

Cryopeeling for treatment of photodamage and actinic keratosis: liquid nitrogen versus portable system *

Crioapeeling para tratamento de fotodano e ceratoses actínicas: comparação entre nitrogênio líquido e sistema portátil

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Abstract: BACKGROUND: Cryopelling uses diffuse cryotherapy not only on lesions of actinic keratosis but all over the photodamaged skin.

OBJECTIVES: The aim of this study was to compare two cryopeeling methods (liquid nitrogen- LN and portable system - PS) and demonstrate their efficiency in the treatment of actinic keratoses, patient tolerance, researcher and patient preference and aesthetic results.

METHODS: Sixteen patients (N = 16) with multiple actinic keratoses on the forearms were subjected to cryopeeling with LN on one of the forearms and PS on the other, randomly.

RESULTS: In the treatment of actinic keratoses, LN obtained 74% efficiency and PS, 62% (p = 0.019). The mean visual analogue scale (0-10) was 5.7 ± 1.61 with LN and 4.3 ± 1.44 with PS (p = 0.003). There was no significant statistical difference between the two methods in terms of researcher and patient preference. An analysis of the photos showed improvement of the skin appearance with both treatments (p < 0.001). Treatment with LN obtained some degree of improvement in 62.5% of the cases, while treatment with PS obtained some degree of improvement in 52% of the cases (p > 0.05). Discussion: Treatment with the PS showed better tolerance, but was less efficient than LN. Although LN has been the preferred method, there was no statistical difference between the methods.

CONCLUSIONS: The cryopeeling technique may be an option in the treatment of photodamage. The PS can be an interesting alternative in clinical practice with good tolerance and acceptable results in the treatment of actinic keratoses.

Keywords: Actinic keratosis; Cryotherapy; Skin aging

Resumo: FUNDAMENTOS: O *criopeeling* utiliza a crioterapia difusa não somente nas lesões de ceratose actínica, mas em toda a pele fotodanificada.

OBJETIVOS: Comparar dois métodos de *criopeeling* (nitrogênio líquido e sistema portátil de éter dimetilico, propano e isobutano) quanto à eficiência no tratamento de ceratoses actínicas, tolerabilidade do paciente, preferência do paciente e do pesquisador e resultado estético.

MÉTODOS: Dezesesseis pacientes (n=16) com múltiplas ceratoses actínicas nos antebraços foram submetidos ao *criopeeling* com nitrogênio líquido em um dos antebraços e com o sistema portátil no outro, randomicamente.

RESULTADOS: No tratamento das ceratoses actínicas, o nitrogênio líquido obteve 74% de eficiência e o sistema portátil, 62% (p=0,019). A média da escala visual analógica (0-10) foi 5,7±1,61 com o nitrogênio líquido e 4,3±1,44 com o sistema portátil (p=0,003). Não houve diferença estatística entre os métodos quanto à preferência do paciente e do pesquisador. Na análise das fotos, observou-se melhora do aspecto da pele nos dois tratamentos (p<0,001). Com o nitrogênio líquido, em 62,5% das vezes houve algum grau de melhora; com o sistema portátil, em 52% (p>0,05).

CONCLUSÕES: A técnica de *criopeeling* pode ser uma opção no tratamento de fotodano. O sistema portátil pode ser uma alternativa interessante na prática clínica, com boa tolerância e resultados aceitáveis no tratamento de ceratoses actínicas.

Palavras-chave: Ceratose actínica; Crioterapia; Envelhecimento da pele

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Conflict of interest / *Conflito de interesse*: O sistema portátil foi fornecido gratuitamente pela empresa Neolatina, mas sem qualquer auxílio financeiro para realização do estudo. Não há, portanto, conflito de interesses entre os pesquisadores.

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INTRODUCTION

Actinic keratosis is a sun-induced neoplasm that affects the epidermis and which could evolve into squamous cell carcinoma (SCC).^{1,2} It is estimated that the chance of developing invasive SCC is 0.075 to 0.096% per lesion per year.³ These data justify efficient treatment of actinic keratosis, especially in cases of multiple lesions. Over 80% of the lesions are found in sun-exposed areas such as face, neck and limbs.⁴

Conventional treatment can be based on various therapeutic modalities, including cryotherapy, in which freezing of the cells causes necrosis. Cryotherapy using liquid nitrogen (LN) is the most common modality in the treatment of actinic keratoses.^{5,6} A portable system (PS) is a recent alternative to cryotherapy, which uses gases (dimethyl ether, propane and isobutane) in a portable plastic container. One of its advantages is the practicality of the method, since periodic substance refills are not necessary, as it occurs with liquid nitrogen, and it has a shelf-life of up to three years.

Cryopeeling is a technique that uses cryotherapy in a diffuse manner throughout all the skin region damaged by the sun in order to promote exfoliation and cellular renewal, with possible benefits in the appearance of new lesions. Few studies have been conducted on the technique of cryopeeling so far. In a study by^{7,8} STEPHEN and CHIARELLO (2001) with 373 patients with actinic keratoses, the results obtained were satisfactory and more efficient than 5-fluorouracil. It was concluded that the use of cryopeeling appears to be efficient, accessible and easy to apply.⁸

It is necessary to clarify what the best option is in terms of practicality and efficiency in the treatment of photodamage and actinic keratoses, which are so prevalent in tropical countries. The aim of this study was to compare the two methods of cryotherapy (liquid nitrogen and portable system) in terms of efficiency in the treatment of actinic keratosis, patient tolerance, preference of physician and patient and aesthetic results.

METHODOLOGY

We selected sixteen patients (n = 16) seen in dermatology offices with significant photodamaged skin that presented multiple actinic keratoses on the upper limbs. We included men and women aged 50-80 years. Patients with uncompensated chronic diseases or coagulation disorders were excluded. The study was approved by the Hospital's Ethics Committee in accordance with the current official norms (Resolution CNS 196/96, Law 6.638/79 and Normative Resolution 04/97).

Patients were subjected to standardized

photographic documentation before and after the procedure. They underwent treatment with cryopeeling using the portable system (PS) on one of the forearms and liquid nitrogen (LN) on the other forearm, randomly. Topical anesthetic with occlusion (lidocaine 5% and prilocaine 5%) was applied for two hours before the procedure. In order to guide the application quadrants and lesions of actinic keratosis to be individually treated were demarcated. Cryopeeling was performed by applying the freezing substance with movements of a brush along the length of the forearm until whitening of the skin.⁸ Actinic keratosis lesions were then treated individually with variable freezing time, which was stipulated by the researcher. Following the manufacturer's guidelines for use of the portable system, the valve was pressed until a few drops of the product were eliminated through the tip. After that, the applicator was rotated 90 degrees and we waited a few seconds until freezing of the tip. Then, it was slid over the skin with rotational movements causing whitening of the skin. After a few applications, the process was repeated to guarantee the effectiveness of the procedure. We used topical vaseline in the postoperative period to moisturize the skin and reduce the discomfort of healing. Soon after the procedure, the patients answered a visual analogue

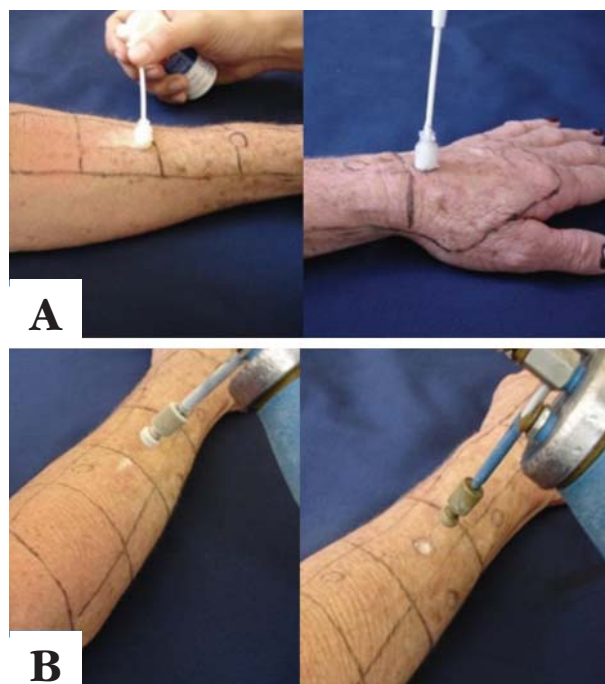


FIGURE 1: Application of portable system (A) and liquid nitrogen (B) with movements of a brush followed by individual treatment of actinic keratosis lesions

scale (VAS) from zero (no discomfort) to 10 (worst discomfort possible).⁹

The patients were periodically followed up on the 7th, 14th, 21th, 30th and 60th days after the procedure. On these occasions, new photographs were taken for documentation of the progress of healing.

We evaluated the effectiveness of the methods by means of the previous demarcation of the lesions with acetate sheets and permanent-ink pen. After sixty days, we counted the lesions that had healed completely, that is, that showed no sign of a previous lesion.

After sixty days, the patient and the physician responded to a five-point scale which ranged from -2 (right much better than left) to +2 (left much better than right),⁹ taking into account the result until that moment.

The aesthetic result was evaluated by comparing the photos before the procedure and sixty days after the procedure. Three professional dermatologists evaluated how much the appearance of the skin had improved following a standardized scale: 0 = no improvement / 1 = a little better / 2 = much better. The raters were blind to the treatment that was being evaluated.

Statistical analysis was performed using the nonparametric test of comparison of two paired samples, known as the sign test. For analysis of the improvement of the appearance of the skin, we used the Student's t-test.

RESULTS

The percentage of lesions completely healed with treatment with liquid nitrogen was 74%, while it was 62% with the portable system, taking into account the average of initial lesions and remaining lesions two months after the treatments. Both treatments were effective in the treatment of actinic keratoses ($p < 0.0001$). Treatment with liquid nitrogen was more efficient when compared with treatment with the portable system ($p = 0.019$) (Graph 1).

The mean visual analogue scale (VAS) score for treatment with liquid nitrogen was 5.7, while it was 4.3 for treatment with the portable system. The patients showed significantly ($p = 0.003$) higher tolerance to pain with the portable system (Graph 2).

With respect to global preference of the patient and physician sixty days after the procedure, it was found that 37.5% of the patients preferred liquid nitrogen, 18.75% preferred the portable system and 43.75% had no preference between the two methods. As for the physician, these percentages were 50%, 18.75% and 31.25%, respectively (Graph 3). There was no statistical difference in preference between the methods ($p > 0.05$).

The aesthetic result was evaluated by means of

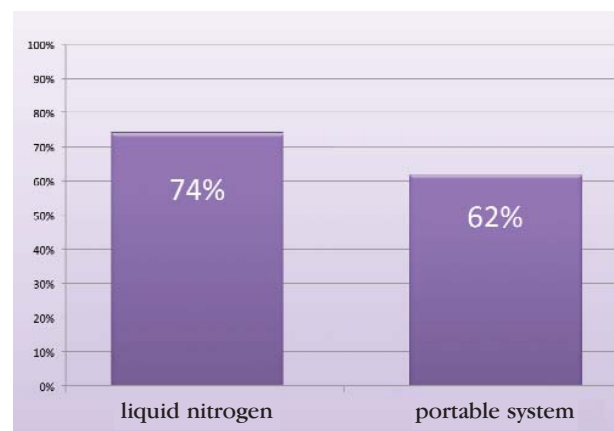
photographic documentation (Figure 1). In an analysis of the photos before the procedures and sixty days after the procedures, the observers noted statistically significant improvement of the appearance of the skin with both treatments ($p < 0.001$). Treatment with liquid nitrogen resulted in some degree of improvement (scores 1 and 2) in 62.5% of the cases and no improvement in 37.5% of the cases (score 0). With the portable system, the percentage of cases in which there was improvement was 52% compared to 48% of the cases without improvement. There was no statistically significant difference between the treatments in this analysis (Graph 4).

DISCUSSION

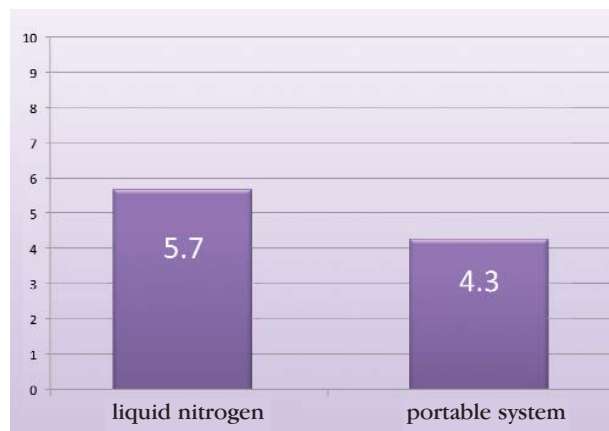
Although cryotherapy is a method widely used in clinical practice, few studies on the cryopeeling technique had been conducted so far.^{7,8} Freezing not only the lesions of actinic keratosis but the entire photodamaged area may be interesting in terms of improving the appearance of the skin and, combined with intensive photoprotection, it may prevent the appearance of new lesions.

From a practical standpoint, there was difficulty in using liquid nitrogen in the cryopeeling technique due to freezing of the tip after a few applications. Since many patients were treated on the same day, this inconvenience may be minimized in office applications with shorter periods of time. Regarding the use of the portable device, it was observed that during individual treatment of lesions of actinic keratosis there was often an abrupt increase of the frozen area. This fact deserves attention, since there may be an uncontrolled increase of the frozen area.

The decision to randomize the choice of which treatment to be used on each forearm was made in order to reduce interference from higher sun exposure



GRAPH 1: Efficiency of treatments based on the number of lesions completely healed. $74.1 \pm 23.74\%$ of the lesions healed with LN, while 62.1 ± 22.75 healed with the PS ($* p = 0.019$)

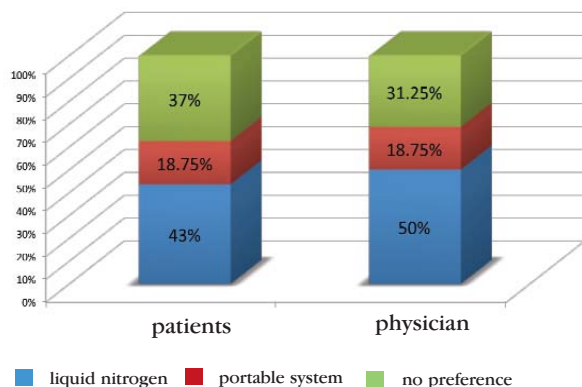


GRAPH 2: Visual analogue scale means for pain. The mean visual analogue scale score ranging from 1 to 10 was 5.7 ± 1.61 with LN and 4.3 ± 1.44 with the PS. There was better tolerance to treatment with the portable system (* $p = 0.003$)

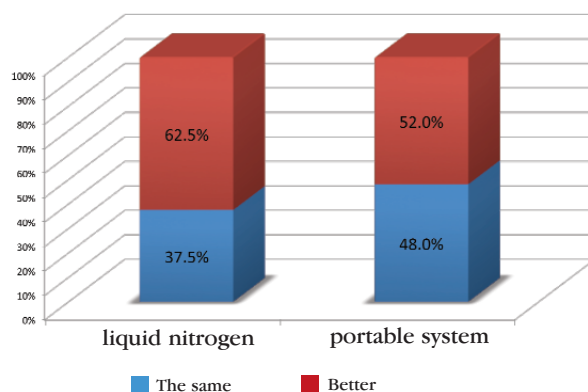
of one of the arms; for example, patients who drive and therefore expose their left arms to the sun more often.

The rate of efficiency of cryotherapy varies a lot in the literature and the duration of freezing influences the success of the treatment. In a prospective study of 90 patients using cryosurgery for treating actinic keratoses¹⁰, we observed a complete response of 69% with freezing times longer than 5 seconds. Similar results were observed in this study: 74% of the lesions healed completely with LN and 62% with the PS. Since the freezing time was not predetermined, the fact that all patients were treated by the same researcher is important to reduce variation in the results.

Some studies have examined new strategies to address the treatment of actinic keratoses, such as photodynamic therapy.¹¹ A multicenter randomized intraindividual (right-left) study with 119 patients compared the use of photodynamic therapy and



GRAPH 3: Analysis of global preference of patients and physician sixty days after the procedures. No statistically significant difference was observed between the methods



GRAPH 4: Analysis of the appearance of the skin by means of photographic documentation and standardized scale 0 = no improvement / 1 = a little better / 2 = much better. The graph shows the percentage of cases in which there was improvement of the appearance of the skin to some degree with both treatments. The observers were blind to the treatments evaluated. There was no statistically significant difference between the treatments in this analysis

cryotherapy in the treatment of actinic keratoses.⁹ The patient's and investigator's preference was evaluated using a five-point scale varying from -2 (right much better than left) to +2 (left much better than right). The individuals measured their discomfort using a visual analogue scale (VAS) from zero (no discomfort) to ten (worst discomfort possible) immediately after the procedure. Photodynamic therapy was the method preferred by the patients, with efficiency comparable to cryotherapy. Both the visual analogue scale and the five-point scale were used as tools for evaluating the methods of cryotherapy in this study.

Both methods were well tolerated by the patients, and the contribution of the topical anesthetic in this finding is undoubtedly important. However, there was better tolerance with the portable system, with a statistically significant difference. On the other hand, this method showed to be less efficient in the treatment of actinic keratoses. There may be minor tissue damage with the portable system, which could explain these findings. In addition, less experience with the use of this method may have influenced these results.

Both methods were able to improve the appearance of the skin, without statistical differences between them. We observed an improvement in skin texture to the touch with a noticeable decrease in skin roughness. The fact that the dermatologists analyzing the photos were blind to the types of treatments used renders a more reliable conclusion in terms of not finding differences between the two methods. It is interesting to consider that although the portable system showed to be less effective in the treatment of actinic keratoses, there was no difference between the

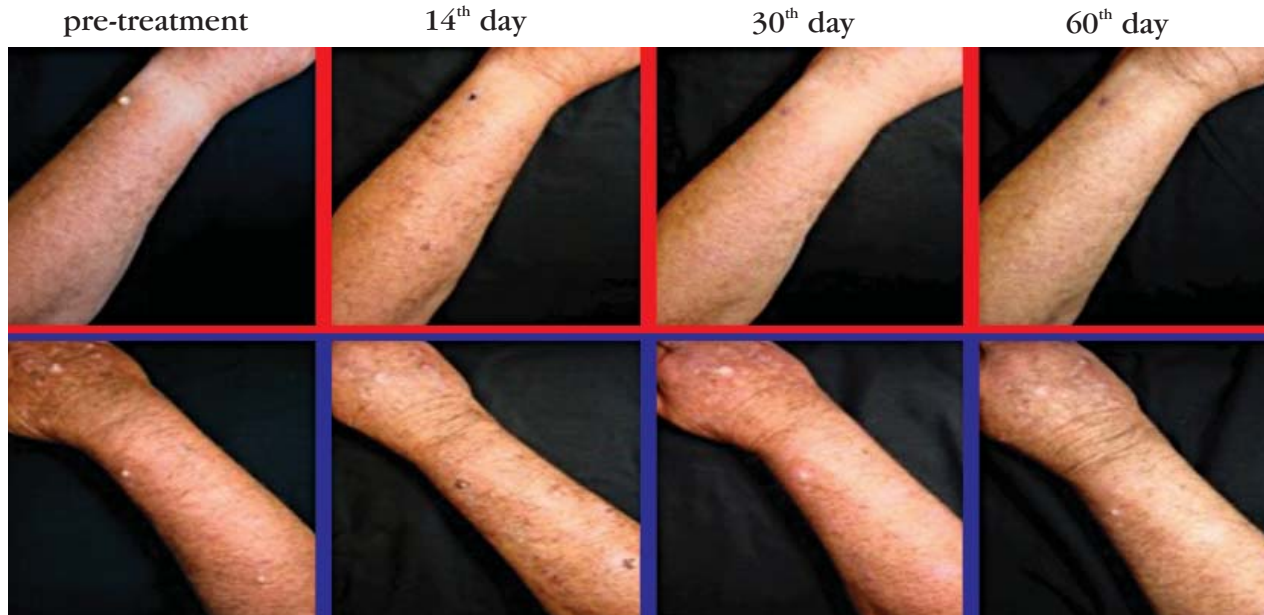


FIGURE 2: Photographic documentation of one of the sixteen cases studied. Pre-treatment photos followed by photos of the 14th, 30th and 60th days after the procedure. Treatment with liquid nitrogen shows border in red and portable system, in blue. In the analysis of improvement of skin appearance, pre-treatment photos and photos taken after sixty days of the procedure were compared without the observers knowing which treatment they were evaluating

two methods in the analysis of global preference on the part of the physician and the patient or in the analysis of the photos. Therefore, one can infer that the portable system can be a valid alternative when the goal is to improve the appearance and texture of the skin.

The recovery of all patients was satisfactory, with good healing. The main complaint was pruritus in the postoperative period. All patients were satisfied with the results.

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CONCLUSION

The cryopeeling technique is well tolerated by patients with good efficiency in the treatment of actinic keratoses and improvement of the appearance of photodamaged skin. From a practical standpoint, the portable device may be considered a viable alternative in the application of cryopeeling in medical offices. □

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