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ORIGINAL ARTICLE

Efficacy of Topical Silymarin and Intradermal Injection of Tranexamic Acid in the Treatment of Melasma: A Comparative Study

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ABSTRACT

Background: Melasma is a skin disorder that mostly effect females in reproductive age. Modern treatment techniques are needed to address these issues.

Objective: The aim of this study was to explore the efficacy of topical silymarin and intradermal injection of tranexamic acid in the treatment of melasma.

Material and Method: The current randomized control trial study was carried out at PGMIQ/ BMC Hospital Quetta from January 2023 to June 2023 after taking approval from the ethical board of the institute. A total of 76 individuals of both gender and different age groups (15-45 years) presented with melasma to the dermatology department were included. The study participants were randomly divided equally in to two groups of 38 individuals each. Group A was administered silymarin cream twice a day for 12 weeks, whereas Group B got weekly intradermal injections of tranexamic acid. The modified Melasma Area and Severity Index score was determined at the beginning of therapy, at each follow-up appointment, and at the end of treatment. At the end of three months of therapy, efficacy was evaluated, and a mMASI score reduction of more than 50% from the baseline considered effective. To analyze the data, SPSS version 24.0 was used. To investigate effect modifiers, data stratification was carried out for age, gender, lesion location, severity, and disease duration. The Chi Square test was used to compare the effectiveness of the two groups and post-stratification, with a P-value of ≤0.05 being considered statistically significant.

Results: A total of 76 individuals participated in this study out of which 58(76.3%) were females and 18(23.6%) were male. Participants in Group A had a mean mMASI score of 11.91±4.95 at baseline, while those in Group B had a mean score of 14.36±4.93 (the p-value=0.038). Patients in Group A had a mean mMASI score of 7.33±3.74 at the end of therapy, while those in Group B had a mean score of 6.67±2.89 (p-value=0.41). The mean change in the mMASI score was 8.58±3.11 in Group B and 4.6±1.95 in Group A. The p-value was less than 0.05, indicating that the difference was significantly different**.** Our study's findings revealed that 17 (44.7%) of the 38 participants in Group A experienced efficacy and 21(55.2%) did not. However, 26 (68.4%) of the 38 participants in Group B confirmed that the therapy was effective. The difference was considered statistically significant, with a P-value of 0.03**.** There was no statistically significant variation in the effectiveness stratification according to age and gender, (p value was greater than 0.05).

Conclusion: Our study concluded that for the treatment of melasma topical silymarin is not statistically as effective as intradermal injection of tranexamic acid.

Keywords: Efficacy; Topical; Silymarin; Intradermal injection; Tranexamic acid; Melasma

INTRODUCTION

A pigmentary condition called melasma is frequently seen in females of reproductive age and can be caused by hypermelanosis.[1] Clinically, it appears as symmetrically dispersed hyperpigmented macules that may be reticulated, punctate, or confluent. The majority of people with Fitzpatrick skin types III–V have this disease.[2] It mostly affects regions exposed to UV rays, including the forehead, cheeks, temples, and upper lips.[3] Affected individuals range from 5 to 70%, with just 10% being men.[4] Melasma has a detrimental impact on the patient's life as it can lead to psychological distress and interfere with their social life and emotional well-being.[4] The over activity of the melanin pigment causes this medical condition, which leads to melanin accumulation in the afflicted skin's dermal, epidermal, or both layers.[2] Sunscreens, topical hydroquinone, topical tretinoin, azelaic acid, kojic acid, local chemical peeling agents, lasers, and dermabrasion are all used to treat melasma, either alone or in combination.[4] Although there are many possibilities, the best therapy with fewer side effects still needs to be found since response is inconsistent, unsatisfying, takes a long time, and is typically resistant to existing therapies.

Thus, new treatment techniques are needed to address these issues.[5] The complex combination of polyphenolic compounds known as silymarin is isolated from the milk thistle plant, Silybum marianum.[6]Its primary active ingredient, silibinin, possesses potent anti-inflammatory and antioxidant qualities. When silymarin is used dose-dependently, melanin synthesis is decreased without compromising cell viability.[7-8]As a plasmin inhibitor, tranexamic acid binds to the lysine binding sites of plasminogen molecules in a reversible manner.[9-10] This causes the tyrosinase activity to drop, the generation of prostaglandins to decrease, and the amount of free arachidonic acid to decrease. Healthy skin that is not exposed to the sun is unaffected by it.[4] An earlier study by Lee et al. examined the effectiveness of localised transexamic acid in treating melasma. One hundred female patients with melasma were chosen for this study; of them, 9.4% had good responses and 76.5% had fair responses.[11] It has a significant recurrence rate even with the use of several therapeutic techniques. Tranexamic acid used intradermally produces greater local side effects and requires particular handling. Self-administration is a benefit of silymarin treatment, which is also inexpensive. Limited international data and lack of local research exist on silymarin. Therefore the current study was conducted to find out the efficacy of topical silymarin and intradermal injection of tranexamic acid in the treatment of melasma.

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MATERIAL AND METHOD

The current randomized control trial study was carried out at PGMIQ/ BMC Hospital Quetta from January 2023 to June 2023 after taking approval from the ethical board of the institute. A total of 76 individuals of both gender and different age groups (15-45 years) presented with melasma to the dermatology department were included while pregnant women ,lactating mother ,individuals taking treatment for the last three months for melsma, those on oral contraceptive pills in last 1 year, or taking photosensitive drugs or anticoagulants were excluded from the study. By lottery the study participants were randomly divided equally in to two groups of 38 individuals each. Their personal information, including age, gender, and length of sickness, was recorded in the proforma.

At the beginning of therapy, at follow-up appointments (weeks four and eight), and at the conclusion of therapy, the participants were photographed. Group A was administered 1.4% silymarin cream twice a day for 12 weeks, whereas Group B got weekly intradermal injections of tranexamic acid at 1-cm intervals in the affected region using an insulin syringe with 1ml and a 30-gauge needle. Each insulin syringe had 4 mg/ml of tranexamic acid since it contained 0.04 ml (four units of insulin syringe) of tranexamic acid & 0.96 ml of normal saline. The modified Melasma Area and Severity Index score was determined at the beginning of therapy, at each follow-up appointment, and at the end of treatment. At the end of three months of therapy, efficacy was evaluated, and a mMASI score reduction of more than 50% from the baseline considered effective. Data was entered into the pre-made Performa, and data confidentiality was maintained. The area and darkness of facial melasma are the two components that are scored in order to get the modified MASI Score. The four primary parts of the face are the forehead (30%), chin (10%), left malar (30%), and right malar (30%). A numerical number is allocated to region (A) of engagement based on the percentages of the affected region. 0 indicates that no region is engaged. 1 indicates <10% impacted area, 2 = 10-29% impacted area 3 = 30–49% impacted area, 4 = 50–69% affected area, 5 = 70–89% affected area, and 6 = 90% or over 90% affected area. The following scale is used to assess skin for Darkness of Melasma (D): 0 denotes normal skin colour, 1 somewhat noticeable pigmentation, 2 mild hyperpigmentation, 3 moderate hyperpigmentation, and 4 severe hyperpigmentation. The mMASI score, which is determined by summing the scores for the four facial regions, ranges from 0 to 24. The overall mMASI score is equal to 0.3 × A (right malar) × D (right malar) + 0.3 × A (left malar) × D (left malar) + 0.3 × A (forehead) × D (forehead) + 0.1 × A (chin) × D (chin). To analyze the data, SPSS version 24.0 was used. The mean and standard deviation of age, illness duration, and mMASI score at baseline and after therapy were displayed. Frequencies and percentages for gender, lesion location, and effectiveness were shown. To investigate effect modifiers, data stratification was carried out for age, gender, lesion location, severity, and disease duration. The Chi Square test was used to compare the effectiveness of the two groups and post-stratification, with a P-value of ≤0.05 being considered statistically significant.

RESULTS

A total of 76 individuals participated in this study out of which 58(76.3%) were females and 18(23.6%) were male .the mean age of the study participants was 31.30±8.69 years. Group A's mean age was 29.65±6.92 years, whereas Group B's was 30.95±8.16 years. According to study findings, patients' lesion durations ranged from a minimum of one month to a maximum of twelve months, with an average of 6.043±2.76 months. Participants in group A had an average lesion duration of 6.41±2.73 months, whereas those in group B had a mean period of 5.78±2.80 months. Out of the total individuals of the study in both groups 20(26.3%) individuals in A group and 44(57.8%) had lesions on cheeks as presented in figure 1. Out of 38 individuals in A group 9(23.4%) participants had mild disease, 19 (50%) had moderate and 10(26.3%) had sever disease but in B group 5(13.1%) participants had mild, 14(36.8%) had moderate and 19(50%) had sever disease. Participants in Group A had a mean mMASI score of 11.91±4.95 at baseline, while those in Group B had a mean score of 14.36±4.93 (the p-value=0.038). Patients in Group A had a mean mMASI score of 7.33±3.74 at the end of therapy, while those in Group B had a mean score of 6.67±2.89 (p-value=0.41). The mean change in the mMASI score was 8.58±3.11 in Group B and 4.6±1.95 in Group A. The p-value was less than 0.05, indicating that the difference was significantly different.as presented in table 1. Our study's findings revealed that 17 (44.7%) of the 38 participants in Group A experienced efficacy and 21(55.2%) did not. However, 26 (68.4%) of the 38 participants in Group B confirmed that the therapy was effective. The difference was considered statistically significant, with a P-value of 0.03 as presented in table 2. There was no statistically significant variation in the effectiveness stratification according to age and gender, (p value was greater than 0.05) as presented in table 3.

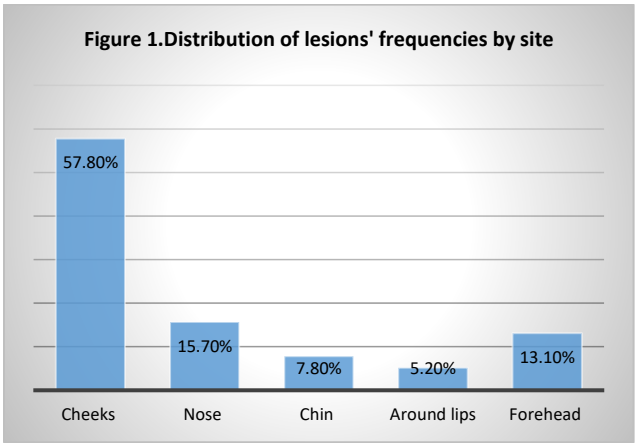

Table 1: Group-to-Group Comparison Of MMASI and MMASI Change

MMASI	Group A	Group B	P- Value
Baseline	11.91±4.95	14.36±4.93	0.038
End of Treatment	7.33±3.74	6.67±2.89	0.41
Change	4.6±1.95	8. 58±3.11	Less than 0.05

Table 2: Comparing the Effectiveness of the Two Groups

Groups	Effectiveness Yes (%)	No (%)	Total
Tranexamic acid (Group-B)	26(68.4%)	12(31.5%)	38
Silymarin (Group-A)	17(44.7%)	21(55.2%)	38

Table 3: Data stratification

		Efficacy	A group	B group	Vale of P
Age in years	30 or below	Yes No	12(31.5%) 15(39.4%)	12(31.5%) 7(18.4%)	0.177
	Above 30	Yes No	5(31.1%) 6(15.7%)	14(36.8%) 5(13.1%)	0.123
Gender	Male	Yes No	3(7.5%) 5(13.1%)	8(21%) 4(10.5%)	0.152
	Female	Yes No	14(36.8%) 16(42%)	18(47.3%) 8(21%)	0.078

DISCUSSION

Melasma is a hyperpigmentary condition that is quite frequent in Asian and Latin American women. Approximately 5–70% of the global population is affected. It significantly impacts the individual's emotional health and standard of life.[12]The guiding principles of treatment include UV protection, melanocyte activity inhibition, melanin production, and the disruption and elimination of melanin pigments.[1] There are many different treatment methods for melanomas, however sunscreens are typically used in combination with other ingredients like steroids, tretinoin, local chemical peeling agents, laser monotherapy, or dermabrasion.[4]Melasma has a high recurrence rate and is resistant to several therapeutic methods even after numerous treatments.[12-13] The milk thistle plant, Silybum marianum, is the source of silymarin. It is a strong antioxidant that lessens and inhibits the negative effects of sunlight's ultraviolet radiation (UVR).[8] Tranexamic acid (TA) was just recently become available as a treatment for melasma. Tranexamic acid (TA) was just recently become available as a treatment for melasma.[14]The use of intralesional TA injection for melanomas is justified by the fact that it is economical and free of systemic adverse effects.[15] Therefore the current study was conducted to find out the efficacy of topical silymarin and intradermal injection of tranexamic acid in the treatment of melasma. A total of 76 individuals participated in

this study. The mean age of the study participants was 31.30±8.69 (15-445) years. The mean age of those participating in a study by Elfer and El Magharby et al. was 40.07, with ages ranging from 28 to 52, which is higher than in our study.[1] In our study 58(76.3%) were females and 18(23.6%) were male. In a research by Sharma et al.[16], of 100 participants, 8% were male and 92% were female. This is similar to our study, where females were more than men. In our study 44(57.8%) of the lesions were on cheeks, 12(15.7%) were on nose, 10(13.1%) were on forehead and 6(7.8% were on chin. Out of 42 individuals, 32 (76.2%) had centrofacial involvement and 10 (23.80%) had malar region involvement, according to a research by Elfer & El Magharby et al.[1] The majority of patients in our research had centrofacial involvement, thus this was comparable. Our study found that melasma lasted anywhere from one month to a year, however Ahmad Nofal et al.'s study found.[3] It ranged from three months to twenty years.[17] Our study's findings revealed that 17 (44.7%) of the 38 participants in Group A experienced efficacy and 21(55.2%) did not. However, 26 (68.4%) of the 38 participants in Group B confirmed that the therapy was effective Elfar & ElMaghraby et al. examined the effects of silymarin cream (Group B), glycolic acid peel (Group C), and tranexamic acid intradermal injection (Group A) in a research they conducted in 2015. With a mean of 41.85%, Group B shown the most efficacy, followed by Group A with a mean of 39.24%, and Group C with a mean of 20.10%, which demonstrated the lowest efficacy. These outcomes went opposed to our research, which found that Group B (intradermal tranexamic acid) was more effective.[1] Researchers Sharma et al. & Shetty et al. evaluated the effects of oral and intradermal tranexamic acid injections. Research' findings indicated that intradermal tranexamic acid injections were more effective, and our study's findings were similar to those of other research.[16-18]In our study participants in Group A had a mean mMASI score of 11.91±4.95 at baseline, while those in Group B had a mean score of 14.36±4.93 (the p-value=0.038). Patients in Group A had a mean mMASI score of 7.33±3.74 at the end of therapy, while those in Group B had a mean score of 6.67±2.89 (p-value=0.41). The mean change in the mMASI score was 8.58±3.11 in Group B and 4.6±1.95 in Group A. our study findings are with in contast with the previous study.[1] Melasma responded to both treatment choices in our study, although the intradermal transxamic acid group demonstrated statistically significant superior effectiveness as compared to the silymarin group. An innovative and cutting-edge melasma therapy method with few adverse effects is intradermal tranexamic acid injection. The sample size for this study was small, and it was carried out in a single place. Therefore, it is advised that future research be multicentric and carried out with a larger sample size in order to minimize bias. Another research limitation was the short follow-up time; thus, future studies should include long-term follow-up with melasma patients.

CONCLUSION

Our study concluded that for the treatment of melasma topical silymarin is not statistically as effective as intradermal injection of tranexamic acid. An effective treatment option that may be used in outpatient settings is the intradermal injection of tranexamic acid.

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