Superiority of a vitamin B12-barrier cream compared with standard glycerol-petrolatum-based emollient cream in the treatment of atopic dermatitis: A randomized, left-to-right comparative trial

S. P. Nistico1 | E. Del Duca2 | F. Tamburi3 | E. Pignataro3 | N. De Carvalho4 | F. Farnetani4 | G. Pellacani4

1Department of Health Sciences, University Magna Graecia, Catanzaro, Italy
2Department of System Medicine, University of Tor Vergata, Rome, Italy
3Institute of Dermatology, Catholic University of Rome, Rome, Italy
4Department of Dermatology, University of Modena and Reggio Emilia, Modena, Italy

Correspondence
Francesca Farnetani, MD, Department of Dermatology, University of Modena and Reggio Emilia, Modena, Italy. Email: farnetani.francesca@gmail.com

Abstract
Atopic dermatitis (AD) is a result of complex genetic, epigenetic, environmental, and immunological interactions with an overlapping epidermal barrier defect. The study evaluates the efficacy and tolerability of topical Vitamin B12-barrier cream (MB12) compared with standard glycerol-petrolatum-based emollient cream (GPC) used three times a day for mild AD. The study was conducted as a one-hemi-body randomized, controlled, single-blind, intra-patient left-to-right comparative trial by patients with clinical diagnosis of mild AD measured with total SCORAD index over 4 months. MB12 was compared on one hemi-body treated (GPC). The comparisons of score values were performed primarily by using non-parametric procedures: Mann–Whitney-U test (for independent samples) and Wilcoxon test (for dependent samples). All 22 patients were randomized (left or right side treated with MB12 or GPC). At week 12 a reduction from baseline in SCORAD index was assessed in both body sites with 77.6% SCORAD index reduction in the MB12 treated body sites versus 33.5% in the GPC treated body sites. These results suggest that MB12 could represent a new option in the treatment of mild AD.

KEYWORDS
atopic dermatitis, hydration, skin barrier

1 | INTRODUCTION
Atopic dermatitis (AD) is a common chronic inflammatory skin disorder affecting 10% of world population in developed countries (Eichenfield et al., 2014). Nowadays, several drugs are available to treat atopic dermatitis (Garmhausen et al., 2013; Saeki et al., 2016), but, despite the large number of drugs available, patients are often dissatisfied with their treatments (Kessel & Goldenberg, 2016). Under this aspect, MB12 may represent a safe alternative to the currently available topical therapies. Cobinamide, a cobalamin (vitamin B12) precursor that binds NO with high affinity, has been shown to have a potent action as a NO-scavenger in biologic systems (Broderick et al., 2005). Since the important renal excretion (nearly 90%) vitaminB12 requires high concentrations to reach peripheral target which can be associated with toxicity. To avoid toxicity, cutaneous application has been recently considered by Stucker, Memmel, Hoffmann, Hartung, and Altmeyer (2001) the most appropriate way of administration. Few articles have been carried out to assess the efficacy of vitamin B12 in atopic dermatitis skin (Stucker et al., 2004).

The aim of the present study is to assess the therapeutic effects of a new topical treatment containing vitamin B12: Mavena® B12 barrier cream (0.07% Cyanocobalamin) on patients affected by AD. We evaluated the therapeutic response, in a prospective, intra-individual, right versus left clinical trial, comparing MB12 treatment to a standard GPC.

2 | MATERIAL AND METHODS
Vitamin B12 in the barrier cream is imbedded in a Polysorbate carrier system to penetrate the skin with a lipidic concentration of 24 and 1% Urea. Male or female Caucasian patients with a confirmed clinical
diagnosis of mild AD measured with total SCORAD index up to 25 points have been enrolled in this study.

The study has been conducted as a hemi-body randomized, controlled, single-blind, intra-patient trial design. Patients suffering from mild AD, were treated with MB12 on one hemi-body GPC on the other body side. The hemi-body treating with MB12 or GPC was randomized, thus any bias will be avoided.

The Scoring Atopic Dermatitis (SCORAD) was determined at baseline week 0, week 2, week 4, week 8, week 12, and 4 weeks after the end of treatment (F1).

For 12 weeks, MB12 or GPC was applied two to three times a day in the evening and at bedtime on the atopic lesions of one hemi-body, per the randomization scheme.

The study was approved by the Institutional Review Board of University of Catanzaro Number of experimentation register 49/15 of 8/10/2015, and the investigation was conducted in accordance to the Declaration of Helsinki.

2.1 | Statistical methods

The comparisons of score values were performed primarily by using non-parametric procedures: Mann–Whitney-U test (for independent samples) and Wilcoxon test (for dependent samples) based on rank sums. Parametric procedures (t tests) supplemented the analysis based on mean and standard deviation. The analysis of correlation was performed referred to Pearson.

3 | RESULTS

About 22 randomized Caucasian patients over 18 years old have been treated (left or right side with MB12 or GPC), 14 males (14 of 22; 63.6%) and 8 females (8 of 22; 36.4%), pUex = 0.876. Mean (SD) SCORAD index was 5.64 (2.08) and 5.50 (1.97), pUex = 0.876 (0.823) for male and female, respectively.

At baseline (T0), mean (SD) SCORAD index was 5.64 (2.08) for the MB12 treated (M treated) and 5.50 (1.97) for the GPC treated (C treated) hemi-body sides (Figure 1).

At T2 in 63.6% of the patients the SCORAD values statistically significant decreased on M treatment hemi-body sides were compared with ones observed in C treatment hemi-body sides T2 (pWex < 0.001; Power = 78.0%). The mean SCORAD of patients decreased on both treatment body sides, (SD) SCORAD T2 was 2.64 (0.79) for M treated and 4.86 (1.86) for C treated patients. Significantly more M treated sides (81.8%) achieved the primary endpoint (total SCORAD reduction) than C treated sides (59.1%) (Figures 1 and 2).

At T4 in 72.7% of the patients the SCORAD values statistically significant decreased on M treatment hemi-body sides then ones observed in C treatment hemi-body sides (pWex < 0.001; Power = 78.0%). Significantly more M treated sides (95.5%) achieved the primary endpoint (total SCORAD reduction) than in the C treated side sides (72.71%). Moreover, 50.0% of patients of M sides showed a reduction in SCORAD from T2 to T4 versus a minor reduction achieved from C sides, 40.9% (Figures 1 and 2).

At T8 90.9% of the patients with SCORAD values observed on M treatment hemi-body sides were statistically significant lower than the ones observed in C treatment hemi-body sides (pWex < 0.001; Power = 78.0%). Significantly more M treated sides (95.5%) achieved the primary endpoint (total SCORAD reduction) than C treated sides (45.5%). Moreover, 54.5% of patients of M hemi-body sides showed a reduction in SCORAD from T4 to T8 versus a minor reduction achieved from C hemi-body sides (40.9%) (Figures 1 and 2).

At T12, all cases (100%) showed lower values of SCORAD index on M treatment hemi-body sides compared with the ones observed in C treatment hemi-body sides (pWex < 0.001; Power = 78.0%).

FIGURE 1 Absolute SCORAD values M versus C hemi-body treated sides
Statistically significant more M treated sides (100%) achieved the primary endpoint (total SCORAD reduction) than C treated sides (63.6%). Moreover, 59.1% of M hemi-body sides showed a reduction in SCORAD from T8 to T12 versus a minor reduction achieved in the C hemi-body sides, 36.4% (Figures 1 and 2).

At F1 4 weeks after stopping the treatment 86.4% of the phemi-body sides in the M treatment hemi-body sides were lower on observed SCORAD values than those observed in C treatment hemi-body sides \( p \leq 0.001 \); Power = 78.0% (Figures 1 and 2).

Reduction of pruritus and high level of tolerability was measured to assess the QoL (quality of life) improvement in patients’ daily life. Mean pruritus generally decreased from 8.7 (1.09), value measured at T0, to 1.7 (1.5), value measured at T12 (Figure 3). Both parameters have been evaluated for both split-body-sides, improving indirectly the quality of life of the patients.

4 | DISCUSSION

Our findings show the significant statistical superiority of MB12 treatment compared with standard GPC in the total SCORAD index reduction \( p \leq 0.001 \) (Figures 1 and 2). While the mean SCORAD values in the M treatment hemi-body sides significantly decreased, the values measured in the C treatment hemi-body sides showed a non-significant decrease. There were statistically significant differences in

![Relative SCORAD values M versus C hemi-body treated sides](image1)

![Itching mean pVAS 0–10 M and C treatment over treatment period](image2)
SCORAD between M treatment hemi-body sides compared with the C
treatment hemi-body sides at all point in time from T2 to F1 (each with
pWex < 0.001) (Figures 1 and 2). The relative changes in SCORAD
score from T0 to T12 was 80% in the M treated sides, while the mean
score of SCORAD based on the C treatment decreased only by 15%
(Figures 1 and 2).

Reduction of pruritus and high level of tolerability was achieved in
all patient’s treatment sides, showing in both hemi-body sides a statisti-
cal significant reduction on erythema, pruritus with a good tolerability
(Figure 3).

5 | CONCLUSIONS

Efficacy and tolerability of a MB12 compared with standard GPC was
assessed by SCORAD index. All patients referred an improvement in
clinical symptoms and decrease of itching, measured through SCORAD
index and pVAS. These results are consistent with other studies (Baker
& Comaish, 1962; Kim et al., 2014; Stalder, 1969). In conclusion,
accoring our experience, MB12 can be considered a valid therapeutic
option in the treatment of atopic dermatitis to the traditional topical
drugs now available, and it can be used in the treatment of mild AD.

REFERENCES
