

Original Article

Efficacy and safety of pseudo-ceramide containing moisture cream in the treatment of senile xerosis

一種含有偽神經酰胺的保濕乳霜對老年乾燥症治療的功效及安全性

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Objective: To study the efficacy and safety of a pseudo-ceramide containing moisture cream among Chinese patients with xerosis. **Method:** This was a single arm study with 30 elderly home residents recruited. After two-week wash out period, a pseudo-ceramide containing moisture cream were applied twice daily to the test areas (volar aspect of forearm and lateral aspect of calf) by nursing staff. The clinical symptoms, clinical xerotic severity scores and dermoscopic pictures were obtained before and after 3 weeks of treatment. The skin hydration and trans-epidermal water loss were measured before and at 1, 2 and 3 weeks after treatment commenced. Any adverse effect during the study was recorded. The acceptability of the test moisture cream was also enquired at the end of the study. **Results:** After 3 weeks of treatment with the moisture cream, there was a significant time-dependent improvement in skin hydration. The effect of the moisture cream on the trans-epidermal water loss (TEWL) was equivocal with a transient beneficial effect during the first two weeks but was not sustainable in the third week. On the clinical symptoms, there was a significant improvement in dryness, roughness and itch, but with no difference in the symptoms of tightness, scaliness, erosions and hotness. There was also a significant improvement in the clinical severity scores and dermoscopic appearance. No adverse event was reported. The moisture cream was well accepted by the subjects. **Conclusion:** A pseudo-ceramide containing moisture cream was able to increase skin hydration and might be able to decrease trans-epidermal water loss in elderly patient with xerosis. It improved some of the subjective symptoms of xerosis, the clinical xerotic severity score and dermoscopic appearance.

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目的：研究一種含有偽神經酰胺的保濕乳霜對華裔皮膚乾燥症患者的功效及安全性。**方法：**這是一個邀得三十位安老院長者參與的無對照研究。經過兩週的沖洗期後，護理員每天兩次把含有偽神經酰胺的保濕乳霜塗抹在患者的指定皮膚測試位置（前臂掌側和小腿肚外側）。研究錄取了患者治療前及治療三週後的臨床病徵、臨床乾燥症的嚴重度評分和皮膚鏡圖像。治療前及治療後第一、二、三週的皮膚含水度和經皮水份散失度都一一測定量度；而研究期間所發生的不良反應亦作記錄。研究結束時，查詢了患者對測試的保濕乳霜之接受程度。**結果：**經過三週潤膚乳霜治療後，皮膚含水度有時間依賴性的明顯改善。至於潤膚乳霜對經皮水份散失度的療效則有待商榷，因首兩週的即時正面效果未能延續至第三週。臨床病徵方面，皮膚乾燥、粗糙和瘙癢程度得到顯著改善，但繃緊、脫屑、糜爛和灼熱程度則相差無幾。此外，臨床乾燥症的嚴重度評分及皮膚鏡下之外觀亦有顯著改善。治療中沒有任何不良反應的報告，而保濕乳霜亦得到參與者的滿意接受。**結論：**使用上述含有偽神經酰胺的保濕乳霜，能增加皮膚乾燥症之老年患者的皮膚含水度，並有可能減少其經皮水份的散失。此外，皮膚乾燥症的部分主觀病徵、臨床乾燥症的嚴重度評分及皮膚鏡下之外觀亦有所改善。

Keywords: Epidermal functions, moisture cream, pseudo-ceramide, senile xerosis

關鍵詞：表皮功能，潤膚乳霜，偽神經酰胺，老人乾燥皮膚

Introduction

Senile xerosis is a common skin problem among the elderly. The prevalence of senile xerosis in an elderly home was more than 40%.^{1,2} The clinical features of xerosis include scaling, papulation, roughness, loss of luster and secondary changes of excoriation and fissuring. Patients may feel itchy especially at night time.³ The causes of senile xerosis are multifactorial.⁴ One of the main causes is the reduced production of ceramide with age which is an important component of stratum corneum in maintaining skin hydration.^{5,6} The present study aimed to assess the effect of 3 weeks twice daily application of a pseudo-ceramide containing moisture cream (*Curel*[®], Kao, Japan) on (i) subjective symptoms, (ii) clinical signs and (iii) parameters of epidermal barrier function at volar forearm and lateral leg among elderly Chinese patients with xerosis. The safety and acceptability of the test moisture cream was also assessed.

Methods

Thirty elderly patients (age >65) with xerosis were

recruited at a nursery home under the care of Shatin Hospital, Hong Kong in early January of 2009. Informed consent was obtained after detailed explanation. After a two-week washout period, the test cream (*Curel*[®], Kao, Japan) was applied to the volar aspect of the forearm and the lateral aspect of the lower leg by nursing staffs twice a day for a period of 3 weeks. The subjects were allowed bathing with soap or bathing liquid but were forbidden to use any other moisture cream on the test sites. Before the application, the subjects were asked about the symptoms of xerosis. The baseline signs of xerosis was assessed by attending physicians according to EEMCO guidance.⁷ Dermoscopic pictures were taken of the tested sites. The procedures were again repeated 3 weeks later at the end of the study period. Skin hydration and trans-epidermal water loss (TEWL) of the test sites were measured with Corneometer[®] CM 825 and Tewameter[®] TM 300 (C+K, Germany) respectively according to the instructions^{8,9} at the beginning of the study. The measurements were taken in the afternoon within an enclosed room under a regulated temperature of 25±2°C and relative humidity of 50±5% after an acclimatizing period of 15 minutes. The measurements were repeated 1, 2 and 3 weeks

after the start of the study. Any adverse effect encountered was to be reported to the investigator immediately by the nursing staffs during the study. At the end of the study period, the subjects were also asked about the acceptability of the tested product. This study was approved by the ethical committee of the Chinese University of Hong Kong.

Statistical analysis

SPSS (version 10) was used for analysis. The Wilcoxon Sign Ranked test for paired results of skin hydration and trans-epidermal water loss was used to see the difference before and 3 weeks after treatment. Fisher's exact test was used to analysis for the change in clinical severity of xerosis.

Results

Subjects

Thirty-four subjects were recruited at the beginning of the study. However 4 patients dropped out for varies reasons. One died after admission into the hospital. Three refused further participation in the study. Thus, 30 subjects remained for analysis. The age distribution and medical diseases were shown in Figures 1 and 2. Fifty percent of the male subjects had the habit of using moisture cream

while only 5% of the female subjects had. Both groups did not have any history of drug allergy and 1 female patient had a history of allergic bronchitis.

Skin hydration

There was a time-dependent increase in the mean skin hydration at the test sites. Before treatment, the mean baseline skin hydration was 32.3 ± 1.6 a.u. (volar forearm) and 26.5 ± 1.1 a.u. (lateral leg). After 1 week of treatment, these values increased to 38.6 ± 1.6 a.u. (volar forearm) and 33.4 ± 1.7 a.u. (lateral leg). After 2 weeks of treatment, they were further increased to 39.7 ± 1.3 a.u. (volar forearm) and 34.1 ± 1.6 a.u. (lateral leg). At the end of the third week, the values reached the highest 42.8 ± 1.5 a.u. at the volar forearm and 39.3 ± 1.5 a.u. at the lateral leg, which were 32% and 48% above the baseline level (Table 1, Figures 3 & 4).

Trans-epidermal water loss

The mean TEWL decreased significantly in the first two weeks but was not sustained in the third week. The mean baseline trans-epidermal water loss was 6.4 ± 0.4 g/m².hr (volar forearm) and 7.2 ± 0.4 g/m².hr (lateral leg). After 1 week of treatment, they were significantly ($P < 0.05$) decreased to 5.3 ± 0.4 g/m².hr (volar forearm) and 6.2 ± 0.3 g/m².hr (lateral leg). After 2 weeks of treatment, they further dropped to 5.0 ± 0.2 g/m².hr (volar forearm) and 5.8 ± 0.2 g/m².hr (lateral leg). However at the end of the 3 week, the TEWL rose

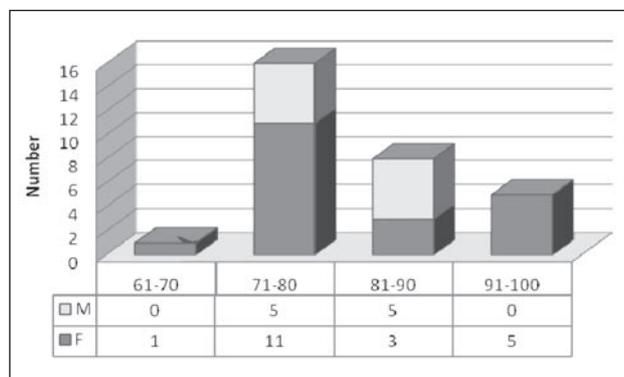


Figure 1. Age distribution of subjects.

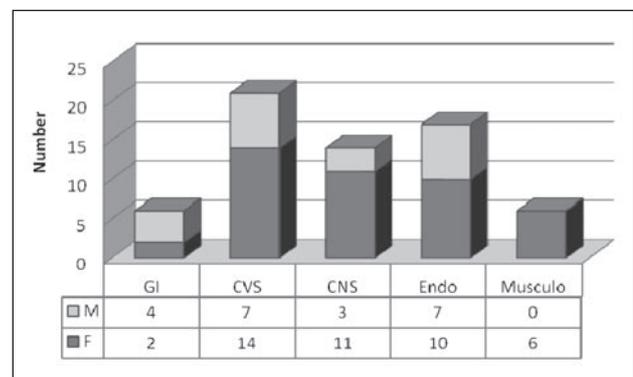


Figure 2. Medical diseases of subjects.

Table 1. Patients characteristics and results of study

Patient population				
Enrolled (N=34)				
Males/Females (completed the study)	10		20	
Discontinued	1		3	
Lost to follow-up	–		0	
Evaluable (N=30)				
Efficacy				
	Baseline	1 week	2 week	3 week
Skin hydration				
Volar forearm	32.3±1.6	38.6±1.6*	39.7±1.3*	42.8±1.5*
Lateral leg	26.5±1.1	33.4±1.7*	34.1±1.6*	39.3±1.5*
TEWL (Trans-epidermal water loss)				
Volar forearm	6.4±0.4	5.3±0.4*	5.0±0.2*	6.0±0.2
Lateral leg	7.2±0.4	6.2±0.3*	5.8±0.2*	6.0±0.2*
Subjective symptoms (n=27) [†]				
	No	Yes	p value	
Q1 (tightness)				
Baseline	21	6	0.100	
Week 3	26	1		
Q2 (dryness)				
Baseline	11	16	0.005*	
Week 3	22	5		
Q3 (roughness)				
Baseline	8	19	0.001*	
Week 3	21	6		
Q4 (itchiness)				
Baseline	5	22	0.000*	
Week 3	19	8		
Q5 (severity)				
Baseline	4	23	0.000*	
Week 3	21	6		
Q6 (scaliness)				
Baseline	17	10	0.054	
Week 3	24	3		
Q7 (erosion)				
Baseline	18	9	0.544	
Week 3	21	6		
Q8 (hotness)				
Baseline	16	11	0.066	
Week 3	23	4		
Clinical xerotic severity scores (n=30) [‡]				
	Grade 0 or 1	Grade 2 or above	p value	
Baseline	2	28	0.000*	
Week 3	25	5		

Safety

No report of any adverse event with the use of curel moisture cream during the study

Acceptability

Curel moisture cream was well accepted by the subjects

Dermoscopic appearance

There was an improvement in the dermoscopic appearance of the tested sites

Notes: *Statistically significant. †3 subjects were too deaf to communicate, hence only 27 subjects were assessed; For the symptom scores: those with no symptoms will be designated 0, while those with symptom 1. (For question 5, those with mild symptom will be designated as 0 and those with moderate, severe or very severe itch will be designated 1). ‡For the clinical severity scores: grade 0 and 1 was designated as 1; grade 2 and above was designated 2 in the analysis.

back to 6.0 ± 0.2 g/m².hr (volar forearm) and 6.0 ± 0.2 g/m².hr (lateral leg). Hence, the maximum percentage decrease was at the second week with 21% at the volar forearm and at 19% lateral leg (Table 1, Figures 5 & 6).

Subjective symptoms

Eight questions based on symptoms of xerosis were enquired. Though there was a general improvement of symptoms in all these questions, only questions on dryness, roughness, and itch showed statistical significance. However there was

no significant difference in tightness, scaliness, hotness and erosions before and after treatment (Table 1 and Appendix 1).

Clinical xerotic severity scores

Before treatment, 2 subjects had a severity score of 1, 13 subject had a severity score of 2, 14 subjects had severity score of 3 and one subject had a severity of scores of 4. After 3 weeks of treatment, 25 subjects had no more xerosis while 5 subjects suffered from a mild degree of xerosis with a score of 1 (Table 1).

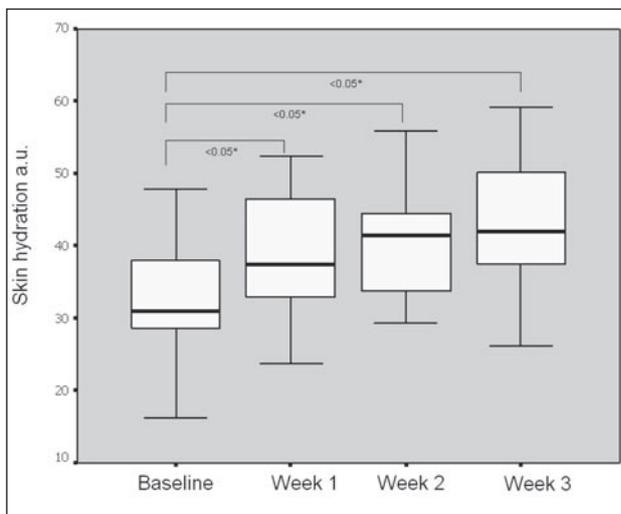


Figure 3. Change of volar forearm skin hydration over time.

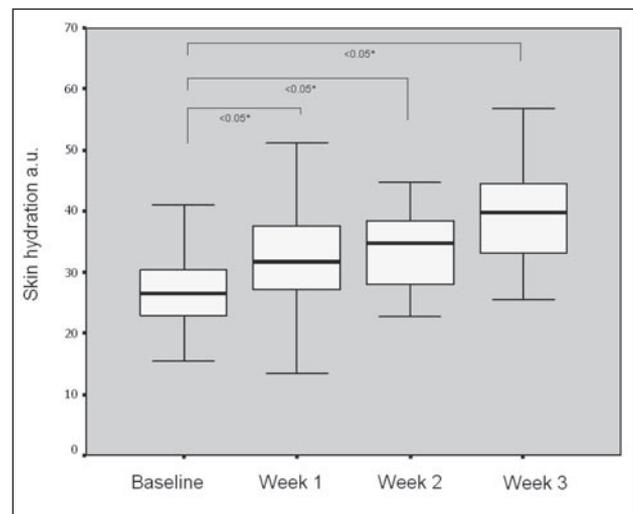


Figure 4. Change of lateral leg skin hydration over time.

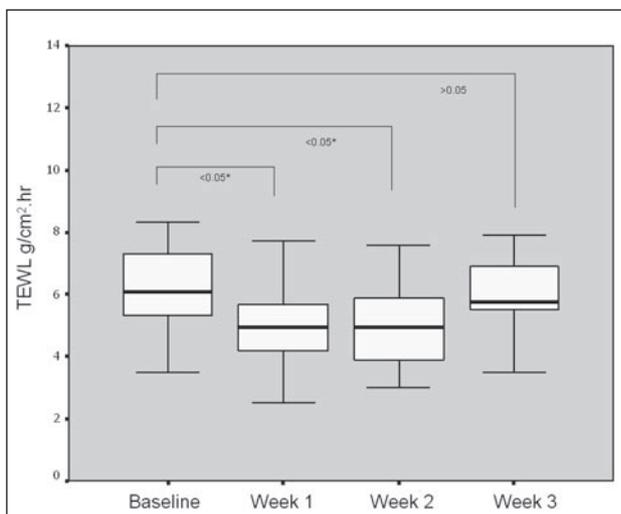


Figure 5. Change of TEWL of volar forearm over time.

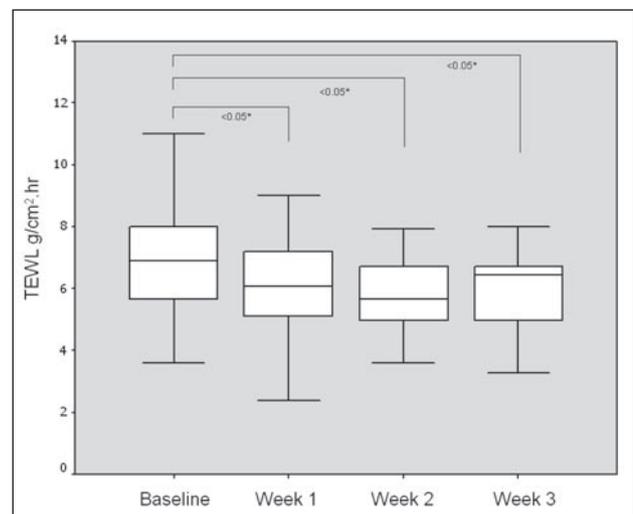


Figure 6. Change of TEWL of lateral leg over time.

Adverse events

Adverse effects were reported according to the guideline of good clinical practice. There was no adverse event reported during the course of the study (Table 1).

Acceptability

The pseudo-ceramide containing moisture cream was well accepted by the subjects.

Dermoscopic appearance

There was improvement in the dermoscopic appearance with decreased scaliness and increase in shininess of the treated areas (Appendix 2).

Discussion

Senile xerosis (SX) is a common skin problem among elderly and account for more than 40% of the skin problems within institutionalized elderly. In a survey involved 300 elderly patients living in 3 nursing homes in Ankara, Turkey, it was found that 45.3% of patients had xerosis.¹ In another study of 398 patients in Tainan City, southern Taiwan, 58.3% of the subject had xerosis which was statistically correlated with an age range of 80-90 years.²

Dry skin is itchy and especially so at night time. It is not uncommon to find elderly patients frequently scratch their skin or use very hot bath to alleviate their symptom. Lichenification and excoriation could result and sometimes even secondary bacterial infection and cellulitis. It is therefore important to treat senile xerosis.

There are multiple causes for senile xerosis. Low ambient humidity, cold winds, frequent or prolonged bathing in hot water, overuse of soap and infrequent use of moisture cream⁴ and decrease of intercellular lipids in stratum corneum with age are important factors in the development of xerosis.¹⁰ To replenish the decreased ceramide in elderly skin is one of the strategies to revert xerosis.

Ceramide is an important component of stratum corneum lipid (SCL) and has been shown to possess the highest water holding capacity in the bi-lamellar lipid layer of the extra-cellular space.¹¹ Since natural ceramides are expensive to produce and may cause apoptosis,¹² synthetic ceramides had been used in moisture creams to mimic the function of natural ceramides. It has been shown in various studies that pseudo-ceramides are able to decrease transepidermal water loss and to improve skin hydration.^{13,14}

The present study tried to assess the usefulness of a pseudo-ceramide containing moisture cream (*Curel*[®], Kao, Japan) in elderly patients with xerosis. Our study has demonstrated the beneficial effect of pseudo-ceramides in improving the skin hydration in elderly after three weeks of treatment in a time-dependent fashion. The arm hydration increased from 32.3 to 42.8 a.u. while the leg hydration increased from 26.5 to 39.3 a.u. The percentage of improvement was higher (49%) at the drier lower leg than the less dry arm (33%). The continual increase in the skin hydration could signify that our subjects had a very dry skin and a steady hydrated state was not achieved even with three weeks of treatment.

The symptom of itch, qualitatively and quantitatively has significant improvement. It is important as it probably reduces the itch-scratch cycle which may reduce the chance of excoriation and secondary bacterial infection. It would be of interest if we could actually measure the scratching behaviour in these patients.

Dermoscopic appearance has shown improvement in patients with mild, moderate and severe xerosis. We found that it is a useful adjunct tool for assessing dry skin and is superior to clinical photography. However, it is important to mark the exact sites for legitimate comparison.

We could only demonstrated a transient improvement in the trans-epidermal water loss. The skin barrier function was improved in the first two weeks with the TEWL dropped from the initial

6.4 and 7.2 to 5.0 and 5.8 g/m².hr for the arm and leg respectively. However the TEWL started to rise on the third week. Whether the test cream could repair the degenerated epidermal dysfunction remained to be shown. A larger sample size may be able to answer this important question.

Nonetheless, the test product is relatively safe as there was no adverse event encountered in the study and all the subjects graded the product as acceptable.

Limitation

The present study is just a single arm study and the exact role of the pseudo-ceramide could not be unequivocally demonstrated. It would be better if we could compare the test product with and without the pseudo-ceramide in order to define the exact role of the pseudo-ceramide component.

Conclusion

It is important to pay attention to dry skin in the elderly patients and it is essential we should advise elderly patients to avoid exposure to factors that may damage the epidermis. To use moisture cream containing pseudo-ceramide is one of the strategies that could be adopted as it has been shown to decrease itch and improve the skin hydration. Besides, it is also relatively safe. The role of the pseudo-ceramide in epidermal repair need to be further investigated.

Competing interests

This study was sponsored by Kao, Japan.

Acknowledgements

We would like to thank Prof. Jean Woo, Miss Ivy Lau, Miss Zoe Lau, Dr. TM Leung, Dr. Elsie Hui

and all the staffs of Shatin Cambridge nursing home in contributing in this study. We also would like to thank Kao, Japan for sponsoring this study.

References

1. Kilic A, Gul U, Aslan E, Soylu S. Dermatological findings in the senior population of nursing homes in Turkey. *Arch Gerontol Geriatr* 2008;47:93-8.
2. Smith DR, Sheu HM, Hsieh FS, Lee YL, Chang SJ, Guo YL. Prevalence of skin disease among nursing home patients in southern Taiwan. *Int J Dermatol* 2002;41:754-9.
3. Patel T, Ishiujji Y, Yosipovitch G. Nocturnal itch: why do we itch at night? *Acta Derm Venereol* 2007;87:295-8.
4. Proksch E, Lachapelle JM. The management of dry skin with topical emollients-recent perspectives. *J Dtsch Dermatol Ges* 2005;3:768-74.
5. Waller JM, Maibach HI. Age and skin structure and function, a quantitative approach (II): protein, glycosaminoglycan, water, and lipid content and structure. *Skin Res Technol* 2006;12:145-54.
6. Imokawa G, Akasaki S, Kuno O, Zama M, Kawai M, Minematsu Y, et al. Functions of lipids on human skin. *J Dispers Sci Technol* 1989;10:617-41.
7. Pierard GE. EEMCO guidance for the assessment of dry skin (xerosis) and ichthyosis: evaluation by stratum corneum strippings. *Skin Res Technol* 1996;2:3-11.
8. Pinnagoda J, Tupker RA, Agner T, Serup J. Guidelines for transepidermal water loss (TEWL) measurement. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 1990; 22:164-78.
9. Berardesca E. European Group for Efficacy Measurements on Cosmetics and Other Topical, EEMCO guidance for the assessment of stratum corneum hydration: electrical methods. *Skin Res Technol* 1997; 3:126-32.
10. Imokawa G, Abe A, Jin K, Higaki Y, Kawashima M, Hidano A. Decreased level of ceramides in stratum corneum of atopic dermatitis: an etiologic factor in atopic dry skin? *J Invest Dermatol* 1991;96:523-6.
11. Imokawa G, Akasaki S, Hattori M, Yoshizuka N. Selective recovery of deranged water-holding properties by stratum corneum lipids. *J Invest Dermatol* 1986;87:758-61.
12. Uchida Y, Holleran WM, Elias PM. On the effects of topical synthetic pseudoceramides: comparison of possible keratinocyte toxicities provoked by the pseudoceramides, PC104 and BIO391, and natural ceramides. *J Dermatol Sci* 2008;51:37-43.
13. Takagi Y, Nakagawa H, Higuchi K, Imokawa G. Characterization of surfactant-induced skin damage through barrier recovery induced by pseudoacylceramides. *Dermatol* 2005;211:128-34.
14. Vavrova K, Hrabalek A, Mac-Maary S, Humbert P, Muret P. Ceramide analogue 14S24 selectively recovers perturbed human skin barrier. *Br J Dermatol* 2007;157: 704-12.

Appendix 1. Xerotic symptoms questionnaire

姓名： 男／女 _____ 日期： _____ 狀況： _____
 相片號： _____ 溝通能力： _____ 聽覺： _____

參照過去兩星期中的經驗回答以下問題：

1. 皮膚有沒有拉緊的情況

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

2. 皮膚有沒有乾燥或皺縮的情況

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

3. 皮膚有沒有粗糙(好鞋)的感覺

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

4. 皮膚有沒有痕癢的感覺

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

5. 痕癢的程度

A 輕微 B 麻麻地嚴重 C 幾犀利 D 嚴重(好犀利)

6. 有沒有皮屑脫落的現象

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

7. 皮膚有沒有損裂或流血的現象

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

8. 皮膚有沒有紅熱的現象

A 從沒有 B 有時 C 很多時候 D 經常 / 常常

Appendix 2. Dermoscopic appearances of different xerotic severity before and after treatment at volar forearm and lateral leg. Upper panel, mild xerosis; middle panel, moderate xerosis and lower panel severe xerosis.

