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Neural therapy—A review of the therapeutic use of local anesthetics

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ABSTRACT

Neural therapy, or therapeutic local anesthesia (TLA), is the diagnostic and therapeutic use of local anesthetics. This review summarizes the scientific and clinical evidence, indications, methods of application, and possible future research.

In the literature, there is a gap between the multitude of data supporting a number of different molecular effects and the few clinical trials that are available. The available clinical studies and case reports, however, show effectiveness in acute and chronic pain, functional disorders, vegetative diseases such as the complex regional pain syndrome (CRPS), and chronic inflammation.

Five administration methods are described: local, segmental, regional, and systemic application, as well as injections into the so called "stoerfeld" (disturbance field, interference field).

Local anesthetics have been used for therapy for over 120 years, which suggests that this therapy may be an important, effective, and efficient therapy that has few side-effects. Possible clinical studies to reveal the potential effectiveness and benefit-risk ratio of this holistic approach are described.

1. Definition of neural therapy

Neural therapy (neuraltherapy), therapeutic local anesthesia (TLA), or therapeutic neural blockade [1], are common names for the diagnostic and therapeutic use of local anesthetics (LA). In contrast to the well-defined and short-time use for analgesia in surgery, the neural therapy approach aims for long-term relief of pain and functional disorders.

2. Neural therapy and acupuncture

There are multiple interrelationships between neural therapy and acupuncture. Both are minimally invasive, both have knowledge of distant phenomena, and both have few side effects. They are both forms of regulatory therapy and aim to influence the whole organism by following a holistic approach. This review summarizes the scientific and clinical evidence, indications, methods of application, and possible future research in this field.

3. Scientific evidence

The long-term effects of LA, which are useful in therapy, have been known since the discovery of LA in 1884 by Sigmund Freud and Carl Koller [2]. Freud's goal in investigating cocaine was to find new therapeutic treatments for his patients with chronic pain, particularly a male with severe trigeminal neuralgia. However, Freud's congenial coworker, Koller, immediately recognized cocaine's potential as a perioperative analgesic agent, and 14 days after Koller's historic lecture in Heidelberg in 1884, the whole medical world knew about this fascinating new method for pain-free surgery. Local anesthesia for operations found its way into medical routines worldwide, and its therapeutic use was nearly forgotten. Today, trigeminal neuralgia and similar forms are major indications for the therapeutic application of LA [3], and Freud's idea of therapy with LA is now close to a new renaissance.

Local anesthetics have a multitude of effects on the nervous system. Beside the well-known action on sodium ion channels in excitable cells, they also seem to provide neuroprotection to the CNS [4], protect against sympathetic sprouting in neuropathic pain [5], and reduce intracranial hypertension [6].

There is some evidence in basic science that pleiotropy (i.e., the "alternative effects") of LA on non-excitable cells [7,8] has a longer lasting effect than the pharmacological half-life of the drug in the sodium ion channel.

Some studies have revealed additional molecular mechanisms in neural therapy. Local anesthetics induce Gq–protein-complex mediated intracellular anti-inflammatory mechanisms [9],

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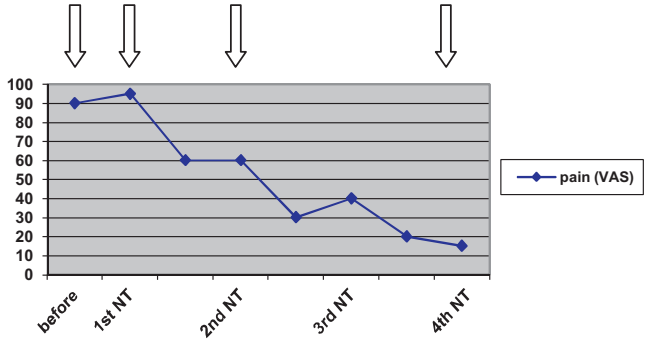

Fig. 1. The concept of "pain holidays". Repeated interventions with increasing intervals based on the improvement of patient complaints. Scale: VAS (0-100). Arrows: Treatment session with local anesthetics.

deactivate overactive granulocytes, inhibit the signaling of human NMDA receptors [10], and affect the synthesis and release of inflammatory mediators as eicosanoids, histamine, prostaglandins, and cytokines [11]. LA induce vasodilatation [12], reduce a pathologically increased capillary permeability in a hyperoxic lung injury in rabbits [13], have antimicrobial properties [11], and exhibit a sympatholytic effect [14]. Furthermore, the interesting concept of neurogenic inflammation [15] opens new perspectives into the therapy of chronic sterile inflammation by local anesthetics, thereby reducing the release of pro-inflammatory substances. Although Tracey has already suggested this approach [16], there are no data available proving this idea.

Neural therapy works best if it is repeated several times with increasing intervals as complaints are decreasing. This concept of "*salutogenesis by pain holidays*" (Fig. 1) may reflect the central nervous system action of local anesthetics. Memory effects are important mechanisms in the development of chronic pain disease. A central mechanism of LA action is likely. Procaine, for instance, shows a selective proclivity for activating limbic structures [17] without inducing the adverse effects of cocaine [18].

4. Clinical research

In contrast to this expanded knowledge concerning the underlying mechanisms of neural therapy and its frequent use in Central Europe [19], there is an obvious lack of clinical evidence. A recent systematic review of neural therapy in musculoskeletal diseases [20] could not identify any high-quality studies that proved an effect of neural therapy in this context. The few exceptions to the lack of data are randomized clinical trials (RCTs) on neural therapy in multiple sclerosis [21], on the therapy of distal colitis [22], and on acute pancreatitis [23]. Some reports have also shown high cost effectiveness [24] and a significantly higher treatment and care-related patient satisfaction with primary care for musculoskeletal diseases provided by physicians practicing neural therapy [25]. A HTA report in Switzerland worked-up approximately 3000 case reports from non-peer-reviewed journals (best case analysis) and recommended maintaining this method in the Swiss health system [26]. Since January 2012, Switzerland has reintegrated neural therapy into its basic medical insurance refunding [27].

5. Five groups of indications

Based on clinical experience, at least five indication groups and five administration methods have evolved.

Indications for the therapeutic use of LA can be divided into the following groups:

5.1. Acute pain and chronic pain disorders

Headache and migraine can be addressed by injections to the major occipital nerve [3] or by the intranasal or intravenous application of lidocaine [28,29]. Trigeminal neuralgia has been successfully treated with 10% lidocaine injections [30] and with trigger point injections [31].

Postherpetic neuralgia (PHN) could be successfully treated with local LA injections. Early reports [32,33] were confirmed by recent studies using neural therapy with procaine in a multifaceted integrated CAM concept [34]. In most recent studies, however, neural therapy was only used in combination with steroids [35,36]; therefore, a clear conclusion on the value of local anesthetics alone cannot be drawn. A promising approach to ophthalmic PHN is the topical use of lidocaine in eye drops [37]. Similarly, the topical use of 5% lidocaine plaster has been established as a first-line option for treating patients with PHN [38].

Myofascial pain is characterized by the frequent occurrence of muscular trigger points; in fact, myofascial pain and trigger points are nearly synonymous. One of several publications on successful LA use in this disease was conducted in Taiwan, with cervical facet joint injections for shoulder pain [39].

Visceral pain. An important example of abdominal pain conditions is chronic pelvic pain without organic origin. A French group reviewed the literature and found a significant diagnostic effect of autonomic nerve blocks (ganglion impar, hypogastric plexus and L2 lumbar sympathetic blocks) [40]. Further research may reveal a therapeutic effect in repeated interventions.

Postamputation pain syndrome. There is some evidence that contra-lateral injections of LA relieve phantom pain in soldiers [41]. Recent observations support the idea of treating postamputation pain with LA [42].

5.2. Functional disorders without organic findings

Vulvodynia. Clinical experience in our unit (with 10 patients) yielded the first evidence that LA injections around the pudendal nerve and the hypogastric plexus provided long-term relief of this painful condition [43].

Chronic colitis. In a review with description of their own experience, a Swedish group [22] described the results of a treatment of colorectal mucosa with a topical application of 2% lidocaine gel. The clinical results were promising and no side effects were observed.

Reportedly, **tinnitus** may respond well to the application of local anesthetics. The first known publication reported on successful nasal application of procaine (Barany, 1935). In a recent report, a Japanese group performed intravenous lidocaine injections with good success [44].

5.3. Vegetative (systemic) disorders

"Sympathetic pain" describes sympathetically induced vasoconstriction, ischemia, tissue damage, and chronic pain in the respective area. Well-known examples are reflex or vasospastic disorders, such as Raynaud's phenomenon and thromboangiitis obliterans (Buerger's disease). Early sympatholysis with LA injections or infusions to the respective ganglion or artery is an auspicious method of relieving these conditions [45,46]. Also causalgia and reflex dystrophy (Sudeck's disease, CRPS) are vegetative disorders. Therapy with LA injections to sympathetic ganglia is a promising approach for relieving these severe conditions [45,47–49].

Probably, based on clinical experience, also non-specific vegetative disorders, such as menopausal flushes, can be addressed with LA injections to the sympathetic ganglia. Case reports are available, but there is no available RCT data.