THE ROLE OF CRYOANALGESIA FOR CHRONIC THORACIC PAIN: RESULTS OF A LONG-TERM FOLLOW UP

Carmen R. Green, MD, A. Michael de Rosayro, MD, and Alan R. Tait, PhD
Ann Arbor, Michigan

Cryoanalgesia (the use of cold to provide anesthesia or analgesia) is the oldest anesthetic and analgesic still in current clinical use. Its intraoperative use in providing postoperative analgesia for acute thoracic pain problems via an open thoracotomy is well described. The long-term efficacy of cryoanalgesia for the management of chronic thoracic pain due to intercostal neuralgia is less clear.

We retrospectively examined the medical records of patients who received percutaneous cryoanalgesia following successful intercostal nerve blockade for chronic chest pain. Sixty percent of the patients (N=43) reported significant pain relief immediately following their procedure. Three months following cryoanalgesia, 50% continued to report significant pain relief. There were no reports of neuritis or neuroma formation and only three patients had a pneumothorax. This work provides evidence that cryoanalgesia is a safe and efficacious method of providing analgesia for chronic thoracic pain due to intercostal neuralgia. (J Natl Med Assoc. 2002;94:716-720.)

Key words: cryoanalgesia ♦ chronic thoracic pain ♦ analgesia ♦ anesthesia ♦ intercostal neuralgia

Freezing of peripheral nerves, also known as cryoanalgesia, has been used to treat many different types of pain syndromes, e.g., occipital neuralgia, coccydynia (S5 and coccygeal nerves), and interstitial cystitis. It also has been used to provide local destruction of brain tissue, e.g., cranial and spinal nerves, intractable facial pain, trigeminal neuralgia, as well as head and neck cancer pain (involving the maxillary and mandibular nerves).

More specifically, cryotherapy has been successfully utilized to provide analgesia for acute thoracic pain following thoracotomy or pain due to percutaneous drainage tubes, as well as traumatic or pathologic rib fractures.5 When used to provide analgesia in this manner, it has been shown to reduce postoperative opioid analgesic requirements.5 Although the duration of pain relief under these circumstances is brief, estimated to last about two weeks, it also can be used to treat chronic thoracic pain problems, e.g., post thoracotomy syndrome, post herpetic neuralgia, and intercostal neuralgia (pain that travels along the distribution of the intercostal nerve), as well.

The long-term efficacy of cryoanalgesia in
the management of chronic thoracic pain due to intercostal neuralgia or post herpetic neuralgia is less clear. Few papers have specifically attempted to address this issue, although percutaneous cryoneurolysis is currently utilized for the management of chronic thoracic pain with encouraging results.³

At the University of Michigan’s Multidisciplinary Pain Center, cryoanalgesia has been routinely used for the treatment of chronic thoracic pain due to intercostal or post herpetic neuralgia with good results for more than 10 years. Based on our experience, we hypothesized that cryoanalgesia was a valuable and safe therapeutic tool for the management of chronic thoracic pain. We designed a study that retrospectively reviewed the charts of patients undergoing cryoneurolysis for chronic chest pain due to intercostal neuralgia in order to evaluate the efficacy of this technique.

METHODS

This study was approved by the University of Michigan’s Institutional Review Board for research involving human subjects. All adult patients over 18 years of age who were evaluated at the University of Michigan Multidisciplinary Pain Center for chronic thoracic pain due to intercostal neuralgia were included in this study. Basic demographic information was obtained from patient report and chart review. All patients received a diagnostic intercostal nerve block of the affected intercostal nerves, which provided substantial pain relief by the patient’s report. The subjects were then scheduled one week later for cryoneurolysis of the same affected intercostal nerves. Patients with a history significant for chronic obstructive pulmonary disease are routinely excluded from cryoanalgesia in our practice since pneumothorax is a potentially devastating complication in this patient population.

Written informed consent was obtained for all subjects for the chart review. Prior to cryotherapy, patients were instructed to assess their pain on a 10-point verbal analogue pain scale (VAPS; 0 = no pain, 10 = severe pain). The affected intercostal nerve and rib were identified for cryoneurolysis, as well as the intercostal nerve above and below.

With the patient positioned in the semilateral position, all of the skin levels were anesthetized with 1% lidocaine via a 25-gauge ½-inch needle at the posterior axillary line. The cryoprobe (which was inside a 14-gauge angiocath) was inserted vertically through the skin and “walked off” percutaneously until it was just below the rib. A cryolesion was formed and confirmed by temperature. Cryoneurolysis was accomplished using a single four-minute freeze cycle at −60°C for each affected intercostal nerve with a cryoprobe (Neurostat®, Westco, San Diego). There was no purposeful attempt to elicit paresthesias (an abnormal sensation which can be spontaneous or evoked) with our technique, since it has not been shown to improve outcome.

After completion of the single freeze cycle, the cryoprobe was withdrawn when it was fully thawed. The VAPS was repeated periodically to assess the patient’s immediate post procedure pain. Pain scores were recorded pre-block, immediately following the block, and 24-hours after the procedure, as well as at one week, one month, and three months following the procedure. Follow-up information on the patient’s post-procedure progress was obtained via chart review and telephone interview.

Statistical Analysis

Non-parametric data were analyzed by the Wilcoxon Rank Sum Test, while interval data were analyzed by repeated measures two-factor analysis of variance (ANOVA). Categorical variables were analyzed using Chi-square (contingency table). Demographic data was presented in a descriptive fashion. A P-value <0.05 was considered to be statistically significant.

RESULTS

Forty-three patients with chronic chest pain underwent treatment with cryoanalgesia during the period of November 1992 through January 1993. Patient ages ranged from 26 to 84
years, with a mean age of 57 years. Fifty-eight percent (25/43) of the population were male and 42% (18/43) were female. Patients had two main causes for their pain. Ninety-one percent (39/43) of the patients had intercostal neuralgia secondary to thoracotomy incisions, and 9% (4/43) had post herpetic neuralgia.

The mean duration of pain prior to cryoneurolysis was 31 months (range 0.5 months to 24 years). Sixty percent of the patients reported a diminution of their pain immediately after and 24-hours after the procedure. Three months after cryoneurolysis, 50% of the patients reported significant pain relief. Table 1 describes the percentage of patients with pain relief and VASs at the different time intervals. Three patients developed pneumothorax, which required medical or surgical intervention. There were no reports of neuritis or neuroma formation after cryoanalgesia. The decreasing number of patients observed in the follow up studies can be explained by the death of some patients secondary to their primary disease process. None of these deaths were attributable to their treatment.

Table 1. Percentage of Patients with Pain Relief and VAS at Different Time Intervals

<table>
<thead>
<tr>
<th></th>
<th>Pre Block</th>
<th>Immediate</th>
<th>24 hours</th>
<th>1 week</th>
<th>1 month</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>43</td>
<td>43</td>
<td>42</td>
<td>35</td>
<td>29</td>
<td>22</td>
</tr>
<tr>
<td>% of pts with pain relief</td>
<td>0</td>
<td>60</td>
<td>60</td>
<td>54</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>VAS (mean ± SE)</td>
<td>8.2 ± .38</td>
<td>2.0 ± .47*</td>
<td>1.8 ± .44*</td>
<td>2.7 ± .62*</td>
<td>2.6 ± .72*</td>
<td>2.7 ± .72†</td>
</tr>
</tbody>
</table>

*p < 0.01 vs. pre-block.
†p < 0.05 vs. pre-block.

In general, cryoanalgesia provides pain relief via destruction of nerve endings or blocking peripheral nerves without the side effects associated with other methods of peripheral nerve destruction. For instance, although phenol is a local anesthetic, it may cause an incomplete conduction blockade. Cutting, burning, or crushing the affected nerve may cause neuritis and neuromas, as well as a neuralgia that is worse than the patient’s presenting symptoms. The use of alcohol for neurolysis may cause permanent destruction with scarring, neuritis and neuralgia. Continuous local anesthetic infusions via epidurals, peripheral nerve blocks, and intercostal nerve blocks may provide analgesia and anesthesia for acute thoracic pain, but are of limited duration. Thus, these techniques have limited use for chronic chest pain syndromes. In contrast, the application of a cryolesion leads to the formation of intracellular and extracellular ice in the tissue with minimal disruption of the endoneurium, basal lamina, and connective tissue.

The cryolesion subsequently causes Wallerian degeneration with axonal disintegration and disruption of myelin sheaths with resultant destruction of nerve endings and the blocking of peripheral nerves. Despite second-degree nerve injury, the analgesia is reversible with

DISCUSSION

Cold traditionally has been used therapeutically to provide both analgesia and anesthesia. In fact, Hippocrates recorded the use of cold. Anglo Saxon monks in the 11th century discussed its use to decrease sensation prior to surgery. Larrey reported less painful amputation of limbs in soldiers during the Napoleonic wars when cold was applied. In modern times, the introduction of the cryoprobe allowed for the therapeutic application of cold to provide analgesia. Lloyd et al. coined the term cryoanalgesia for the destruction of peripheral nerves by extreme cold when a cryoprobe was used to yield pain relief. Thus, ice or cold is one of the oldest anesthetics and analgesics known that remains in clinical use today.
function returning when the nerve regenerates. Zhou et al. showed that cryotemperatures lower than \(-140^\circ\)C resulted in permanent alteration of the nerve morphology in rabbits.\(^8\) A cryotemperature of \(-60^\circ\)C was found to be the optimal temperature for cryoneurolysis in this study. Thus, the main advantages of cryoneurolysis at \(-60^\circ\)C is that function is maintained with greater sensory than motor blockade with less fibrous reaction, when compared to other neurolytic techniques.\(^1\)

From a physiological standpoint, cold causes decreased blood flow, which decreases tissue metabolism. Effective blockade of peripheral nerves via prevention of the conduction of peripheral nerves can be obtained at temperatures of \(10^\circ\)C, with motor function generally preserved. The cryoprobe uses the Joule Thompson effect and temperatures of \(-50^\circ\)C to \(-60^\circ\)C. The factors that are ultimately responsible for the conduction blockade are temperature, rate of freezing, rate of thawing, and duration of freezing. The resultant conduction blockade with cryoanalgésia is reversible. The subsequent duration of cryoanalgésia is dependent upon the rate of axonal regrowth and distance of the cryolesion from the organ.

Previous studies have demonstrated that cryoneurolysis produces a reversible cryolesion that regenerates in approximately 42 days.\(^1\) Moorjani et al. varied the duration of cryoanalgésia in anesthetized dogs and subsequently biopsied their intercostal nerves periodically over six months.\(^6\) From a histologic perspective, recovery occurred after one month for the 30 and 60-second freeze cycle. Longer freeze cycles proportionally increased the pain relief for periods well in excess of the cryolesion.

In this study, we showed that our patients had significant analgesia for at least three months. Although the information was obtained from chart review, there are inherent limitations in retrospective studies of pain. A potential for a recall bias is present. Furthermore, pain, e.g., VAPS, is only one domain of health status or quality of life. Another limitation of this study is that we only used one measure of quality of life, and as such, this limits any determination of the individual’s overall health status in the context of their chronic chest pain. Therefore, a larger number of subjects utilizing a randomized double blind methodology may help to further clarify the long-term outcomes of this technique.

We did not find any of the disabling side effects, which have been associated with other neuroablative techniques, i.e., phenol, alcohol, cutting, or crushing the affected nerve.\(^7\) This is consistent with the literature supporting that cutaneous sensory changes occur and usually resolve within six months with complete restoration of function. Other potential complications of cryoanalgesia are similar to other nerve blocks and include pneumothorax, infection, bleeding, neuralgia, scarring, local anesthetic toxicity, and damage to the neurovascular bundle. Furthermore, cryoanalgesia is not recommended for use in mixed nerves or in the paravertebral area. Our subjects did not report numbness, rigidity of the chest wall, or bulging of the abdominal wall as described by Maiwand.\(^5\) However, the ability of cryoneurolysis to circumvent many of the problems associated with the more traditional techniques makes its application very appealing for chronic thoracic pain.

Our only adverse event associated with the technique was pneumothorax. Although, ideally the incidence for pneumothorax should be less than 1%, the incidence following cryoanalgesia with a 14-gauge angiocath in our residency training program is considered to be acceptable.

One major difference between our study and previous works is that the manufacturer of the cryoprobe suggests the use of two 2-minute freeze cycles instead of a single 4-minute freeze cycle. Maiwand et al. compared a single 30-second freeze cycle to two 30-second freeze cycles and found equally good results in patients with acute post thoracotomy pain.\(^4\) The results suggest that one 30-second freeze cycle is sufficient when performing cryoneurolysis in an open thorax. Our use of a single 4-minute
freeze cycle is based mainly upon our experience over a period of three years prior to the study period. It is unclear whether our favorable results in chronic thoracic pain are due to the increased duration of the freeze cycle, or if conversely, increased time is necessary when using a blind technique, compared to its use intraoperatively for acute thoracic pain syndromes. It does make sense that, overall, open intraoperative techniques have some intrinsic advantages over blind techniques. Although the technique has evolved for acute thoracic pain, there is no literature to guide us in the use of cryoanalgesia for chronic thoracic pain. We currently continue to use this technique at the Multidisciplinary Pain Center with good results.

Our results demonstrate that cryoanalgesia yields a significant diminution in pain with relief extending past 42 days when this therapeutic modality is used for the management of chronic thoracic pain due to intercostal neuralgia. The potential for bias in this study is consistent with the nature of retrospective studies in general. This preliminary study serves as a platform for future prospective double-blinded randomized control studies. However, our results suggest that cryoneurolysis is a safe and efficacious technique that is currently underutilized in the management of chronic thoracic pain.

REFERENCES