

Relieve the pain of post herpetic neuralgia using a non-freezing technique: clinical trial

Alivio del dolor en neuralgia postherpética usando una técnica no congelante: estudio clínico

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ABSTRACT

We used non-freezing technique (NFT) in 112 patients with post herpetic neuralgia, with similar results and as an extension to the previously published study (Calandria L, Cryoanalgesia for post-herpetic neuralgia: a new treatment, *Int J Derm* 2011, 50: 746-50).

In 93% of the cases we obtained an excellent (> 70%) or very good improvement in pain (30-70% improvement) and very mild responses (< 30%) or failure in 7% of cases.

We used liquid nitrogen in the form of NFT in 99 patients with post herpetic neuralgia and in 13 patients with acute evolution zoster neuralgia (one week to one month of neuralgia).

We believe that the technique offers a totally painless, ambulatory and rapidly effective treatment, using liquid nitrogen as a cooling factor in the area and non-freezing. The action is hypothesized to occur through the release of repairing cytokines from damaged nerve sheaths. Proudfoot *et al.*⁷ have been identified molecular receptors for cooling in sensory nerves, and they demonstrate there how activation of one of these, TRPM8, produces profound and mechanically novel analgesia in states of chronic pain.

This technique (NFT) is performed through the skin and not by the exposure of the open-air nerve as previously rhizotomies were performed even by cryosurgery or minor interventional percutaneous balloon rithotomy.

KEYWORDS: non-freezing technique, post herpetic neuralgia, cryoanalgesia.

Introduction

The frequency of appearance of herpes zoster (HZ) is approximately between 200 and 300 patients per 100 thousand inhabitants (USA and Europe).

RESUMEN

Usamos una técnica no congelante (NFT) en 112 pacientes con neuralgia postherpética, con resultados similares y extensión a un estudio previamente publicado (Calandria L, Cryoanalgesia for post-herpetic neuralgia: a new treatment, *Int J Derm* 2011, 50:746-50).

En 93% de los casos obtuvimos un resultado excelente (> 70%) o muy buena mejoría del dolor (30 a 70%) y respuesta mediana (< 30%) o falla en 7%.

Usamos nitrógeno líquido en la forma de NFT en 99 pacientes con neuralgia postherpética y en 13 pacientes con evolución aguda de la neuralgia de zóster (de una semana a un mes de neuralgia).

Creemos que la técnica ofrece una ausencia total de dolor, es un tratamiento ambulatorio y con efectividad rápida usando nitrógeno líquido como un factor de enfriamiento en el área y no congelante. Se cree que la acción ocurre a través de la liberación de citocinas reparadoras de las vainas del nervio dañado. Proudfoot y colaboradores⁷ identificaron receptores moleculares para enfriamiento en nervios sensitivos y demostraron su activación, los receptores TRPM8 producen profunda y mecánicamente analgesia en estados de dolor crónico.

Esta técnica (NFT) se realiza a través de la piel y no por la exposición abierta del nervio, como se hacía previamente en rizotomías con criocirugía en intervenciones menores percutáneas con rizotomía con balón.

PALABRAS CLAVE: técnica no congelante, neuralgia postherpética, crioanalgesia

Post herpetic neuralgia (PHN) is a complication of HZ, defined as the pain of the affected area, important, intolerable and persistent a month after the disappearance of the vesicle stage.

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Post-herpetic neuralgia is an extremely painful condition that affects a greater number of patients as older are the patients affected by zoster. It occurs in 16% of patients aged under 60 and in 47% of those over 60 years old, increasing the occurrence with the older the age of onset.¹

The intolerance and persistence of pain can invalidate the daily life of the individual, affecting night rest and there have even been reports of patients with suicidal thoughts.²

Conventional treatments have had variable responses. Pain relief was attempted with minor and major pain relievers (opioids), capsaicin, gabalin, pregabalin, and valproic acid.

Another method used was to anesthetize the area with topical use of lidocaine or locoregional block.

Another method, more recently used, is the use of botulinum toxin intradermal injected on the affected skin area, but with less satisfactory results (10% of patients with a 50% response to pain improvement at 12 weeks) in addition to the cost of the treatment and the need of repeating the process frequently.³

Rizotomies were performed (removal of painful nerves) by different methods, including open cryosurgery, for the destruction of the affected nerve fibers.⁴

We have asked ourselves if cryosurgery could produce cryoanalgesia, even in cases of unexposed nerve and if there could be a method without causing tissue injury. This is how we developed the NFT technique and applied it to patients with PHN. Later we found an article by doctor Suzuki⁵ who used carbon dioxide in 14 patients with a positive result of 71%, similar results to ours.

According to Douglas and Malcom,⁶ the small peripheral nociceptive fibers of the unmyelinated nerves of the skin are more sensitive to cold. The zoster's tissue injury causes release of $H + K + ATP$ that increases the sensitivity of the nociceptive nerves. The release of histamine and substance P by inflammatory mast cells worsen the situation. This would help to raise a pathophysiological hypothesis exposed later.

According to Proudfoot *et al.*,⁷ the activation of sensitive cooling receptors, TRPM8, produces analgesia in state of chronic pain, explaining the physiopathology hypothesis.

Method

The sample included 112 patients with PHN originating in the dermatological consultation, with ages ranging from 30 to 98 years (average 79 years). 73 women and 39 men. The location of the zoster was in various topographies: cephalic, face, neck, trunk and limbs. We performed the NFT

technique in all of them (13 were in the acute vesicular period or with a neuralgic pain of less than 30 days after HZ and 99 patients had neuralgia more than one month after the acute period). We used liquid nitrogen in CryAC Brimill® device.

The technique consists of cooling the area affected by neuralgia; nitrogen applied, perpendicular to the skin, at a distance of approximately 15 cm, without freezing, cooling the area by circular or brush strokes. We perform slow movements for approximately 30 seconds. During that time, we exercise a cooling of the area, producing a cloud of nitrogen. The nitrogen is passed several times (4-5) emphasizing the cooling in the most algid zone. It is very important due to be not the prior basic idea of cryosurgery, because is not freezing. Only a nitrogen cloud form. Not freezing the skin. No blister.

Weekly repeated cycles for approximately six weeks. Even sometimes, the pain disappears before (especially in acute cases or with shorter evolution).

The improvement is subtle at the beginning, better night rest, and use of fewer analgesics for the relief of pain, reduction of the size of the affected area, change in the type of pain, less intensity or even the appearance of pruritus instead of pain. The reduction of the affected area is not very visible to the patient, many times, we have to examine the area and see its nociceptive response in order to quantify it.

In order to assess pain and its evolution, we asked the patient to prepare a diary with specific data. They should quantify the pain in a range of one to 10, where the pain is minimal in one, and maximum in 10. Even they should also answer what is the duration of pain each time it appears, as well as if they have different cycles of pain during the day or the night. They should also answer if their pain wakes them up at night and with what type of analgesics they obtain relief. These questions help to focus on the quantification of pain and improvement. Anxiety and expectation about relief sometimes make it difficult to show initial subtle improvements. Generally, after the 3rd week of treatment, the change is more evident. It is very important to help patients stay alert to subtle changes and not lose hope of improvement, since they come to the consultation dejected by the pain and the chronicity of the process.

For the interpretation of the data, we considered that the improvement is excellent when the reduction in the assessment of pain intensity was at least 70%.

If the improvement is between 30 and 70% we considered that it is notorious and poor response or failure when improvement was less than 30%.

Results

We maintained results with slight variations with respect to the previous publication. 75 patients (67%) rated an improvement between 71 and 100% ranked as excellent. 29 patients (26%) evaluated the improvement between 31 and 70%, graded as a marked improvement. And eight patients (7%) were classified as treatment failure since the improvement was scarce (corresponding < 30% or null). In short, we observed a successful response in 93% of the cases (**graph 1**).

The number of sessions was one to six in 83 patients (74%); seven to 10 in 25 patients (22%) and more than 11 in four patients (4%) (see **graph 2** and comments).

Of the 13 patients who had episodes of acute zoster, seven of them improved 100% in only one session, two patients needed two sessions to improve 100%. One patient improved 100% in three sessions, other one patient improved 90% in three sessions. Only two patients of this group needed four sessions or more to get some improvement and it was 30 and 80% each one considering one of them was an HIV-AIDS patient in treatment and the other one a very old patient with multiple pathologies attached.

Very often, they get immediate transient relief from pain, which gives them the strength to follow the protocol.

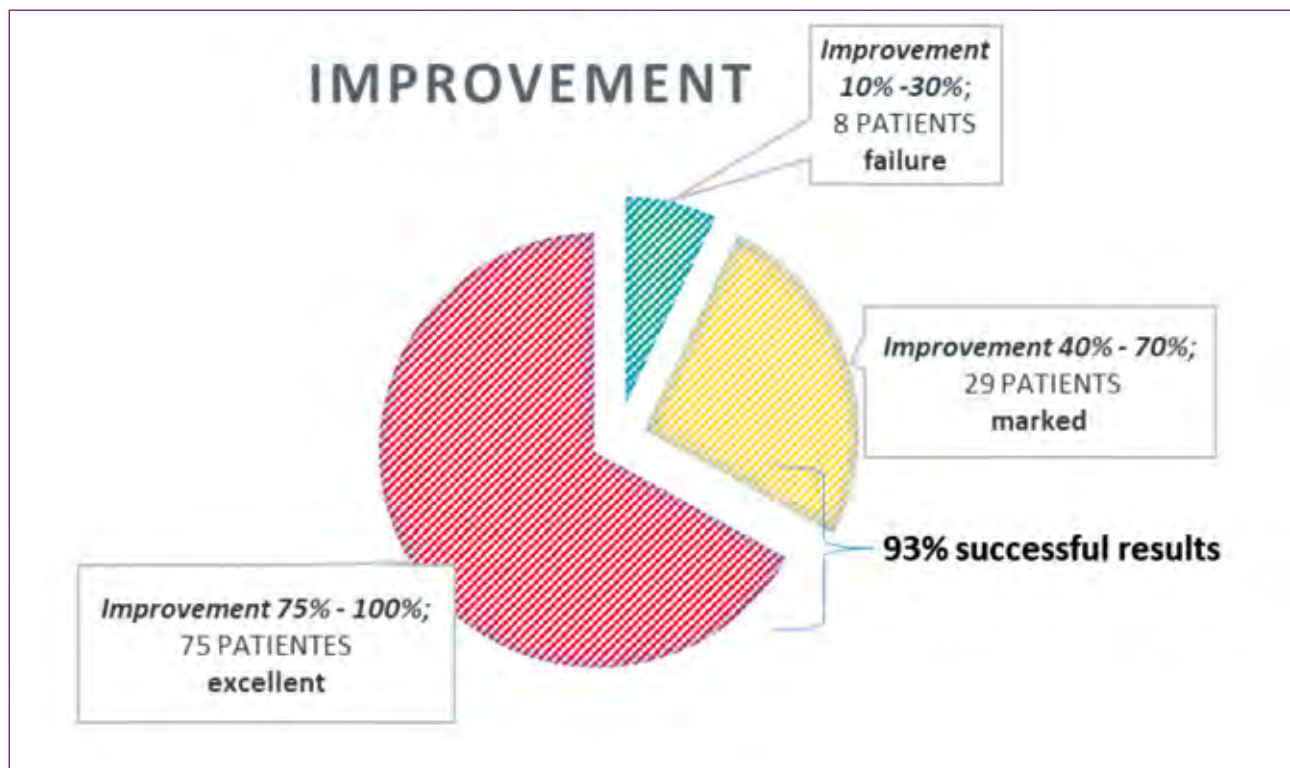
Comments

In previous unpublished studies, we observed that the progression of cycles to more than six sessions had no noticeable influence on the improvement of the process. That is why we mark six as the number of sessions to be performed. Despite this, we have practiced it more than six times in some cases, especially at the beginning of our study.

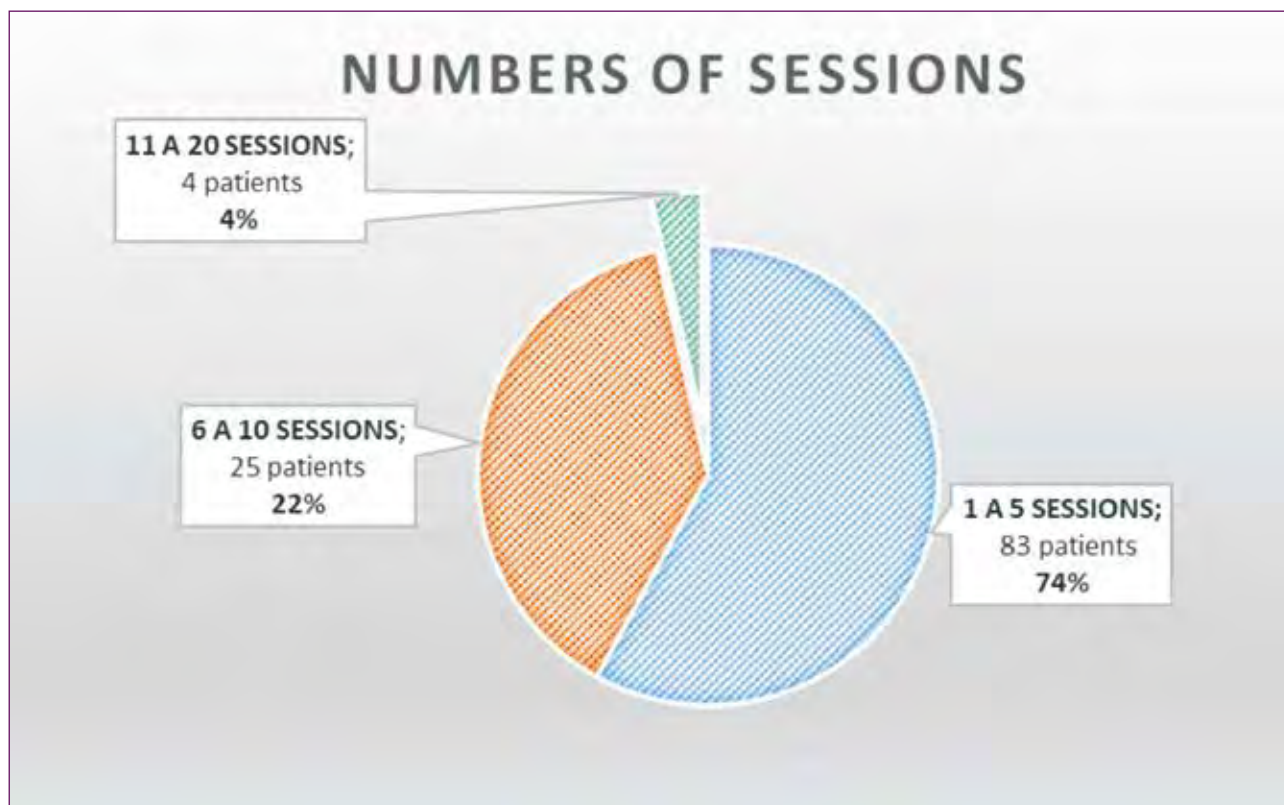
In addition, we observed that, for the result to be more effective, the flow of nitrogen has to be more powerful than the usual flow of "A" tips to cool without freezing in a short time. We designed an adapter between the free tip of the device and the placement of a plastic device (called Abbocath® No. 14 orange used in venoclysis). This is a metal adapter, made by a turner. After our initial study, Brimill® made their own adapters, available to anyone.

We also noticed that, in some cases, some colleagues, in the absence of metallic adapters, use the free device without any point or tip device, but there is a risk that the cooling is too powerful and causes freezing with formation of phlyctenas (blisters).

According to previous authors, the peripheral nociceptive unmyelinated fibers would be very sensitive to cold, and in this way we could propose a percutaneous cryoanalgesia hypothesis, in which the release of cytokines,



Graph 1. Improvement, $n = 112$ patients.



Graph 2. Number of sessions.

by the same inflammatory process due to cooling, would contribute to further improve the cryoanalgesia.

In this way, Proudfoot *et al.*⁷ identified molecular receptors for cooling in the sensory nerves, demonstrating how the activation of the TRPM8 produces profound and mechanically novel analgesia in chronic pain states.

Finally, we emphasize that this percutaneous cooling procedure relieves pain with very promising results in less than six weeks for post herpetic neuralgia defined as persistent pain a month of relieve cutaneous lesions; however, it was also useful in the 13 patients who were treated during the acute evolution of the zoster. What is more, the response in these patients was much faster, in one-two sessions they completed improvements of more than 90%. Only in two cases the improvement was lower and slower, perhaps due to concomitant aggravating pathologies such as HIV-AIDS or very elderly multi-treated patients.

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