Vitamin B_{12} ointment containing avocado oil in the therapy of plaque psoriasis

Markus Stücker[1], Ulrike Memmel[1], Matthias Hoffmann[1], Joachim Hartung[2], Peter Altmeyer[1]

[1] Department of Dermatology and Allergology, Ruhr University, Bochum
(Director: Prof. Dr. Peter Altmeyer)

[2] Department of Statistics of the University of Dortmund and project 'Meta-Analysis in Biometry and Epidemiology', SFB 475 of the DFG

To appear in:

DERMATOLOGY

Correspondence: Dr. Markus Stücker, Clinic for Dermatology and Allergology, Ruhr University, Bochum, Gudrunstrasse 56, D-44791 Bochum/Germany, Tel: +49 234 509 3448, +49 234 509 1, Fax: +49 234 509 3409, E-mail: M.Stuecker@derma.de

Summary

Background: There are already many effective topical therapies available for use in the treatment of chronic plaque psoriasis. Unfortunately, these treatments are often associated with a not insignificant risk of undesirable effects.

Objective and methods: In the randomized, prospective clinical trial discussed in the following, the therapeutic effects of the standard vitamin D_3 analog calcipotriol were evaluated against those of a recently developed vitamin B_{12} ointment containing avocado oil preparation in an intraindividual right/left-side comparison. The efficacy of vitamin B_{12} in the treatment of psoriasis has already been demonstrated. The trial collective consisted of 13 patients, ten men and three women, with chronic plaque psoriasis. The observation period was 12 weeks; the effects of therapy were assessed on the basis of a PASI score adapted to the right/left-side comparison technique, the subjective evaluations of the investigator and patients and the results of 20 MHz sonography.

Results: There was more rapid development of beneficial effects with use of calcipotriol in the initial 8 weeks, although differences in effects were significant only at the time point therapy week 8 ($p<0.05$). After 12 weeks, neither the PASI score nor 20 MHz sonography showed significant differences between the two treatments. While the efficacy of the calcipotriol preparation reached a maximum in the first 4 weeks and then began subsequently to subside, the effects of the vitamin B_{12} ointment containing avocado oil remained at a constant level over the whole observation period. This would indicate that the vitamin B_{12} preparation containing avocado oil may be suitable for use in long term therapy, a hypothesis further supported by the fact that the investigator and patients assessed the tolerability of the vitamin B_{12} ointment containing avocado oil as significantly better in comparison with that of calcipotriol.

Conclusion: The results of this clinical trial provide evidence that the recently developed vitamin B_{12} ointment containing avocado oil has considerable potential as a well tolerated, long term topical therapy of psoriasis.

Key words:

Psoriasis, Vitamin B_{12} ointment containing avocado oil, Calcipotriol

1. Introduction

Many effective preparations for use in the topical therapy of psoriasis are currently available. In addition to the antipsoriatics dithranol, topical retinoids and corticosteroids, which have long been established as the standard therapeutic agents, vitamin D_3 analogs are being increasingly used in the topical therapy of psoriasis. One factor that is common to these topical agents is a significant potential for causing irritation (1). It has proved possible to reduce the risk of such undesirable effects by combining various topical agents or topical and systemic antipsoriatics and, at the same time, to reduce the costs of treatment (2,3,4).

An unfavorable benefit/side-effect profile will reduce compliance in patients who are already experiencing marked deterioration of quality of life as a result of psoriasis. For this reason, it is a recognized need to find topical antipsoriatics with a more positive side-effect profile. An exploratory investigation of the effects of an innovative vitamin B_{12} ointment containing avocado oil was conducted in the clinical trial discussed in this article.

Initial reports of therapeutic success after (mainly) parenteral administration of vitamin B_{12} in the treatment of psoriasis were made some 40 years ago.

Ruedeman et al. administered 1100 µg vitamin B_{12} i.m. daily over a period of 10 - 20 days in 34 patients with psoriasis vulgaris. There was complete remission in 11 cases, near complete remission in a further 11 cases, and significant improvement in symptoms in six cases (5). Cohen reported on psoriasis patients who had received 1000 µg vitamin B_{12} i.m. daily on 6 days per week over a 3-week period. In at least 50% of this collective, complete or near complete healing was achieved (6).

It can be assumed that the effects of the substance in the skin after systemic administration of vitamin B_{12} are relatively slight, as up to 90% of a dose is eliminated by the renal pathway within 48 hours and is therefore not available to the target organ – the skin (7). With topical application, the excellent depot characteristics (8) of the skin ensure that a large percentage of the vitamin B_{12} present in the ointment base remains continuously available. The fact that dermal vitamin B_{12} levels are reduced in psoriatic plaques and in apparently healthy skin in patients with psoriasis (9) is a reason for the use of vitamin B_{12} in psoriasis.

Any new antipsoriatic agent should exhibit innovative activity and a favorable cost-benefit profile while the recurrence rate should be low after discontinuation of therapy with the agent. The therapeutic efficacy should not be less than that of standard topical antipsoriatics. As the basic efficacy of vitamin B_{12} in the treatment of psoriasis has already been demonstrated, the aim of the clinical trial discussed here was to investigate whether the therapeutic effects of the new vitamin B_{12} ointment containing avocado oil[1] differ from those of a contemporary vitamin D_3 analog, calcipotriol[2]. The therapeutic effects were evaluated in a randomized, prospective clinical trial in an intraindividual right/left-side comparison.

2. Patients and methods

2.1 Patient collective

Included in the trial were 13 patients with stable psoriasis vulgaris; ten men and three women aged 38 - 67 years (52.9 ± 12.2 years). Mean duration of the disorder was 20.8 ± 12.7 years. Two patients were excluded from the analysis due to deviations from the trial protocol; one female patient who exhibited insufficient compliance by occasionally discontinuing use of the ointment and receiving intensive UV irradiation, and one male patient who applied calcipotriol to the skin sites allocated to vitamin B_{12}

---

[1] Regividerm®, Regeneratio AG, Wuppertal, Germany

[2] Psorcutan® ointment, Schering AG, Berlin, Germany

ointment containing avocado oil. Exclusion criteria were use of corticosteroids, topical retinoids, dithranol or vitamin D_3 analogs in the 7 days prior to commencement of the trial, modification of systemic therapy in the past 3 months or phototherapy during the past 6 weeks, the presence of pustular or erythrodermic forms of psoriasis or age less than 18 or greater than 70 years. Prior to inclusion, it was established that patients had no known hypersensitivity to calcipotriol or to vitamin B_{12}. Other exclusion criteria were avocado oil allergy and $\geq 60\%$ of body surface area requiring treatment on one side of the body (a contraindication for the use of calcipotriol).

The trial medication vitamin B_{12} – avocado oil contains only naturally occurring substances in a simplified formulation with few ingredients: these are vitamin B_{12} in a concentration of 700mg/kg, methylglycoside stearate (Emulsan®), avocado oil and distilled water, whereas avocado oil was added from cosmetic point of view, because of its physico-chemical properties, i.e. it spreads easily on the skin. The avocado oil of our trial preparation contents vitamin E (α Tocopherol) in a dosis of 82,9 mg/kg, whereas the values of vitamin A and D_3 were not detectable in the investigated preparation.

Patients received detailed information on the intended trial and gave their written informed consent. The trial had been approved by the Ethics Committee of the Faculty of Medicine of the Ruhr University in Bochum.

2.2 Trial design

During the 12 week observation period of the prospective, randomized trial, two ointment preparations containing calcipotriol or vitamin B_{12} with avocado oil were applied to psoriatic plaques on the contralateral body sides of each patient. The preparations were applied twice daily, once in the morning and once in the evening, by the patients themselves. Effects were monitored in control examinations after 2, 4, 8 and 12 weeks.

The primary target variable was the PASI score. The differences in treatment effects were evaluated on the basis of the severity and extent of psoriasis on the two body sides of each patient at baseline and final examinations as shown in the form of the modified PASI score. The modification made for the purposes of this trial concerned the area evaluated only; it is usually the whole body that is evaluated using a PASI score. As the method involved comparison of contralateral body sides, the PASI score per body side was given a 50% weighting and the head/neck area was ignored for practical reasons. Secondary variables were the subjective evaluations of efficacy made by the patients and the investigator. In addition, the effects of each treatment were quantified using 20 MHz sonography (DUB 20, Taberna pro medicum, Lüneburg, Germany) by measuring the width of the echo lucent area (which shows the extent of acanthosis and inflammatory infiltration) prior to initiation of therapy and 2, 4, 8 and 12 weeks after commencement of treatment (14). The echo density of the corium was also measured to provide an indication of cellular infiltration (15).

2.3 Statistics

In addition to descriptive methodologies, the t-test for paired samples was used. Bowker’s symmetry test for connected samples was used to analyze the results of subjective evaluation of the two tested preparations in the form of 2 x 2 contingency tables. Results with a significance level of $\alpha \leq 0.05$ were considered to be statistically significant.

3. Results

- **Evaluation of efficacy on the basis of the PASI score**

The baseline PASI score for the body side to which the vitamin B_{12} ointment containing avocado oil was applied was 9.1 ± 4.8. After 12 weeks therapy, the score had fallen to 0.8 ± 0.7 (PASI score range: 0 - 2.1).

The baseline PASI score for the body side to which calcipotriol was applied was 9.2 ± 5.1. After 12-weeks therapy, PASI scores were in the range 0 - 1.8 (mean: 0.8, SD: ±0.7). The effects of the vitamin D_3 analog were more rapid in the initial 8 weeks, as the reduction in mean scores shows (**Fig. 1, Tab. 1a, 1b**). However, there was no significant difference in the treatment effect (adjusted for baseline) after 2 weeks ($p=0.056$) or after 4 weeks ($p=0.055$). Only after 8 weeks the reduction of the PASI score was significantly more marked for calcipotriol therapy in comparison with vitamin B_{12} ointment containing avocado oil therapy ($p<0.05$). However, after 12 weeks (the target end point of the trial), the difference in treatment effect was only 0.09 (PASI score) in favor of calcipotriol ($p=0.534$).

If the mean PASI scores at two successive examination time points are compared, the differences between baseline and results after 2 weeks and between 2 weeks and 4 weeks are highly significant for both preparations ($p<0.0001$ in each case). However, there is no significant difference in the reduction of the PASI score between the examination time point 4 weeks and 8 weeks for the calcipotriol preparation ($p=0.067$). The effects of this preparation therefore stagnated, while there continued to be a significant improvement in symptoms during therapy with the vitamin B_{12} preparation containing avocado oil ($p<0.05$). As a result, the treatment effect approached equivalence after 12 weeks.

- **Subjective evaluation of the two topical preparations by patients and the investigator**

To increase the value of the results of statistical analysis, the originally 4 x 4 contingency tables were reduced to 2 x 2 contingency tables, whereby the results "very good" and "good", and "moderate" and "poor" were evaluated in one group.

Due to a random effect, the evaluation of efficacy by the investigator was better for the calcipotriol preparation than for the vitamin B_{12} ointment containing avocado oil ($p=0.56$). The global evaluation of efficacy by patients was identical with the investigator’s evaluation on the basis of the reduced contingency tables (**Figs. 2a, 2b**).

In the patients’ evaluation of the feeling of skin and the effects on clothing, there was a significant superiority of the vitamin B_{12} ointment containing avocado oil over calcipotriol ($p<0.05$).

The two preparations were identically evaluated for odor, while the color of the calcipotriol preparation (white) was tendentially more acceptable than that of the vitamin B_{12} preparation containing avocado oil (pink) ($p=0.32$).

- **Evaluation of tolerability by patients and the investigator**

In the global evaluation of tolerability by the investigator, there was a significant superiority of the vitamin B_{12} ointment containing avocado oil over the calcipotriol preparation ($p<0.05$). On the basis of the reduced contingency tables, the patient evaluation was identical with that of the investigator ($p<0.05$) (**Figs. 3a, 3b**). The evaluation of tolerability includes a consideration of undesirable effects (safety collective: n = 15 patients). Four patients (26.7%) reported skin irritation during calcipotriol therapy that necessitated a dosage reduction. Local pruritus occurred in one case (6.7%) during topical therapy with vitamin B_{12} ointment containing avocado oil : the symptoms subsided on continuation of therapy.

- **Evaluation of treatment effects using 20 MHz sonography**

As in the case of the PASI score, there were significantly more marked decreases in the width of the echo lucent area (ELA) in the initial 4 weeks of therapy during treatment with calcipotriol in comparison with the vitamin B_{12} preparation containing avocado oil. From therapy week 8, there was only a tendentially more marked decrease in ELA ($p=0.062$) for calcipotriol, while by the end of therapy week 12, there were no significant differences between the therapy regimens for this parameter ($p=0.389$) (**Fig. 4**).

The density of the corium indicates the extent of inflammatory infiltration. If there is a decrease in inflammatory infiltration during therapy, there is a corresponding increase in the density of the corium. There were no significant differences between the two treatments in respect of increases in corium density, except at the time point therapy week 4, when there was a significantly greater increase in density during calcipotriol therapy compared with the vitamin B_{12} preparation containing avocado oil therapy ($p<0.05$) (**Fig. 5**).

4. Discussion

Psoriasis is one of the most frequently occurring skin diseases, with a prevalence of 1 - 3%. Although this inflammatory dermatosis seldom becomes life-threatening, it is commonly perceived as a major disorder on a level with myocardial infarction and cancer (16). To date, no causal therapy of psoriasis has been developed. A multicausal pathomechanism is postulated which principally involves, in addition to hereditary predisposition, a ten-fold increase in epidermopoiesis and inflammatory-immunological factors (17). The topical and systemic antispsoriatics interfere with this pathomechanism.

The mechanism of action of calcipotriol is attributable to its antiproliferative effects on keratinocytes (18,19). Holland et al. (20) report a reduction of epidermal hyperproliferation and a return to normal keratinocyte turnover rates after a 10 week course of topical therapy with vitamin D_3 analogs. The range of potential undesirable effects associated with this class of medicaments include skin irritation and inflammation (1) and, in rare cases, hypercalcaemia. It is therefore recommended that calcipotriol should not be applied to more than 30% of body surface area and should not be used for longer than 12 months.

In this prospective clinical trial, the efficacy of a recently developed topical vitamin B_{12} preparation containing avocado oil was compared with that of the topical vitamin D_3 analog[1]. Vitamin B_{12} modifies nucleic acid synthesis, particularly during hematopoiesis and other cell maturation processes, but cannot be endogenously produced in the human body. At present, generally accepted therapeutic indications for vitamin B_{12} are restricted to the prevention and treatment of complications arising from vitamin B_{12} deficiency, such as hyperchromic macrocytic anemia and funicular myelosis (7). There are individual case reports in which good efficacy in psoriasis is described for systemically administered vitamin B_{12} preparations (5, 6). Other research groups have been unable to confirm beneficial effects of systemically administered vitamin B_{12} in the therapy of psoriasis (21,22). It should be borne in mind that due to pharmacokinetic characteristics the bioavailability of systemically administered vitamin B_{12} is poor. However, the results of our clinical trial demonstrate that topically applied vitamin B_{12} with avocado oil is effective in the treatment of psoriasis. The data on the amount of vitamin are contraditory. However, it is generally agreed that the main part is vitamin E (α Tocopherol), whereas vitamin A is not found at all, or like vitamin D, only in a very small amount (10,11,12,13). Furthermore, it must be considered that the therapeutic potency of retinoids and vitamin D_3 analogs is considerably higher than the vitamins from which they are derived, except for calcitriol. Since the contents of vitamin A and D were below the provable limit in our trial preparation, the therapeutic effect of avocado oil on psoriasis can be considered as marginal or not demonstrable. Avocado oil was used in some cases for treatment of atopic dermatitis and was seen as less potent than Evening primrose oil regarding its efficacy. In literature, no reference can be found on the use of avocado oil as popular scientific therapy for psoriasis. On the contrary, the use of fish oil as monotherapy for psoriasis was more thoroughly investigated and a low therapeutic effect could be proven, which could be based on an effect on the 5-lipooxygenase metabolism pathway, as well as on a reduction of the of leucotrien B4 formation. For avocado oil these effects were never discussed or examined, since fatty acids, that are responsible for these action mechanism, are not found in vegetable oils. The interaction of avocado oil with connective tissue metabolism was described, showing an anti-inflammatory effect by catabolic activitiy on collagen (23,24).

---

[1] Psorcutan® ointment, Schering AG, Berlin, Germany

After a 12-week course of therapy, there were no significant differences in treatment effect of calcipotriol and the vitamin B_{12} ointment containing avocado oil. Neither the clinical evaluation on the basis of the PASI score nor sonographic analysis showed differences in the effects of therapy.

More recent research has demonstrated an immunomodulatory effect of vitamin B_{12} *in vitro*. Immunomodulatory effects on T-lymphocyte subpopulations have been demonstrated, such as increased induction of T-suppressor cells (25). When this trial was extended to include 27 patients with rheumatoid arthritis, there was a significant reduction in the use of non-steroidal anti-inflammatory drugs and prednisolone with concomitant oral administration of 1500 µg vitamin B_{12} (25). Another group reports dose-dependent *in vitro* suppression of IL 6 and INF γ in the presence of vitamin B_{12} (26). At present, there is no adequate qualified data on the mode of action and efficacy of vitamin B_{12} *in vivo*.

In our prospective clinical trial, we were able to demonstrate the efficacy of topically applied vitamin B_{12} with avocado oil in the therapy of psoriasis. There were no significant differences in efficacy to that of the reference preparation calcipotriol. It is of interest that, after 4-weeks therapy, there was a marked diminution of the efficacy of calcipotriol while the frequency and severity of skin irritation increased, whereas the efficacy of the vitamin B_{12} ointment containing avocado oil remained largely constant over the whole observation period. It can therefore be proposed that the vitamin B_{12} ointment containing avocado oil may be suitable for use in the long term therapy of psoriasis. In follow-up trials, we intend to further evaluate the efficacy of vitamin B_{12} with avocado oil in the treatment of psoriasis as the *in vitro* results as well as these initial *in vivo* results proved to be very promising.

Acknowledgement:

This investigation was supported by Regneratio AG, Wuppertal, Germany

References

1. Fullerton A, Avnstorp C, Agner T, Dahl JC, Olsen LO, Serup J: Patch test study with calicipotriol ointment in different patient groups, including psoriatic patients with and without adverse dermatitis. Acta Derm Venerol (Stockh) 1996:76:194-202
2. Marchetti A, LaPensee K, An P: A pharmacoeconomic analysis of topical therapies for patients with mild-to-moderate stable plaque psoriasis: a US study. Clin Ther 1998:4:851-869
3. Sander P, Happe M, Stücker M, Hermes N, Hoffmann K, Altmeyer P: Tazaroten verstärkt den antipsoriatischen Effekt von Dithranol bei der chronisch stationären Psoriasis (CSP). Hautarzt 1999:50:723-727
4. Sander P, Stücker M, Hermes N, Hoffmann K, Altmeyer P: Mometason und Calcipotirol optimieren den therapeutischen Initialeffekt von Dithranol auf die chronisch stationäre Psoriasis (CSP). Hautarzt 1998:49:291-294
5. Ruedemann R, Albany NY: Treatment of psoriasis with large doses of vitamin B12 1100 micrograms per cubic centimeter. Arch Derma Syph (Chic.) 1954:69:738
6. Cohen EL: Some new treatments for psoriasis. Practitioner 1958:181:618-620
7. Europäisches Arzneibuch, Band II, S.1366. Deutscher Apotheker-Verlag Stuttgart, Govi-Verlag GmbH Stuttgart, 1975
8. Howe EE, Dooly CL, Geoffroy RF, Rosenblum C: Percutaneous absorption of vitamin B12 in the rat and guinea pig. J Nutrition 1967:92:261-266
9. Stankler L: The vitamin B12 level in psoriatic skin and serum. Br J Dermatol 1969:81:911-918
10. Anonymus: Final report of the safety assessment for avocado oil. J Environ Pathol Toxicol 1980:4:93-103

11. Heller H, Asche W. Zusammensetzung des Avocado-Öls. Seifen-Öle-Fette-Wachse 1985:111:164-165
12. Albert K. Avocadoöl DAC 1979. Pharmazeutische Zeitung 1986:131:2279-2281
13. BIBRA working group. Avocado oil. Toxicity profile BIBRA Toxicology International 1990:1-3
14. Hoffmann K, Dirschka K, Schwarze H, el-Gammal S, Matthes U, Hoffmann A, Altmeyer P: 20 MHz sonography, colorimetry and image analysis in the evaluation of psoriasis vulgaris. J Dermatol Sci 1995:9:103-110
15. Altmeyer P, Hoffmann K, Stücker M, el Gammal S: General phenomena of ultrasound in dermatology; in Altmeyer P, Hoffmann K, el Gammal S (eds): Ultrasound in Dermatology. Berlin, Springer, 1992; 55-79
16. Windemuth D, Stücker M, Altmeyer P: Implizite Persönlichkeitstheorien in der Dermatologie. Eine empirische Studie zu dem Bild, das Ärzte von Patienten unterschiedlicher dermatologischer Diagnosegruppen habe. Hautarzt 2000:51:176-181
17. Ackermann L, Harvima IT, Pelkonen J, Ritamaecki-Salo V, Naukkarinen A, Harvima RJ, Horsmanheimo M: Mast cells in psoriatic skin are strongly positive for interferon-gamma. Br J Dermatol 1999:140:624-633.
18. Berardesca E, Vignoli GP, Farinelli N, Vignini M, Distante F, Rabbiosi G: Non-invasive evaluation of topical calcipotriol versus clobetasol in the treatment of psoriasis. Acta Derm Venerol (Stockh) 1994:74:302-304.
19. Lamaud ME, Miskulin M, Robert AM, Wepierre J. Biochemical modifications of connective tissue induced by the non-saponifiables of avocado and soja-bean oils administered percutanously in the “Hairless” rat (author´s trans.). Pathol Biol (Paris) 1978:26:269-274

20. Trevoux R. Les insaponifiables de l´avocat soja en gynécologie. J Gynec Obs Biol Reprod 1977:6:99-105
21. Kragballe K, Wildfang IL. Calcipotriol (MC 903): A novel vitamin D3 analogue stimulates terminal differentiation and inhibits proliferation of cultured human keratinocytes. Arch Dermatol Res 1990:283:164-167.
22. Holland DB, Roberts SG, Russel A, Wood EJ, Cunliffe WJ: Changes in epidermal keratin levels during treatment of psoriasis with the topical vitamin D3 analogue MC 903. Br J Dermatol 1990:122:284
23. Alexander S: Vitamin B12 in psoriasis. Lancet 1957:1:738
24. Baker H, Comaish JS: Is vitamin B12 of value in psoriasis? Br Medical J 1962:ii:1729-1730
25. Sakane T, Takada S, Kotani H, Tsunematsu T: Effects of methyl-B12 on the in vitro immune functions of human T lymphocytes. J Clin Immunol 1982:2:101-109
26. Yamashiki M, Nishimura A, Koska Y: Effects of methylcobalamin (vitamin B12) on in vitro cytokine production of peripheral blood mononuclear cells. J Clin Lab Immunol 1992:37:173-182

Table 1a, b

PASI score evaluation of both treatment groups (vitamin B12 – avocado oil, Calcipotriol) for each of the 13 patients at 0, 2, 4, 8, 12 weeks.

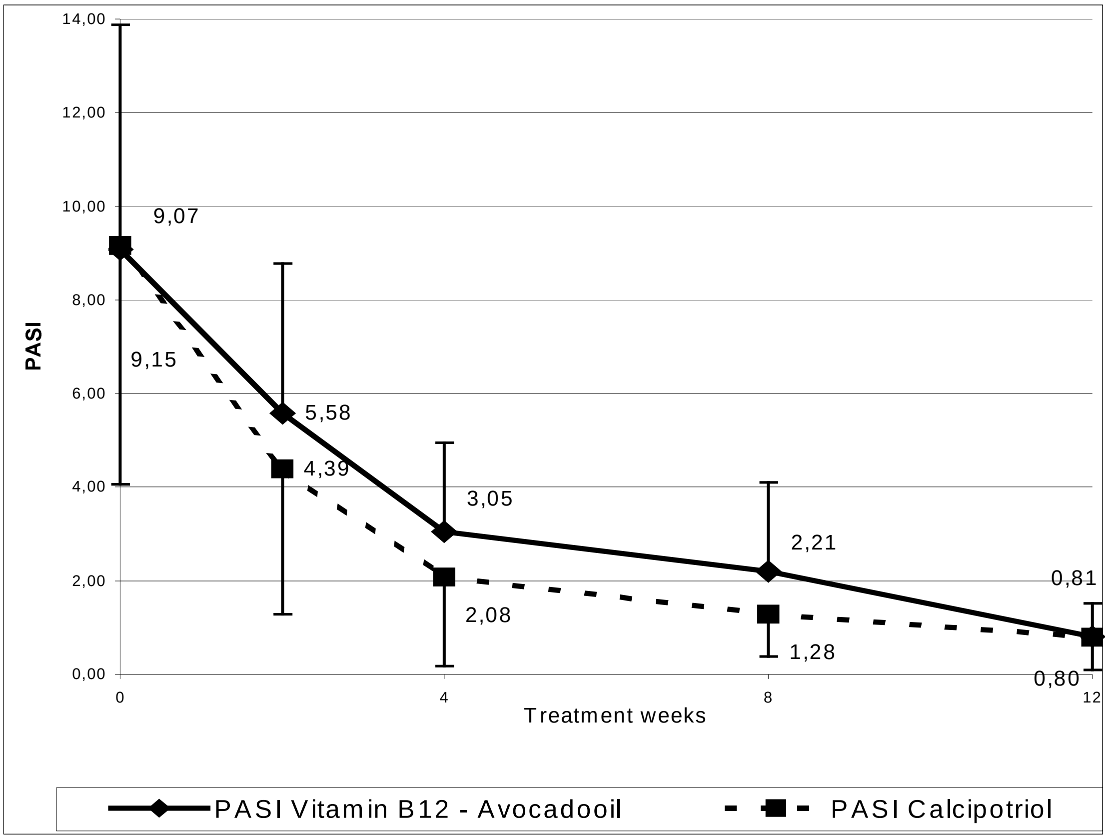
Table 1a

	PASI score Vitamin B12 containing avocado oil				
Patient	Before treatment	After 2 weeks of treatment	After 4 weeks of treatment	After 8 weeks of treatment	After 12 weeks of treatment
1	4,50	3,30	1,90	0,90	0
2	16,20	9,90	4,95	1,65	0,55
3	2,80	1,40	0,80	0,30	0,20
4	4,50	3,30	1,00	1,50	1,20
5	10,80	6,60	4,05	1,70	0,45
6	5,40	2,40	0,60	0,20	0
7	8,85	4,85	4,45	2,55	1,20
8	4,95	2,20	1,10	0,45	0
9	12,00	7,20	6,00	6,00	2,10
10	8,10	5,40	2,70	1,30	0,80
11	12,60	8,40	4,20	4,20	1,40
12	18,70	11,90	5,10	5,10	1,70
13	8,55	5,70	2,85	2,85	0,95
mean	9,07	5,58	3,05	2,21	0,81
±SD	4,8	3,2	1,9	1,9	0,7

Table 1b

	PASI score Calcipotriol				
Patient	Before treatment	After 2 weeks of treatment	After 4 weeks of treatment	After 8 weeks of treatment	After 12 weeks of treatment
1	4,50	3,30	2,00	2,10	0
2	17,85	9,90	6,60	1,65	1,80
3	2,20	1,20	0,80	0,40	0
4	4,50	3,00	0,20	0,20	0,30
5	10,80	6,60	2,10	1,45	0,45
6	5,40	2,40	1,20	0,60	0,90
7	8,85	3,80	1,60	0,65	0,45
8	4,95	1,65	0,55	0,45	0
9	12,00	3,60	1,20	1,20	1,20
10	8,10	1,80	0,90	0,90	0,65
11	12,60	2,00	1,40	1,40	1,40
12	18,70	10,20	3,70	3,40	1,70
13	8,55	7,60	4,75	2,25	1,50
mean	9,15	4,39	2,08	1,28	0,80
±SD	5,1	3,1	1,9	0,9	0,7

Fig. 1



In the initial 8 weeks, the effect of calcipotriol therapy were more rapidly manifested than those of vitamin B_{12} with avocado oil therapy. The difference was not significant after 2 weeks (p=0.056) or after 4 weeks (p=0.055) but only after 8 weeks therapy (p<0.05). After 12 weeks, there were no significant differences in the efficacy of treatment (adjusted for baseline) between the two therapy regimens (p=0.534). Mean ± SD.

Fig. 2a

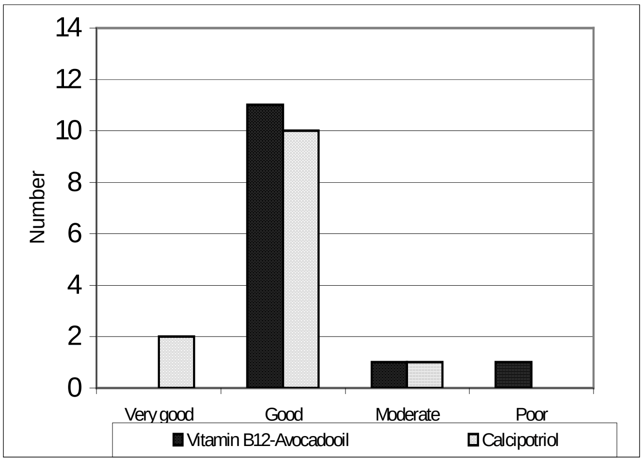
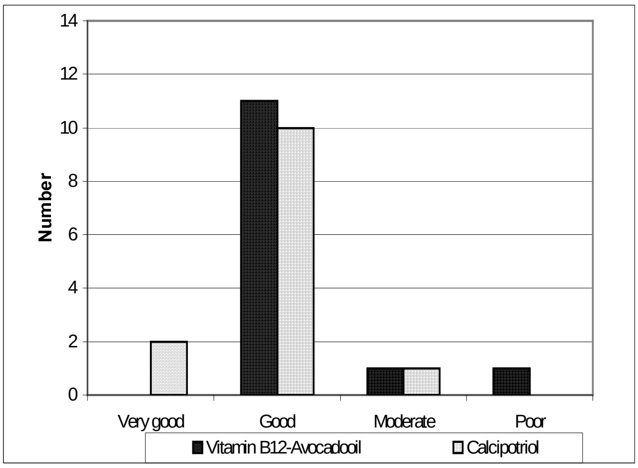


Fig. 2b



Evaluation of efficacy by the investigator (**Fig. 2a**) and by patients (**Fig. 2b**). In both cases, there is tedentially better efficacy of the calcipotriol preparation in comparison with the vitamin B_{12} – Avocadooil preparation (p=0.56); investigator and patient evaluations are identical).

Abb. 3a

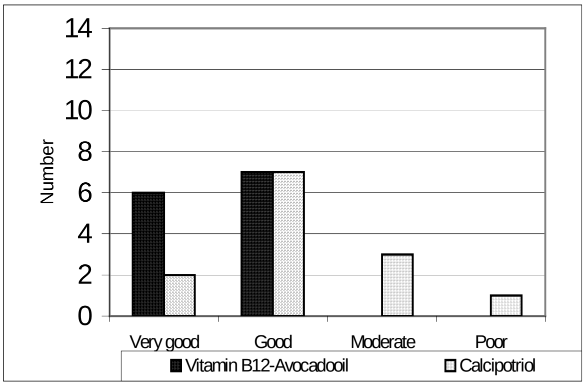
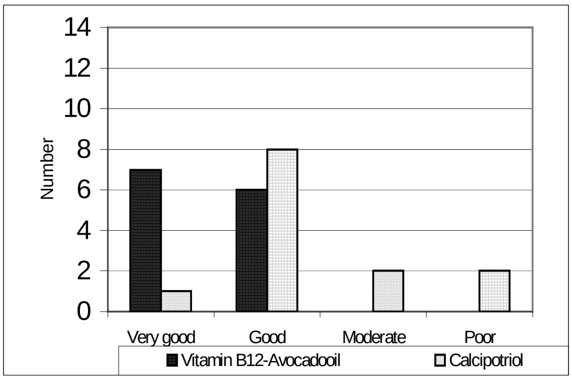
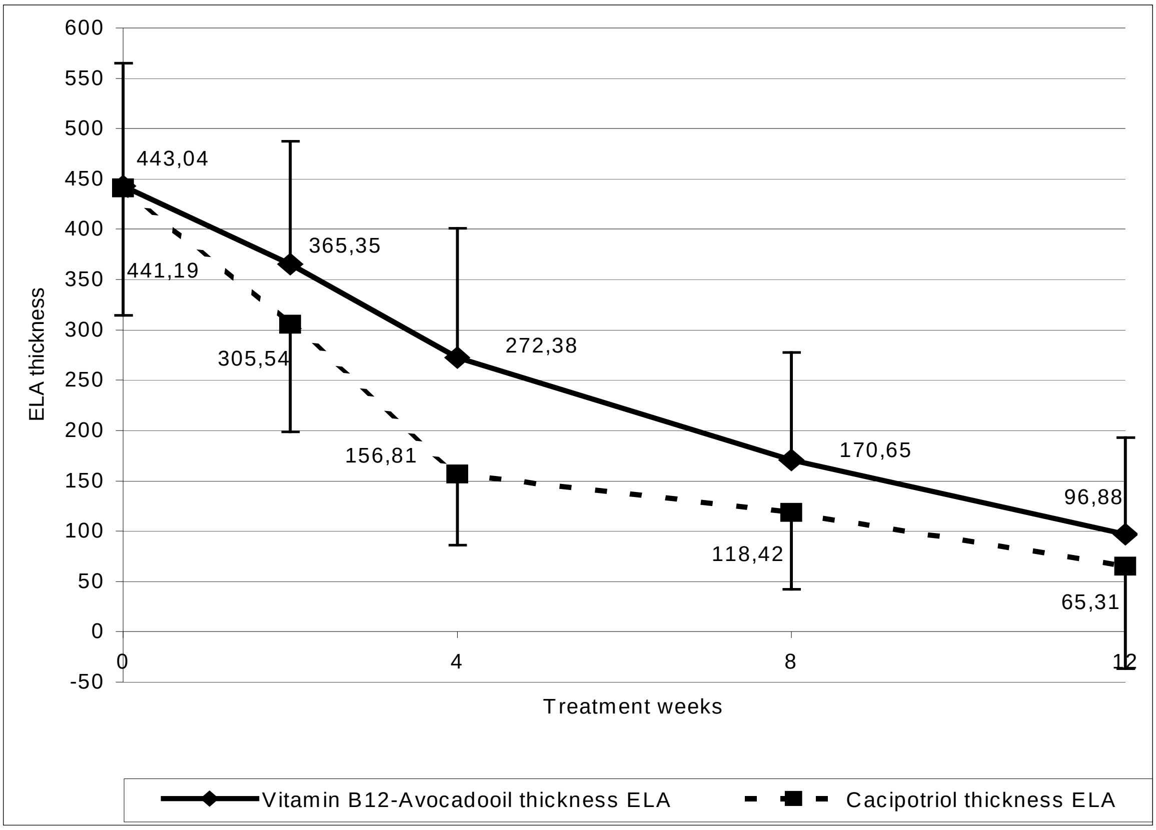


Abb. 3b



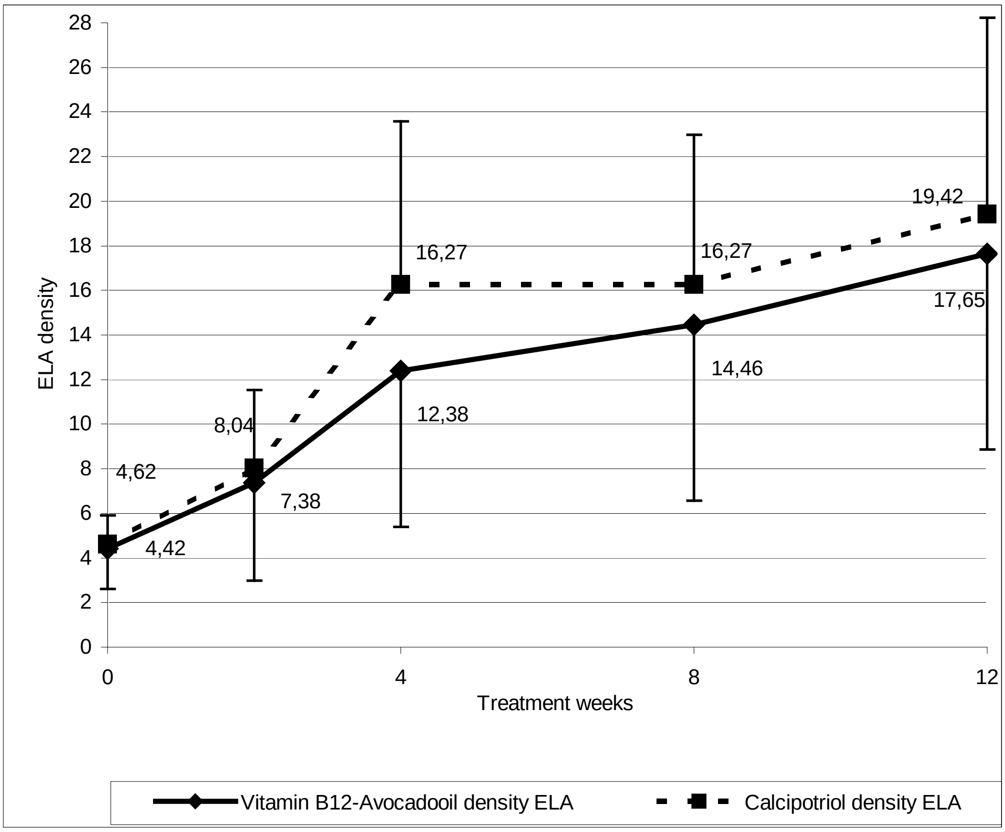
Evaluation of tolerability by the investigator (**Fig. 3a**) and the patients (**Fig. 3b**). In both cases, there is significant superiority of tolerability of the vitamin B_{12} - Avocadooil preparation in comparison with calcipotriol (p<0.05 in each case).

Fig. 4



20 MHz sonography of a reference plaque: width of the echo lucent area (ELA). In the initial 4 weeks of therapy, there was a significantly more marked reduction during therapy with calcipotriol in comparison with vitamin B_{12} ointment containing avocado oil ($p<0.05$). After 8 weeks ($p=0.062$) and 12 weeks ($p=0.389$), there were no significant differences in the thickness of echo lucent area. The figure shows the mean values with the standard deviation before treatment as well as 4,8 and 12 weeks after the beginning of the treatment.

Fig. 5



20 MHz sonography of a reference plaque: density of the echo lucent area (ELA). In week 4, there was a significantly greater density for calcipotriol therapy in comparison with vitamin B_{12} ointment containing avocado oil ($p<0.05$). At all other measuring time points and on completion of therapy (therapy week 12) ($p=0.106$), there were no significant differences in the density of the echo lucent area. The figure shows the mean values and the standard deviation before treatment as well as 4, 8 and 12 weeks after the beginning of the treatment.