ABSTRACT
Melasma is one of the most common, therapy-resistant forms of acquired hyperpigmentation. The aim of the present study was to assess the efficacy and side effects of chemical peels with 35% glycolic and 15% trichloroacetic acid (TCA) in conjunction with 20% azelaic acid cream in the treatment of melasma. Twenty-six women aged 22-54 years with different forms of melasma have been treated. Six of them were with phototype II, 11 with phototype III and 9 with phototype IV. Disease severity was assessed at the beginning and at the end of therapy according to the Melasma Area and Severity Index (MASI). Patients were randomly divided in two groups – Group I (n=12) treated with 35% glycolic acid and Group II (n=14) treated with 15% TCA. A significant reduction in MASI values after therapy was observed in all patients without significant difference between Group I and Group II (t=0.12; p>0.05). No statistical difference was established among final MASI values of women with phototypes II, III and IV (t=0.25; p>0.05). Side effects were light and negligible. Therapy was positively assessed by the patients. In conclusion, chemical peels with 15% TCA and 35% glycolic acid in conjunction with 20% azelaic acid reduce significantly MASI values after therapy and are equally effective in the treatment of melasma.

Key words: melasma, peel, glycolic acid, TCA

INTRODUCTION
Melasma is an acquired hyperpigmentation of the face affecting predominantly women. Multiple etiologic factors have been implicated: high estrogen states (pregnancy, oral contraceptives), genetic factors, cosmetics and autoimmune thyroid disease. Sunlight exposure appears to be essential for its development.

Conventional therapy for melasma consists of keratolytic (tretinoin, resorcin, glycolic and trichloroacetic acids etc) and depigmenting agents (hydroquinone, kojic and azelaic acids). It has been established that chemical peels potentiate the effect of the depigmenting agents and reduce significantly the Melasma Area and Severity Index (MASI) (3, 4, 5, 6).

AIM
The aim of the present study was to assess and compare the efficacy and side effects of chemical peels with 35% glycolic and 15% trichloroacetic acids (TCA) in conjunction with 20% azelaic acid cream in the treatment of melasma.

PATIENTS AND METHODS
PATIENTS
Twenty-six women aged 22-54 years (mean 25) were enrolled in the study. The pattern of melasma was as follows - six patients with centrofacial, four with mandibular, four with malar and twelve with mixed melanos. The mean duration of the disease was 10.6 years. Six women had Fitzpatrick skin type II, 11 were with skin type III and 9 with skin type IV. Thirteen had had previous pregnancy, 11 had received oral contraceptives and 2 had been on estrogen replacement therapy. Fifty percent of the patients used no photoprotection outdoors. Ten women had undergone previous treatment with other agents with different, but as a whole poor response. Nursing and pregnant patients as well as those who had conducted depigmenting therapy during the previous three months were excluded from the study. According to their birth date patients were randomly allocated in two groups - Group I (n=12) treated with 35% glycolic acid peel and Group II (n=10) treated with 15% TCA peel.

METHODS
Patients were pretreated with tretinoin (Acnederm gel 0.05%) for two weeks. A series of four peels spaced 15 days apart was applied to each patient.

The face was first treated with a mild cleanser and water and prepared with a pre-peel toner. TCA was applied with two cotton-tipped applicators. Hydrating mask was spread on the whole face after the appearance of even pinkish-white frosting. Glycolic acid was applied with a soft fan-like brush. The peeling solution was neutralized and removed with water after the development of slight erythema and/or frosting.

After the peel the patients were directed to use emol-
Assessment of therapeutic efficacy

The same investigator evaluated all patients. This was performed before and after treatment and six months after the end of the therapeutic course. Melasma severity was scored using the MASI (2). In this system the face is divided into four areas: forehead, right malar, left malar and chin that correspond respectively to 30%, 30%, 30% and 10% of total face area. The melasma in each of these areas was graded on three variables: percentage of total area involved on a scale from 0 (no involvement) to 6 (90-100% involvement); darkness on a scale from 0 (absent) to 4 (severe); homogeneity on a scale from 0 (minimal) to 4 (maximum). The MASI was then calculated by the following equation:

\[
\text{MASI} = 0,3(\text{DF+HF})\text{AF} + 0,3(\text{DMR+HMR})\text{AMR} + 0,3(\text{DML+HML})\text{AML} + 0,1(\text{DC+HC})\text{AC},
\]

where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar, C is chin and the values 0,3 and 0,1 are respective percentages of total facial area.

At the end of the treatment patients were asked to give their subjective assessment of their clinical response to the peels.

Statistical methods

Statistical analysis was performed with the help of Student's t-test for comparing MASI values before and after treatment and among patients with phototypes II, III and IV.

RESULTS

Clinical results

A statistically significant decrease in average MASI scores after treatment was observed in both Group I and Group II (Group I – MASI before treatment 13,8±9,4; after treatment 5,0±1,2; t=18,9; p<0,001; Group II - MASI before treatment 14,6±7,7; MASI after treatment 6,2±1,9; t=16,3; p<0,001). No statistically significant difference was found between MASI values after the two therapeutic regimens (t=0,12; p>0,05), as well as among MASI scores of patients with phototypes II, III and IV (MASI after treatment for phototype II - 6,0±2,7, for phototype III - 6,8±1,5 and for phototype IV - 7,7±2,2; t=0,25; p>0,05).

Patients' subjective assessment

After treatment patients were asked to evaluate the discomfort from the two different peeling solutions. They found the TCA peel caused more discomfort – slight pain and strong stinging during the application, excessive desquamation during the next 4-5 days, which interfered with their daily activities. The glycolic acid procedure was associated with stinging and nipping, which were most pronounced during the first procedure.

Sixteen of the patients (8 from Group I and 8 from Group II) assessed therapeutic efficacy as greater than 90% improvement, 8 (6 from Group I and 2 from Group II) – as greater than 50% improvement and 2 (Group I) - as greater than 30% improvement.

Adverse reactions

They were observed in eight patients from Group I and included persisting postpeel erythema (on the cheeks, chin and around the nose). It was treated with moderately potent topical corticosteroids. In two patients crusting developed as a result of a deeper penetration of the solution. In six women from Group II postlesional hyperpigmentation was observed.

Long-term follow-up

Seventeen (65%) of the patients were followed-up six months after the treatment. Only the ten of them, who continued topical therapy with sunscreens and azelaic acid maintained improvement. The others experienced relapse, although they were still improved over the pretreatment measurements.

DISCUSSION

Melasma is a serious medical and esthetic problem, especially in dark-skinned people. Despite the impressive number of available therapeutic agents treatment results are often disappointing, as the condition usually recurs. The principle rules in the treatment of melasma include avoidance of excessive sun exposure, retardation of melanocyte proliferation, inhibition of melanosome formation and promotion of melanosome degradation (6). This could be achieved by regular use of depigmenting agents and sunscreens with or without keratolytics.

Superficial and medium-depth chemical peels are recommended for the treatment of melasma, mainly in fair-skinned individuals. People with higher phototype are usually resistant to therapy and therapeutic results are unsatisfactory (5). However, this was not observed in our patients probably because of the small number of women with phototype IV. Chemical peels act by increasing the penetration of medical therapy, not only by “peeling off” the pigment (3). This was confirmed in the study conducted by Sarkar R et al (5) in two groups of Indian patients. The first group was treated with 30 and 40% glycolic acid peels and a topical regimen of a modified Kligman formula (0,05% tretinoin, 2% hydroquinone and 1% hydrocortisone). The other group received the topical regimen alone. After a total of six peels a significant decrease in MASI values was established in both groups (p<0,001). The women who received the glycolic acid peel showed a statistically
significant trend toward a more rapid and greater improvement ($p<0.001$).

Azelaic acid is a naturally occurring, straight-chained, saturated dicarboxylic acid that acts as a competitive inhibitor of tyrosinase and interferes directly with melanin biosynthesis. Various studies report “good” to “excellent” results in 63-80% of the patients with melanosine after 6 months of treatment with 20% azelaic acid cream in conjunction with broad-spectrum sunscreens (1). Azelaic acid has practically no effect on normal melanocytes and its long-term use has not been associated with ochronosis. Such changes were not observed in our patients also.

The results of the present study demonstrate that chemical peels with 35% glycolic and 15% TCA in conjunction with azelaic acid and tretinoin are equally effective in the treatment of melasma and are positively accepted by the patients. This was confirmed by the fact that 16 (62%) of them assessed therapeutic efficacy as excellent (greater than 90% improvement) and 8 (31%) as good (greater than 50% improvement). Side effects were light and negligible except for the postlesional hyperpigmentation, which disappeared in about 4 weeks. It developed most often around the mouth and on the chin in TCA-treated patients probably as a result of the premature desquamation of the epidermis in these regions due to the active contraction of the muscles during speaking and eating.

The long-term follow-up of the patients demonstrated that therapeutic results persist only in those of them, who continued the topical application of azelaic acid and broad-spectrum sunscreens. This confirms the necessity of a constant maintenance therapy of melasma - an obligatory condition for the achievement of long-lasting therapeutic results (4).

REFERENCES:

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