Original Article

The Probity of Conditioned Pain Modulation (CPM) in Patients with Myofascial Pain Syndrome - Clinical Study

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Abstract

Purpose: Abstract Introduction: Temporomandibular joint disorders can affect the temporomandibular joint and/or the surrounding muscle component. Many theories were provoked to explain the pathophysiology of its chronic pain. Impaired endogenous pain modulation mechanism theory is considered one of the most widely accepted explanations of the pain controlling theories. Conditioned pain modulation can be considered as reliable test to assess the pain inhibits pain phenomena, which represents the inhibitory component of the endogenous pain modulating mechanism. Aim: To evaluate the integrity of endogenous analgesia in patients suffering from muscular pain related to myofascial pain dysfunction syndrome. Patients and methods: Fifteen patients were recruited in this study. Trigger points in the masseter muscle were identified and the pain rate was recorded after applying manual pressure on these trigger points. A cold pressor test was then performed, and the pain rate was recorded again. Results: There wasn't a statistically significant difference between the mean value of test pain stimulus scored by the patients before and after performing the cold pressor test (P value 0.0961). Conclusion: The results of this study showed that the endogenous pain inhibitory system is impaired in temporomandibular joint disorders patients, however further studies are recommended.

Keywords: Conditioned pain modulation, Temporomandibular disorders, Myofascial pain

I. INTRODUCTION

Temporomandibular disorders (TMDs) is a general term used to describe a wide array of painful conditions that affect the TMJ and/or surrounding muscles (Trindade et al., 2021). Ranked only second to toothache, TMDs are considered to be one of the most common forms of orofacial pain, yet its pathophysiology represents an unsolved mystery that stands as a major obstacle to find the optimal method for its treatment or even predicting its prognosis (Moana-Filho, Babiloni and Theis-Mahon, 2018). To understand the pathophysiology of TMD induced pain, various hypotheses were proposed, one of these hypotheses suggests that patients with chronic pain may suffer from an impaired endogenous pain modulation mechanism (EPMM). EPMM is a term with wide range, describing the reaction of the central nervous system toward pain. This reaction can be translated to pain inhibition or pain augmentation (Harper, Schrepf and Clauw, 2016) (Sarlani and Greenspan, 2005) (Millan, 2002). Two pain controlling pathways were recognized throughout literature; top to bottom pathway in which the brain transmits pain messages to the brainstem and bottom to top pathway in which spinal cord and peripheries send messages to the brainstem pain control centers. The bottom to top pathway was figured out as the pain-inhibits –pain phenomena. Throughout literature the animal application of this phenomena was given a term "diffuse noxious inhibitory controls," abbreviated as DNIC however term "conditioned pain modulation" (CPM) was given to human protocols that evaluate the human DNIC-like phenomena (Yarnitsky, 2015).

Conditioned pain modulation (CPM) is a reliable method to assess the integrity of endogenous analgesic which is the term used to distinguish the inhibitory component of the EPMM. The core of CPM relay on the face that "pain inhibits pain" thus applying a painful (conditioning) stimulus will amend a second painful (test) stimulus (Oono et al., 2014).

The aim of this study was to evaluate the integrity of endogenous analgesia in patients suffering from muscular pain related to myofascial pain dysfunction syndrome.

II. PATIENTS AND METHODS

This was a study that was performed at the oral and maxillofacial surgery department, Faculty of Dentistry, Cairo University, on 15 patients all recruited from the department's outpatient clinic. Patients' ages were ranging between 32 and 58 with a mean of 43.7 \pm 8.9 years at the time of the study. In order to be enrolled in this study, all selected patients have met the following inclusion criteria:

- Suffered from unilateral myofascial pain related to the masseter for the last 3 years.
- Free from any orofacial pain of joint origin.

- Free from any previous or current injuries &/or medical conditions that may affect normal pain perception.
- Should not have done any dental procedures during the week prior to the study.

The diagnosis of myofascial pain was performed based on the diagnostic criteria of disorders temporomandibular (DC/TMD) (Schiffman et al., 2014) that defined myofascial pain as the muscular pain that can be modified by jaw function and that radiates within the boundaries of the involved muscle following palpation. Before performing the study, informed consents were obtained from the patients after explaining the nature, steps and aim of the study to them in clear words. The study design was reviewed and approved by the ethical and research committee at Cairo university.

A. Conditioning stimulus

The cold pressor test was performed according to Kennedy's recommendations (Kennedy et al., 2016). All patients were asked to immerse their preferred foot into a bowl filled with cold water with a temperature of 10 degrees Celsius for 2 minutes (figure 1).

B. Test stimulus

During patients recruiting phase, the masseter muscle of each patient was divided into 9 equal small squares (figure 2), manual examination was performed to each single square to locate the site of the trigger point in each patient. After checking the square containing the trigger point, it was recorded in the patient's file for later use.

At the time of study set-up, digital pressure (test stimulus) was applied by the examiner index finger to the pre-determined trigger point containing square. The patients were asked to rate the pain they felt as a result of this digital pressure on a visual analogue scale (VAS) ranging from 0 to 10 with zero indicating no pain while 10 indicates the worst imaginable pain. For standardization, clinical examination and test stimulus were performed by the same examiner. Test stimulus was performed before applying the conditioning stimulus (baseline pain) and repeated 15 minutes following conditioning stimulus (conditioned pain).

C. Statistical analysis

SPSS12 (Statistical Package for the Social Sciences - IBM Corp., Armonk, NY) was used to perform statistical analysis. Data of the test stimulus pain level were represented as mean \pm standard deviation. Variables between

the two sets (before and after cold pressor test) were compared with each other using paired ttest. If the p-value was less than 0.05, the results were statistically significant.

III. RESULTS

The mean value of test pain stimulus scored by the patients before and after performing the cold pressor test were 6.0 ± 0.85 and 5.67 ± 0.72 respectively (figure 3) The difference between the two groups was statistically insignificant (P value 0.0961) as shown in table 1.

 Table (1): Table 1 showing descriptive statistics and comparison between baseline and conditioned pain levels. (Paired t-test)

VAS	Mean	95% confidence interval	P-value
Baseline pain	6.0 ± 0.85		0.0961
Conditioned pain	5.67 ± 0.72		
Significance level	P>0.05, *insignifican	t	



Figure (1): Patient immersing his leg in cold water (Conditioning stimulus).



Figure (2): Master muscle divided into 9 equal squares.

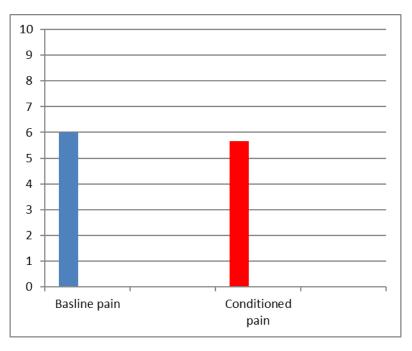


Figure (3): Bar chart showing the mean of test stimulus pain values before and after cold pressor test (Baseline versus conditioned pain levels)

IV. Discussion

Temporomandibular disorders were associated with chronic pain in 15% of the cases, this pain is the main reason why these patients seek medical help owing to its devastating impact on their daily activities such as eating and talking (Moana-Filho, Babiloni and Theis-Mahon, 2018). The presence of trigger point is considered a diagnostic feature for myofascial pain. Since the 1950s and despite the on-going improvements in diagnostic aids yet manual palpation of the involved muscle is still considered the gold standard in locating the trigger points (Shah et al., 2015), (Do et al., 2018).

The chronicity of TMD induced pain that does not correlate well with peripheral pathology promoted the scientists to assume that TMD is associated with somatosensory abnormalities concerning the abolished ability of the CNS to suppress pain via endogenous pain modulation (EPM) (Harper, Schrepf and Clauw, 2016). EPM is the process through which the CNS can either facilitate or inhibit the perception of peripheral painful stimulation (Arendt-Nielsen et al., 2018). The ability of CNS to inhibit pain perception can be evaluated by using conditioned pain modulation (Yarnitsky, 2010), (Kothari et al., 2015).

The rationale of CPM techniques depends on the evaluation of painful test stimulus both before and after (or during) the application of another conditioning painful stimulus (Yarnitsky et al., 2010). In healthy subjects with an intact endogenous inhibitory pain pathway, the use of the conditioning stimulus will result in a marked reduction in pain perception of the test stimulus (Kennedy et al., 2016).

Although the cold pressor test is widely used in the literature as a reliable conditioning stimulus yet there are concerns regarding its repeatability. (Granovsky et al., 2016), (Oono et al., 2011) In an attempt to standardize the technique, Kennedy et al recommended performing the cold pressor test using water ranging from 8 to 12 degrees for 2 minutes (Kennedy et al., 2016). Using these parameters is expected to enhance the repeatability of cold pressor test as all patients will be able to tolerate it ensuring a uniform application of the conditioning pain stimulus to all the patients.

It's also worth mentioning that once the inhibitory pain pathway is activated by a conditioning stimulus of an adequate strength, it will reach a ceiling level thus any increase in the intensity of the conditioning stimulus will have no effect on the efficiency of endogenous pain modulation (Granot et al., 2008).

In this current study, the efficiency of the endogenous inhibitory pain pathway was evaluated in TMD patients suffering from myofascial pain using cold pressor test Kennedy's following recommendations. (Kennedy et al., 2016) The test stimulus used in this study was applying digital pressure to the patient's trigger point located in their masseter muscle. Test stimulus was applied shortly after the application of conditioning stimulus to avoid the bias of distraction (Yarnitsky et al., 2015). The results of this study showed that in TMD patients, the endogenous pain inhibitory system appears not to be working efficiently as there was no statistically significant difference

between the baseline and conditioned pain levels (6 and 5.67 respectively, p value 0.096).

This result is consistent with the results of several studies that showed a marked impartment in the endogenous inhibitory pathway in patients suffering from chronic pain conditions such as irritable bowel syndrome, tension headache and migraine (Moana-Filho, Babiloni and Theis-Mahon, 2018), (Lewis, Rice and McNair, 2012). Interestingly a similar study was conducted to evaluate the integrity of the endogenous analgesia in TMD patients (Oono et al., 2011), yet in that study two test stimuli were applied to the patient, one of this stimuli was applied in the trigeminal region while the other one was applied in an extratrigeminal region, the result of that study showed that although the endogenous pain inhibition was not efficient in the trigeminal area, yet normal endogenous pain inhibitory effect was noticed in the extra-trigeminal segment.

In an attempt to explain these findings, Oono et al., postulated that the localized impartment of condition pain modulation in TMD patients can be attributed to abnormalities concerning the transmission and processing of painful stimuli in the trigeminal nucleus rather than a generalized impartment of the CNS ability to inhibit pain via endogenous analgesia (Oono et al., 2011). In addition to this explanation, the authors would like to shed light in this paper on another possibility, that the localized poor conditioned pain modulation noticed in the pain area may be attributed to the increased cytokine mediated sensitivity of pain receptors located in the involved muscles (Staud, 2013).

V. CONCLUSIONS

Within the limitations of this study, the results of this study showed that the endogenous pain inhibitory system is impaired in TMD patients, however further studies are needed to investigate the cause of such finding.

VI. REFERENCES

- Arendt-Nielsen, L. et al. (2018) 'Assessment and manifestation of central sensitisation across different chronic pain conditions', European Journal of Pain, 22(2), pp. 216–241. doi: 10.1002/ejp.1140.
- Do, T. P. et al. (2018) 'Myofascial trigger points in migraine and tension-type headache', The journal of headache and pain. The Journal of Headache and Pain, 19(1), p. 84. doi: 10.1186/s10194-018-0913-8.
- Granot, M. et al. (2008)'Determinants of endogenous analgesia magnitude in a diffuse noxious inhibitory control (DNIC) paradigm: Do conditioning stimulus painfulness, gender and personality variables matter?', Pain, 136(1-2), 142-149. doi: pp. 10.1016/j.pain.2007.06.029.
- Granovsky, Y. et al. (2016) 'CPM test-retest reliability: "standard" vs "single test-stimulus" protocols', Pain Medicine, 17(3), pp. 521–529. doi: 10.1111/pme.12868.
- Harper, D. E., Schrepf, A. and Clauw, D. J. (2016) 'Pain Mechanisms and Centralized Pain in Temporomandibular Disorders', Journal of Dental Research, 95(10), pp. 1102–1108. doi: 10.1177/0022034516657070.
- Kennedy, D. L. et al. (2016) 'Reliability of conditioned pain modulation: A systematic review', Pain, 157(11), pp. 2410–2419. doi: 10.1097/j.pain.00000000000689.
- Kothari, S. F. et al. (2015) 'Somatosensory assessment and conditioned pain modulation in temporomandibular disorders pain patients', Pain, 156(12), pp. 2545– 2555. doi: 10.1097/j.pain.00000000000325.

- Lewis, G. N., Rice, D. A. and McNair, P. J. (2012) 'Conditioned pain modulation in populations with chronic pain: A systematic review and meta-analysis', The Journal of Pain. Elsevier Ltd, 13(10), pp. 936– 944. doi: 10.1016/j.jpain.2012.07.005.
- Millan, M. J. (2002) 'Descending control of pain Mark', Progress in Neurobiology 66, 66(6), pp. 355– 474. doi: 10.1016/s0301-0082(02)00009-6.
- Moana-Filho, E. J., Babiloni, A. H. and Theis-Mahon, N. R. (2018) Endogenous pain modulation in chronic orofacial pain: A systematic review and meta-analysis, Pain. doi: 10.1097/j.pain.000000000001263.
- Oono, Y. et al. (2011) 'The inter- and intra-individual variance in descending pain modulation evoked by different conditioning stimuli in healthy men', Scandinavian Journal of Pain. Elsevier B.V., 2(4), pp. 162–169. doi: 10.1016/j.sjpain.2011.05.006.
- Oono, Y. et al. (2014) 'Conditioned pain modulation in temporomandibular disorders (TMD) pain patients', Experimental Brain Research, 232(10), pp. 3111– 3119. doi: 10.1007/s00221-014-3997-7.
- Sarlani, E. and Greenspan, J. D. (2005) 'Why look in the brain for answers to temporomandibular disorder pain?', Cells Tissues Organs, 180(1), pp. 69–75. doi: 10.1159/000086200.
- Schiffman, E. al. (2014)et 'Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial

Pain Special Interest Group†', Journal of Oral & Facial Pain and Headache, 28(1), pp. 6–27. doi: 10.11607/jop.1151.

- Shah, J. P. et al. (2015) 'Myofascial trigger points then and now: A historical and scientific perspective', PM R. Elsevier Ltd, 7(7), pp. 746–761. doi: 10.1016/j.pmrj.2015.01.024.
- Staud, R. (2013) 'The important role of CNS facilitation and inhibition for chronic pain', International Journal of Clinical Rheumatology, 8(6), pp. 639–646. doi: 10.2217/ijr.13.57.
- Trindade, D. et al. (2021) 'Biological treatments for temporomandibular joint disc disorders: Strategies in tissue engineering', Biomolecules, 11(7), p. 933. doi: 10.3390/biom11070933.
- Yarnitsky, D. (2010) 'Conditioned pain modulation (the diffuse noxious inhibitory control-like effect): Its relevance for acute and chronic pain

states', Current Opinion in Anaesthesiology, 23(5), pp. 611– 615. doi:

10.1097/ACO.0b013e32833c348b.

- Yarnitsky, D. et al. (2010)'Recommendations on terminology and practice of psychophysical DNIC testing', European Journal of Pain. European Federation of International Association for the Study of Pain Chapters, 14(4), p. 339. doi: 10.1016/j.ejpain.2010.02.004.
- Yarnitsky, D. et al. (2015) 'Recommendations on practice of conditioned pain modulation (CPM) testing', European Journal of Pain (United Kingdom), 19(6), pp. 805– 806. doi: 10.1002/ejp.605.
- Yarnitsky, D. (2015) 'Role of endogenous pain modulation in chronic pain', Pain, 156(4), pp. 24– 31. doi: 10.1097/01.j.pain.0000460343.4684 7.58.