased significantly (Fig 9). The levels of LPO in the plasma of the placebo-prescribed patients decreased also; however, it did not reach significance.

Figure 9. Effect of G. lucidum on the plasma LPO of the OSCC patients. Results are mean ± SE. Data were subjected to paired student’s t-test for a given patient group.

4.11 Effect of G. lucidum prescription on blood TNFα and p53

The levels of TNFα and p53 were significantly higher in the plasma taken on the day of surgery from the OSCC patients, as compared to those of the age-matched control subjects. The levels of TNFα in the plasma of the patients receiving G. lucidum treatment for three months decreased significantly (Fig10A). The prescription of G. lucidum treatment for three months reduced the levels of p53 in the OSCC patients; however, the values did not reach significance (Fig 10B). However, the serum levels of TNFα or p53 in the placebo-prescribed patients were not changed (data not shown).
G. lucidum benefits palliative care in postoperative OSCC patients

Figure 10. Effect of G. lucidum on the plasma TNFα and p53 marker protein. Results are mean±SE. Data were subjected to one-way ANOVA, followed by Fisher’s PLSD test for multiple comparison. Significantly different at \(^{a,b,c}\)P<0.05.

V. Discussion

The aim of the investigation was to demonstrate whether G. lucidum could be used to increase the quality of life in palliative treatment for oral squamous cell carcinoma (OSCC) patients with an emphasis on patients’ clinical status in terms of body weight (BW), body mass index (BMI), conditions of appetite, tolerability to radiochemotherapy, functional impairments by Karnofsky score and efficiency of treatment by visual analog scale against a placebo treatment after the cancerous tissues were removed by surgery and the patients were post-treated with radiochemotherapy; and, if the postoperative treatment with G. lucidum ameliorates or further deteriorates other prognostic parameters such as blood hemoglobin, urea, creatinine, total protein, albumin, globulin, AST, ALT, ALP, LPO (as indicator of oxidative stress) and TNF-α (as indicator of proinflammatory response) in the patients.

In palliative treatment option, the general trend is to make the patient’s lifestyle easy, improved and supportive for themselves, as well as, to increase their life expectancy. For OSCC, average life expectancy is about five years. Therefore, if their lifestyle could be improved and life expectancy advanced, it would definitely add success to the current treatment option. After three months of treatment with G. lucidum, the body weight and BMI of the OSCC patients increased, as compared to those of the placebo-prescribed patients, thus suggesting the beneficial (weight-gaining) effects of G. lucidum treatments. Changes in appetite were common with OSCC patients. In our study, the condition of appetite was significantly higher (68.73%) in the patients who received G. lucidum after surgery, as compared to that of the placebo-receiving subjects (57.62%). Moreover, radiochemotherapy causes weakness, vomiting, mouth sores, difficulty in swallowing and chewing-all ultimately affects the eating behavior. Therefore, research that aims to increase the tolerability to radiochemotherapy has been an interesting field of research in cancer therapy. The effect of G. lucidum on the tolerability was therefore evaluated in this investigation. Higher treatment tolerability (in >81% patients) was observed in the G. lucidum-taking OSCC patients than in the placebo-taking patients (69%). This result thus suggests that G. lucidum prescription helped the patients to withstand the curse made by radiochemotherapy procedures. Finally, the increases in appetite and tolerability to radiochemotherapy might have improved the patient’s digestion/metabolism, which otherwise would have led to weight loss in the patients. Therefore, the results of increased appetite are consistent with the increased BW and BMI in the patients treated with G. lucidum.

The Karnofsky performance score is a widely used method to assess the functional status of a patient [20]. Accordingly, we used Karnofsky score in this investigation to assess patients’ performance status. The Karnofsky score was significantly higher in the G. lucidum-prescribed patients as compared to that of the placebo-treated patients, which demonstrates again the positive effect of the mushroom on the functional status of the patients.

Visual analog scale (VAS) of pain was also recorded for measuring the intensity of the disease state of the OSCC patients. The lower the score is, the higher is the efficacy of the treatment. The results of decreased VAS in the G. lucidum-treated patients as compared to that of the placebo-treated patients demonstrate a betterment of pain, and pain-related depression or anxiety and other affective components of the OSCC patients. Along with this betterment of the clinical status (BW, BMI, appetite, Karnofsky score and visual analog scale) in the OSCC patients, other changes in blood parameters, including Hb, urea, creatinine, AST, ALT, ALP, albumin, globulin and total protein were evaluated. The treatment of the patients with G. lucidum significantly increased the levels of Hb in this investigation, while the treatment with placebo decreased the Hb in the placetreated patients. These results are one of the intriguing aspects of the study. Oral administration of G. lucidum to rats and/or in vitro incubation of G. lucidum extract with RBCs significantly inhibited the in vitro
hemolysis [23]. The results are, thus, consistent with the fact that treatment of OSCC patients with G. lucidum might have, at least partially, inhibited the hemolysis of RBCs in the patients. Furthermore, cancer and its therapies may lead to renal impairment [24] and hepatic damage [25]. The treatment of the patients with G. lucidum significantly decreased the levels of creatinine/urea in the OSCC patients, while the levels of creatinine rather increased in the placebo-treated patients, thus suggesting that the consumption of G. lucidum significantly protected the kidney functions. The levels of liver AST, ALT and ALP also decreased significantly in G. lucidum-treated patients when compared to those in the placebo-treated patients, indicating again the beneficial effects of G. lucidum on liver functions. The oral administration of S. cumini seed extract prevented the oxidatively degenerated parenchymal tissues, tubules and glomeruli of the kidneys [26]. Paracetamol-induced hepatotoxicity was also improved in the G. lucidum-administered rats [27]. Our results are thus qualitatively consistent with the protective roles of G. lucidum against oxidative damages of kidneys and liver in animal models (rats). Also, cancers in the liver may result in hypoalbuminemia [28, 29], leading to symptoms such as muscle weakness, fatigue, and poor appetite. Lower levels of plasma proteins in the OSCC patients of the present investigation is in agreement with earlier studies on oral cancer [30, 31]. The treatment with G. lucidum increased (P

VI. Conclusion

Finally, the improvements of the blood Hb, total protein, hepatorenal parameters, oxidative stress, proinflammatory TNFα by the G. lucidum might contributed to the gaining of BMI, body weight, increased appetite and wellness of other clinical status of the OSCC patients. The improvements of all these parameters are, thus, suggestive of palliative to the lifestyle of the OSCC patients. However, further investigations are obviously necessary to understand the specific mechanism of action of G. lucidum. Also, it is critically important to have a large number of patients in each group in order to have a greater confidence of our results.

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Disclosure statement

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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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