Clinical observation on tranexamic acid combined with reduced glutathione for the treatment of chloasma

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Abstract: To observe and analyze the efficacy of tranexamic acid combined with reduced glutathione in chloasma treatment. The 180 patients diagnosed with chloasma and treated in our hospital from June 2015 to March 2018 were enrolled as study subjects and randomly divided into treatment group (90 cases) and control group (90 cases) using simple digital table method. Where, the control group was treated with pure topical therapy of hydroquinone ointment, and the treatment group was treated with intradermal injection of tranexamic acid and glutathione. The two groups were observed and compared in terms of treatment efficacy. Comparison of the overall treatment efficacy of the two groups shows that the treatment group is superior to the control group, $p<0.05$; observation of chloasma severity and chloasma area in the two groups shows that the treatment group has obvious advantages over the control group, $p<0.05$. The combination of reduced glutathione and tranexamic acid in chloasma treatment can better improve the overall treatment efficacy, lower the severity of the disease, and reduce the chloasma area.

Keywords: Reduced glutathione, tranexamic acid, combination therapy, chloasma.

INTRODUCTION

Chloasma as a chronic pigmentation disease difficult to treat mainly attacks young and middle-aged women. The incidence of chloasma is gender-neutral, and men can also suffer from this disease which not only affects the quality of life, but also deeply affects work (Zhao, 2013; Zhao, Tang, 2015). Timely diagnosis of patients and adoption of targeted and effective symptomatic treatment control plan has become a key research topic in the current medical community.

Chloasma, also known as melasma, is a result of yellow-brown pigmentation on the face (fig. 1). It is mostly in butterfly-shaped symmetrical distribution in the cheek. For female patients, the high level of estrogen in the blood is the main reason, and its incidence is related to pregnancy, long-term oral administration of contraceptives and menstrual disorders. It is also found in women with reproductive system disorders, tuberculosis, cancer, chronic ethanol poisoning, liver disease, and sunlight can promote the disease (Yu, *et al*., 2015; Luo, Yang, 2016). Male patients account for about 10%. Some studies suggest that male incidence is genetic related. Currently, an important method for the disease is drug therapy, and widely used drugs include tranexamic acid and reduced glutathione. This study is to observe the clinical efficacy of tranexamic acid combined with reduced glutathione in chloasma treatment, with report contents as follows.

MATERIAL AND METHODS

General information

The 180 chloasma patients treated in our hospital from June 2015 to March 2018 were selected as the study subjects. This paper has a rigorous structure, and the conclusion has been approved by relevant ethics and relevant departments. All cases met the diagnostic criteria for chloasma. In addition, all cases in this study have signed informed consent, have fully understand the experimental nature of the treatment before the treatment, and agreed to receive this treatment. The patients' front, lateral views were photographed with a digital camera (fig. 2 and fig. 3, respectively) The exclusion criteria for patients include (Rivas, Pandya, 2018; Kashanian, *et al*., 2017): pregnant and lactating women; those with history of photosensitivity, recent sun exposure; thrombophilia; treatment with other drugs or whitening products in the past 3 months; those with abnormal blood routine examination and coagulation function; patients with history of gynecology and liver disease; other types of skin diseases such as malar greenish brown spot, skin melanosis, freckles, trauma, post-inflammation pigmentation, etc.; outdoor workers, those with cicatricial diathesis and poor compliance.

In this prospective study, patients were randomly divided into treatment group and control group according to simple digital table method. Each group had 90 cases. Where, the treatment group had 76 female and 14 male patients. Aged between 36 and 60 years, the patients had an average age of (42.3±0.8) years. The control group had 80 female and 10 male patients. Aged between 35 and 58 years, the patients had an average age of (40.5±0.5) years.

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Comparison of the relevant data of the two groups indicates comparability, p>0.05.

All the patients in this study signed the informed consent form, fully understood the experimental nature of this treatment before treatment and agreed to accept this treatment. Meanwhile, digital cameras were used to take the front-view and lateral-view photos of the patients. The exclusion criteria of the patients were [5-6]: Pregnant and lactating women; patients with history of light sensitivity, or recent history of solar exposure; patients who are prone to thrombosis; patients who applied other drugs or whitening products for treatment within 3 months; patients with abnormal blood routine and coagulation function; patients with a history of gynecology and liver diseases; patients with other types of skin diseases, such as zygomatic brown and blue spots, skin melanosis, freckles, trauma, pigmentation after inflammation; outdoor workers, those with scar physique or poor compliance.

Fig. 1: A patient with chloasma

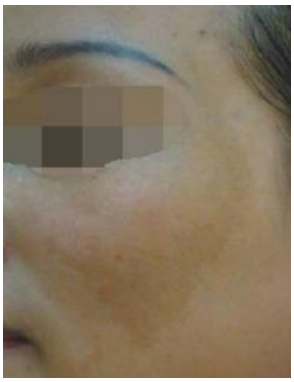


Fig. 2: Front view of a patient with chloasma

Methods

Different treatment regimens were performed on the two groups. The treatment group received intradermal injection of tranexamic acid and glutathione plus hydroquinone ointment for external use, while the control group only received normal conventional hydroquinone ointment for external use.

For the treatment plan for hydroquinone ointment, appropriate amount of cream was externally applied to the spot once a day before sleep at night. For the treatment plan of intradermal injection of reduced glutathione, prepare tranexamic acid 5ml: 0.25g, take 2ml for standby use; inject reduced glutathione into 3ml normal saline, take 1.5ml after mixing for standby use; mix the 2ml tranexamic acid and 1.5ml glutathione with t-branch pipe; adjust the injection depth at 0.8-1.2mm according to the specific skin lesion location, adjust injected volume according to the lesion area, set the return ratio at 35%. The treatment is performed once every 4 weeks, and one treatment course includes 3 treatments.

Observation indicators

The two groups were observed and compared in terms of overall treatment efficacy: forehead score = 0.3×(D+H)×A, the right malar score = 0.3×(D+H)×A, the left malar score = 0.3×(D+H)×A; chin score = 0.1×(D+H)×A; Total Score = Total Score Decrease Index = (Total Score Before Treatment - Total Score After Treatment)/ Total Score Before Treatment * 100% . Basically cured: spot area fading in naked eye≥ 90%, the color basically disappears (Chen, Deng, 2014); post-treatment decrease index calculated by scoring method≥ 0.8. Markedly: spot area fading in naked eye≥ 60%, the color is lighter obviously; post-treatment decrease index calculated by scoring method≥0.5. Improved: spot area fading in naked eye≥30%, the color is lighter; post-treatment decrease index calculated by scoring method≥0.3. Invalid: spot area fading in naked eye <30%, the color change is not obvious, post-treatment decrease index calculated by scoring method<0.3. Melasma area severity index (MASI) is adopted for evaluation (Zheng, 2017). Where, severity criteria include no, slight, mild, moderate, and severe degrees, with respective scores of 0, 1, 2, 3 and 4. Area criteria include no, slight, mild, remarkable and maximum area, with respective scores of 0 (0%), 1 (10% or less), 2 (10%-29%), 3 (30%-49%), 4 (50% and the above).

STATISTICAL ANALYSIS

The statistical analysis software used was SPSS 21.0. Where, the measurement data were expressed as mean ±average ($\bar{x}$ ±s), and t was used for comparison between groups; the count data was expressed using natural numbers (n) and percentages (%), and X2 was used for comparison between groups. P<0.05 indicates statistical value. All the patients were scored in terms of area, color. The facial images were photographed with results presented as absolute scores for analysis standard. The analysis results are presented in the form of absolute scores and facial photographs, and treatment effect is visually compared via images.

RESULTS

Comparison of Overall Treatment Efficacy between the Two Groups

As shown in table 1 below, the overall treatment efficacy is higher in the treatment group than in the control group, P<0.05.

Table 1: Comparison of overall treatment efficacy between the two groups [n(%)]

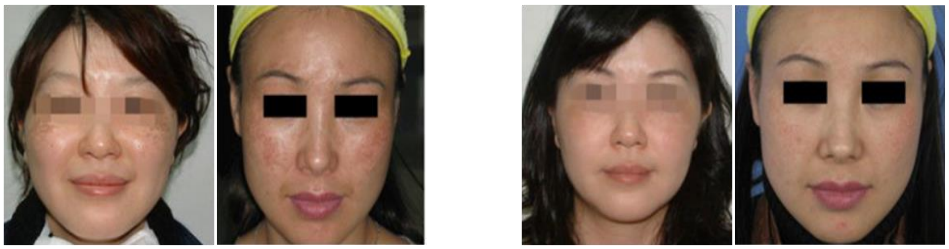
Group	Case number	Basically cured	Markedly	Improved	Invalid	Total effective rate
Treatment group	90	35	30	19	6	84(93.33)
Control group	90	20	38	12	20	70(77.78)
x2						12.18
p						<0.05

Table 2: Comparison of severity of chloasma between the two groups (x±s)

Group	Case number (n)	Severity score of chloasma(point)
Treatment group	90	1.68±0.23
Control group	90	3.36±0.19
t		8.93
p		<0.05

Table 3: Comparison of chloasma area in the two groups (x±s)

Group	Case number (n)	Chloasma area score (point)
Treatment group	90	2.02±0.57
Control group	90	4.70±0.23
t		11.63
p		<0.05



Before treatment After treatment

Fig. 3: Comparison chart before and after chloasma treatment

Comparison of severity of chloasma between the two groups

As shown in table 2 below, comparison of average scores of the severity of chloasma in the treatment group and the control group shows that the treatment group is significantly lighter in severity, P<0.05.

Comparison of chloasma area in the two groups

As shown in table 3, the chloasma area is smaller in the treatment group than in the control group after treatment, P<0.05. The comparison of chlosma area before and after treatment of two cases of treatment group patients is shown in fig. 3.

DISCUSSION

Chloasma is a chronic pigmentation disease, which is difficult to be treated. Both male and female patients can develop chloasma disease. Once chloasma disease occurs, not only the quality of life will be affected, but also the work life of patients will be profoundly influenced. The exact pathogenesis of chloasma is not clear. The possible pathogenic factors are as follows: first, pregnancy and oral contraceptives; second, some chronic diseases; third, sunlight exposure; fourth, drugs; fifth, genetic factors, which is mainly for men; sixth, emotional factors. The current treatment measures are mainly local treatment and systemic treatment. Systemic treatment is to take vitamin C treatment in the form of intravenous injection, and promote hypopigmentation. Local treatment includes topical drug therapy, peeling therapy, facial mask therapy, laser or pulsed light therapy, etc (Jutley *et al*., 2016). The treatment of chloasma by western medicine mainly involves the usage of tranexamic acid, reduced glutathione, vitamin C, vitamin E, hydroquinone ointment, etc. The single application of hydroquinone ointment has certain limitations. The results of this study showed that patients in the treatment group treated with tranexamic acid combined with reduced glutathione had better advantages than those in the control group treated with hydroquinone ointment, P<0.05. According to recent clinical observation of tranexamic acid injection combined with glutathione and vitamin C in the treatment of chloasma by Chen Hengru, the patients in the observation group who received tranexamic acid injection combined with glutathione and vitamin C treatment had a

higher overall effective rate than those in the control group who received conventional treatment, which is consistent with the results of this study.

Many reports have pointed out that treatment of chloasma with reduced glutathione combined with tranexamic acid has certain effectiveness. The hemostatic tranexamic acid has a good hemostatic effect in the fibrinolytic system. Sharing consistent chemical structure with tyrosine, it can induce competitive inhibition (Ma, Sivamani, 2015), avoid binding of tyrosinase and tyrosine, reduce the production of melanin and thus exert a good therapeutic effect on chloasma. Glutathione exists in human body in the form of oxidation type and reduction type. It belongs to a tripeptide compound containing a hydrophobic group. Reduced glutathione can activate the hydrophobic enzyme and plays the role of activating the REDOX system, thus forming the detoxification effect. The composition of reduced glutathione includes glycine, cysteine, and glutamic acid. By participation into the sugar metabolism process in vivo, it can promote the generation of high-energy in the body to achieve the effect of coenzyme. Plus its ideal effect in integrated detoxification and anti-oxidation, tranexamic acid combined with reduced glutathione has significant effect on chloasma.

CONCLUSIONS

In summary, implementation of combination therapy of reduced glutathione and tranexamic acid in patients with chloasma disease can better improve the overall treatment efficiency, while effectively lowering severity of the disease and reducing chloasma area. In this study, tranexamic acid is a typical hemostatic drug with the same chemical structure as tyrosine, which can induce the formation of competitive inhibition, prevent the binding of tyrosinase to tyrosine, thus significantly reducing melanin production. Meanwhile, glutathione exists in both oxidized and reduced forms in the human body. Reduced glutathione can stimulate thiolase and exert the effect of activating the redox system, resulting in good detoxification. The composition of reduced glutathione including glycine, cysteine and glutamic acid participates in the process of glycometabolism in the human body, which can promote high energy production in the body to achieve the effect of coenzyme, demonstrating ideal integrated detoxification and anti-oxidation effect. The combination of the two can better display the treatment effect. In addition, the sample size of this study is limited, and larger sample data research is needed in the future to better demonstrate this conclusion.

REFERENCES

Chen HR and Deng LH (2014). Recent clinical observation of tranexamic acid injection combined with glutathione and vitamin C for the treatment of chloasma. *China Medicine and Pharmacy,* **4**(02): 10-12+63.

Jutley GS, Rajaratnam R and Halpern J (2016). Systematic review of randomized controlled trials on interventions for melasma: An abridged Cochrane review. *J. Am. Acad. Dermatol.,* **70**(2): 369-373.

Kashanian M, Shahpourian F and Zare O (2017). A comparison between monophasic levonorgestrel-ethinyl estradiol 150/30 and triphasic levonorgestrel-ethinyl estradiol 50-75-125/30-40-30 contraceptive pills for side effects and patient satisfaction: A study in Iran. *Eur. J. Obstet. Gynecol. Reprod. Biol.,* **150**(1): 47-5.

Luo DQ and Yang W (2016). A comparison of topical application of 1% tetracaine gel before and after the procedure in removal of cutaneous pigmentation with Q-switched neodymium-doped yttrium aluminium garnet laser (1064/532nm). *Photomed. Laser Surg.,* **28**(2): 213-217.

Ma C and Sivamani RK (2015). Acupuncture as a Treatment Modality in Dermatology: A Systematic Review. J Altern Complement Med. , **21**(9): 520-529.

Rivas S and Pandya AG (2018). Treatment of melasma with topical agents, peels and lasers: An evidence-based review. *Am. J. Clin. Dermatol.,* **14**(5): 359-376.

Yu H, Liang H, Ju XL, Su JW and Du K (2015). Clinical observation of laser combined with tranexamic acid, glutathione and vitamin C for the treatment of chloasma. *Progress in Modern Biomedicine*, **15**(27): 5295-5298.

Zhao Y (2013). Clinical analysis of tranexamic acid combined with reduced glutathione for the treatment of chloasma. *China Practical Medical*, **8**(05): 174-175.

Zhao Y and Tang Y (2015). Clinical analysis of tranexamic acid combined with reduced glutathione for the treatment of chloasma. *China Medical Abstracts (Dermatology),* **32**(05): 538.

Zheng H (2017). Clinical observation of laser combined with tranexamic acid, glutathione and vitamin C for the treatment of chloasma. *China Medical Cosmetology*, **7**(03): 46-48.