TIVIC HEALTH™

White Paper

ClearUP™
Sinus Pain Relief

Scientific Theory for Use of Microcurrent Neuromodulation for Relief of Sinus Pain

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NASAL/SINUS SYMPTOM PATHOPHYSIOLOGY

Congestion, pain, and pressure are common symptoms of rhinitis and rhinosinusitis. These symptoms are caused by mucosal inflammation, venous engorgement, increased nasal secretions, edema, and hypersensitivity of sensory perception. Inflammatory and neurogenic mediators are key drivers of vasodilation leading to edema and swelling of the nasal mucosa and subsequent reduction in nasal airflow and increases in pain and pressure.

ClearUP™ Sinus Pain Relief Device

NEUROMODULATION TODAY

Neuromodulation is defined as the alteration of nerve activity via targeted stimulus. Neuromodulation technologies can be either implantable (e.g., deep brain stimulation for Parkinson's disease tremor, vagus nerve stimulation for rheumatoid arthritis) or non-invasive (e.g. transcranial magnetic stimulation for drug-resistant depression) and rely upon the use of electrical current, magnetic fields, or ultrasound, among other modalities. In the last 15 years, neuromodulation technologies have proliferated and are quickly forming a new vertical in medicine. The adoption of neuromodulation therapies is driven in part because these treatment approaches have excellent safety profiles and often exhibit clinical effectiveness in difficult-to-treat clinical populations.

CLEARUP™ SINUS PAIN RELIEF: SCIENTIFIC THEORY

Tivic Health's ClearUP™ Sinus Pain Relief (ClearUP™) device uses electrical current in the microamp range to provide a non-invasive neuromodulation approach found to be beneficial in patients suffering from symptoms of rhinosinusitis including pain.

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The handheld device delivers a pulsed electrical current to the skin near the nose and paranasal sinuses. When a decrease in impedance is detected by the device, a vibration prompts the user to hold the device in place for treatment.

1. VASOCONSTRICTION VIA ACTIVATION OF SYMPATHETIC NERVES AND SMOOTH MUSCLE CONTRACTION

The paranasal sinuses are four paired air-filled spaces that are adjacent to the nasal cavity and include the maxillary, frontal, ethmoid, and sphenoid sinuses. The nasal cavities are air-filled spaces that are a continuation of the nostrils behind and above the nose. The blood supply for the sinuses and nasal cavities come from the branches of both the internal and external carotid artery, including branches of the facial artery and maxillary artery.

Importantly, there is pervasive sympathetic innervation of the blood vessels that supply the sinus and nasal mucosa. This sympathetic innervation by postganglionic nerve fibers facilitates vasoconstriction by the release of norepinephrine and subsequent smooth muscle contraction.[1]

Stimulation of sympathetic nerve fibers can promote release of norepinephrine and vasoconstriction as evidenced by several peer-reviewed studies[2-4] investigating frequency ranges similar to that of the ClearUp device (i.e., < 20 Hz). Vasoconstriction of arterioles and venous vessels, in the context of rhinosinusitis, results in smaller vessel diameter, reduced edema and extravasation of inflammatory immune cells, as well as less nasal resistance to air flow, all of which contribute to reduced symptom severity.

2. MODULATION OF ASCENDING PATHWAYS CONVEYING PAIN AND SENSORY PERCEPTION

In addition to symptom relief via vasoconstriction, there is neuromodulation of ascending pain and pressure signals that are relayed from the cranial nerves of the face (trigeminal and facial nerves) to the central nervous system.[5]

The sinus and nasal cavities are innervated by branches of the trigeminal nerve (Cranial Nerve V) and the facial nerve (Cranial Nerve VII) which provide sensory (afferent) input to the central nervous system via thalamocortical projections and also descending (efferent) parasympathetic projections that regulate mucous production. The afferent inputs to the central nervous system include touch, position, temperature and pain.

Cranial nerve projections are relayed via the thalamus to regions including primary somatosensory cortex (sensory perception) and cingulate cortex/insula (pain processing). Patients with rhinosinusitis often have hypersensitivity leading to augmented perceptions of pain, pressure, and congestion. Stimulation of the nerves that send ascending sensory information to the brain can disrupt and attenuate perception of pain and discomfort as has been shown by several studies.[6-7]

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2. *Mandel, Yossi, et al. "Vasoconstriction by electrical stimulation: new approach to control of non-compressible hemorrhage." Scientific reports 3 (2013).*
3. *Franco, O. S., et al. "Effects of different frequencies of transcutaneous electrical nerve stimulation on venous vascular reactivity." Brazilian Journal of Medical and Biological Research 47.5 (2014): 411-418.*
4. *Malm, L. "Stimulation of sympathetic nerve fibres to the nose in cats." Acta oto-laryngologica 75.2-6 (1973): 519-526.*
5. *Wilson-Pauwels, L., Akesson, E. J., Stewart, P. A. Cranial Nerves: Anatomy and Clinical Comments. B. C. Decker, 1998.*
6. *Slavin, Konstantin V., et al. "Trigeminal and occipital peripheral nerve stimulation for craniofacial pain: a single-institution experience and review of the literature." Journal of Neurosurgery: Neurosurgical focus 21.6 (2006): 1-5.*
7. *Hansson, Per, and Anders Ekblom. "Transcutaneous electrical nerve stimulation (TENS) as compared to placebo TENS for the relief of acute oro-facial pain." Pain 15.1-4 (1983): 157-165.*

ClearUP™ Sinus Pain Relief is an investigational technology. Claims have not been evaluated by the FDA. This device is not currently for sale in the U.S. FDA 510 K clearance is pending.