Cryotherapy for Trigeminal Neuralgia

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Key Points

- Cryotherapy causes reversible ablation of nerves thereby providing pain relief
- It is yet another modality for treatment of trigeminal neuralgia; may be used as an adjuvant therapy to medical management
- It is a simple and repeatable procedure with less reported side-effects

Introduction

Cryotherapy means treating with cold. Cold causes reversible ablation of peripheral nerves and provide pain relief. The utility of cooling therapy is known since the time of Hippocrates [1]. James Arnott (1797–1883), an English physician, first published work on use of cold for treatment of pain in breast, skin and uterine cancers. Due to makeshift agents used and vague technique of delivery, the modality remained less popular. Irving S Cooper, a neurosurgeon contributed enormously to cryosurgery by designing a cryoprobe utilizing liquid nitrogen. The probe could attain a temperature of −196 °C and was used to freeze thalamus for treatment of Parkinson's disease and other movement disorders [2]. Thereafter, liquid nitrogen became popular and was used across many specialities. The advent of cryoprobe enabled clinicians to precisely control area of lesion and also minimise destruction to neighbouring tissues. Lloyd et al. (1976) used it to treat facial pain and found its utility in patients

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with TGN [3]. Thereafter, its benefit for relieving chronic facial pain especially due TGN was reported by many clinicians [4, 5].

Mechanism of Action

Cryotherapy in neuralgia works by freezing nerve cells and thus, blocking transmission of pain. The mechanism of action of Cryotherapy can be divided into three parts:

1. **Heat transfer/heat exchange**: The heat between target area and cryogenic agent is exchanged due to temperature gradient between the two. The common agents used to produce sub-zero temperatures are liquid nitrogen, nitrous oxide, and carbon dioxide. Liquid nitrogen has a boiling point of −196 °C, nitrous oxide −88 °C, carbon dioxide −79 °C [6]. The agent can be delivered by spraying, direct application with a cotton applicator, or with a cryoprobe. When liquid nitrogen is sprayed on the target tissue, it gets evaporated immediately and heat exchange occurs due to evaporation. With a cryoprobe, the heat transfer occurs through conduction.
2. **Cell Injury**: Due to reduction of temperature, the cellular water gets converted to ice crystals resulting in cell injury. Cellular hyperosmolarity prevents cellular freezing unless temperature reaches −5 to −10 °C. Freezing causes concentration of extracellular solutes and results in creation of osmotic gradient which further adds to cellular injury.
3. **Inflammation** is the result of cellular destruction. With use of cryotherapy there occurs minimal tissue destruction and thus, limited inflammation and neuroma formation. Cryogenic nerve injury is characterized by axonal and myelin sheath disintegration causing type-2 nerve injury (Wallerian degeneration). Since the epineurium, perineurium, and endoneurium are preserved, nerve regeneration occurs. Histological changes are suggestive of axonal degeneration within 7 days of treatment. Axonal regeneration occurs at a rate of 1–1.5 mm/week and takes weeks to months for proximal neurons to regenerate. Progressive axonal regeneration and recovery to normal structures is seen around 24 weeks post treatment [6]. With completion of re-innervation symptoms may recur.

Technique

Cryogenic agents such as liquid nitrogen, liquid nitrous oxide, or carbon dioxide decrease temperature of the target tissue when delivered by means of spraying, direct application, or through a cryoprobe. **Cryoprobe** is a hand-held device used to deliver compressed liquid gas via small gauge needle (cryo-needle) for reversible nerve lesioning. The cryoprobe using liquid nitrogen can attain a temperature of −190 °C at its tip. The cryoprobe is based on Thompson Joule principle and depending upon the agent used could attain a temperature up to −50 °C to −70 °C. It is a double

lumen probe with an outer and an inner cannula. The outer cannula is connected to a gas source and cryogen is delivered down it at a high pressure (600–800 psi). Since gas under pressure escapes through a small lumen near the probe tip, there is massive fall in pressure to about 10–15 psi which leads to cooling and formation of an ice ball at the tip of probe. The size of ice ball varies from 3.5 to 6 mm depending upon the size of needle used and type of tissue being cryolyzed. In general, bigger the probe, bigger is the ice ball, and more is the area of damage. The inner cannula is used to vent out the gas. Usually14 G/18 G probes are used for cryoneurolysis [6].

The cryoprobe designed for neurolysis has an inbuilt nerve stimulator and thermistor for nerve localization and monitoring target temperature at its tip. After cryolesioning probe should be withdrawn only after thawing to avoid nerve avulsion. The use of introducer needle is recommended to avoid damage to cryo-needle. Both hand held and console tethered cryprobes are available in the market. The hand piece of the probe should remain vertical while lesioning. The freeze and thaw cycles depend upon the type of probe and agent used. Manufacturer's recommendations should be followed. The system is cooled down for about 40 s and the subsequent freezing is done lasting for 90 s. After a period of thawing the freezing is to be repeated.

Application in Trigeminal Neuralgia

Patients with TGN, in whom high dose of drugs has caused considerable side effects can benefit from cryotherapy [7–9]. It produces a reliable, prolonged and reversible trigeminal nerve block without aggravation of symptoms. It is a simple and repeatable procedure in patients who want to avoid major surgery or when the latter is contra-indicated. Cryotherapy has been shown to produce symptomatic pain relief due to primary as well as secondary TGN [10].

Open dissection, percutaneous and transmucosal approach has been used for Cryo-lesioning of trigeminal nerve and its peripheral branches. Cryo-lesioning has been done for inferior alveolar, buccal, mental, lingual, auriculotemporal, supraorbital, and infraorbital nerves. Peripheral branches of trigeminal nerve at the infraorbital or mandibular foramen can be frozen without exposing the nerve or damaging the surrounding tissue. The cryoprobe can be applied in the same way as a needle for a nerve block at infraorbital or mental foramen, by an intraoral approach. Computed tomography (CT) guided imaging has been used to precisely position the probe near the central nerve endings. Dar et al. documented use of CT guidance and treatment of secondary TGN using percutaneous cryoablation. Palliative cryoablation procedures were performed under CT guidance in recurrent head and neck malignancy [10].

The procedure is not painful and does not require general anesthesia. Reduction of pain is seen within 5 days and complete pain relief is seen in another 15 days. The dose of drugs can be titrated down after the procedure. The duration of pain relief in patients receiving cryosurgery may range from 0 days to 4 years [11]. In various case reports average duration of pain relief is limited to 6–12 months. Small

duration of procedure, small wound, lesser rate of infection and ease of technique makes it user friendly. Recurrence and partial benefit is common but due to lack of side effects the procedure can be repeated as many times as required [12]. The reported adverse effects include temporary sensory loss, migration of pain to another division of trigeminal nerve and oedema. Cryotherapy comes with inherent risk of trauma during needle placement, bleeding, infection and nerve damage. Since cryotherapy produces type 2 nerve injury, it is less likely to result in neuroma formation, hyperalgesia, deafferentation pain. However, allodynia, hypersensitivity after cryolysis has been reported by few. Anesthesia is seen in few cases though the sensations return back within 6 months.

Other treatment modalities for TGN have their own risk benefit profile. Microvascular decompression (MVD) is an invasive procedure requiring craniotomy and subsequent risk of severe adverse effects. These are relatively contraindicated in elderly patients and in patients with multiple comorbidities. Cryosurgery can be a complement to the medical management in such patients. Electrocoagulation is known to produce side effects like permanent loss of sensation, motor disturbances, including weakness of the masseter muscle and palsy of muscles innervated by oculomotor nerve. Glycerol injection and gamma knife radiosurgery have minimal such problems. However, glycerol injection may be associated with development of deafferentation pain, neuroparalytic keratitis, or anesthesia dolorosa [13]. Though cryotherapy is not associated with significant side effects but its effectiveness has not been proven in large studies. It has been documented only on basis of clinical reports. There are only a few RCTs comparing effectiveness of cryotherapy with other available modalities of treatment.

Conclusion

Although not popular, cryotherapy is one of the promising treatment modalities for TGN. It produces a reliable, prolonged and reversible nerve block without aggravation of symptoms. It is a simple and repeatable procedure in patients who want to avoid a major neurosurgery or where the surgery is contra-indicated. However, the effectiveness of cryosurgical procedures need to be evaluated with large RCTs.

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