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Quantitative Sensory Testing, A Pristine in Orofacial Pain : Review on Literature with Emphasis on Temperomandibular Disorders and Trigeminal Neuralgia

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Review Article

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ABSTRACT

The principal aim was to include as many as reports, and salient areas of those reports stating the efficacy of QST in detecting orofacial pain. The primary research question for this systematic review is “Does QST have supremacy in diagnosing the nature of orofacial pain compared to routine methods?”.

INTRODUCTION

Reckoning of pain has scored denotation in contemporary years by the virtue of assorted ascribing factors. Formerly treatment was done on a generalized axiom and priority was catered only for major conditions. Neurologic pain ensemble was treated as an exclusive entity. Now various research rostrums have steered to find out how these pains vary between every single condition. These had driven to the revelation of various pathways of pain thereby spawning a forum for actualizing treatment or diagnostic modalities that would revamp those indicated pathways in lieu of treating a condition as a whole [1]. This perception of pain based treatment modification has encased its hypothesis from the concept that each condition divulges different clinical signs and symptoms [2].

Various experimentation procedures were contrived to reckon the functions of nerves. Among which the Quantitative sensory Testing (QST) has scored denotation over the last few decennaries. This has proved to be the most decisive contraption used in reckoning the function of sensory nerves [3].

QST is based on precise definition of the stimulus attributes (modality, intensity, spatial and temporal characteristics), analysis of the quality of sensation so conjured and quantification of the intensity. It alleviates in the assessment of sensory thresholds that encompasses both the espial of threshold for a peculiar stimulus and that in accession to assessment of sensory thresholds (i.e., detection threshold for innocuous stimuli and pain threshold), QST includes the assessment of sensations conjured by supra-threshold stimuli [3]. QST also proffers an inherent advantage over other electrophysiological tests used to appraise the sensory phenomena in what respect it can intensify both decline or upsurge in sensory or pain thresholds to a stimuli and also enumerates all these idiosyncrasies [4]. The main gimmick of this approach is that it is psychophysical in temperament and it obligates reciprocity of the patient. Since every sensation is discerned in a diversified way, thus the aftermath also hinges on the subjective counter from a patient [5].

SYSTEMATIC REVIEW

The approach follows the systemic review procedure set as in case of other oral and maxillofacial lesions. The strategy was based on the research question set above.

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Search Strategy

PubMed search was made up to march 2017. We used the following MeSH terms in a Boolean search: Pain AND (Pain assessment methods) OR (Orofacial Pain) OR (Quantitative sensory testing) OR (Temporomandibular Disorders) OR (Trigeminal Neuralgia) OR (Applications of QST) AND (Pain Threshold). In addition, we targeted orofacial pain and quality of life in Temporomandibular Disorder patients using a similar strategy. The search results were imported into a computerized database e (Reference Manager Version 12). Grey literature search and reference cross check was performed to detect eligible articles that were not encountered during previous search. The search was conducted without restriction on language or the date of publication. The results so obtained by above mentioned search method were combined and duplicate publications were eliminated.

Inclusion and Exclusion

We included studies that reported basics about quantitative sensory testing, Methodology so performed, we included studies that reported orofacial pain, but not those where the location of pain was not specifically stated to be from the head and neck region.

We excluded the following publication types from the systematic review: previous systematic and non-systematic reviews; studies not reporting actual data, or data from previous publications, or if later, relevant follow-up publications were identified; phase I and II clinical studies, opinion papers, editorials and case reports; articles published before 1980. The search was limited to English language and articles from other languages were excluded. We excluded interventional studies with a focus on oral mucositis and not oral pain. We also excluded data so obtained on non-standardised grounds.

Components of QST

The quantitative Sensory System (QST) device subsists of two dissimilitude, one that implicates divulging the individual to vibratory and other thermal stimuli and the other that divulges the individual to these stimuli at specific frequencies. This is done by the two components of the device itself [5]. Vibration is a form of mechanical stimulation that has scored denotation in contemporary years in the study of various physiological and pathological conditions. It has also been hypothesized that low amplitude, high frequency vibratory stimuli is a reliable and decisive way of revamping muscle clout, body balance and mechanical dexterity of bone [6]. Appraisal this vibratory sensation abets the clinician to ascertain the plenum of mechanoreceptors in the skin as these regions are equipped by rapidly conducting large-diameter afferent fibers. Therefore any abated vibratory sensation is a decisive finding in the diagnosis of disorders affecting the dorsal column-medial leminiscial system and may proffer as sign of peripheral neuropathies [7]. These vibratory stimuli are used in QST using stimulators that releases the stimuli at a designated frequency and adjustable amplitude. The frequencies are usually perpetuated in the range of 200-300 Hz as it would be peerless to sensitize the Pacinian corpuscles. In order to stimulate both Meissner's and Pacinian Corpuscles, the frequency is fixed at 128Hz [5]. The device so handled in QST is based on the peltier principle, in which the intensity and direction of current flow curbs the surface temperature of the electrode, which is termed Thermode. The thermode is made to approximate the skin and the subject is asked to report sensation and is recorded as temperature change or heat or pain. In lieu of vibratory stimuli, electrical stimuli of variable frequency and intensity so as to determine sensory thresholds [5].

Method of Application

As intimated formerly, the patient is subjected to the effects of thermostat and is asked to report the sensation so felt. Two accustomed technique have customarily been bestowed based on the method of limits and method of levels. In the former method the patient should assert as soon as a strong stimulus is perceived which is termed as ascending ramp or as decreasing stimulus is erstwhile detected termed as descending ramp. While in the method of levels the patient is disclosed to a specific stimuli of curbed intensity level and is checked if a specific level is detected or not [5]. This method was first acquainted into clinical practice by Sekuler et al. [4]. The method of levels has a major detriment wherein the subject is forced to excerpt whether or not stimulus is felt: hence it is also referred to as a "forced choice" paradigm was used by Dyck et al. [5]. Compared to the method of limits, method of levels tends to produce more fickling results as it depends upon the rate of change of stimuli and the analogous response of the individual. This is related to the subject's reaction time. The subject needs to deliberately perceive the stimulus and process the information and should engender as action to indicate a response. The problem arises during the period of information processing where in before the subject could engender a response the stimuli conduce to increase or decrease thereby provoking a small error in threshold measurement. The response of the individual can be a binary decision task, the subject is catechized to say 'yes' or 'no' as to whether stimulus is felt or not or subject may be asked to rate the stimulus intensity on a previously recorded scale [4]. The method of limits is modified into a "Reaction time inclusive" technique whereabouts the response is independent of the speed of response. But it takes protracted time to complete and the amount of error is subjected to attention level of the subject [5] (6-9 of 5) practical performance of such a measurement encompasses a reaction time artifact which hovers insignificant for rapidly conducted sensations and it increases in value in comparably slower conducted sensations like thermal sensations. The values are higher for warming compared that of cooling. This artifact can be reduced by changing the temperature at a slower rate [4]. Simpler methods were developed which includes 'levels' '4, 2, 1'. In these methods a series of stimuli is given to the patient based on the response of the individual to the previous. Initially a stimuli of certain intensity is given,

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and the subjective response of the individual is recorded if the subject detects it then a stimulus of lower intensity is given if the subject fails to detect the stimuli then the next higher stimulus is given. Thus the process is repeated for a certain fixed number of times in direction and threshold is determined by the intensity of final stimuli. Thus these intervals between the levels can be related linearly or exponentially based on amount of differences [4].

QST Interpretation

Various factors including that of electrode size, site of stimulation and frequency and rate of change of the stimuli perturbs the sensory threshold measurements [5-11]. Reproducibility is also an important factor. There is no proper consensus on how the results can be defined. One advent is correlation techniques to compare results between separate sessions [5-13]. Another method is where in the repeatability factor "r" for which there is a 95% CI that two fortitudes made on the same subject would digress by less than "r". [5-9,14,15]. These testing methods should follow a standardized approach so as to effectuate reproducible result. The users should follow manufacturer's instructions properly and it should be evidently elucidated to the subject. The room should be reticent with nay beguilement. The test should always be done in an explicit manner and the perpetual examiner should do the follow-up testing. Not much of studies have been done so far to compare the different methods of reproducibility [5].

Applications

All these different methods of QST can be used to do the following:

1. To study the anatomic and physiologic basis of normal and pathological sensory and pain perception.

2. To detect pain syndromes clinically presenting with similar symptomatic paradigms.

3. To Perform qualitative and semi quantitative assessment of those illnesses that show poor correlation of patients' symptoms and signs with respective pathological changes, or have no obvious changes.

4. To evaluate patient's response to pharmacologic or non-pharmacologic therapeutic approaches under experimental [8].

Quantitative Sensory Testing in Oral Related Disorders

Temporomandibular disorders

Temporomandibular Disorders interpolates a fraction of disorders concerning the temporomandibular joint and the associated structure, it usually flaunts with pain, unusual sounds, locking of jaw and discomfort midst eating or chewing. TMD's is comprehensively composed of varied conditions including Myofacial Pain Dysfunction Syndrome (MPDS), Osteoarthritis, osteoarthrosis etc. [10]. The diagnosis and treatment of TMD retreats to early 19th century [10]. Thus pertinent diagnosis at the primal possible time can lead to effective treatment planning for the patient [11]. Though Prevalence rate is marked up, the varied group of patients consistently present with the solely feature, pain [10]. Various studies have also shown that patients with these symptoms may additionally endure from associated systemic conditions such as neuromuscular, vascular and mental or a consolidation of disorders. Thus, amending the treatment modalities established on the diagnosis made using various techniques and also choosing appropriate methodology plays a vital role in tailor-made treatment planning [10]. Pain in TMJ ensues due to inflammatory reaction embroiling the structures associated with it; this consecutively contributes to release of various pro inflammatory cytokines, mainly Tumor Necrosis Factor - alpha and Interleukins, which consecutively draws to articular cartilage remodeling and decadence [12]. These inflammatory mediators dynamize the nociceptors of the TMJ and escalate the release of CGRP (calcitonin gene related peptide) along with substance P release which contributes to swelling, redness and escalation of temperature, which is termed as neurogenic stimulation. Intensified Nociceptive stimulation induces central sensitization [13].

C-fibers are the first nociceptors implicated in the onslaught of central sensitization. They gravitate to conceive slow synaptic currents and monotonous stimuli and thus broaching the calcium channels for a short period of time by AMPA (α-Amino-3-hydroxy-5-methyl-4- isoxazole propionic acid) receptors. Thus, accrediting calcium ions to penetrate the cell and facilitates depolarization of wide dynamic range neurons which consecutively can counter to a large variety of stimuli. In addition to activating ionotropic receptors, glutamate and substance P also activate metabotropic receptors, so that releasing more calcium to intracellular vesicles, escalating the concentration of calcium ion and, as a result, activating protein-kinase enzymes that phosphorylate the N-methyl-D-aspartate (NMDA) receptor. Usually these NMDA receptors are impeded by magnesium ions, once these phosphorylated magnesium ions are released which opens the channel and thus allowing continuous inflow of calcium ions, consecutively causing elevated excitability of neuronal membrane, facilitation of synapses and abated inhibitory influence of dorsal horn neurons. Thus, central sensitization might coax pain in contempt of omission of pathologies or peripheral pain stimuli [12]. TMD disorders can be diagnosed by varied methods including tomography, arthroscopy, computed tomography (CT) scan and magnetic resonance imaging [10]. Various studies have shown that there is an assured relationship between clinical symptoms and various imaging methods and instruments expended, thus pain epitomizes as a guiding symptom in decision making and treatment planning [14]. Pertinent preference of diagnostic technique, which shows a positive correlation as of the clinical symptom, is very much important [15]. Radiographic technique which was interpreted to be the conventional method was introduced in clinical practice by Schueller.

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The idiopathic evaluation was by dynamic imaging using open and shut mouth images. Subsequently various modifications were developed like oblique projections and posterior anterior craniogram but the above mentioned were meager to show the soft tissue change and floundered to correlate with clinical symptom [16]. Ultrasonography intrinsically has three major fields of interest in TMJ, which includes assessment of disk position abnormalities, joint effusion and bone pathologies. But determining the disk position fundamentally cannot aid in treatment planning [17]. Diagnostic accuracy of posturography successively varies between various methodologies so used, few tends to show a positive correlation with disease condition set side by side to that of other [18]. Arthrography is a method in which injection of contrast media is used with pre-articular or transmeatal puncture site so as to visualize the internal joint structures. This technique is used as an adjuvant to other diagnostic techniques in case where internal TMJ imaging was impossible by other methods. The ambit of risk and discomfort endured by the patient eclipses the diagnostic information so procured from arthrography [19]. Magnetic Resonance Imaging (MRI) is one of the golden imaging methods for descrying the heterogeneous group of TMD's. Westesson et al. had shown the diagnostic veracity of MRI in fresh autopsy to be 95% and 93% in estimating the disc position and bone status. For patients without disc displacement with synovial involvement obliges contrast enhanced imaging technique due to its ineptitude to show the synovial thickening. Thus MRI also flounders to diagnose the condition in the early stages [20]. Innumerous amount of studies have been done so far to test the accuracy of MRI but these exhibited no clear evidence of relationship between clinical and MR findings [14]. According to Bell et al. TMD'S is a term used to chronicle all functional brawl associated with masticatory muscles. Electromyography (EMG) is the study of muscle function through scrutiny of the electrical signals produced during muscular contractions. But there is no scientific evidence to prove the efficacy of EMG in diagnosing TMD's [21].

The former mentioned methods contribute to show very limited correlation with the pain factor which consecutively acts as a driving force and decision dynamic in treatment planning. QST holds an upper hand in this sector which persists as a lacunae unfilled by other diagnostic methods. Efficacy of QST in studying the somatosensory profile for some body parts such as hand; foot and face have heretofore been established [22]. The chronic nature and sensitization of TMD pain is bordered on by using Quantitative sensory testing. It commences with the assessment of positive and negative somatosensory signs and symptoms in relation to the ambit of pain so experienced by the patient which is the first step towards understanding pain profile of the patient [23]. As for TMJ Standardized battery of QST was compiled according to the protocol of German Research Network on Neuropathic Pain (DFNS). The QST battery encompasses of 7 tests measuring 13 parameters that cover germane nerve function [24]. In summary, the protocol investigates the following sensory functions: Thermal thresholds: cold detection (CDT), warmth detection (WDT), cold pain (CPT), heat pain (HPT), and thermal sensory limen (TSL); Mechanical thresholds: mechanical detection (MDT), vibration detection (VDT), mechanical pain (MPT), and pressure pain (PPT); Stimulus response functions: mechanical pain sensitivity (MPS), dynamic mechanical allodynia (DMA), windup ratio that is pain summation to repetitive pinprick (WUR), and paradoxical heat sensations (PHS) during the TSL procedure [2]. QST is usually performed on the skin overlying the TMJ on both the sides [24]. Studies have shown that patients with Temporomandibular Disorders (TMDs) have limited thermal pain threshold, ischemic pain threshold and ischemic pain tolerance values not only near the jaw but also at the distal extremities. In TMD patient's thermal pain tolerance also tends to be limited. These patients also show increased thermal C-fiber-mediated temporal summation in contrast with pain-free individuals [8]. Conclusively somatosensory abnormalities were commonly detected in TMD pain patients denoting the major role of central sensitization in the pathophysiological mechanism leading to onset or perpetuation TMD pain.

Trigeminal Neuralgia

The characteristic feature of Trigeminal Neuralgia (TN) is unilateral pain attacks that lingers for few minutes, exhibiting as sharp, shooting, lancinating, electric shock-like, burning and excruciating pain. The attack usually is initiated by non-physical stimulation of specific areas or trigger zones which are located in the ipsilateral area. There also prevails a refractory period between successive attacks. This consecutively depends upon the individual's susceptibility and sensitivity [25]. Earlier methods of pain evaluation in neurological literature confided on a composite scale of pain, Visual Analog Scale (VAS). Composite scales have been useful because they have obliged some grade of standardization across treatment modalities, but their reliability and validity have not been tested assiduously [26]. QST seems to be more reliable method in estimating the sensitization levels. Various small QST studies have shown that patients gravitate to have elevated thresholds for touch and thermal detection and declining thresholds for thermal and mechanical pain [27]. According to a study done by Younis et al they have found escalated mechanical detection threshold in the symptomatic side vs. asymptomatic side. Thermal and mechanical hyperalgesia was detected bilaterally both in the face and the hand. Thus, they had shown that trigeminal neuralgia patients with no sensory abnormalities at neurological examination had generalized subclinical hypoesthesia, which contributes to be more pronounced on the symptomatic side. This could indicate pain induced hypoesthesia and sensitization induced by central mechanisms [27].

CONCLUSION

Diagnosing the sensory nerve damage and formulating a tailor-made treatment plan for each patient is at times challenging which the QST eases out. Though QST excels in estimating the pain threshold levels in case of neuropathic pain, its guise in

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defining the mechanism is yet to be completed. The ultimate aim to conclude the direct relationship between the clinical symptom and pain so experienced is hitherto being proved. Thus, impending studies should aim to comprehend the relationship betwixt somatosensory profile, clinical symptom, pain pathways and importantly the etiological factor which controls the rest.

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