

CONFIDENTIAL

Universitäts-Hautklinik Freiburg
Research group for phytopharmakology and dermatotherapy
Research group für pharmaco-economics and outcomes research

Head: Dr. M. Augustin

in Cooperation with

**IFKS - Private Institute for
Research Management & Clinical Studies**

Head: Dipl. Psych. I. Zschocke

Final Biometric Report

On the Study:

Ointment Preparation containing NADH in Teleangiectasis"

Sponsor: Labor Birmayer, Vienna

Study Participants: Prof. Dr. W. Vanscheidt, Study Manager
Dr. M. Augustin, Study Manager
Dr. D. Trefzer, Coordinator, Optical Research
Dr. N. Denig, Study Physician
Dipl. Psych. I. Zschocke, Biometry

Monitoring: PD Dr. H. Schlachter, Munich

1. Summary

Objective Investigation of the efficacy of an ointment preparation containing NADH with respect to the reduction of facial telangiectasis.

Methods Prospective, open observational study with randomized-blinded assessment over 6 weeks. Weekly follow-ups. As part of a wrinkle study, n=36 patients with facial wrinkles were recruited. Of these, n=17 presented with telangiectasis. These were treated and assessed as the second target structure.

The telangiectases were examined independently prior to therapy and during the course of the study by two blinded, dermatologically experienced raters on the basis of photos recorded in standardized procedures. Two methods were applied:

1) Score by rank (Scale from 1=best picture to 6=worst picture).

2) Quantitative telangiectasis score

The raters' results were averaged, the interrater correlation continuously checked. It was always in the range of highly significant correlations.

Results There was significant improvement in the telangiectases, with no exception, and usually to complete healing.

Conclusion

The test preparation with NADH is extremely effective in practically all patients in the reduction of telangiectases.

Recommendations on procedure:

With respect to efficacy in the area of telangiectases, there is a considerable benefit and marketing potential. It is recommended that the effects be tested in a further study using skin-physiological methods. Thereafter, a further application observation should be performed on patients with relevant skin diseases, such as Rosacea telangiectatica, spider vein varicosis.

2. Methods

2.1 Methods of Study Performance and Documentation

Please refer to the detailed study protocol.

The foto processing was performed by Optical Research Inc., Freiburg. The assessments of efficacy were performed by the two raters using prints of the digital photos.

2.2 Methods of Rating the Degree of Teleangiectasis

Corresponding to the procedure of assessment during the course of therapy with respect to degree of wrinkles, two blinded raters examined the degree of teleangiectasies at various points of time. In order to attain greater methodological certainty, both score values and rank values were determined.

The interrater correlation of the rank values was between 0.52 and 0.86, whereby the time points „Therapy begin“ and „Therapy end“ as the main target criteria attained values of 0.78 and 0.66. Thus the reliability of the assessment of degree of teleangiectasies is given and the formation of averaged rank values to increase the validity was appropriately performed. Comparable interrater correlations in the score values provided the basis for the formation of averaged score values.

3. Results

3.1 Assessment of the Teleangiectases

3.1.1 Treatment outcome measured on the Teleangiectasis-Score

A teleangiectasis score was determined as one of the two assessment types in this study. Two blinded dermatological raters independently rated the degree of telangiectasis on a 10-point scale from 1 (slight telangiectasis) to 10 (very severe telangiectasis). A „teleangiectasis score“ was formed from the means of the two ratings.

Under therapy with the test preparation, the mean degree of telangiectasis prior to therapy was 3.6 ± 1.2 , at the end of therapy (5 wks) 1.5 ± 0.5 (Fig. 1). This difference was significant, as was the difference between 4 weeks and therapy begin.

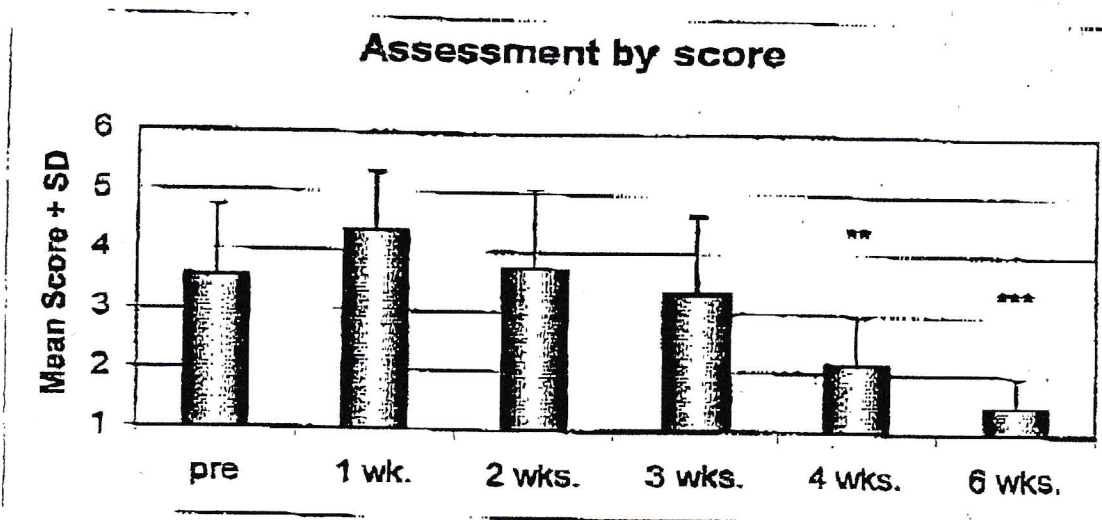


Fig. 1: Course of wrinkles under treatment with ointment containing NADH in the group of therapy responders (n=17). The rank course is shown as the mean of 2 independent ratings (Scale: 1=best picture to 6=worst picture) * $p < 0.05$, ** $p < 0.01$ versus the time prior to therapy.

3.2.2 Course of therapy measured on the Teleangiectasis Rank Values

In order to achieve greater methodological certainty, a second assessment mode was applied. The two blinded raters assigned a ranking to the skin findings. The finding with the mildest degree of teleangiectasis was assigned rank „1“, the finding with the greatest degree of teleangiectasis was assigned rank „6“.

Under therapy with the test preparation, the mean rank prior to therapy was 4.1 ± 1.1 , at the end of therapy (6 wks) 1.4 ± 0.5 (Fig. 2). This difference, like all other differences within the various observation times, was not significant.

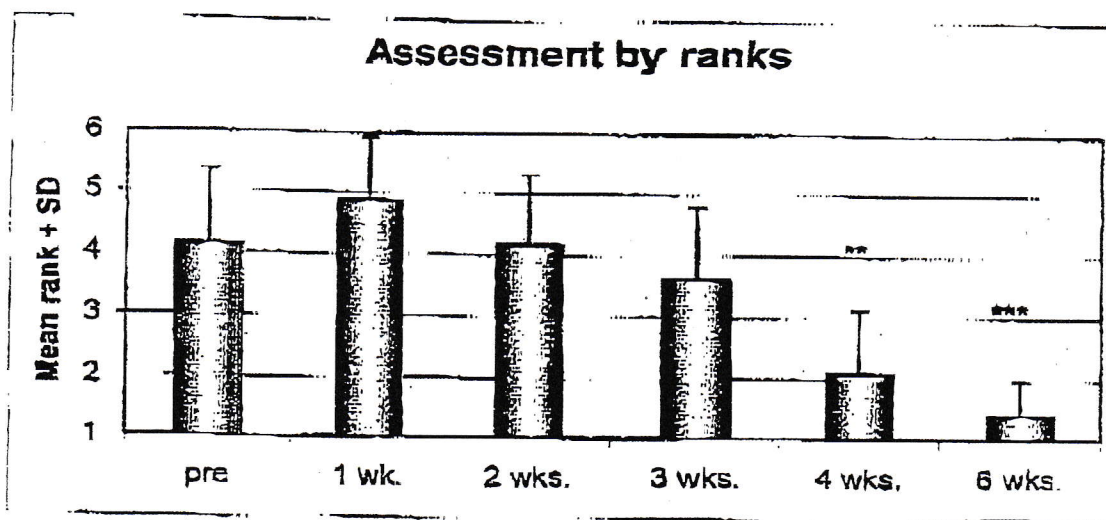


Fig. 2: Course of wrinkles under treatment with an ointment containing NADH in the group of therapy responders (n=17). The figure shows the rank course as mean of 2 independent ratings (Scale: 1=best picture to 6=worst picture) **p<0.01, ***p<0.001 versus time before therapy.

4. Conclusions and Recommendations

Conclusion

The test preparation containing NADH is extremely effective in practically all patients in the reduction of telangiectases.

Recommendations on Procedure

With respect to efficacy in the area of telangiectases, there is a considerable clinical potential. It is recommended that the effects observed in this study be tested in a further confirmative study using skin-physiological methods. Thereafter, a further application observation should be performed on patients with relevant skin diseases, such as Rosacea telangiectatica, spider vein varicosis.

Consideration should also be given to repeating the present study with the new NADH-preparation.

Freiburg, 27.10.00

Merzhausen, 29.10.00

Checked for correctness:

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