MedCrave
Step into the World of Research
International Journal of Family & Community Medicine

Review Article

Open Access

CrossMark

Reduction of work hour loss due to absenteeism and presenteeism a novel algorithm in the treatment of chronic – episodic migraine in workman force

Volume 5 Issue 5 - 2021

Faro T Owiesy
MD, Corona Doctors Medical Clinics, 802 Magnolia Ave., Suite 106, Corona, CA, 92879, USA

Correspondence: Faro T Owiesy, MD, Corona Doctors Medical Clinics, 802 Magnolia Ave., Suite 106, Corona, CA, 9289, USA, Email owiesymd@gmail.com

Received: September 19, 2021 | **Published:** October 28, 2021

Background and objectives

According to many studies in Europe and the United States, migraine and other related disorders lead to widespread suffering, reduced quality of life, and marked impairment of participation, both in work and social activities. Patients that experience migraine and migraine-like symptoms also experience substantial psychological and economic impairment. The traditional treatment goal is to prevent attacks and limit recurrent pain and disability experienced by headache sufferers. In this challenge, the American Headache Society's (AHS) role and several other Headache societies are appreciated. Not less appreciated is the challenge of the scientists in the pharmacological industry and other societies.

Migraine treatment in all its subcategories practically is still empirical and hypothetical

Unfortunately, the introduction of CGRP monoclonal antibodies as the newest trend in the preventive and abortive measures did not differ substantially from previous preventive or abortive pharmaceutical challenges. It also added to the increased cost of treatment and a new burden to patients. Migraine is an episodic disorder with a substantial socioeconomic burden on the productivity of industrialized countries. Migraine affects millions of individuals worldwide and significantly impairs the sufferers' ability to function. Researchers' collected data show that excess medical and pharmaceutical treatment costs for employees with migraines averaged almost $ 2000 a year. They also had 2.2 days of sicker leave per year, averaging approximately $ 600 in wages and benefits.[1] Different studies found marked variations between countries, both concerning prevalence and burden of headaches. In the USA and Europe, the estimated days per year lost to migraine at work, and school are 250,000,000. In the Global Burden of Disease Study, updated in 2004, migraine itself responsible for 1.3% of all years of life lost to migraine disability worldwide.[2] Migraine is an episodic disorder with a substantial socioeconomic burden on the productivity of industrialized countries. Migraine affects millions of individuals worldwide and significantly impairs the sufferers' ability to function normally and be productive. Collected data shows that excess medical and pharmaceutical treatment costs for employees with migraine attacks averaged almost $ 2000 a year. They also had 2.2 days of sicker leave per year, averaging approximately $ 600 in wages and benefits.[3]

Different studies showed marked variations between countries and industries, both concerning prevalence and burden of headache. In some studies, the level of disability due to migraine has been evaluated with the Migraine Disability Assessment Scale (MIDAS). With this instrument, days with work absence (job or household chores), days with 50% reduction in productivity, and days with an inability to participate in social activities were counted for three months. For instance, in France, among those with active migraines, 22% (1.5% of the whole population) had grades III or IV disability (moderate or severe disability, indicating 11 days or more during the last three months' period when headache affected 50% or more work/household chores or leisure activities).[4] The most recent study of indirect migraine costs found that a cohort of migraineurs incurred significantly higher indirect costs in all categories studied, including absence, short-term disability, and worker's compensation. Compared with a propensity score-matched cohort of patients without migraine, the total indirect costs for migraineurs were $2,834 more than for the matched cohort ($4,453 vs. $1,619 per year, respectively). The total estimated indirect burden, excluding presenteeism, was $12 billion.[5]

Among the chronic disorders, the costs of headache disorders are enormous; the costs only for migraine accounted for €27 billion in the EU countries between 2016 and 2017, and the cost for other headaches is probably as high. Socioeconomic data search revealed dimensions of high tendency for unemployment in the workforce cohort with chronic and episodic migraine causing low income due disability and absence from work. They provides pattern of measurable low quality of life and diminished leisure activities. Also, socially seen there was marked impact on family life, and migraine headaches pose considerable strain on partners and children.[6] The economic impact of migraine on the employed labor force in Taiwan in 2008 revealed that migraine resulted in (1.7 million people who experienced migraine over one year) 3.7 million estimated missed workdays and an estimated cost of $ 4.6 billion due to absenteeism in 2005, 56% of whom accounted for the female labor force. The cost and impact of migraine headaches in developing countries are enormous but not statistically present in the literature.

Current understanding of the economic impact and corresponding social malfunction in all levels of productivity in our society requires rethinking the migraine treatment strategy. Historically, with 61 years of the collective international approach to migraine treatment, we are still puzzling, and our approach is empirical. New developments in understanding the molecular physiology of cells, in particular neurons, promote novel elements in cost-effective and universal treatment for migraine headaches. Given the increasingly high indirect costs of headaches, more significant investment in health care that treats headaches effectively may well be cost-saving overall. Instruments to assess the impact of headache are used routinely in only 24% of countries and extraordinarily little in developing countries.[7]

There are widely available drugs for treating migraine headaches; however, they are expensive and may not be covered by insurance. It is noticeable that there are professional headache organizations in advanced industrialized economies, raising awareness, educating, and creating guidelines routinely for migraine treatment. Many low-income countries are lacking these costly privileges. A cost-effective means a financially affordable treatment, and a practical approach for treating migraine headaches should reduce or even eliminate the costly excessive use of abortive and preventive drugs and procedures. Unsuccessful new drugs burden the research associate scientists, headache specialists, and primary care physicians and often conflict with their enthusiastic feelings. We deal with failure after failure in our effort to heal.

An analysis of the scientific papers demonstrates that most treating physicians select harsh off-label drugs, and sometimes in high doses for their patients. A questionnaire of patients with migraine headaches revealed that they tried more than 50-90 drugs in their lifetime. Data from world health organization WHO showed Worldwide, headache is rarely included in national expenditure surveys: in their collected data only 7 % of the countries responded, all of which are within three regions – Eastern Mediterranean (15 %), European (11 %), and the Americas (5 %). None are low-income countries.[8] Regarding those facts, discussing the matter with high valued experts, and attending many annual conferences, we were encouraged to bypass the existing instruments and hypothesis. We conducted our studies and evaluation of the past to reach a simple, affordable, and curative future approach. We neared our goal in 2013 by analyzing the results of our approach. In this paper, we present the results on the workforce cohort after months and years of treatment.

Introduction

The patient-centered outcomes of this retrospective study were to evaluate the effectiveness and results of the simultaneous administration of Dexamethasone, Lidocaine, and Thiamine into the trigeminal nerve branches, the greater and lesser Occipital nerve bilaterally for the treatment of acute and chronic trigeminal neuralgia and episodic/chronic migraine headaches. Evaluation of collected follow-up data from 2008-2018 from the workman force cohort with long- and short-term disabilities were outsourced and analyzed. Between 2008-2017, we treated over 551 patients with chronic migraine headaches, indifferent of subtype. We did not differentiate patients with migraine with aura versus without aura because all categories responded with the same results. Our concept and techniques emerged from the unsatisfying results using traditional treatment approaches and patients' frustration with failed treatment results. In the face of challenges and frustrations with unsuccessful past treatments for headaches, we built a comprehensive guide to better understand the craniofacial pain in general and migraine headache in particular. Clinical guides were prepared to address the long-term resolution of migraine headaches. The material represents the epitome of over 20 years of personal research and treatment of migraine headaches.

Eligibility criteria

The study was conducted by Corona doctors' medical clinics, a multispecialty clinic, an educational and treatment center in Corona, Southern California. Patients were recruited through the media announcement and among those who approached our clinic directly for treatment. We included patients aged 12-87 years who were able to distinguish migraine attacks from other headaches, able to read, comprehend, and legibly and reliably record information, able to provide written, informed consent, and respond to pre-and post-treatment questionnaires (in minors legal guardian provided symptomatic history and consent). All selected patients for this study were in the workman cohort, among which one already had comprehensive diagnostic procedures and distinct abortive and preventive medications and treatment history.

Exclusion criteria

Patients with malignant hypertension, history of stroke, Transient Ischemic Attack or diagnosis of a brain aneurysm, neuro-stimulator implant, trigeminal tractotomy, TGN/occipital nerve neurectomy, microvascular decompression procedure, allergies, chronic sinusitis, glaucoma or gross ophthalmologic disorders, and hypersensitivity to Dexamethasone, Lidocaine, or Thiamine were excluded from the study.

Randomization and study drug administration

Patients were randomly recruited at the time of the acute attack and evidence of chronic-episodic migraine by agreeing to try the proposed treatment vs. currently available alternatives. Medical records were obtained and evaluated before the procedure. Consent for procedure and possible publications, also California experimental subject's bill of right were obtained from all participants. Patients of all selected ages received the same dosage and composition of medications. A fresh, aseptic, and sterile solution was prepared for each patient consisting of Dexamethasone phosphate (pH adjustment 7.0-8.5) 20 mg, Lidocaine HCI 1% (each ml contains lidocaine HCI 10 mg), Sodium Chloride 7 mg, Methylparaben 1 mg, water for Injection q.s. (pH range 5.0-7.0) 40mg, and composed thiamine (a water-soluble vitamin 100mg per 10 ml vial). Medication is prepared in a sterile fashion in 10 ml vials, withdrawn in 1ml syringes using 30G and 27G needle for injections. At each site, a total of five of 1 ml syringes were used. According to the protocol at each injection site, 0.1 ml of composed medication was administered at the proposed anatomical sites. A volume of 0.3 ml - 0.4 ml was considered for the ascending and descending branches of the greater Occipital nerve and the Lesser Occipital nerve at each side. Retrobulbar space and pterygopalatine ganglion PGP were approached upon severity and resistance of symptoms. If patients returned with a new trigger point(s), we treated only certain branches involved in neuralgia Figure 1.

Results

Patients in the workforce and disability category were followed with an appointment, telephone call, email, and follow-up results from 2008-2018 were corroborated. Thirty-six individuals who were working were followed up after treatment administration between 2008-2017. Thirty-three White and Hispanic individuals, 24 female and nine males, responded to our inquiry in full. Three individuals were lost to follow up due to address changes or did not respond. Each individual was evaluated for clinical symptoms parameters and symptom relief length. We considered each patient's comorbidities, previous medications and abortive interventions, and psycho-social lifestyle changes. Out of 33 patients, almost 100% reported consequent steady work performance without interruption of their job performance or loss of work hours following their treatment. A

modified MIDAS (Migraine Disability Assessment Questionnaire) was put together to measure headaches' impact on the patients' work environment and disability after De-Novo treatment. The information in this questionnaire was analyzed to evaluate the treatment's effect on the study cohort, Figure 2.

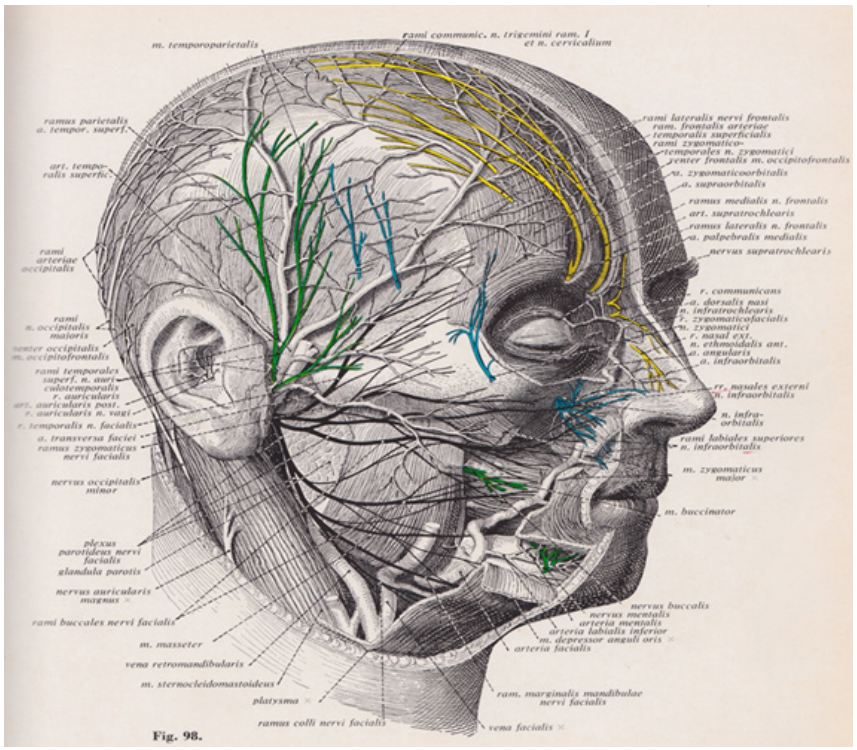

Figure 1 Branches of trigeminal nerve, greater and lesser occipital nerve we approach.

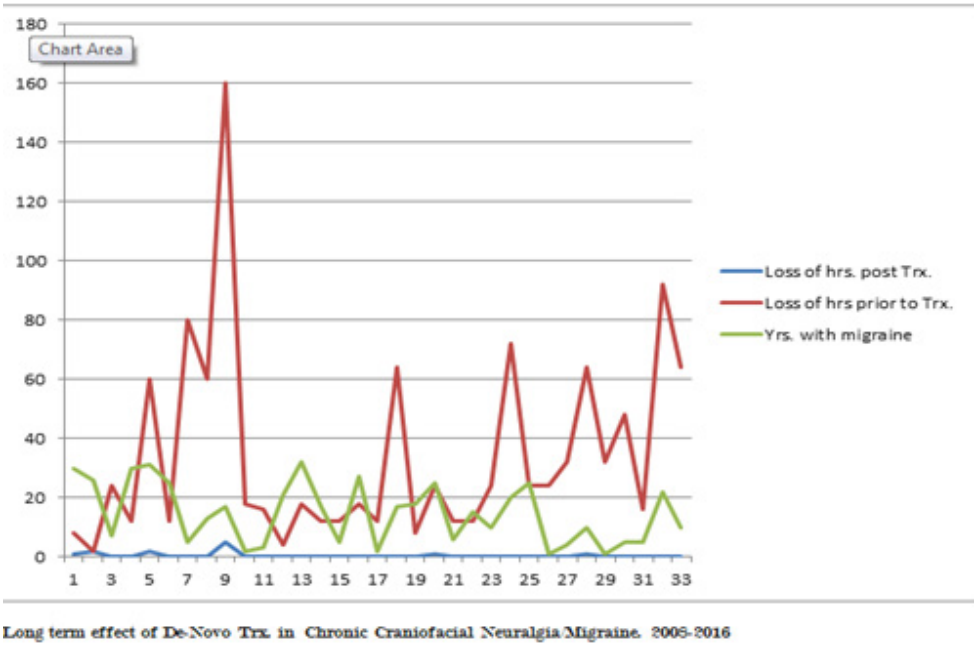

Figure 2 Loss of Work Hours per month prior and post-treatment/years lining without migraine headaches: Significant changes witnessed in the post-treatment reduction of hour's loss at any headaches-migraines occurrences at the workplace.

Citation: Owiesy FT. Reduction of work hour loss due to absenteeism and presenteeism a novel algorithm in the treatment of chronic – episodic migraine in workman force. *Int J Fam Commun Med.* 2021;5(5):168–175. DOI: 10.15406/ijfcm.2021.05.00240

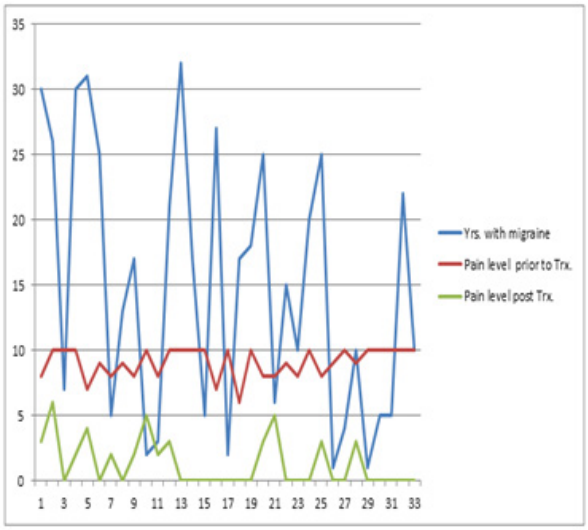

Figure 3 The long-term effect of De-Novo treatment: Years with migraine headaches and pain level before De Novo treatment vs. pain level post-De-Novo treatment.

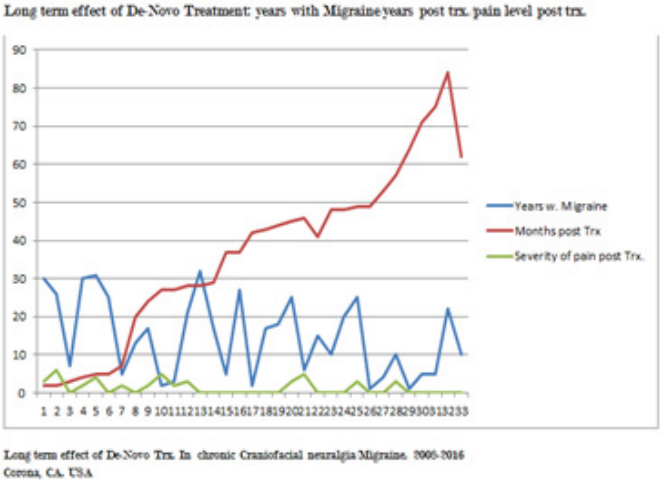

Figure 4 Long term effect of De-Novo treatment years with Migraine, vs. years' post-treatment, pain level post-treatment.

Data analysis

We used a descriptive data analysis in this retrospective research analysis. Survey data obtained by our clinic between 2008 to 2018. Data were collected from patients' medical records and a history of chronic and episodic migraine headaches and disability at work. We did not restrict our selection and treatment to cohorts with aura or without aura. Data was collected as homogenous chronic and episodic migraine nonresponsive to current conventional therapies. Following treatment, individual data was collected by email, phone call, and in-person encounter for 80 months following treatment based on patients' accessibility and cooperation. We made multiple comparisons to evaluate the significance of the treatment formula and algorithm. Thirty-three eligible individuals participated in data collection and follow-ups. Data revealed a total of 1152 working hours lost in the months before treatment, averaging 34.91 hours and a median of 21 hours per month. The shortest hours per month loss was 2 hours, and the most prolonged 160 hours, depending on the frequency of migraine attacks and timing.

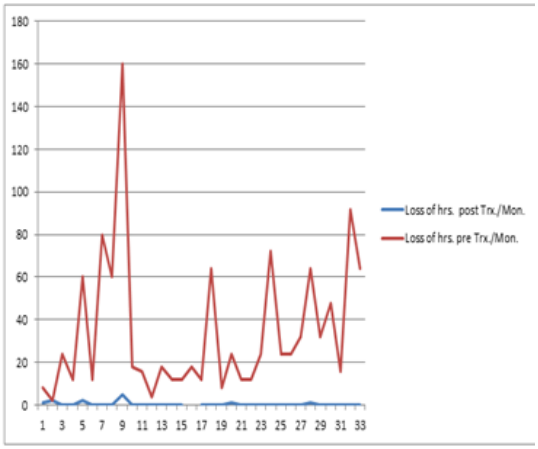

Figure 5 Comparison of hour loss per month prior and post De-Novo treatment.

Data collected after treatment for the longest 80 months and shortest one month revealed a total of hours loss at work 11hours per month in cohort, an average of 0.36 hours/month, varied from 0 as minimal and six as the highest level of pain. Additionally, pre-treatment data showed scores of pain at the level of 0/10, with an average of 8.7 of 0/10, median 9/10, and mode of 10. The lowest pain level given was 6, and the highest was 10 out of 10. All individuals demonstrated a headache frequency of 10-20 per month (considering episodic <15 Days/month and chronic migraine 15+ days/month). The cohort revealed a total of 50.4 years of migraine history with an average of 15.3 years, a median of 16 years, and mode 30 years of chronicity of headaches per individual. The shortest period of migraine headaches was one year, and the most extended period was 32 years—. In the same table, we plotted the severity of pain before treatment and after treatment, pain level for an objective efficacy comparison. Data collected showed scores in numerical rating scales (NRS) of pain in the cohort after treatment a minimum of 0/10 and a maximum of a pain level of 6/10. Average was 1.9, and mode of 0 respectively.

17 individuals reported 0/10 pain (51.52%)

1 individual reported 2/10 pain (3.03%)

6 individual reported 3/10 pain (18.18)

3 individual reported 4/10 pain (9.09%)

5 individual reported 5/10 pain (15.15%), and

1 individual reported 6/10 pain (3.03%).

An average score of 1-4/10 after treatment considered sufficient positive satisfactory result. Statistic demonstrated 81.81% with complete relief with respective score of 0-4 of 10 and 18.18% with respective score of 5-6/10 considered moderate results with significant improvement. Score of 6/10 determined as mild relief or no relief. Both groups did not take any preventive, abortive medications post-

treatment as they did before treatment. Frequency of migraine attacks reported from 0-3 per month after treatment. None of the participants returned for the second treatment within 80 months post-treatment, Table 1.

Table 1 Workhours loss pre and post treatment

	Total work hrs. lost/month	Average work hrs. loss/month	Average months free of migraine	Total Pain level in a month	Average daily pain level	Total yrs. with migraine
Before Trx.	1152	34.91	0	287	9.26	504
After Trx.	11	0.34	1.9	63	1.65	0

Discussion

The autonomic nervous system is an internal alert system that communicates with our physical world. The fragile human body is defenseless against physics laws, such as gravity, weight, light, rays, velocity, acceleration, and electricity. The human body, like most species, has a warning system that includes signals. These signals are provided to different organs in all vertebrates, including pain, nausea, vomiting, diarrhea, bronchospasms, vision loss, ophthalmoplegia, and photophobia. Molecular receptors of the somatosensory systems modify these warning signals. Easing the suffering of migraine headaches and craniofacial neuralgia in human beings seems a painful and costly challenge. Frustrations of patients and physicians are going hand in hand. We did study the cause and path of migraine headaches for over 20 years. We came upon an analysis of our own studies outcomes and hypothesis of the physical environmental cause. We discovered a combination formula that demonstrated good long-term results compared to other treatments and pharmaceuticals we used in the past. Our goal is to achieve rapid abortive and longer-lasting freedom of migraine pain with the minimum dosage and no harm. This could be a halt to centuries of moaning and mourning of migraine headaches. As we demonstrate below, our goal is to inject the medications into the connecting branches of Pterygopalatine ganglion demonstrated below. We do not intend to deliver the medications toward the olfactory mucosa and Olfactory nerve branches. The olfactory nerve and its' anatomical properties per se do not demonstrate a direct physiologic communication with Pterygopalatine ganglion and trigeminal nerve divisions and branches. In the presence of aura with anosmia associated with frequent migraine attacks, we recommend applying our formula to the Olfactory Mucosa and nerves.

Background- hypothesis

Anatomical properties of Pterygopalatine ganglion and trigeminal nerve branches

Clinical and animal research data demonstrate that the pterygopalatine ganglion plays a significant role in the vasodilation/vasoconstriction event in the peripheral and central blood supply of CNS. The maxillary nerve courses forward through the cavernous sinus wall and leaves the skull through the foramen rotundum. It crosses the pterygopalatine fossa, where it gives branches to the pterygopalatine ganglion, a parasympathetic ganglion. This ganglion gives several branches, now containing visceral motor and sensory fibers, to the mucous membrane of the mouth, nose, and pharynx.

The branches of significance include:

I. Greater palatine branch enters the hard palate

II. Lesser palatine branch enters the soft palate

III. Nasopalatine branch enters the posterior or superior lateral nostrils runs downward and forward on the nasal septum

IV. Posterior superior alveolar branch

V. Infraorbital nerve

VI. The Middle superior alveolar branch arises from the infraorbital nerve and runs through the maxillary sinus's lateral wall.

Anatomical properties of Pterygopalatine ganglion and trigeminal nerve branches

Clinical and animal research data demonstrate that the pterygopalatine ganglion plays a major role in the vasodilation/vasoconstriction event in the peripheral and central blood supply of CNS. The maxillary nerve courses forward through the wall of the cavernous sinus and leaves the skull through the foramen rotundum. It crosses the pterygopalatine fossa, where it gives branches to the pterygopalatine ganglion, a parasympathetic ganglion. This ganglion gives several branches, now containing visceral motor and sensory fibers, to the mucous membrane of the mouth, nose, and pharynx.

The branches of significance include:

I. Greater palatine branch enters the hard palate

II. Lesser palatine branch enters the soft palate

III. Nasopalatine branch enters the posterior or superior lateral nostrils runs downward and forward on the nasal septum

IV. Posterior superior alveolar branch

V. Infraorbital nerve

VI. The Middle superior alveolar branch arises from the infraorbital nerve and runs through the lateral wall of the maxillary sinus.

Anatomical understanding of autonomic craniofacial ganglia

Having a broad knowledge of anatomy is essential for practicing neurology. Certain anatomical structures call for detailed studies due to their anatomical and functional importance. Nevertheless, some structures are difficult to visualize and identify due to their small volume and complicated access. Such is the case of the parasympathetic ganglia located in the cranial, facial part of the autonomic nervous system, which includes: the ciliary ganglion (located deeply in the orbit, laterally to the optic nerve), the pterygopalatine ganglion (located in the pterygopalatine fossa), the submandibular ganglion (located laterally to the Hypoglossus muscle, below the lingual nerve) and the Otic ganglion (located medially to the mandibular nerve, right beneath the oval foramen).[9]

A ganglion is a mass of nervous tissues found in some peripheral nerves. Ganglia are located on the roots of spinal nerves and the sensitive roots of the trigeminal, facial, glossopharyngeal, Vagus, and Vestibulocochlear nerves. Ganglia also appear in association with the autonomic nervous system. Each ganglion is covered by a smooth and dense capsule of fibrous connective tissue, with cells similar to associated flattened fibrocystic, which extends to the nerves' perineurium, sending numerous extensions to the ganglion's interior. Ganglia vary considerably in size, shape, and location.[10] The pterygopalatine ganglion is also known as sphenopalatine ganglion lies deep within the pterygoid fossa, rostral to the anterior opening of the pterygoid canal and inferior to the maxillary nerve.[11] It is the main parasympathetic ganglion of the upper jaw and related structures. The ganglion is about 3 mm long, containing about 56,500 tightly packed ovoid nerve cell bodies, 20 □m X 30 □m in diameter, with thick branching dendrites, often bearing knob shaped endings.[12] Some neurons have long, multi-branched dendrites that contribute to dense dendritic glomeruli.[12] Preganglionic axons reach the pterygopalatine ganglion from the facial nerve, via the greater superficial petrosal nerve and the pterygoid canal nerve (Vividian nerve). Small groups of nerve cell bodies occur in the distal portion of the pterygoid canal nerve, proximal to its junction with the pterygopalatine ganglion.[13] Ocular rami carry postganglionic vasodilator fibers projecting to blood vessels of the eye.[14]

Most neurons in human pterygopalatine ganglion are cholinergic; however, other studies revealed staining, demonstrating VIP, peptide histidine methionine (PHM), helospectin, and pituitary adenylate cyclase-activating peptide (PACAP), NOS.[15] Other investigators show that a specific set of vasodilator neurons innervates the cerebral arteries.[16] The pterygopalatine ganglion is essential for intraocular pressure balance and cerebral vasodilatation associated with vascular originated headaches. It is located deeply in the pterygopalatine fossa, close to the sphenopalatine foramen, and front of the pterygoid canal. The pterygopalatine ganglion was located in the pterygopalatine fossa and was functionally attached to the facial nerve. This ganglion had the largest size compared to the other ganglia, and it had a flattened form.[17] Concerning morphology: there are several descriptions of the pterygopalatine ganglion. According to some researchers, the pterygopalatine ganglion is slightly flat, with a triangular and flat form, and is the cranial parasympathetic system's biggest peripheral ganglion. However, for others, this ganglion is polymorphic and can be rhomboidal, pear-shaped, semi-lunar, triangular, or fusiform, with volume similar to that of a lentil (5 mm to 7 mm length). In our study, the pterygopalatine ganglion had a flat form and presented the largest size (3 to 5 mm); hence, our results concur with the description made by Warwick, Williams (1979).[18]

Our understanding of the biological process of migraine:

Migraine headaches seem to demonstrate a dysbalance between sympathetic and parasympathetic innervations of the cerebrovascular system rather than an isolated central cortical process. The brain is complicated hardware programmed by its five sensory organs connecting it to the physical environment for its existence. Through those sensory organs, the brain gets with the time programmed to the physical world's laws such as light, different rays length, and hazardous effect—a perception of those effects programming the brain's centers. Now, any abnormal and hazardous impulse damaging or incapacitating the brain's specific hardware, its applications programming, in this case, eyes may deprive the visual cortex of its capacity. For instance, a visually deprived individual may not experience visual dreams because of a lack of visual reception of his/her physical environment in the visual cortex. The same could be accepted upon the other four sensory organs. A brain without its sensory organs is similar to computer hardware without useful programs and apps. Sensory organs without a functioning brain are useless programming tools. The sensory organs' role is not only to secure the programmed and highly functional brain but also to continue completing the programming with unlimited capacity. Giga bite capacity of the human brain is speculated indefinitely. We came upon the conclusion that inputs for migraine headaches are peripheral. CNS molecular biologic events are just cellular events to recognize the inputs, analyze hazardous levels, and imbalance in the autonomic system. Events of pain incorporated in the CNS are reversible unless they destroy mitochondrial machinery in neurons and end the brain's existence.

In his testimony, Nicola Tesla stated once," When a child is born, its sense-organs are brought in contact with the outer world. The waves of sound, heat, and light beat upon its feeble body, its sensitive nerve-fibers quiver, the muscles contract and relax in obedience: a gasp, a breath, and in this act a marvelous little engine, of inconceivable delicacy and complexity of construction, unlike any on earth, is hitched to the wheel-work of the universe. The little engine labors and grows, performs more and more involved operations, becomes sensitive to ever subtler influences and now there manifests itself in the fully developed being - Man - a desire mysterious, inscrutable and irresistible: to imitate nature, to create, to work himself the wonders he perceives*".*[19] Medicine is one of the sophisticated and respected materialistic tools serving human existence. However, spiritual tools accompanied human beings' weakness to answer and uncover all dark sides of life and the universe. Pain is the best and the only messenger of the upcoming dangerous and damaging condition to any peripheral sensory organs.

This phenomenon is embedded in the sympathetic part of the autonomous nerve system covering the peripheral nerve's vascularity. Every physical stimulus must enter through the sensory organs before it reaches the brain centers for analysis and action. No exception. The sensory organs' role here is speculated as a safety gate for the brain's healthy functionality. Pain per se is peripheral and locally determined, acknowledged by the brain in the pattern of perceptive logic to handle the confrontation of life with the physical world. To experience all types of pain, humans need to have intact and functional five sensory organs. Perception of pain is a learning process; it is not the intuitive capacity that every single individual mammal caries automatically. Navigation of animal life for survival responds to a physical environment controlled by one and each of the somatosensory organs as a first-line defense mechanism. The somatosensory system is the only efficient, intelligent programming resource for the brain. 1- Gustatory system (taste), 2-Olfactory system (smell), 3-Vestibulo-Auditory system (balance/hearing), 4-Visual system, and 5- Somatosensory, tactile system (touch), are managed by a higher sophisticated regulatory system in the brain centers.[20-27]

Interpretation

How humans and other mammals defend their life against the physical world? Humans and animals and our planet's lifeless, physical world crush with grime results in living creatures. Human makes gear for defense, and get wiser. Upon the journey of life, pain

understands the straightforward escaping the distress of the physical world. Primarily, pain caused by hypoxia. The sympathetic and parasympathetic nervous system is genetically designed as an initial primitive internal defense mechanism. It is universal to almost all species on the earth. Its mechanism and pattern may differ on the ground and in avian environment living species. The autonomous nervous system is an internal alert system communicating with our physical world. The plasticity and highly fragile human body system are defenseless against the law of physics such as gravity and weight, wavelength and light, velocity and acceleration, electricity, and more. A question arises: how the warning system inside us works? There is a warning system with its signals embedded in our whole system as a human being. The fundamental defense mechanism in almost all species is the same. Its warning signal is pronounced mostly by pain or other symptoms such as nausea, vomiting, diarrhea, spasm of the airways and throat, visual loss. Warning signals modified by molecular receptors of five somatosensory systems:

1- Gustatory system (taste), 2-Olfactory system (smell), 3-Vestibulo-Auditory system (balance/hearing), 4-Visual system, and 5- Somatosensory, tactile system (touch), are managed by a higher sophisticated regulatory system in the brain centers. Navigation of animal life for survival responds to a physical environment controlled by one and each of the somatosensory organs as a first-line defense mechanism. The somatosensory system is the only efficient, intelligent programming resource for the brain. However, later in the evolution process arises the emotional, sensory system from communication in the path of the civilization. Therefore, the power of emotional sense is genetically embedded in the civilized animal's brain and behavior. The limbic system is responsible for the awareness threshold and is our major emotional center. It receives input from all somatosensory organs and analyses the data to determine how safe the physical and emotional environment we are entering is. Emotional sense modifies the concept of an internal stressor as a modifier of sympathetic signals in a self-defense approach. Factors such as bright lights and ultraviolet waves, flickering lights, as well as specific visual patterns, smells, noises, tastes may trigger a migraine. Lifestyle stressors may also trigger a migraine attack, and it has been hypothesized that visual cortical hyperexcitability can be responsible for migraine. We witnessed that migraine is bilaterally induced. However, the dominant reaction with a significant pain pattern reveals itself at one side. We did try first to treat the dominant side in several cases. Patients returned with more severe unusual pain pattern on the opposite side. We experimented with patients with mainly occipital neuralgia complaints, and they returned with a new expression of trigeminal neuralgia symptoms later. The mentioned selective experiences shape the conclusive pattern of our algorithm.

A profound study into the mechanism of medications utilized in treating the trigeminal neuralgia and migraine, their adverse reaction, and their role as rescue or abortive agent did not satisfy our ambition of migraine treatment. Major studies of the 21st Century at the level of molecular biochemistry and molecular biology indicated that the signaling system at the cellular and cell -organelle level plays a significant role. Genetic modification of altered balanced signals in autonomous nerve system components was the key understanding in our approach. Our medications' gene suppressive effect may be switching the key signals by silencing the hyper-activated proinflammatory signals. The promotion of those signals may encode balance between sympathetic/parasympathetic mechanisms at the level of vascular-neuronal capillaries. Induction of nitric oxide synthase changing hypoxia's status consequently relieves pain by inhibiting COX-2 and inhibiting nearly all proinflammatory cytokines-genes[28] that play an essential role in the **pain signaling.** Thematically, biological signals affecting neurovascular regulation. Cell surface receptors are the gateway through which the cell senses respond to the environment. Most physiologically important processes are initiated by cell-surface receptors' interaction with extracellular mediators resulting in an intracellular signal transduction cascade. Step by step understanding of molecular biologic action of glucocorticoids by sophisticated worldwide research in molecular biochemistry and molecular biology provides significant insight into cell membrane receptors, their activation and deactivation, genetic signaling, and structural genetic biology. These novel subjects may disclose the magic of neural and neurovascular diseases, migraine, and trigeminal neuralgia. So far, the author believes regulatory gene elements play a significant role in silencing and de-silencing neurovascular disorders such as craniofacial neuralgia (migraine) and high possibly also in Chronic Cerebrospinal Venous Insufficiency disorder (CCSVI), ALS, and stroke. These diseases are acquired later in the path of life, and they are not born defects as the etiology and pattern of disease demonstrates.

Conclusion and relevance

In the present study, we demonstrated a selective understanding and approach to treatment of episodic and chronic migraine headaches. The present retrospective study demonstrated the efficacy and stability of a combination of algorithm and a drug formula. Our algorithm materialized our hypothesis and understanding of achieving long term results in migraine headaches treatment. We predict capability of this model as significant in eliminating the anxiety of overdose and uncertain adverse reactions by utilizing harsh off label drugs. Also, by application of our experience millions of lost work hours may be preserved, less human suffering, and burden to families and communities may be achieved. We predict this approach may save billions of dollars for each country's economy in eradicating loss of work hours by saving billions of Euro and dollars. This approach provides long term resolution, if not a full resolution of symptoms. Notably, this approach may decrease the volume of hypothetical therapeutic approaches by utilizing off label drugs with major adverse reactions.

Although for better understanding of our proposed approach a comparative clinical study may provide a unique and powerful tool for broader acceptance and use. In our trial, all participants tolerated the treatment well without an incident or major adverse event. In major number of participants, no abortive or preventive drugs prescribed or utilized after the treatment. Most of the working patients with a history of current disabilities were returned to work with No Evidence of Disease Activity (NEDA). These results, also combined with other population treated in our clinic in the past 15 years indicates that our approach is closely nearing the affordable, one treatment session with long-lasting, satisfying results. Our algorithm and formula are cost-effective, safe, and eradicate the need for polypharmacy and other off label drug use and surgical as well as mechanical tool utilization. Our approach's superiority is embedded in gene expression modification peripherally, which is fundamental for all subtypes of migraine and trigeminal neuralgia. Administration of de novo treatment requires minimal education for providers' smooth training at any level in low-income countries and rural communities.

Conflict of interest and disclosure

The author has no financial relationship with any pharmaceutical organization. The study was sponsored by Corona doctors' medical clinics in Corona, CA 92879-USA. This manuscript is a combination of a review of scientific research articles, books, and online libraries, and a clinical study. The author declares he has no conflict of interest except with CDMC. All introduced formula and algorithm (pat.) are protected by copy and patent right.

Author contribution

Faro Ted Owiesy, M.D had full access to all data in the study and takes full responsibility for the integrity of the data and accuracy of data analysis.

References

1. Jaime Rosenberg. *Migraine has an impact on both Healthcare cost and lost productivity- AJMC- managed markets Network 06/2018*. 2018.
2. *Atlas of headache disorders and resources in the world 2011 A collaborative projects of World Health Organization and Lifting*. The Burden.
3. Edmeads J, Mackell JA. The economic impact of migraine: an analysis of direct and indirect costs. *Headache*. 2002;42:501–509.
4. Hawkins K, Wang S, Rupnow MF. The indirect cost burden of migraine in the United States. *J Occup Environ Med*. 2007;49:368–374.
5. Lars Jacob Stovner, Colette Andre. Impact of headache in Europe: a review for the Eurolight project. *J Headache Pain*. 2008;9:139–146.
6. *Atlas of headache disorders and resources in the world 2011 A collaborative projects of World Health Organization and Lifting*. The Burden.
7. Selma Siéssere, Mathias Vitti, Luiz Gustavo de Sousa, et al. Anatomic variation of cranial parasympathetic ganglia. *Braz Oral Res*. 2008;22(2):101–105.
8. Warwick R, Williams PL. *Gray Anatomie*. 35 ed. In: Rio de Janeiro, et al., editors. Kuntz 1945; Mitchell 1953. 1973.
9. Haviv Levi, Karl Schoknecht, Ofer Prager, et al. Stimulation of the Sphenopalatine Ganglion Induces Reperfusion and Blood-Brain Barrier Protection in the Photothrombotic Stroke Model. *PLoS One*. 2012;7(6):e39636.
10. Om Rastko's Network Website. *Man's Greatest Achievement by Nicola Tesla*. New York American- July. 1930.
11. https://en.wikipedia.org/wiki/Na%2B/K%2B-ATPase.
12. Stephen T Smale. Selective Transcription in Response to an Inflammatory Stimulus. *Cell*. 2010;140(6):935–95.
13. Charles A Dinarello. Anti-inflammatory Agents: Present and Future**.** *Cell*. 2010;140(6):833–844.
14. Shohami E, Novikov M, Bass R, et al. Closed head injury triggers early production of TNF alpha and IL-6 by brain tissue. *J Cereb Blood Flow Metab*. 1994, 14:615–619.
15. Juergen K Mai, George Praxinos. *The human nervous system*. 3rd edition Elsevier. 2011. p. 1428.
16. Perez GM, Keyser RB. Cell Body Counts in Human Ciliary Ganglia. *Investigative Ophthalmology & II-Kawasaki A*. 1986;27(9):1428–1231.
17. A Kawasaki. Physiology, assessment, and disorders of the pupil. *Curr Opin Ophthalmol*. 1999;10(6):394–400.
18. H Stanley Thompson, Randy H Kardon. Irene Loewenfeld Ph. D. Physiologist of the Pupil. *J Neuroophthalmol*. 2006;26:139–148.
19. Izci Y, Gonul E. The microsurgical anatomy of the ciliary ganglion and its clinical importance in orbital traumas: an anatomic study. *Minim Invasive Neurosurg*. 2006;49(3):156–160.
20. Yaday UC, Kalariya NM, Srivastava SK. Protective role of benfotiamine, a fat-soluble vitaminB1 analog, in lipopolysaccharide-induced cytotoxic signals in murine macrophages. *Free Racial Biol Med*. 2010;48:1423–1434.
21. National Institute of Neurological Disorders and Stroke. *"Holmes-Adie syndrome Information Page"*. Retrieved 2008-01-21-Wikipedia. 2-Harriman DGF and Garland H: The pathology of Adie's syndrome. Brain 91:401, 1968.
22. From Alberts. *Molecular Biology of the Cell*. 2nd edn. Year introduced: 1994(MeSH-Database. 1994. p. 693–695.
23. Baud V, Karin M. Signal transduction by tumor necrosis factor and its relatives. *Trends Cell Biol*. 2001;11:372–377.
24. Aida Maddahi, Lars S Kruse, Qing-Wen Chen, et al. The role of tumor necrosis factor-α and TNF-α receptors in cerebral arteries following cerebral ischemia in rat. *J Neuroinflammation*. 2011;8:107.
25. Wajant H, Pfizenmaier K, Scheurich P. Tumor necrosis factor signaling. *Cell Death Differ*. 2003;10:45–65.
26. Arvin B, Neville LF, Barone FC, et al. The role of inflammation and cytokines in brain injury. *Neurosci Biobehav Rev*. 1996;20:445–452.
27. del Zoppo G, Ginis I, Hallenbeck JM, et al. Inflammation and stroke: putative role for cytokines, adhesion molecules, and iNOS in brain response to ischemia. *Brain Pathol*. 2000;10:95–11.
28. Liu T, Clark RK, McDonnell PC, et al. Tumor necrosis factor-alpha expression in ischemic neurons. *Stroke*. 1994;25:1481–1488.
29. Lambertsen KL, Clausen BH, Fenger C, et al. Microglia and macrophages express tumor necrosis factor receptor p75 following middle cerebral artery occlusion in mice. *Neuroscience*. 2007;144:934–949.
30. Wang X, Yue TL, Barone FC, et al. Concomitant cortical expression of TNF-alpha and IL-1 beta mRNAs follows early response gene expression in transient focal ischemia. *Mol Chem Neuropathol*. 1994;23(2–3):103–114.
31. Ali S, Mann DA. Signal transduction via the NF-kappaB pathway: a targeted treatment modality for infection, inflammation, and repair. *Cell Biochem Funct*. 2004;22:67–79.
32. Melendez RR. Importance of water-soluble vitamins as regulatory factors of genetic expression. *Rev Invest Clin*. 2003;54:77–83.
33. Lu' o" ng KV, Nguyen LT. The Role of Thiamine in Cancer: Possible Genetic and Cellular Signaling Mechanisms. *Cancer Genomics Proteomics*. 2013;10(4):169–185.
34. Shoeb M, Ramana KV. Anti-inflammatory effects of benfotiamine are mediated through the regulation of the arachidonic acid pathway in macrophages. *Free Radic Biol Med.* 2012;52:182–190.