

Original article

Pain in the elderly: Prospective study of hyperbaric CO₂ cryotherapy (neurocryostimulation)

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Abstract

Objective: To evaluate the analgesic effects of hyperbaric CO₂ cryotherapy in elderly inpatients.

Methods: An open-label prospective study was conducted in two geriatrics departments in patients with a broad range of pain characteristics. Each patient underwent a physical evaluation followed by hyperbaric CO₂ cryotherapy sessions, whose spacing and number were at the discretion of the physiotherapist. Patients completed a 100-mm visual analog scale for pain severity before and after the sessions.

Results: We included 51 patients, who were treated between May 2 and June 30, 2005. Mean age was 83.7 years, and the female-to-male ratio was 4/1. The patients had acute or chronic pain whose origin was usually musculoskeletal (80.3%) or neurological (18.6%). Pain scores decreased significantly after four sessions, from 52 mm to 13 mm ($P < 0.001$) in patients with acute pain and from 45 mm to 13 mm ($P < 0.001$) in those with chronic pain.

Conclusion: Hyperbaric CO₂ cryotherapy is an innovative tool that should be incorporated within the non-pharmacological armamentarium for achieving pain relief in older patients.

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Keywords: Hyperbaric gaseous cryotherapy; Neurocryostimulation; Older patients; Pain

1. Introduction

Hyperbaric gaseous cryotherapy using CO₂ is an innovative analgesic treatment that is generating considerable interest. Microcrystals of dry ice at very low temperature are sprayed under high pressure on the painful site. The result is a sudden, quasi-immediate drop in skin temperature that induces far greater analgesic, antiinflammatory, vasomotor, and muscle-relaxing effects than conventional methods of cold application.

Hyperbaric CO₂ cryotherapy was developed by a French company and rapidly gained popularity among physiotherapists, rheumatologists, and athletes. However, scientific efficacy data are scant.

The objective of this study was to conduct a prospective evaluation of the analgesic effect of hyperbaric CO₂ cryotherapy in older patients.

2. Methods

An open-label prospective study was conducted in follow-up care and extended-stay wards of the geriatric Émile Roux Teaching Hospital in Limeil-Brévannes, France. The physicians and nurses on the wards identified patients with pain of any type or severity. Using previously developed criteria, 51 patients were included. The reasons for hospital admission in these 51 patients included recovery after orthopedic surgery,

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various rheumatic and neurological diseases, and age-related conditions. Patients were not included if they had contraindications to cryotherapy such as cold allergy, cryoglobulinemia, Raynaud's phenomenon, hemoglobinopathy, cutaneous sensory abnormalities, and skin lesions. Pain severity was assessed on a 100-mm visual analog scale (VAS) where 0 indicated no pain and 100 the worst possible pain. Patients who were unable to use the VAS and those whose Mini Mental Status Examination (MMSE) score was lower than 23/30 were not included in the study. Acute pain was defined as pain of less than 1 month's duration. Ongoing analgesic treatments were continued.

Each patient was examined by a physician, who evaluated the type and severity of the pain and determined that cryotherapy was in order. Cryotherapy sessions were given by trained physiotherapists until two consecutive pre-session VAS pain scores were less than 30 mm. The frequency of the sessions was at the discretion of the physiotherapist. The Cryotron™ (Cryonic Médical, Salins-les-Bains, France) device was used. It consists of medical-grade liquid CO₂ in a cylinder equipped with an electrovalve and an immersed tube, a spray gun, and a nozzle. The CO₂ is sprayed on dry skin over the painful site using a slow, regular, sweeping movement. The tip of the nozzle is kept 7–10 cm away from the skin. Microcrystals of dry ice can be seen to form on the skin. An infrared pyrometer incorporated in the spray gun serves to control the degree of skin cooling. Treatment duration can be pre-programmed on a screen. In patients with acute pain, it ranges from 30 s for small surface areas to 90 s for large surface areas (low back, knee, or shoulder). A light switches on when that skin temperature drops to about 4 °C, which is the threshold for local thermal shock. In patients with chronic pain, treatment duration varies according to the sensations reported by the patient: treatment is usually stopped when the patient describes a burning sensation. In the treatment of chronic neuropathic pain, the CO₂ is sprayed in concentric circles along the painful limb segment, and several thermal shocks are produced along the relevant nerves.

2.1. Data collection

Standardized forms were used to record age; sex; MMSE score; pain characteristics: type, duration, site, and severity before and after each cryotherapy session; and number and frequency of cryotherapy sessions.

2.2. Statistical analysis

VAS pain scores were compared using Student's *t*-test. Results were expressed as means ± SD or as percentages. *P* values smaller than 0.05 were considered statistically significant.

3. Results

Between May 2 and June 30, 2005, 51 patients were included. Their mean age was 83.7 ± 8.6 years (range, 65–97), and the female-to-male ratio was 4:1. In all, 201 cryotherapy sessions were performed in the 51 patients. The pain was acute in 23 (45%) patients and chronic in 28 (55%). The source of pain was the musculoskeletal system in 41 (80.3%) patients, whereas 10 (19.6%) patients had neuropathic pain.

Significant pain relief occurred in both the group with acute pain and the group with chronic pain. After four sessions, the VAS pain score decrease in the group with acute pain was 39 ± 0.4 mm (*P* < 0.001). VAS pain score decreases were 31.5 after five sessions in patients with metabolic joint disease, 44.6 ± 7.5 mm after 4.7 sessions in patients with spinal pain, and 31.4 ± 3.1, *P* < 0.001 after 2.7 sessions in patients with postsurgical pain (Table 1). In patients with chronic pain (often due to multifocal osteoarthritis), the VAS pain score decreased from 45.2 ± 11.6 to 13.2 ± 10.8 (*P* < 0.001) after 3.6 sessions (Table 2). Finally, pain relief was obtained in patients with acute or chronic neuropathic pain (paresthesia due to carpal tunnel syndrome or spasm related to previous stroke, amyotrophic lateral sclerosis, or tetraplegia).

No meaningful side effects were recorded during the study.

Table 1
Effects of neurocryostimulation in patients with acute pain (duration <1 month)

Site	<i>n</i>	Number of sessions	Number of sessions/week	Baseline VAS score	Final VAS score	
Acute pain	23	4.2 ± 2	2.1 ± 0.9	52.2 ± 9.4	13 ± 9	<i>P</i> < 0.001
Crystal-induced arthritis (knee, wrist)	4	5 (3–8)	2 (1–3)	47.2 ± 8.4	15.7 ± 0.9	–
Back pain	5	4.7 (2–6)	2 (1–3)	53.8 ± 8.4	9.2 ± 8.5	–
Trauma or orthopedic surgery to the hip and pelvis (postoperative pain, posttraumatic pain)	8	2.7 (2–7)	1.6 (1–7)	48.5 ± 6	17.1 ± 9.1	<i>P</i> < 0.001
Intercondylar fracture of the knee	1	10	5	63	0	–
Shoulder pain (fracture, reflex sympathetic dystrophy syndrome after stroke)	2	3 (2–4)	2	52.5	7.5	–
Carpal tunnel syndrome	2	4	3	56	13	–
Head-and-neck cancer	1	4	2	68	17	–

Table 2
Effects of neurocryostimulation in patients with chronic pain

Site	<i>n</i>	Number of sessions	Number of sessions/week	Baseline VAS score	Final VAS score	
Chronic pain	28	3.6 ± 1.8	2 ± 1.8	45.2 ± 11.6	13.2 ± 10.8	<i>P</i> < 0.001
Spine	9	3.4 (1–5)	2 (1–3)	45.7 ± 8.2	12.5 ± 9.9	<i>P</i> < 0.001
Cervical osteoarthritis	2	2.5 (1–4)	1.5 (1–2)	44.5 ± 3.5	19.5 ± 4.9	
Back pain	5	3.6 (1–5)	2 (1–5)	41.2 ± 4.7	6.8 ± 9.7	
Sciatica	2	4	2.5 (2–3)	58.5 ± 3.5	20 ± 2.8	
Peripheral joints	13	3.8 (1–6)	2 (1–4)	43.9 ± 12.7	13.6 ± 12	<i>P</i> < 0.001
Hip osteoarthritis	3	4 (2–6)	2 (1–3)	41.6 ± 4.1	16.3 ± 5.1	
Knee osteoarthritis	7	3.5 (1–7)	2 (1–4)	45.7 ± 17.6	14.4 ± 15.6	
Frozen shoulder	3	4.3 (1–8)	1.3 (1–3)	42 ± 1	9 ± 7.9	
Neurological disease	6	3.6 (2–6)	2.3 (2–3)	47.1 ± 14.7	13.6 ± 11	NS
Shoulder spasticity (stroke, ALS)	4	4	2.5 (2–3)	47.7 ± 17	14.2 ± 9.9	
Hand spasticity (stroke)	1	2	2	36	0	
Tetraplegia (C6–C7)	1	4	3	56	25	

ALS: amyotrophic lateral sclerosis; NS: non-significant.

4. Discussion

Although cryoanalgesia was long used empirically, recent studies have elucidated the mechanisms involved in the pain-relieving effect of cold.

4.1. Effects of cryotherapy

4.1.1. Antiinflammatory and vasomotor effects

Tissue injury leads to an inflammatory response characterized by the release of numerous substances, many of which contribute to cause pain. These substances come from three main sources. Factors released by the injured cells activate local nociceptors, which are sensitized by substances from inflammatory cells. Finally, the nociceptors themselves release factors that activate or sensitize the same nociceptors via direct or indirect mechanisms [1,2]. Local application of cold causes vasoconstriction of deep arteries and capillaries, which is rapidly followed by a vasoconstriction-vasodilation cycle that promotes edema resorption.

4.1.2. Analgesic effect

With local cold application, pain relief occurs when the skin temperature drops below 13.6 °C. At lower temperatures, nerve conduction velocity in nociceptive afferents decreases significantly [3–5].

4.1.3. Muscle-relaxing and spasm-relieving effects

Muscle spasm is alleviated by cold application. The underlying mechanism may involve decreased nerve conduction and excitability of muscle spindles (reverse myotatic reflex) or, at 5 °C, complete blockade of neuromuscular transmission [6].

4.2. The limitations of conventional cryoanalgesia

Large temperature decreases within the muscles and joints must be obtained to relieve pain from injury to the musculo-skeletal system [7,8]. The thickness of subcutaneous fat in

each individual governs the duration of cold application needed to obtain a given analgesic effect. For instance, 25 min are required when the fat pad is smaller than 20 mm compared to 60 min when the pad is 30–40 mm [9,10].

The temperature drop varies according to the cryogenic device, duration of application, and initial temperature. The temperature must drop below 13.6 °C to result in significant cutaneous analgesia, 12.5 °C to reduce nerve conduction velocity by 10%, and 11 °C to decrease local enzymatic metabolism by 50% [11–15].

Available methods for cryotherapy cover a broad range, from immersion of a limb or limb segment in cold water and whole-body cryo-chamber exposure through ice-pack and pre-refrigerated gel applications to cryogenic sprays and inflatable splints [3,16–19]. Selection of the optimal method is based on efficacy, ease of handling, storage conditions, modalities of use, and cost. Most of the conventional cryotherapy methods fail to meet all the above criteria, so that their use is confined to adjuvant analgesic therapy. A panel of experts recently developed recommendations for optimal cryoanalgesia that take these limitations into account [20].

4.3. Gaseous cryotherapy

Gaseous cryotherapy with CO₂ (neurocryostimulation) overcomes many of the limitations of conventional cryotherapy. Cluzeau et al. developed an innovative method in which high pressure and cold temperatures are combined to magnify the analgesic and antiinflammatory effects of cryotherapy [21]. Two main characteristics differentiate neurocryostimulation from conventional cryotherapy: the large magnitude of the temperature drop and the short time needed to achieve it. As a result of these two characteristics, the reactive arterial and capillary vasodilation is more marked and occurs at deeper sites than with conventional methods.

Conventional ice-pack therapy acts via conduction, with the heat from the body being transferred by direct contact to the ice pack. CO₂ cryotherapy, in contrast, acts via convection

and sublimation. A spray of dry-ice microcrystals exits the nozzle at a pressure of 2 bars (within the sonic range) and a temperature of -78°C . The sudden intense cold and the high pressure cause a drop in skin temperature to 2°C within 45 s; with conventional cryotherapy, in contrast, 15–30 min are needed to decrease the skin temperature to $13\text{--}15^{\circ}\text{C}$. The sudden drop, or cold shock, achieved with neurocryostimulation, achieves specific effects. The cold is transferred through the three layers of the skin. A sudden decrease in skin temperature to 4°C results in activation of cutaneous and subcutaneous receptors, including nociceptors, Ruffini corpuscles (which respond to temperature changes), and Pacinian corpuscles (which are sensitive to pressure). The resulting nerve impulses travel to the diencephalon, where they trigger an autonomic nervous response involving the sympathetic and parasympathetic systems (hence the term neurocryostimulation). The duration of cold exposure is too short to induce meaningful tissue damage. Pure dry CO_2 is used, which ensures that the procedure is not painful. In addition, CO_2 exerts bacteriostatic and fungistatic properties that eliminate the risk of infection, so that neurocryostimulation can be used on open or recently healed wounds and on surgical sites in the immediate postoperative period. Medical grade CO_2 is colorless, odorless, and unflammable.

Neurocryostimulation is being increasingly used to treat acute sports-related injuries (e.g., ligament and tendon injuries, muscle injuries, fractures, and dislocations) and chronic sequelae of trauma (tendinopathy, muscle lesions, adhesive capsulitis, and reflex sympathetic dystrophy syndrome) [22]. Its beneficial effects are more marked than those of conventional cryotherapy.

Vasomotor and anti-edema effects develop almost immediately; these effects have not been proved to occur with conventional cryotherapy. Thus, the initial 40% vasoconstriction peak is achieved within 7 s (compared to 30 s with ice) and is followed by a 117% vasodilation peak within 20 s (compared to only 80% after 20 min with conventional cryotherapy). The high pressure used to spray the cold gas contributes to the beneficial effects [22–24].

As a result of its specific effects, neurocryostimulation is a full-fledged treatment for many forms of pain. The fast drop in skin temperature to values associated with analgesia, anti-inflammatory effects, and impaired nerve conduction, together with the high spray pressure, leads to quasi-instantaneous decreases in intramuscular and intraarticular temperatures to ranges associated with symptom relief. The beneficial effects are obtained regardless of subcutaneous fat thickness, which is a limitation to the efficacy of conventional cryotherapy. Measurements of skin temperature, intraarticular temperature, pain, and laboratory markers for inflammation have established that neurocryostimulation exerts significant and lasting effects [24].

We evaluated neurocryostimulation in an open-label prospective study of older patients with pain related to various conditions. Many of the patients had several sources of pain that interacted with one another and with underlying diseases. Furthermore, over half the patients had long-standing pain.

Our primary objective was to evaluate the efficacy of neurocryostimulation in older patients with acute or chronic pain from musculoskeletal or neurological conditions.

4.3.1. Effects of neurocryostimulation on acute pain

Many older patients experience pain from acute joint disease (gout and acute chondrocalcinosis in our study). Acute neck pain, thoracolumbar pain, and tenosynovitis are also common in the elderly. We found significant reductions in acute pain severity after four to five neurocryostimulation sessions. Mean VAS score decreases were $47.2\text{--}15.7$ mm for crystal-induced arthritis and $53.8\text{--}9.2$ for thoracolumbar pain. In a prospective controlled study, Schlesinger et al. found that local ice application in addition to prednisone and colchicine induced a 77-mm VAS score decrease, compared to 44 mm without ice [24]. In another controlled study, the severity of acute mechanical low back dysfunction in athletes as assessed using the McGill Pain Questionnaire and VAS scores decreased significantly [25]. In a study of local ice to treat synovitis, cold was associated with increased joint fluid viscosity, which inhibited the influx of leukocytes and the intraarticular inflammatory response [26].

Several patients in our study population were admitted for rehabilitation therapy after orthopedic surgery on the hip, knee, or shoulder. Cryotron[®] therapy resulted in rapid relief from postoperative pain, with a VAS score reduction from 48.5 mm to 17 mm after 2.7 sessions. In a controlled study of Cryotron[®] therapy, Meeusen et al. found similar results in patients treated after shoulder arthroscopy [27]. A controlled study in hip arthroplasty patients showed that continuous cooling with a pad started immediately after surgery reduced the severity of pain as assessed on a VAS [28].

4.3.2. Effects of neurocryostimulation on chronic pain

Neurocryostimulation was effective in our study in patients with chronic spinal or joint pain due to osteoarthritis. Mean VAS pain score reductions were 33 mm after 3.4 sessions for spinal pain and 30 mm after 3.8 sessions for joint pain. Neurocryostimulation combined with radial shock waves was effective in a study of 333 athletes with a variety of sports-related injuries [29]. A randomized controlled study showed that neurocryostimulation was more effective than conventional treatments in athletes with pain from acute tendinitis [30].

Neurocryostimulation effectively relieved pain related to spasms in patients with amyotrophic lateral sclerosis, tetraplegia, or chronic stroke. Petrilli et al. obtained similar results in patients who had multiple sclerosis [6].

Neurocryostimulation was effective in the limited number of patients with neuropathic pain in our study (bilateral carpal tunnel syndrome or orofacial pain from head-and-neck cancer, in keeping with earlier results [31,32]).

Our study has the limitations inherent in its open-label uncontrolled design. Only elderly patients were included, and most patients had multiple sources of pain. The types of pain varied widely. We did not include patients with cognitive impairments that would have precluded the use of the VAS.

We cannot exclude a placebo effect. Nevertheless, this is the first study of the analgesic efficacy of neurocryostimulation in older patients with a variety of types of pain. Pain relief was achieved consistently, although the magnitude of the effect varied somewhat across subgroups. No adverse reactions were reported. The indications for neurocryostimulation are not confined to musculoskeletal and neurological pain. Thus, neurocryostimulation has also been used successfully to prevent pain caused by arterial catheterization [33].

5. Conclusion

The response to neurocryostimulation is greatest in patients with acute musculoskeletal pain and increases with earlier treatment. However, our results show that other types of pain, including chronic pain, respond significantly to neurocryostimulation. The effect may be transient, most notably in chronic pain, requiring repeated sessions, which are often requested by the patient.

Neurocryostimulation is an innovative analgesic treatment that is simple and rapid to use. There are few contraindications, and the cost is reasonable. Neurocryostimulation is neither toxic nor invasive and relies on natural factors. Its indications extend far beyond pain relief in athletes with sports-related injuries. Older patients with pain from multiple sources can derive significant benefits from neurocryostimulation. Studies are ongoing to investigate additional indications. Randomized controlled trials in larger populations are needed, in particular to define the optimal protocol for each type of pain. Additional basic research will help to further elucidate the biological mechanisms that underlie the analgesic effect. Neurocryostimulation may rapidly achieve a prominent position among non-pharmacological treatments for pain.

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