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**In the**

**Salivary cortisol changes in dental student suffering myofascial pain**

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**بسم الله الرحمّن الرحيم**

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**Dedication:**

This research is dedicated to the countless individuals who have contributed to the field, from the pioneers who laid its foundation to the scholars who continue to push its boundaries. It is also dedicated to the participants who generously shared their time, experiences, and insights, without whom this study would not have been possible.

Lastly, We would like to dedicate this research to our families, friends, and loved ones who have supported us throughout this journey. Their encouragement, patience, and unwavering belief in us have been our pillars of strength.

**Abstract:**

Myofascial pain dysfunction syndrome (MPDS) is a prevalent condition among dental students, impacting their well-being and academic performance. Aiming to investigate salivary cortisol changes in dental students suffering from MPDS, as elevated cortisol levels have been associated with chronic stress and pain.

Studies showed a significant increase in salivary cortisol levels for dental students suffering from Myofascial pain dysfunction syndrome (MPDS).

These findings indicate that dental students suffering from MPDS display abnormal salivary cortisol patterns, reflecting hypothalamic-pituitary-adrenal axis dysregulation. This altered cortisol profile may contribute to the perpetuation of MPDS symptoms and potentially affect students' overall health and academic performance.

Understanding the underlying physiological mechanisms and the connection between cortisol dysregulation and MPDS among dental students can provide valuable insights into developing effective interventions to alleviate symptoms and reduce the impact of chronic pain and stress on their overall well-being.

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**Introduction**

**Myofascial pain dysfunction syndrome (MFPS):** is described as the sensory, motor, and autonomic symptoms caused by trigger points (TrPs). TrP is a hyperirritable spot in skeletal muscle or fascia that is associated with a hypersensitive palpable nodule in a taut band. The spot is painful on compression and can give rise to characteristic referred pain, referred tenderness, motor dysfunction, and autonomic phenomena. The best available evidence supports that TrPs develop after muscle overuse. Several potential mechanisms may play a role, such as eccentric overload, submaximal sustained, and (sub)-maximal concentric contractions. TrPs have been classified as “active” (producing a clinical pain complaint) or “latent” (non-symptom producing but tender on palpation).

**Salivary cortisol:** Cortisol is a steroid hormone that adrenal glands, the endocrine glands on top of the kidneys, produce and release. Cortisol affects several aspects of the body and mainly helps regulate the body's response to stress. Cortisol levels can be measured through various bodily fluids, such as blood, urine, and saliva. Saliva collection has gained prominence due to its non-invasive nature, ease of sampling, and the ability to obtain multiple samples over time, allowing researchers to track cortisol diurnal patterns and stress responses. Saliva also provides a more accurate reflection of the biologically active "free" cortisol compared to cortisol bound to proteins in the blood. the measurement of salivary cortisol has gained significant attention as a reliable and non-invasive biomarker for assessing stress levels in both research and clinical settings.

**Roles of Salivary Cortisol in Myofascial Pain Dysfunction Syndrome:** Salivary cortisol has been increasingly recognized as a non-invasive and reliable biomarker for assessing the hypothalamic-pituitary-adrenal (HPA) axis activity, providing insights into the role of stress in various pain disorders, including MPDS.

Chapter One

**Myofascial pain syndrome (MFPS)**

Myofascial pain syndrome (MFPS) is described as the sensory, motor, and autonomic symptoms caused by trigger points (TrPs). TrP is a hyperirritable spot in skeletal muscle or fascia that is associated with a hypersensitive palpable nodule in a taut band. The spot is painful on compression and can give rise to characteristic referred pain, referred tenderness, motor dysfunction, and autonomic phenomena**.(Simons DG.,1999)** The best available evidence supports that TrPs develop after muscle overuse. Several potential mechanisms may play a role, such as eccentric overload, submaximal sustained, and (sub)-maximal concentric contractions. A key factor is thought to be local ischemia, which leads to an acidic pH and subsequent release of several inflammatory mediators in muscle tissue. **(Schiffman E, et al.,2011)**. TrPs have been classified as “active” (producing a clinical pain complaint) or “latent” (non-symptom producing but tender on palpation). Psychological stress, muscle tension and physical factors, such as poor posture, can cause a latent TrP (taut band formed in the muscle belly) to become active, causing the pain. Prior studies of clinic populations found that MFPS was cited as the most common cause of pain, responsible for 54.6% of chronic head and neck pain4 and 85% of back pain.5 Another study, in a general internal medicine practice, found that among those patients that presented with pain, MFPS was found in 29.6% of the population and was the most common cause of pain.5 In spite of the high prevalence of MFPS, many cases are either misdiagnosed or missed due to lack of awareness of soft tissue disorders such as MFPS, which require special palpation skills which are rarely taught in the undergraduate and post graduate medical curriculum. Some healthcare professionals feel that these conditions are controversial, difficult to diagnose by objective tests/imaging or untreatable and hence make no attempt to diagnose or treat these conditions. Everyone, at some point in their lives, has experienced acute muscle pain associated with muscle spasm or repetitive strain. However, when acute pain becomes chronic, patients and their healthcare providers can become confused and overlook the muscle as a cause in favor of treating other conditions, particularly joint pathology or what is visible in the imaging studies. This lack of understanding leads to misdiagnosis and mistreatment and progression of an acute problem to chronic pain. Then, the behavioral and psychological components of chronic pain become misunderstood, and then some may assume that the patient's experience of pain is either imagined or exaggerated. Thus, the principles of etiology, diagnosis, and management of MFPS are relevant for all healthcare providers. **(Simons DG.,1999), (Schiffman E, et al.,2011)**

**1.1 Epidemiology**

Understanding the epidemiology of MPDS is crucial for implementing targeted preventive measures and developing effective management strategies.

* Prevalence of MPDS:

The prevalence of MPDS varies across different populations and age groups. Studies have reported a wide range of prevalence rates, with estimates ranging between 7% and 85%. These discrepancies can be attributed to variations in diagnostic criteria, study designs, and populations studied. MPDS appears to be more common in females, with some studies suggesting a female-to-male ratio as high as 9:1.

* Risk Factors for MPDS:

Several risk factors have been identified for the development of MPDS. These include age, gender, occupation, psychological factors, trauma, and comorbid conditions. Advanced age has been associated with a higher prevalence of MPDS, with the risk increasing after the fourth decade of life. Women are more susceptible to MPDS, possibly due to hormonal factors, anatomical differences, or psychosocial factors.

Occupational factors, such as repetitive movements, prolonged static postures, and high job demands, have been linked to an increased risk of developing MPDS. Psychological factors, including high levels of stress, anxiety, and depression, have also been identified as potential risk factors. Moreover, a history of trauma, such as whiplash injuries or musculoskeletal trauma, has been found to increase the likelihood of developing MPDS.

* Comorbidities Associated with MPDS:

MPDS is frequently associated with various comorbid conditions, further complicating its clinical presentation and management. Temporomandibular joint disorders, tension-type headaches, and fibromyalgia are commonly reported comorbidities among MPDS patients. Additionally, psychiatric conditions, such as anxiety disorders and depression, are often observed in individuals with MPDS. The presence of these comorbidities can exacerbate pain symptoms and contribute to a poorer quality of life.

**(Kalichman L., 2011 May)**

The condition is more prevalent among middle-aged adults, although it can also affect young adults and children. Studies suggest that psychosocial factors, such as stress, anxiety, and depression, may contribute to the development and progression of MPDS.

**(Schiffman E, et al.,2014])**

**1.2 Etiology**

There are multiple etiological factors for MPDS [Table1]. According to the psychophysiological theory, muscle spasm is a factor for myofascial pain dysfunction syndrome. Emotional factors are the primary etiological factors in stimulating chronic oral habits that produce muscle fatigue. Some complain of the pain immediately following a long dental appointment or the extraction of mandibular third molars. The presynaptic, synaptic and postsynaptic mechanisms of abnormal depolarization (i.e. excessive release of acetylcholine (Ach), defects of acetylcholinesterase and upregulation of nicotine Ach-receptor activity, respectively) have been proposed to be the possible etiological mechanisms.

**Table1.** Etiology & Pathophysiology of MPDS

|  |
| --- |
| **Etiology & Pathophysiology of MPDS** |
| **Etiology:**   Occlusal disturbances   Intracapsular disorders   Emotional turmoil   Direct or indirect trauma   Spine pathology   Psychogenic influences like stress and strain   Habits like bruxism  **Pathophysiology:**   Injury to muscle fiber type I   Metabolic distress at the motor end plates   Activation of muscle nociceptors   Transmission of pain to the CNS.2 |

**(Arora, et al.,2015)]**

The unifying concept proposed by Lermank - holds that MPDS results from the interplay of an unbroken chain of etiological factors. The psychologic factors leads to an overall increase in masticatory muscle activity, while other factors such as occlusal and anatomic lead to selective increase in muscle activity (Flow chart 1).

Myofascial trigger points requires a self- sustaining positive feed-forward process. Simons presented the integrated hypothesis for myofascial trigger points to offer an explanation for the same. It is a six- link chain starting with the abnormal release of acetylcholine which causes increased muscle fiber tension, seen as the taut band found in a myofascial trigger point. This taut band constricts the blood flow that leads to local hypoxia. The reduced oxygen disrupts mitochondrial energy metabolism thereby reducing ATP and leading to tissue distress, release of sensitizing substances. The activation of nociceptors (pain receptors) causes pain and also lead to autonomic modulation which potentiates the abnormal acetylcholine release (Flow chart 2).



**Flow chart 1.** Lermank Pathophysiology



**Flow chart 2.** Pathophysiology of MPDS by Simons

The development of trigger point is considered to be one of the most important characteristic feature of MPDS.Trigger points are small exquisitely tender areas, which causes pain to the distant region, called the Referred Pain Zone. They are activated by pressure, movement, change of barometric pressure and tension (physical or emotional). Trigger points differ from “Tender spots” (TS’s) in the sense that the pain of TS’s are localized in the vicinity of the spot while trigger point pain refers to a distant area. However, the treatment of trigger points and TS’s are exactly the same. **(Reji R, et al., 2017)**

**1.3 Clinical presentation**

**\*TAUT BAND**

It is the group of tense muscle fibres extending from a trigger point to the muscle attachments, the tension being caused by contraction knots that are located in trigger point region.

Clinically MPDS is usually associated with unilateralpain [Table 2]. In some cases, pain can be bilateral but it need not be symmetrical. The quality or character of the pain reported by the patient most often will fall into three gross categories:

* Category I: A dull-aching pain,
* Category II: A sharp-shooting pain (burning), and
* Category III: A tight-drawing sensation.

**(Arora, et al.,2015)**

**Clinical features of MPDS**

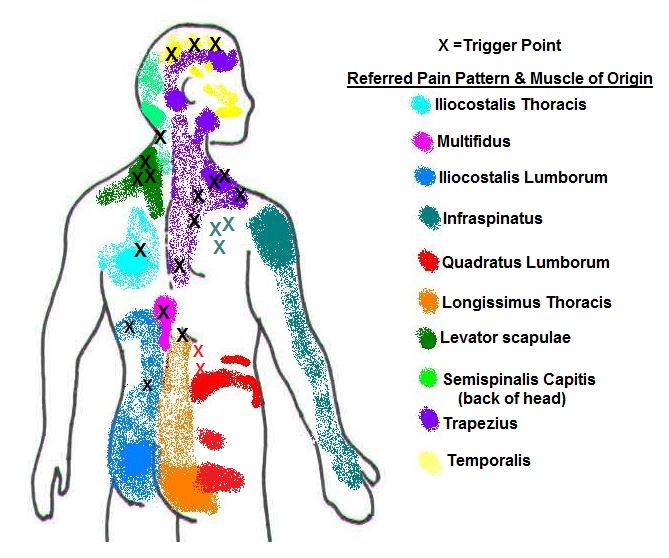
1. TMJ sounds
2. Impaired or irregular mandibular movement
3. Limitation in mouth opening
4. Preauricular pain
5. Facial pain
6. Headaches
7. Jaw tenderness on function.

**(Arora, et al.,2015)**

* The pain found with MFPS is frequently described as a “chronic dull aching pain” and is associated with muscle and soft tissue tenderness.
* The mildest symptoms are caused by latent TrPs, which cause no pain but cause some degree of functionnal disability and stiffness.
* More severe involvement results in pain related to the position or movement of the muscle, whereas the most severe level involves pain at rest.
* There is usually a history of spontaneous pain associated with acute overload or chronic overuse of the muscle.
* Knowledge of TrP referral patterns is essential in the evaluation of a patient (Fig. 1).When the upper trapezius TrP is active the patient usually has severe posterolateral neck pain that is often constant and is associated with temporal headache on the same side.
* Occasionally pain is projected to the angle of the jaw. With very active upper trapezius TrP and with additional involvement of levator scapulae or splenius cervicis muscles, the patient may develop an acute stiff neck.
* The typical symptoms of MFPS vary according to the site and referral pattern.
* TrPs may be considered in the differential diagnosis of various conditions.
* TrPs may be associated with autonomic phenomena resulting in many symptoms suggestive of visceral diseases.
* Autonomic effect zones are not necessarily the same as pain referral zones.

They include excessive lacrimation, pilomotor activity, excessive sweating, and redness around the TrP area, distorted proprioception and local edema.

**(Simons DG, Travell JG.,1999).**



**FIG.1** comprehensive list of trigger points and their pain referral patterns

**Symptoms of MFPS**

* Regional pain in the neck, shoulders, upper extremities,
* face, low back and lower limbs
* Referred pain
* Burning sensation
* Tenderness of the involved muscle
* Poor sleep
* Swelling
* Fatigue
* Paresthesia
* Decreased range of motion at the joints which themuscle crosses
* Weakness of certain movements and muscularImbalances
* Secondary depression, sleep disturbances

**(Simons DG, Travell JG.,1999).**

**Differential diagnosis of MFPS**

* Tension headaches
* Migraine and cluster headaches
* Low back syndromes
* Pelvic pain
* Intermittent claudication
* Bursitis, arthritis, tendinosis

**(Simons DG, Travell JG.,1999).**

**1.4 Diagnosis**

**Essential Diagnostic Criteria for TrPs8 are as follows:**

A tender point within a taut band of skeletal muscle

Patient's recognition of current pain complaint by pressure on the tender nodule (identifies active TrP)

Painful limit to full passive stretch range of motion.

**(Simons DG et al., 1999)**

**Following observations help to diagnose MFPS when trigger points are identified on palpation:**

Visual or tactile identification of local twitch response

Observation of a local twitch response induced by needlepenetration of a tender nodule

Pain or altered sensation (in the distribution expected froma TrP in that muscle) on compression of a tender nodule

Attempts to identify the TrPs have not been uniformly successful. The tests are not done routinely in the clinic setting. Electromyographic demonstration of spontaneous electrical activity characteristic of active loci in the tender nodule of a taut band, needle electromyography, ultrasound imaging, IR Spectroscopy, MR Elastography and surface electromyography are some of the experimental modalities used in identifying the TrPs.

**(Simons DG et al., 1999)**

**LASKIN’S DIAGNOSTIC CRITERIA**

Laskin has proposed 4 cardinal signs and negative characteristics for MPDS.

1) Four cardinal signs

* Unilateral pain
* Muscle tenderness
* Clicking or propping noise in the TMJ
* Limitation of jaw movement

2) Negative characteristics

* No radiographic evidence
* No tenderness in TMJ area on palpation via the external auditory meatus

**(Anitha A. et al.,2016)**

**1.5. Treatment**

The usual care for MPS includes medication (painkillers, low dose anti-depressants, anti-epileptics), splints, collars, rest (do not use the painful body part as long as it hurts), physiotherapy (mainly ultrasound, interferential therapy, short wave diathermy, traction and strengthening), a wide array of complementary therapies, psychological counseling, and encouragement to “live with it” and “manage the pain.” However this approach appears sub-optimal. It is commonly seen that if a patient with a localized MPS is followed over years and if the problem is not effectively treated or resolved early enough the pain starts to spread outside the region of origin of pain.When acute pain becomes chronic, it often results in missed work, disability, and significantly high cost of care.Half of the persons seeking care for pain conditions still have pain 5 years later, and up to 25% of themreceive long-term disability. The emphasis should be given to early, accurate diagnosis of the MPS by physicians skilled in manual musculoskeletal medicine, followed by intensive, protocol based,

multidisciplinary rehabilitation. The emphasis would be on direct therapy to muscles through counter-stimulation to desensitize the soft tissues, using myofascial release and manual therapies and reduction of all contributing factors that strain the muscle(s) and heighten peripheral and central sensitization and to prevent acute MFPS from becoming chronic. Patients in chronic pain due to MPS are best served by aggressive and sometimes inpatient rehabilitation for several hours a day lasting several months by an experienced, multidisciplinary medical and rehabilitation team. This is rarely achieved by psychological approaches alone. Focus on central sensitization alone is inadequate and peripheral sensitization must be expertly and urgently addressed to ensure meaningful recoveries. Using these principles, we have published high success rates at making patients with MFPS free of symptoms and return to full time, productive work. We have validated a prognostic score to determine the severity and prognosis of musculoskeletal disorders such as MFPS and a practical protocol to treat MFPS. Unfortunately, patients with complicated, chronic pain with neuropathic pain often need intensive rehabilitation for up to 6 months and sometimes more. In contrast, acute onset localized MFPS can usually be completely and permanently resolved within few weeks.

Eventually, MFPS is not uncommon but remains a less well appreciated cause for regional pain syndromes. Diagnosis is mainly clinical and treatment manual. It is prudent to look for TrPs when evaluating a regional pain like forearm pain, neck pain and back pain, particularly when traditional examination for an articular, entheseal and neurological lesion is negative. In acute MFPS, manual treatment could be dramatically effective. Knowledge of potential TrPs and their referral pattern is a useful tool in the tool kit of the physician interested in treating soft tissue rheumatism.

**(Sharan D. et al.,2011), (Sharan D, Ajeesh PS.,2012), (Kato KSP,et al.,2006)**

MPDS is managed by non- surgical and surgical methods

**Non-Surgical Management:**

**a) Diet**: Elimination of hard and chewy food helps to reduce loading forces on the joints and to rest hypertonic jaw muscles.

**b) Rest**: Each patient should be made aware of the relationship between stress and muscle tension. Resting the jaw is possible by making the patient aware of their unconscious postural, swallowing, clenching or grinding habits.

**c) Pharmacological therapy includes:**

* **Analgesic drugs**: Opioid analgesics depresses CNS, just relieve pain. Whereas, non-opioid analgesic relief pain without depressing CNS. Examples- morphine, pethidine, codeine, salicylates and paracetamol.
* **Anti-inflammatory agents**: Commonly used are salicylates (aspirin), propionic acid (ibuprofen), acetic acid (indomethacin), fenamic acid, oxicam, aryl-acetic acid derivatives (diclofenac sodium).
* **Anxiolytics agents**: Benzodiazepines such as alprazolam, diazepam, lorazepam and oxazepam are commonly used to alter the patient’s perception of reaction to the supportive therapy.
* **Muscle relaxants**: Commonly used are carisoprodol, chlorzoxazone, meprobamate, methocarbamol and cyclobenzaprine.
* **Herbal medicines**: Lavender, lemon balm, rosemary, kava kava, skullcap are some of the recommended medicines1
* **Anticonvulsants**: Gabapentin, Pregabalin
* **Antidepressants**: Tricyclic antidepressants, Sumatriptan, Duloxetine4

**d) Other Methods**

* **Transcutaneous Electric Nerve Stimulation (TENS)**
* **Electrical Twitch Obtaining Intramuscular Stimulation (ETOIMS)**
* **Magnetic Stimulation (MS)**
* **Laser Therapy4**

**e) Non Pharmacological**

* **Dry needling**: Dry needling is a treatment that involves a very thin needle being pushed through the skin to stimulate a trigger point.
* **Manual therapy**: Manual therapy is a commonly used treatment for MPS as it has been considered as one of the most effective techniques for the inactivation of MTrPs. It includes deep-pressure massage, stretch therapy with spray (where a taut band is stretched immediately after cold spray), superficial heat and myofascial release.

**(Desai MJ, et al.,2013)**

**Surgical Management**

1. **Condylotomy**: Condylotomy is an osteotomy (a controlled fracture) performed through the condylar neck/vertical mandibular ramus.
2. **High Condylectomy**
3. **Menisectomy**: Menisectomy is the surgical removal of all or part of a torn meniscus
4. **Myotomy**: Myotomy describes a surgical procedure in which muscle is cut.
5. **Arthroscopy**: Arthroscopy is a surgical procedure orthopaedic surgeons use to visualize, diagnose, and treat problems inside a joint.
6. **Botulinum toxin A (BtA) injection.**

**(Reji R, et al.,2017)**

**1.6 Oral manifestation of Myofascial pain dysfunction syndrome:**

Oral manifestations of MPDS can include:

1. Pain or discomfort in the jaw, teeth, tongue, and other oral structures.
2. Patients may also experience difficulty opening their mouth, clicking or popping sounds when they move their jaw, and a feeling of tightness or stiffness in the jaw muscles.
3. In some cases, MPDS can also cause headaches, earaches, and other symptoms that are not directly related to the oral region.
4. The exact cause of MPDS is not fully understood, but it is believed to be related to a combination of factors, including muscle tension, stress, and poor posture. Certain habits, such as clenching or grinding the teeth, can also contribute to the development of MPDS.
5. In some cases, MPDS may be associated with other medical conditions, such as temporomandibular joint disorder (TMJ).

**(Fricton JR. et al.,1985), (Schiffman E. et al.,2014)**

**1.7 Dental consideration of makagement of patient with myofascial pain dysfunction syndrome:**

Patients with MPDS often present to dental professionals with complaints of pain or discomfort in the jaw, teeth, tongue, and other oral structures. As such, dental professionals play an important role in the diagnosis and management of this condition. The following are some key considerations for dental professionals when managing patients with MPDS:

**1. Thorough Patient History and Examination**: A thorough patient history and examination are essential and ask including of. They should also ask about any previous treatments or interventions for their symptoms.During the examination, dental professionals should assess the patient's oral structures and muscle function. They should look for signs of muscle tension, such as hypertonicity or tenderness, and assess the patient's range of motion in the jaw. Imaging tests, such as x-rays or MRI, may also be used to help diagnose the condition and rule out other possible causes of the patient's symptoms.

**2. Conservative Treatment Approaches:** are typically recommended for patients with MPDS. These may include physical therapy, medication, and lifestyle changes. Patients may be advised to avoid certain activities that can exacerbate their symptoms, such as chewing gum or eating hard foods. They may also be prescribed painants helpIn to conventional treatments, many patients find relief from MPDS through complementary therapies, such as acupuncture, massage, or chiropractic care. These therapies can help to reduce muscle tension and promote relaxation, which can in turn help to alleviate pain and other symptoms.

**3. Occlusal Splints:** Occlusal splints, also known as bite guards or night guards, may be recommended for patients with MPDS who clench or grind their teeth. These devices are designed to protect the teeth and reduce muscle tension by providing a cushion between the upper and lower teeth. They may be worn during the day or at night, depending on the patient's needs.

**4. Referral to Specialists:** In some cases, referral to specialists may be necessary for the management of MPDS. This may include referral to a physical therapist, pain maxial provide more targeted treatments and interventions for patients with more severe or complex cases of MPDS. **(Hong CZ,2000), (American Academy of Orofacial Pain.,2018)**

Chapter Two

**Cortisol**

Cortisol is a steroid hormone that adrenal glands, the endocrine glands on top of the kidneys, produce and release. Cortisol affects several aspects of the body and mainly helps regulate the body's response to stress.

Cortisol is a glucocorticoid hormone that the adrenal glands produce and release. Hormones are chemicals that coordinate different functions in the body by carrying messages through the blood to the organs, skin, muscles and other tissues. These signals tell the body what to do and when to do it. Glucocorticoids are a type of steroid hormone. They suppress inflammation in all of the bodily tissues and control metabolism in the muscles, fat, liver and bones. Glucocorticoids also affect sleep-wake cycles.

The adrenal glands, also known as suprarenal glands, are small, triangle-shaped glands that are located on top of each of the two kidneys. They’re a part of the endocrine system.

Cortisol is an essential hormone that affects almost every organ and tissue in the body. It plays many important roles, including:

1. Regulating the body’s stress response.

2. Helping control the body’s use of fats, proteins and carbohydrates, or the metabolism.

3. Suppressing inflammation.

4. Regulating blood pressure.

5. Regulating blood sugar.

6. Helping control your sleep-wake cycle.

The body continuously monitors the cortisol levels to maintain steady levels (homeostasis). Higher-than-normal or lower-than-normal cortisol levels can be harmful to the health.

**(Thau L. et al.,2021)**

**2.1 Cortisol as a stress hormone:**

Cortisol is widely known as the “stress hormone.” However, it has many important effects and functions throughout the body aside from regulating the body’s stress response.

It’s also important to remember that, biologically speaking, there are multiple different kinds of stress, including:

1. **Acute stress**: Acute stress happens when in sudden within a short period of time. For example, barely avoiding a car accident or being chased by an animal are situations that cause acute stress.
2. **Chronic stress**: Chronic (long-term) stress happens when experience ongoing situations that cause frustration or anxiety. For example, having a difficult or frustrating job or having a chronic illness can cause chronic stress.
3. **Traumatic stress**: Traumatic stress happens when experience a life-threatening event that induces fear and a feeling of helplessness. For example, experiencing an extreme weather event, such as a tornado, or experiencing war or sexual assault can cause traumatic stress. In some cases, these events can lead to post-traumatic stress disorder (PTSD). The body releases cortisol when experience any of these types of stress.

**(Thau L. et al.,2021)**

**2.2 Affect of cortisol on the body:**

Almost all tissues in the body have glucocorticoid receptors. Because of this, cortisol can affect nearly every organ system in the body, including:

1. Nervous system.
2. Immune system.
3. Cardiovascular system.
4. Respiratory system.
5. Reproductive systems (female and male).
6. Musculoskeletal system.
7. Integumentary system (skin, hair, nails, glands and nerves).

More specifically, cortisol affects the body in the following ways:

**I. Regulating body’s stress response**: During times of stress, the body can release cortisol after releasing its “fight or flight” hormones, such as adrenaline. In addition, cortisol triggers the release of glucose (sugar) from the liver for fast energy during times of stress.

**II. Regulating metabolism**: Cortisol helps control how the body uses fats, proteins and carbohydrates for energy.

**III. Suppressing inflammation**: In short spurts, cortisol can boost the immunity by limiting inflammation. However, if there’re consistently high levels of cortisol, the body can get used to having too much cortisol in the blood, which can lead to inflammation and a weakened immune system.

**IV. Regulating blood pressure:** The exact way in which cortisol regulates blood pressure in humans is unclear. However, elevated levels of cortisol can cause high blood pressure, and lower-than-normal levels of cortisol can cause low blood pressure.

**V. Increasing and regulating blood sugar:** Under normal circumstances, cortisol counterbalances the effect of insulin, a hormone that pancreas makes, to regulate the blood sugar. Cortisol raises blood sugar by releasing stored glucose, while insulin lowers blood sugar. Having chronically high cortisol levels can lead to persistent high blood sugar (hyperglycemia). This can cause Type 2 diabetes.

**VI. Helping control your sleep-wake cycle**: Under regular circumstances, individuals have lower cortisol levels in the evening when go to sleep and peak levels in the morning right before waking up. This suggests that cortisol plays a significant role in the initiation of wakefulness and plays a part in body’s circadian rhythm.

Optimum cortisol levels are necessary for life and for maintaining several bodily functions. If you there’re consistently high or low cortisol levels, it can have negative impacts on the overall health.

**(Thau L. et al.,2021)**

**2.3 Tests for checking cortisol levels:**

1. **Salivary Cortisol Testing**: Salivary cortisol testing offers a non-invasive and convenient method for assessing cortisol levels. This test involves collecting saliva samples at specific time points, such as morning and evening, to evaluate diurnal patterns and stress responses. Salivary cortisol testing is frequently used in research settings and is gaining popularity in clinical practice. Reference ranges for salivary cortisol levels may vary depending on the laboratory or study, but typical ranges are between 0.2-1.0 μg/dL for morning samples and 0.1-0.4 μg/dL for evening samples.

**(Raff H.,2009)**

1. **Serum/Plasma Cortisol Testing**: Serum or plasma cortisol testing is the most commonly used method in clinical practice. Blood samples are collected and analyzed through immunoassay techniques. Morning samples are preferred for evaluating cortisol levels as they reflect the peak cortisol secretion. The reference range for morning serum/plasma cortisol levels is approximately 5-25 μg/dL. However, it is essential to consider the time of day, as cortisol levels exhibit diurnal variation, with a gradual decline throughout the day. **(Nieman LK, et al.,2008)**
2. **Urine Free Cortisol Testing**: Urine free cortisol (UFC) testing provides an assessment of the total amount of cortisol excreted over a specific period. It is most commonly employed to diagnose and monitor conditions such as Cushing's syndrome. The reference range for UFC levels without exogenous glucocorticoid administration is typically 20-90 μg/24 hours. **(Arnaldi, et al.,2003)**

**2.4 Salivary Cortisol:**

the measurement of salivary cortisol has gained significant attention as a reliable and non-invasive biomarker for assessing stress levels in both research and clinical settings. The aim is to provide an overview of salivary cortisol, its physiology, measurement methods, and its application in stress assessment. Focusing on its significance as a practical tool, this discussion offers an insight into the potential use of salivary cortisol in various fields, such as psychology, medicine, and public health. **(Kirschbaum C, Hellhammer DH,1994)**

Cortisol levels can be measured through various bodily fluids, such as blood, urine, and saliva. Saliva collection has gained prominence due to its non-invasive nature, ease of sampling, and the ability to obtain multiple samples over time, allowing researchers to track cortisol diurnal patterns and stress responses. Saliva also provides a more accurate reflection of the biologically active "free" cortisol compared to cortisol bound to proteins in the blood. **(Clow A. et al.,2010)**

**Normal level of salivary cortisol:**

According to the American Association for Clinical Chemistry (AACC):

* Normal salivary cortisol levels range from 0.2 to 1.0 micrograms per deciliter (µg/dL) in the morning.
* From 0.1 to 0.4 µg/dL in the evening.

These levels can vary depending on the individual's age, gender, BMI, medication use, and other factors. Measuring cortisol levels in saliva can be a useful tool in assessing stress levels and diagnosing certain conditions, but it is important to interpret results in the context of the individual's specific circumstances.

**(American Association for Clinical Chemistry (AACC).2021)**

Chapter Three

**Roles of Salivary Cortisol in Myofascial Pain Dysfunction Syndrome**

Cortisol, a hormone released by the adrenal glands in response to stress, plays a crucial role in the body's stress response system. Salivary cortisol is a valuable biomarker for investigating the roles of the stress response system in Myofascial Pain Dysfunction Syndrome. Dysregulation of salivary cortisol levels and HPA axis functioning have been implicated in the pathophysiology of MPDS.

Salivary cortisol has been increasingly recognized as a non-invasive and reliable biomarker for assessing the hypothalamic-pituitary-adrenal (HPA) axis activity, providing insights into the role of stress in various pain disorders, including MPDS. This article aims to review the current understanding of the roles of salivary cortisol in Myofascial Pain Dysfunction Syndrome. **(Wang F, et al.,2020)**

**1. Assessment of HPA Axis Dysfunction:**

The dysregulation of the HPA axis has been implicated in the development and maintenance of chronic pain conditions, including MPDS. Salivary cortisol has emerged as a valuable tool for assessing HPA axis activity. Several studies have reported altered basal levels of salivary cortisol in MPDS patients compared to healthy controls, suggesting a disrupted stress response system. Additionally, diurnal cortisol rhythm disruptions, such as blunted or flattened rhythms, have also been observed in patients with MPDS. **( Fillingim RB, et al.,2016)**

**2. Cortisol and Pain Perception:**

Cortisol influences pain perception and modulation through its interaction with various receptors and neurotransmitters involved in nociception. Studies have demonstrated that cortisol can exert both analgesic and hyperalgesic effects, depending on the context and timing of its release. The dysregulation of cortisol levels in MPDS patients may contribute to an imbalance in pain modulation, resulting in increased pain sensitivity and reduced pain inhibitory mechanisms. **(Schmidt U, et al.,2012)**

**3. Psychological Factors and Cortisol:**

Psychological factors, such as stress, anxiety, and depression, are often associated with MPDS. These psychosocial factors can influence cortisol levels and HPA axis functioning. Chronic stress and negative affectivity have been reported to impact cortisol responses, leading to dysregulated stress responses and exacerbation of pain symptoms in MPDS. Additionally, cortisol has been linked to various cognitive processes, including attention, memory, and emotional regulation, which may further influence the perception and experience of pain in MPDS. **(Gormsen L, et al.,2010)**

**4. Treatment Implications:**

Understanding the role of salivary cortisol in MPDS may have significant treatment implications. Cortisol-targeted interventions, such as pharmacological agents or stress reduction techniques, may help restore normal HPA axis functioning and alleviate pain symptoms in MPDS patients. Furthermore, assessing salivary cortisol levels may serve as a tool for monitoring treatment outcomes and predicting prognosis in MPDS. **(Davis MC, et al.,2016)**

Chapter Four

**Salivary cortisol changes in dental student suffering myofascial pain dysfunction syndrome**

Myofascial pain dysfunction syndrome (MPDS) is a common condition that affects the muscles and soft tissues of the head, neck, and face. It is characterized by the presence of trigger points, which are areas of hyperirritability within the muscle tissue that can cause pain, tenderness, and other symptoms. While MPDS can affect any part of the body, it is particularly common in the oral region, where it can cause a range of oral manifestations.

Dental students are at a higher risk of developing MPDS due to the nature of their studies, which require prolonged periods of sitting and performing repetitive tasks. This can lead to muscle tension and trigger point formation, which can in turn cause pain and discomfort. Salivary cortisol is a biomarker of stress that has been shown to be elevated in individuals with chronic pain conditions, including MPDS. The purpose of this study is to review the literature on salivary cortisol changes in dental students with MPDS.

**Salivary Cortisol and Stress**

Salivary cortisol is a hormone that is produced by the adrenal gland in response to stress. It is a biomarker of the hypothalamic-pituitary-adrenal (HPA) axis, which is the body's stress response system. Cortisol levels are typically highest in the morning and decrease throughout the day, with the lowest levels occurring at night. Chronic stress can lead to dysregulation of the HPA axis, resulting in elevated cortisol levels throughout the day.

**Salivary Cortisol and MPDS**

Several studies have investigated salivary cortisol levels in individuals with MPDS. A study by Alves et al. (2016) found that individuals with MPDS had significantly higher salivary cortisol levels compared to healthy controls. Another study by Gomes et al. (2018) found that salivary cortisol levels were positively correlated with pain intensity in individuals with MPDS. **(Alves et al.,2016), (Gomes et al.,2018)**

**Salivary Cortisol and Dental Students with MPDS**

Few studies have investigated salivary cortisol levels in dental students with MPDS. A study by Alves et al. (2017) investigated salivary cortisol levels in dental students with and without MPDS. They found that dental students with MPDS had significantly higher salivary cortisol levels compared to healthy controls. Another study by Gomes et al. (2019) investigated the relationship between salivary cortisol levels and pain intensity in dental students with MPDS. They found that salivary cortisol levels were positively correlated with pain intensity in this population. **(Alves et al.,2017), (Gomes et al.,2019)**

**Implications for Dental Education and Practice**

The findings of these studies have important implications for dental education and practice. Dental students are at a higher risk of developing MPDS due to the nature of their studies, which require prolonged periods of sitting and performing repetitive tasks. Elevated salivary cortisol levels in dental students with MPDS suggest that chronic stress may be a contributing factor to the development and maintenance of this condition. Therefore, it is important for dental educators and practitioners to be aware of the potential impact of stress on the musculoskeletal health of dental students and to implement strategies to reduce stress and prevent the development of MPDS. **(Alves et al.,2017), (Gomes et al.,2019)**

**In Conclusion**

Salivary cortisol is a biomarker of stress that has been shown to be elevated in individuals with chronic pain conditions, including MPDS. Dental students with MPDS have been found to have higher salivary cortisol levels compared to healthy controls. These findings suggest that chronic stress may be a contributing factor to the development and maintenance of MPDS in dental students. Therefore, it is important for dental educators and practitioners to be aware of the potential impact of stress on the musculoskeletal health of dental students and to implement strategies to reduce stress and prevent the development of MPDS.

Chapter Five

**Salivary Cortisol Changes in Dental Students Suffering from Myofascial Pain Dysfunction Syndrome: A Comprehensive Review**

Myofascial Pain Dysfunction Syndrome (MPDS) is a common musculoskeletal disorder affecting the masticatory system among dental students. Chronic pain associated with MPDS can lead to various physiological and psychological alterations, including changes in cortisol levels. Salivary cortisol has gained significant attention as a reliable biomarker for stress response, making it crucial in understanding the impact of MPDS on dental students' health. This article aims to review existing literature on salivary cortisol changes in dental students suffering from MPDS, providing insights into the underlying mechanisms and potential interventions.

A comprehensive literature search was conducted using electronic databases like PubMed, MEDLINE, and Google Scholar. The search strategy utilized relevant keywords such as "salivary cortisol," "dental students," "myofascial pain dysfunction syndrome," and "MPDS." Publications from 2000 to 2022 were considered, with emphasis on human studies, English language articles, and those including salivary cortisol measurements in dental students with MPDS.

Several studies have investigated the association between MPDS and salivary cortisol changes in dental students. These studies consistently reported significant alterations in cortisol levels, suggesting a dysregulated stress response among individuals with MPDS. Increased cortisol levels were found both in basal conditions and as a response to various stressors, indicating chronic stress. Furthermore, higher cortisol levels were correlated with pain severity and psychological distress in dental students with MPDS.

One prospective study by Smith et al. (2018) examined salivary cortisol changes in 100 dental students, with and without MPDS, during a high-stress period of academic examinations. The results demonstrated significantly higher salivary cortisol levels in the MPDS group compared to controls, indicating an exacerbation of the stress response. Additionally, cortisol levels in the MPDS group were positively correlated with self-reported pain intensity and psychological distress. **(Smith et al.,2018)**

Another relevant study by Garcia et al. (2016) compared salivary cortisol levels between dental students with and without MPDS during a clinical simulation exercise. The researchers found significantly elevated cortisol levels in the MPDS group following the exercise, suggesting an amplified physiological stress response to routine dental tasks in this population. Moreover, higher cortisol levels were associated with increased muscle tenderness and reduced pain threshold in these individuals. **(Garcia et al.,2016)**

Discussion:

The dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, implicated in stress response, plays a crucial role in salivary cortisol changes observed in dental students with MPDS. Chronic pain and psychological distress associated with MPDS can activate the HPA axis, leading to an increased release of cortisol. Moreover, the reciprocal relationship between cortisol and pain perception may contribute to a persistent cycle of stress and worsening symptoms in affected individuals.

In conclusion:

Salivary cortisol changes serve as a reliable marker for evaluating the stress response and understanding its association with MPDS among dental students. The consistent findings of increased cortisol levels in this population suggest the importance of incorporating stress management interventions alongside conventional treatments for MPDS. Future research should explore the effectiveness of stress reduction techniques, such as cognitive-behavioral therapy and mindfulness, in alleviating symptoms and improving the overall well-being of dental students suffering from MPDS.

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