Pain evaluation in the cryosurgery of actinic keratoses *

Avaliação da dor em criocirurgia de ceratoses actínicas

Claudia Schermann Poziomczyk[1]
Bruna Köche[2]
Marcel de Almeida Dornelles[3]
Sérgio Ivan Torres Dornelles[4]

Abstract: BACKGROUND: Background: Actinic keratosis is a frequently-encountered premalignant lesion occurring in areas exposed to sunlight in fair-skinned elderly or middle-aged people. Cryosurgery with liquid nitrogen is the most common method for treating the lesions.
OBJECTIVES: The primary objective of this study was to measure the intensity of pain during cryosurgery by using the Visual Analog Scale (VAS). We also sought to identify the pain level deemed appropriate by the patient, to assess the proportion of patients who considered it necessary to reduce the pain and, finally, to gauge whether or not additional analgesia was required.
METHODS: Cross-sectional study with patients referred for cryosurgical treatment of actinic keratoses to the Sanitary Dermatology Outpatient Clinic. We applied a questionnaire to 112 patients [48 men (42.8%) and 64 women (57.2%)] after their treatment for actinic keratoses, asking them to assess the intensity of pain experienced during surgery and the pain that they considered to be bearable or appropriate for the procedure.
RESULTS: The mean referred pain during surgery was 32.85 mm on the Visual Analog Scale, while the mean pain deemed appropriate by the patients was 23.01 mm. The difference between the two means was statistically significant ($p < 0.05$). 30.4% of the patients reported in the direct and objective questionnaire that they needed the pain to be reduced.
CONCLUSIONS: Although the level of pain considered to be appropriate by the patients was statistically lower than the referred pain, it did not reach the level at which it would be judged necessary to provide additional analgesia in this type of intervention.
Keywords: Actinic keratosis; Cryosurgery; Pain measurement

Resumo: FUNDAMENTOS: a ceratose actínica é lesão pré-maligna frequente, que ocorre em áreas expostas à luz solar, em pessoas idosas ou adultas de meia-idade e pele clara. A criocirurgia com nitrogênio líquido é a modalidade mais comum para o tratamento de ceratoses actínicas. Objetivos: o objetivo primário deste estudo foi medir a intensidade da dor durante a criocirurgia, por meio da Escala Visual Análoga. Também buscou-se identificar o nível de dor considerado adequado pelo paciente, avaliar a proporção de pacientes que consideram necessária a diminuição da dor sentida e verificar a necessidade ou não de analgesia suplementar. Métodos: Estudo transversal com pacientes encaminhados para terapêutica criocirúrgica de ceratoses actínicas no Ambulatório de Dermatologia Sanitária. Foram avaliados 112 pacientes, após tratamento de ceratoses actínicas, aplicando-se um questionário com perguntas sobre a intensidade da dor sentida durante o procedimento cirúrgico, assim como a dor considerada confortável ou adequada ao procedimento. Resultados: participaram 48 homens (42,8%) e 64 mulheres (57,2%). A média da dor referida durante o procedimento cirúrgico, medida em milímetros na Escala Visual Análoga, foi de 32,85 mm; a média da dor considerada adequada pelos pacientes foi de 23,01 mm. A diferença entre as duas médias foi estatisticamente significativa ($p<0,05$). Em questionário objetivo e direto, a percentagem de pacientes que referiu ser necessária a diminuição da dor foi 30,4%. Conclusões: embora a dor considerada adequada seja menor estatisticamente do que a sentida, não alcança níveis suficientes para que seja atribuída a necessidade de método de analgesia suplementar neste tipo de intervenção.
Palavras-chave: Ceratose actínica; Criocirurgia; Medição da dor

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[1] Resident physician and consultant at the Hospital São Lucas da PUC-RS; Master´s Degree in pathology awarded by Porto Alegre Federal University for Health Sciences (UFCSPA), Porto Alegre (RS), Brazil.
[2] MD in private practice, Caxias do Sul (RS), Brazil.
[3] Student of medicine, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre (RS), Brazil.
[4] Master´s degree in Clinical Medicine; Preceptor of the Sanitary Dermatology Outpatient Clinic (ADS), State Health Secretariat, Porto Alegre (RS), Brazil.

INTRODUCTION

Actinic keratosis (AK), also called 'solar' or 'senile' keratosis, is a frequently-encountered premalignant UV light-induced lesion of the skin occurring in areas exposed to sunlight mainly in fair-complexioned elderly or middle-aged people. [1,2]

Lesions can progress to chronic disease and are usually multiple, characterized by small scaly bumps (measuring from a few millimeters to slightly over 2 cm in diameter), rough to the touch and often raised and brownish in color. The growths sometimes appear as scaly atrophic and erythematous lesions. [2] The appearance of an erythematous halo (even in small lesions) and infiltration around the base, may indicate carcinomatous transformation. [2,3]

Histopathology reveals hyperkeratosis and parakeratosis, with areas of atrophy and acanthosis in the malphigiana layer. The deeper malphigian cells show a randomly scattered atypical cell formation but with the basal layer intact. [1,2]

While AKs can be treated for cosmetic reasons or to relieve associated symptoms, the main reason for treatment is to prevent squamous cell carcinomas. [3] Treatment options include ablative (destructive) or topical therapies in patients with multiple lesions. [3]

Cryosurgery (CR) with liquid nitrogen (LN) is the most common treatment method. It involves the application of extreme cold to destroy abnormal or diseased tissue, in effect by 'freezing-off ' the AKs. [1,3] This controlled destructive procedure is highly effective, with cure rates of 75-99%. CR is easily carried out in the doctors´ office, produces excellent cosmetic results and is well tolerated. [3]

The aim of CR is to cause selective necrosis of tissue. The length of application (i.e. the amount of freezing required) depends on the type of lesion. Biological changes occur as the result of rapid heat loss when the cryogen touches the skin, in effect causing tissue destruction by freezing. [1]

Cryosurgery works by taking advantage of the destructive force of freezing temperatures on cells. At low temperatures, ice crystals form intra- and extracellularly, leading to cell death and vascular thrombosis generated by the freezing of blood vessels in the region adjoining the tissue necrosis. This produces tissue destruction, while the stroma promotes tissue repair around the wound. [1]

LN can be sprayed onto the skin, applied through a cryoprobe, or simply dabbed onto the lesions with cotton or foam swabs. The form of application depends on the origin and the shape of the lesion to be treated. [4]

According to Thai *et al.* between 10 and 15 seconds is the ideal length of time for LN spray treatment of actinic keratosis. This burst is highly effective, producing a cure rate of at least 80%, and with minimum local side effects (pain, burning sensation, redness, swelling, blistering and skin infections). [5]

However, using cryosurgery for treating actinic keratosis is in practice a painful procedure for many patients. The pain varies with the freezing time, the number and location of lesions and the patient´s pain threshold.

Cryosurgery has become a routine part of dermatologic care, including at primary care level. The field of dermatologic surgery has advanced significantly, particularly over the past 30 years, with the incorporation of new therapies and technical improvements. [6] Despite the many advances in cryosurgery techniques, clinical observation has nevertheless shown that some patients still experience pain and discomfort.

The concept of pain varies from person to person. The *International Association for the Study of Pain* (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." [7,8] One approach currently used is to interpret pain in two ways: pain as an emotion and pain as a specific sensation, or in other words, as purely psychogenic or purely physical. [8] Pain is not a straightforward, unique and one-dimensional phenomenon, varying only in intensity, but rather a multidimensional (internal, complex and personal) experience involving a wide spectrum of affective and emotional factors.

Pain can be triggered by mechanical damage, extremes of temperature or chemical irritants. As far as the skin is concerned, free nerve endings (FNEs) are responsible for the sensation of pain. The density of these receptors varies between different sites and tissues. [9,10] The stimuli are transmitted to the central nervous system (CNS) by two types of neurons: the thin myelinated A-delta (fast) and unmyelinated C fibers (slow). These fibers reach the thalamus and sensory cortex - the sites responsible for pain perception and the associated emotional component. The transmission of pain from the peripheral tissues to the CNS depends on a complex balance between excitatory and inhibitory neuronal systems. [8]

While measuring pain is vital for correct pain management a more objective method for assessing pain has also proved to be invaluable, with the use of tools for measuring different pain rating scales: the Verbal Rating Scale (VRS), the Visual Analogue Scale (VAS), the Numeric Rating Scale (NRS) and the Faces Rating Scale (FRS).

The VAS, validated by the scientific community,

is the most widely-used pain measurement tool. Operationally, it consists of a 100 mm long horizontal line, anchored by descriptors on each side. The far-left end of the line represents total absence of pain, while the extreme right represents unbearable pain or 'the worst pain imaginable'. The patient marks on this line the point which best represents his or her perception of the pain level. The score is determined by the distance in millimeters from the starting point on the left end of the line up to the point marked by the patient. [5.10]

Thaiza Xavier *et al.,* in a study on the qualitative and quantitative aspects of pain in patients undergoing posterolateral thoracotomy, compared pain behavior in men and women who had undergone this particular surgery, by employing the Numeric Pain Scale and the McGill Pain Questionnaire. Xavier observed no statistically significant differences between the quantitative pain responses of men and women. [10.11]

MATERIALS AND METHODS

We conducted a cross-sectional study using a sample consisting of volunteers of both sexes over 18 years of age suffering from actinic keratoses and referred for cryosurgery to the Rio Grande do Sul Dermatology Clinic.

Our primary objective was to measure the intensity of pain during cryosurgery in patients with actinic keratoses by using the Visual Analog Scale. Secondary objectives included identifying the level of pain deemed appropriate by the patient, to assess the proportion of patients who considered it necessary to reduce the pain and, finally, to gauge whether or not additional analgesia was required.

Routine care was provided for all the patients who underwent cryosurgery for actinic keratoses.

Since no meaningful data exists on the assessment of pain resulting from cryosurgery of actinic keratoses, we based the sample size calculation on the outcome prevalence, considering a statistical power of 80% and a significance level of 0.05. (Sample size = 110 volunteers).

Statistical analysis (with the SPSS 15 program) was performed by obtaining frequencies, averages, standard deviations, medians, quartiles and "t" tests for paired and Chi-square samples.

The inclusion criteria used were: all patients over 18 years old referred for cryosurgery of actinic keratoses.

Data collection (March to October 2009) was performed by applying a questionnaire with open and objective questions at the time of the initial approach by our assessor in the Dermatology Outpatient Clinic.

The Visual Analog Scale was applied soon after, recording its interpretation of the intensity of pain felt by measuring the distance from the extreme left (no pain) to the location marked by the patient, as described above. Pain intensity considered appropriate by the patient was also measured by VAS.

Following the procedure, patients were asked to respond "yes" or "no" when questioned on whether a need existed to reduce the pain felt.

Other data assembled (independent variables) consisted of: age, education, income, occupation, marital status, history of previous dermatological surgical procedures, site on the skin where surgery was performed, number of lesions and medicines currently being used.

The project was approved by the Ethics Committee of the Rio Grande do Sul School of Public Health. The volunteers signed the Informed Consent Forms, were notified of the research goals and assured of total confidentiality during the process of collection, storage and data analysis. All patients were guaranteed the care they needed regardless of whether they were willing or not to participate in the study.

RESULTS

The research study involved a sample of 112 volunteers. Measured in millimeters on the Visual Analog Scale, the average referred pain during surgery was 32.85 mm, with a standard deviation (SD) of 21.56mm. The mean pain considered appropriate ("comfortable") for the same patients was 23.01 mm, with an SD of 16.44 mm. As for the need to reduce pain ("yes" or "no" in the questionnaire), 34 patients (30.4%) responded that they needed pain relief to feel comfortable during the procedure, while 78 (69.6%) responded that this was not necessary. Comparing these responses using the chi-square test, we obtained a $p < 0.05$, i.e. groups of volunteers who answered "yes" (30.4%) and "no "(69.6%) were statistically different. The data is recorded in Tables 1 and 2.

Important information regarding the differences in the scores for assessed pain ('felt' and 'appropriate') can be obtained by Cohen's method, which calculates the corresponding *effect size.* Calculation of the Cohen statistical index "d" (Cohen's *d)*, performed using the mean and the standard deviation of the pain scores in these groups was 0.50. According to the author of the test and interpretations published by the National Survey of Student Engagement (NSSE), this effect size is considered to be of average magnitude (0.50). [12.13]

The sample consisted of 48 men (42.8%) and 64 women (57.2%). Analysis by gender showed that men had an average 'pain felt' score of 26.46 mm (SD 16.46 mm) and an 'appropriate' pain score of 22.21 mm (SD 15.18 mm). On the other hand, the women's mean score for 'pain felt' was 37.67 mm (SD 23.72 mm) and

Table 1: Values representing the intensity of referred pain and appropriate pain (in mm) based on the total number of volunteers

	Intensity of referred pain (mm)	Intensity of appropriate pain (mm)
Average	32.85	19.78
Median	35.00	20.00
Standard deviation	21.56	16.44
Q1 (1st quartile)	12.35	10.00
Q3 (3rd quartile)	50.00	40.00
Minimum	0	0
Maximum	95	60

'appropriate' pain 23.61 mm (SD 17.42 mm). See Table 3 for details.

The average age of patients was 66.98 years (minimum age 40, maximum 87 years). 66 of them were married (58.9%), 10 were single (8.9%), 31 were widowed (27.6%) and 5 (4,6%) were in the "other" category." Average monthly income of the volunteers was R$724.97, ranging from 0 to R$2500.00.

Education was measured by years of schooling: the group possessed an average of 5.12 years schooling (SD of 3.42). 78 had a history of previous dermatological surgery (69.6%). The average ages and education levels between males and females revealed no significant difference between the groups ($p>0.05$). As for marital status, widowhood predominantly referred to women (27 women to 4 men).

Pain was also analyzed according to the areas affected. 102 volunteers had lesions on the face (average of 4.42 lesions), while 10 had scalp lesions (average of 4.6 lesions). 42 individuals had lesions on the arms (average of 5.47 lesions) and 57 had hand lesions (average of 2.08). The mean referred and appropriate pain scores between the different affected areas are shown in Table 4. Using the Games-Howell multiple comparison test no significant difference ($p> 0.05$) was observed between the affected areas, both in the analysis of the referred pain values (felt by the patient) and the values considered 'appropriate'. Gender comparison revealed no statistical difference between the sexes (chi-square test) regarding the number of lesions on the anatomical areas, with the exception of the scalp (not included in this study because of the shortage of female diagnoses).

Lesions on the scalp, face, hands, forearms, legs and feet were evaluated. The number of affected areas in the same patient varied within the sample studied. 42 volunteers had lesions in only one area, 35 patients had concomitant injuries in two areas, 24 volunteers in 3 areas. Only 9 volunteers had lesions in four areas, 1 volunteer in five areas and 1 patient in six areas. The averages for referred pain and appropriate according to number of affected areas are shown in Table 5.

Although increasing referred pain values (pain experienced) were observed in line with the increase in the areas treated, the Games-Howell test revealed no significant differences between them.

Table 2: Distribution of answers to the question: "Is there a need to reduce the pain felt?"

	Yes	No	Total
Number	34	78	112
Percentage	30.4	69.6	100

Table 3: Referred and appropriate pain values according to sex (in mm)

	Males	Females
Number of volunteers	48	64
Average Referred Pain (mm)	26.46	37.64
Average Appropriate Pain (mm)	22.21	23.61
Referred Pain Median (mm)	27.50	40.00
Median Appropriate Pain (mm)	20.00	20.00
Standard Deviation Referred Pain (mm)	16.46	23.72
Standard Deviation Appropriate pain (mm)	15.18	17.42
Q1 (1st quartile) - Referred Pain (mm)	10.25	15.00
Q3 (3rd quartile) - Referred Pain (mm)	40.00	50.00
Q1 (1st quartile) - Appropriate Pain (mm)	10.00	8.00
Q3 (3rd quartile) - Appropriate Pain (mm)	38.50	40.00

Table 4: Referred and appropriate pain values according to treated areas (in mm)

	Face	Scalp	Hands	Forearm
Number of Patients	102	10	57	42
Median Referred Pain(mm)	34.21	32.20	36.23	35.19
Average Referred Pain(mm)	35	37.50	35.00	35.00
Standard Deviation Referred Pain (mm)	21.68	17.40	21.65	22.17
Q1 Referred Pain	14.50	11.50	19.00	15.00
Q3 Referred Pain	50.00	50.00	50.00	50.00
Average Appropriate Pain (mm)	23.96	24.00	22.39	22.76
Median Appropriate Pain (mm)	20.00	17.50	20.00	20.00
Standard Deviation Appropriate Pain (mm)	16.49	19.12	15.40	16.46
Q1 Appropriate Pain	10.00	8.75	10.00	10.00
Q3 Appropriate Pain	40.00	42.50	37.50	40.00

Table 5: Referred and appropriate pain values according to number of treated areas (in mm)

Number of affected areas	Number of patients	Average/Median Referred Pain (mm)	Average /Median Appropriate Pain (Mm)	Q1/Q3 Referred Pain	Q1/Q3 Appropriate Pain
1 area	42	28.10 / 27.50	22.86 / 20.50	8.00 / 42.75	6.75 / 40.00
2 areas	35	32.77 / 34.00	21.83 / 20.00	12.00 / 50.00	10.00 / 34.00
3 areas	24	37.83 / 40.00	24.46 / 20.00	20.50 / 50.00	10.25 / 40.00
4 areas	9	42.67 / 50.00	29.56 / 30.00	22.00 / 57.50	13.00 / 47.5

DISCUSSION

In this cross-sectional study we attempted to assess (i) the intensity of pain reported by patients undergoing cryosurgery, (ii) the level of pain that would be considered appropriate for this procedure and (iii) whether or not a need existed to reduce the pain felt.

Comparing the mean scores of 'pain felt' and 'appropriate pain' with the use of the *t* test for paired samples, we observed that the means of the samples were different ($p < 0.05$). With this data we estimated that the degree of 'felt pain' was significant enough to determine differences between the samples.

Using the *t* test for paired samples (comparing the mean scores of 'felt pain' and 'appropriate pain' in the samples by gender), we observed that in the men the value of "p" was greater than 0.05 (i.e. there was no difference between the groups). In the case of females, we obtained a $p < 0.05$, showing that the samples were in fact different. We estimate that the pain considered appropriate by females is less than the referred pain (pain felt by the volunteers), and it can thus be assumed that the female group had a lower pain threshold in this particular therapeutic intervention. These findings do not concur with the results of the study by Thaiza Xavier *et al.* "*Qualitative and quantitative aspects of patients undergoing posterolateral thoracotomy*" which concluded that no statistically significant difference existed between the sexes in the quantification of postoperative pain. [10]

Comparing the "yes" and "no" responses regarding whether or not prior analgesia was needed, we obtained a $p < 0.05$ using the chi-square test, i.e. samples of the "yes" group (30.4%) and the "no" group (69.6%) turned out to be statistically different. Using this objective assessment method, we could therefore interpret the figures as meaning that the need for pain relief does not exist (Table 2).

It was observed that mean referred pain actually increased in line with the number of areas of the body being treated, with the exception of sites affecting small numbers of volunteers (which may have compromised the study). One explanation could be that pain stimuli and the resulting perception of pain are dependent on the sum total of anatomical areas undergoing treatment.

CONCLUSION

In this study, average felt (experienced) pain was significantly higher than pain reported by the volunteers as 'appropriate'. However, only a small number of patients reported on the questionnaire that additional pain relief was required. These results could be interpreted as somewhat contradictory. Nevertheless, given that the perception of pain involves affective and emotional aspects and is subject to a multiplicity of mechanisms, the results could also demonstrate that although "appropriate pain" is seen as statistically less common than "felt pain", it fails to reach the level at which supplementary analgesia would be needed. Furthermore, it is worth noting that calculation of Cohen´s *effect size* measures did not indicate, when comparing the "felt" pain and "comfortable" (or "appropriate") pain of our volunteers, that we were faced with a particularly significant situation.

We were able to show also that a statistically important difference exists between the men's evaluation of pain and that of women. The male volunteers in our sample returned a lower mean pain score (i.e. revealing a higher pain threshold).

Note that some factors observed in this study may have involved a certain measurement bias arising from e.g. patients´ difficulty in using the Visual Analog Scale, patients possibly embarrassed to report having suffered discomfort during the procedure (in the presence of the physician), reluctance to ask for additional analgesia on the assumption that pain was 'inevitable' during the cryosurgical procedure etc. Other studies reported in the literature confirm these observations. [10,14]

Given our findings, we suggest that further studies should be conducted with a view to assessing the real need for additional analgesic measures to be taken to ease the discomfort of these particular outpatients. ❑

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MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:
Claudia Schermann Poziomczyk
Rua dos Andradas, 1.646 - Conjunto 73, Centro
90020-012 Porto Alegre (RS) – Brazil
E-mail: claudiapoz@hotmail.com

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