REVIEW ARTICLE

Cryoneurolysis: Is it the Future of Neurolysis…?

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Abstract

The various methods available for neurolysis include surgical ablation, chemical ablation, thermal ablation, cryoablation, and mechanical compression. Cryoneurolysis is the direct application of low temperature to ablate nerves to provide pain relief. The cryoprobe consists of a hollow tube with a smaller inner tube. Pressurized gas travels down the inner tube and is released into the larger outer tube through a very fine aperture that allows the gas to rapidly expand into the distal tip. This extracts heat from the tip of the probe resulting in extremely low temperatures at the tip itself forming an ice ball. The severities of cryolesion are dependent on the cryotemperatures. The cryo technology has been used in many other specialities. The sophisticated architecture of the probe was the real limiting factor in manufacturing extremely narrow gauge probes till very recently. The absence of nerve injury beyond second degree makes cryoneurolysis extremely safe weapon. In case of any inadvertent motor damage during cryoneurolysis the fibres recovers completely within a short span where as the pain fibres are ablated for a longer period. Apart from the above, still more facts like minimal procedural pain, immediate onset of action and versatile utility in chronic pain anywhere in the body make it a perfect choice for the future of neurolysis.

Keywords: Cryoablation, Cryoneurolysis, Deafferentiation, Nerve injury, Regeneration.

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Neurolysis is defined as the selective, iatrogenic destruction of neural tissue to secure the relief of pain, or a procedure in which the nerve is electively freed surgically from inflammatory tissues.[1] Neurolysis is a valuable tool designed to produce prolonged interruption of neural transmission. In contrast to the action of local anesthetic block, which is measured in hours, neurolytic block aims to alter neural function for weeks to months, and even for months. The common rationale for neurolytic block is prolonged relief of intractable pain, and most often in patients with malignancy. Neurolytic blocks can be used to treat visceral and somatic pain. Their use for chronic, nonmalignant pain is controversial. Additional analgesic applications may include relief of ischemic pain in occlusive vascular disease.

The various methods available for neurolysis include surgical ablation, chemical ablation, thermal ablation, cryoablation, and mechanical compression.[2] The various agents used to achieve chemical neurolysis are alcohol, phenol, glycerol, and hypertonic saline.[3] Phenol has an immediate local anesthetic effect due to its selective effect on smaller nerve fibers. This differential blocking ability is believed to be the result of small vessel destruction that initially spares large fibers. However, the effects of the block cannot be evaluated until after 24 to 48 hours, to allow time for the local anesthetic effect to dissipate. The neurolytic effect may be clinically evident only after 3 to 7 days. If inadequate pain relief is obtained after 2 weeks, this may indicate incomplete neurolysis and require repetition of the procedure. In case of alcohol, though 50 to 100% alcohol is used as a neurolytic agent, the minimum concentration required for neurolysis has not been established. A local anesthetic is more commonly used as a diluent. Following its injection, the patient complains of severe burning pain along the nerve's distribution, which may last for a minute and is subsequently replaced by a warm, numb sensation.

The disadvantages of neurolysis includes inadvertent damage to adjacent motor, sensory, autonomic fibers, resulting in muscle weakness, paresthesia, bowel, and bladder dysfunction. A more alarming complication is the deafferentation pain. The two main peripheral sensitization mechanisms responsible for deafferentation pain is the development of ectopics and cross talk. Complications of chemical neurolysis include skin and other nontarget tissue necrosis and sloughing, hypotension secondary to sympathetic block and systemic toxic reactions, heart rate and rhythm disturbances, blood pressure changes, and central nervous system excitation and depression.

Regeneration of nerve following a nerve injury usually occurs when the cell body is intact. Nerve damages of up to third degree regenerate. The degrees of nerve injuries can be classified as follows. In the first-degree nerve injury (neuropraxia), there is only conduction block. It usually recovers in a few hours to days. In the second-degree nerve injury, there is only division of intraneural axons. The three coverings, namely, endoneurium, perineurium, and epineurium are intact. There will be full recovery without any sequel within 2 months to 2 years. In the third-, fourth-, and fifth-degree nerve injury, along with axons its coverings up to endoneurium, perineurium, and epineurium, respectively, are damaged. Regeneration is uncertain, and there is a possibility that neuroma and both cross talk and ectopic signals may deteriorate pain.

Cryoneurolysis is the direct application of low temperatures to ablate nerves to provide pain relief. Cryoablation is mostly used for tumor ablation. Cryoanalgesia is application of cold to reduce pain. The history of cryoneurolysis dates back to 1899 when Campbell White first used refrigerants medically. Later in the year 1950, Allington was the first to use liquid nitrogen for medical treatments. But an early cryoprobe that reached –190°C using liquid nitrogen was introduced by Cooper in 1961. Six years later in 1967,

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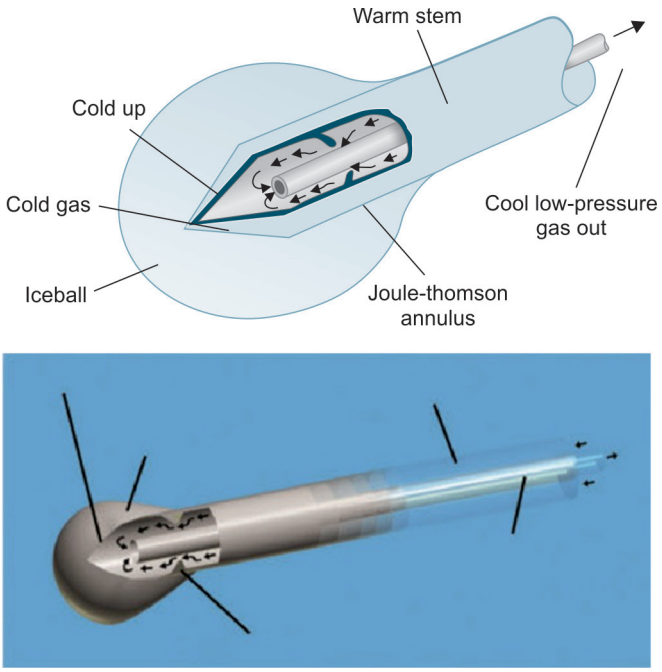

Fig. 1: CRYOPROBE—inner architecture

an ophthalmic surgeon named Amoils used carbon dioxide and nitrous oxide to create a cryoprobe that reached –70°C.[4]

The cryoprobe consists of a hollow tube with a smaller inner tube. Pressurized gas (usually N_2O or CO_2) at 600 to 800 psi travels down the inner tube and is released into the larger outer tube (which is at a low pressure of 10 to 15 psi) through a very fine aperture (0.002 mm) which allows the gas to rapidly expand into the distal tip (Fig. 1).[5] This extracts heat from the tip of the probe, resulting in temperatures as cold as –89°C at the tip itself (Joule–Thompson effect), forming an ice ball, with temperature of –70°C.[6] The temperatures of the cryoprobe are dependent on the characteristics of coolants, pressure of the coolant, and whether gas or liquid is enclosed.

When liquid nitrogen (boiling point of –195.8°C) is used as a coolant in cryoprobe, the treatment is known as cryoablation; whereas if the coolant is nitrous oxide (boiling point of –88°C) or carbon dioxide (boiling point of –79°C), it is termed as cryoneurolysis. Therefore, temperatures of the cryoneedle tip range from –20°C to –196°C. This forms an ice ball at the tip of the catheter. The cold temperature creates neurological dysfunction that ranges from temporary conduction block to Wallerian degeneration.[7,8] Effectiveness of the therapy is dependent on proximity of the probe to the nerve, size of the probe, size of the ice ball formed, rate and duration of freezing, and temperature of the tissues in proximity to the probe.

The severities of cryolesion are dependent on the cryotemperatures. First degree or neuropraxia occurs when the temperature of cryolesion is above –20°C. Second degree or axonotmesis occurs at temperatures from –60°C to –100°C. Third degree to fifth degree or neurotmesis occurs when the temperatures are below –140°C.[9,10] The mechanism of neuroablation in cryoneurolysis involves the following process. The freezing process manifests first in the extracellular space, causing an osmotic gradient to form, leading to cell shrinkage. As the freezing process progresses, intracellular ice crystals form and directly damage organelles. Similar mechanisms result in vascular injury, inducing a coagulative cascade and eventual ischemia-mediated cell damage. During the thaw phase of these procedures, water rushes into previously shrunken cells, causing them to burst.

Due to the highly intricate design, the earlier cryoprobes used to be much thicker than 14 G, but today with the state-of-the-art engineering techniques even 22 G cryoprobes are available. The size of the lesion possible with the recent cryoprobe varies from 7 to 20 mm.

Major advantages of cryoneurolysis include direct visualization of ablation zone and minimal or nil procedural and postprocedural pain. The ability to simultaneously use multiple probes in variable configurations to create tailored additive overlapping ablation zones makes it more favorable. In contrast to surgical or heat-mediated ablation, cryoneurolysis does not cause any nerve lesion beyond second degree, which reduces the risk of deafferentiation pain and may allow eventual nerve regeneration.[11,12] It avoids the risk of systemic toxicity associated with chemical nerve ablation. It is safe because nerve regenerates within 2 months to 2 years. Motor fibers recover early, i.e., within 2 months.

Some of the contraindications include infections, bleeding disorders, cryoglobinemia, cold urtricaria, Raynaud's disease. Major side effects are bleeding, infection, numbness, and motor loss. Major applications of cryoneurolysis include occipital nerve, median branch of facet,[13–16] suprascapular nerve, intercostal nerve, ilioinguinal, iliohypogastric, genitofemoral nerve,[17,18] scar neuralgias, Sacroiliac (SI) joint arthropathies,[14,19–21] cluneal nerve, genicular nerve of knee, medial calcaneal nerve for the heel pain, phantom limb pain, pudendal nerve, postoperative pain, and movement disorders.

So when we consider the aspects like 100% safety, pain-free procedure, on-table onset of analgesia, and full and early recovery of inadvertent motor damage, cryoneurolysis is definitely going to be the future of neurolysis in the days to come.

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