Clinical Observations

Effects of Chinese Herbal Medicine Combined with He-Ne Laser on Lipoperoxide and Superoxide Dismutase in Chloasma Patients

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Objective: To observe the effects of Chinese decoction and ligustrazine hydrochloride injection combined with He-Ne laser on lipoperoxide (LPO) and Superoxide dismutase (SOD) in patients with chloasma. Methods: 90 cases of chloasma were randomly divided into the following two groups: a treatment group (of 54 cases) treated by a self-prepared prescription for toning the kidneys and relieving the depressed liver to remove blood stasis, ligustrazine hydrochloride injection and He-Ne laser therapy, and a control group (of 36 cases) treated with oral administration of Vitamin E and Vitamin C plus external application of 20% Azelaic acid cream. Results: The total effective rate in the treatment group was 79.6%, which was significantly higher than that of the control group ($P<0.05$). After treatment, the LPO level in the treatment group was significantly lowered ($P<0.01$), and the SOD level was significantly elevated ($P<0.05$). Conclusion: The therapeutic methods adopted in the treatment group may show the action of antioxidation, providing good clinical effects for treating chloasma.

Key word: Chloasma; TCM therapy; Lipoperoxide; He-Ne laser; Ligustrazine

Chloasma is a common skin disease characterized by pigmentation on the face with the cause unknown. Recent studies have shown that it is related with the change of oxygen free radicals (OFR), in order to explore the roles of lipoperoxide (LPO) and Superoxide dismutase (SOD) in morbidity of chloasma and try to find better therapy to treat the disease, the authors used Chinese herbal medicine combined with He-Ne laser therapy to observe the effects on LPO and SOD in patients with chloasma. A report follows.

CLINICAL MATERIALS

All 90 cases in this series were females from the Departments of TCM and Dermatology, Guangzhou Red Cross Hospital. They all met the criteria for diagnosis of chloasma. Patients who had taken medicines affecting endocrine functions in the past half a year, those experiencing menopause, pregnancy, diabetes, chronic dysfunction of the liver and kidney, autoimmune diseases, and those who had been treated by other therapies in the past one month were excluded. By drawing lots, the patients were randomly divided into two groups. In the treatment group of 54 cases, the age range was from 19 to 50 years (mean 38.5 years) with the illness course from 2 months to 10 years (mean 5.4 years). In the control group of 36 cases, the age range was from 20 to 49 years (mean 37.6 years) with the illness course from 3 months to 10 years (mean 5.2 years). There were no significant differences in age and course of disease between the two groups. LPO and SOD levels of the peripheral blood were detected before and after treatment in the treatment group. In addition, thirty healthy subjects were taken as the normal controls for comparison of the LPO and SOD levels. The age range was from 18 to 50 years (mean 36.4 years).

METHODS

Chinese herbal medicine combined with He-Ne laser therapy were given in the treatment group. The herbal prescription was composed of Zhen Zhu Mu (珍珠母 Concha Margaritifera Usta) 30g (decocted first), Nü Zhen Zi (女贞子 Fructus Ligustri Lucidi) 20g, Tu Si
Zi (菟丝子  Semen Cuscutae) 20g, Shan Zhu Yu (山茱萸  Fructus Corni) 15g, Sang Shen (桑椹  Fructus Mori) 15g, Yu Jin (郁金  Radix Curcumae) 15g, Fu Ling (茯苓  Poria) 15g, Su Xin Hua (素馨花  jasmine flower) 15g, Dang Gui (当归  Radix Angelicae Sinensis) 10g, Chai Hu (柴胡  Radix bupleuri) 10g, Bai Zhi (白芷  Radix Angelicae Dahuricae) 10g, and Hong Hua (红花  Flos Carthami) 5g. The prescription should be modified according to individual condition of the patients. The decoction was taken one dose daily for 4 weeks as one therapeutic course. The He-Ne laser was used for intravascular irradiation, with a needle inserted into the median cubital vein and connected with optical fibers through the venous catheter. The irradiation of 1.5 mW was given 30 min each time, once daily. Following each irradiation, 10% 500 ml glucose added with 240 mg ligustrazin hydrochloride injection was intravenously dripped. One-week of treatments made up a therapeutic course with a 3-week interval between courses.

In the control group, Vitamin E in a dose of 50 mg and Vitamin C in a dose of 200 mg were orally administered three times daily, with 20% Azelaic acid cream externally applied twice daily on the skin lesions of the face, one-month treatment constituting a therapeutic course.

Two courses of treatments were given for both groups. During the course of treatment, the patients were examined once a week, and the change in the skin lesions was recorded. The therapeutic effects were evaluated after two courses of treatment. LPO and SOD levels of the peripheral blood were detected before and after two courses of treatment respectively by thio-barbituric acid chromatometry and pyrogallic acid autoxidation.

**Statistical Analysis**

SAS10.0 software was used for statistical analysis. The $\chi^2$ test was used for evaluation of the therapeutic effect for chloasma, the rank-sum test for comparison of LPO and SOD between the treatment group and normal control group, and the paired rank-sum test for intergroup comparison of LPO and SOD in the treatment group before and after treatment.

**Criteria for Therapeutic Effects**

Basically cured: The chloasma area was reduced by $\geq 90\%$ with basic disappearance of the color determined with the naked eye. Markedly relieved: the chloasma area was reduced by $\geq 60\%$ but $< 90\%$ with obvious fading of the color determined with the naked eye. Improved: reduction of the chloasma area by $\geq 30\%$ but $< 60\%$ with fading of the color determined with the naked eye. Failed: reduction of the chloasma area by $< 30\%$ with no obvious change of the color determined with the naked eye.

**RESULTS**

Of the 54 cases treated in the treatment group, 17 cases were basically cured, 26 cases markedly relieved, 10 cases improved and 1 case failed, with a total effective rate of 79.6%. Of the 36 cases treated in the control group, 5 cases were basically cured, 15 cases markedly relieved, 12 cases improved and 4 cases failed, with a total effective rate of 55.6%. The therapeutic effect in the treatment group was significantly better than that of the control group ($P<0.05$).

**Comparison of the LPO and SOD Levels Before and After Treatment**

It can be seen from Table 1 that before treatment there are significant differences in the LPO and SOD levels between the treatment group and the normal control group, showing an obvious increase of LPO ($P<0.01$) and a marked decrease of SOD ($P<0.01$). This indicates the imbalance between oxidation and antioxidation, leading to generation or aggravation of chloasma.

After treatment, the LPO and SOD levels were detected only in 34 of 54 cases in the treatment group. As shown in Table 2, after treatment the LPO level is markedly lowered ($P<0.01$) and the SOD level is significantly elevated ($P<0.05$), indicating an improvement in the imbalance between oxidation and antioxidation with removal or alleviation of chloasma.
Table 1. The LPO and SOD Levels before Treatment in the Treatment Group and the Normal Control Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>LPO (μmol/L)</th>
<th>SOD (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>54</td>
<td>5.42±3.87**</td>
<td>29.36±5.11**</td>
</tr>
<tr>
<td>Normal Control</td>
<td>30</td>
<td>3.27±2.68</td>
<td>33.81±6.43</td>
</tr>
</tbody>
</table>

Note: **P<0.01, compared with normal control group

Table 2. Comparison of the LPO and SOD Levels Before and After Treatment in the Treatment Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>LPO (mol/L)</th>
<th>SOD (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretreatment</td>
<td>34</td>
<td>6.37±4.30</td>
<td>29.55±6.01</td>
</tr>
<tr>
<td>Posttreatment</td>
<td>34</td>
<td>3.73±2.90**</td>
<td>33.49±9.06*</td>
</tr>
</tbody>
</table>

Note: *P<0.05 and **P<0.01 for the intragroup comparison in the treatment group.

Adverse Effects

No obvious side effects were found in the treatment group.

DISCUSSION

Chloasma is a facial skin disease related to a disorder of the pigment metabolism, and it often occurs in women. Generally, it is thought to be related to ultraviolet irradiation, endocrine disorder and genetic factors. Recent studies have shown that its generation is related to OFR changes. Under normal conditions, there are many kinds of antioxidant in the human body, such as SOD and catalase (CAT), which can effectively eliminate the oxidation-induced lesion and keep a dynamic equilibrium between oxidation and anti-oxidation. In patients with chloasma, the equilibrium is broken, the physiologically generated oxidative products like peroxidized lipid cannot be effectively removed, resulting in accumulation of LPO. The present study shows that in patients with chloasma the LPO level is obviously higher and the SOD level obviously lower than that of normal subjects. Elevation of LPO can accelerate the oxidizing reaction of tyrosine series and increase the melanin produced by melanin cells. Meanwhile, due to instability of LPO, the degeneration product, malonaldehyde, can make protein molecules cross-linked to form fluorescence chromophore represented by pigment. TCM holds that chloasma results from blood stasis, and it is related to deficiency of the kidneys, depression of the liver, and disorder of qi and blood.

Chinese herbal medicine combined with He-Ne laser therapy is a new method for treating chloasma. The herbal prescription for oral administration functions to tone the kidneys, relieve the depressed liver, and regulate the circulation of qi and blood. According to modern pharmacological studies, Shan Zhu Yu (山茱萸 Fructus Corni), Nü Zhen Zi (女贞子 Fructus Ligustri Lucidi), Sang Shen (桑椹 Fructus Mori), Tu Si Zi (菟丝子 Semen Cuscutae), Dang Gui (当归 Radix Angelicae Sinensis) and Yu Jin (郁金 Radix Curcumae) have the ability to elevate the activities of SOD, removing oxygen free radicals, defending against lipid peroxidation, lowering blood viscosity, dilating blood vessels, and improving blood flow. Ligustrazin hydrochloride extracted from Rhizoma Ligustici is a kind of alkaloid, which can be used to remove blood stasis to promote blood circulation, improve microcirculation, lower whole blood viscosity, protect or enhance SOD activities, eliminate the oxygen free radicals, anti-lipid peroxidation, and inhibit the proliferation of melanocytes, the synthesis of melanocytes and the tyrosinase activities. A low intensity of He-Ne laser for intravascular irradiation can strengthen the activities of SOD and catalase, enhance the plasma copper- protein and endogenous Vitamin K levels, defend against lipid peroxidation, remove oxygen free radicals, improve blood viscosity, micro-circulation and hypoxia, and correct abnormal lipid metabolism. Therefore, after treatment the LPO level was obviously lowered, the SOD level markedly elevated, and the imbalance between oxidation and anti-oxidation regained, thus showing therapeutic effects for chloasma.

REFERENCES

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(Translated by CHEN Zheng-qiu 陈正秋)