Review Article

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Role of Female Hormones on Temporomandibular Joint Disorders: An Unsolved Mystery

Anukriti Vishwakarma[1*] Abhijeet Deoghare[2] Rashmi Nivsarkar[3] Kanak Tripathi[4] Roshan Prabhakar Dhonge[5]

[1]Post Graduate Student, Department of Oral Medicine and Radiology, Chhattisgarh Dental College and Research Institute, Rajnandgaon, India.
[2]Professor and Head, Department of Oral Medicine and Radiology, Chhattisgarh Dental College and Research Institute, Rajnandgaon, India.
[3]Post Graduate Student, Department of Oral Medicine and Radiology, Chhattisgarh Dental College and Research Institute, Rajnandgaon, India.
[4]Post Graduate Student, Department of Oral Medicine and Radiology, Chhattisgarh Dental College and Research Institute, Rajnandgaon, India.
[5]Senior Lecturer, Department of Periodontology and Implantology, Aditya Dental College, Beed, India.

ABSTRACT

Background: Temporomandibular joint disorders (TMDs) are more common in women as compared to men, with its peak during the reproductive years. The age and gender predilection suggests a possible link between the female hormones and the TMDs. Female hormones have been associated with development, restitution and metabolism of temporomandibular joint. These hormones also play a role in pain regulation. The recent studies have established the use of exogenous hormone and the risk of TMDs among women after menopause. This article throws a light on the role and effect of female hormones chiefly estrogen and progesterone on the temporomandibular joint leading to TMDs.

Keywords: TMDs, Female hormones, Progesterone, Estrogen, Relaxin.

INTRODUCTION

Temporomandibular joint disorders (TMDs) are a set of clinical conditions which are related to the temporomandibular joints (TMJ) and masticatory muscles of the face and neck.[1] The increased incidence of occurrence of temporomandibular joint disorders in women have been proved by the various epidemiological studies which state that it is most common in the reproductive years of women (20-40 years).[2,3]

The prevalence pattern of TMDs indicate that endogenous as well as exogenous female hormones play a role in causing TMD pain.[4,5] Although the exact mechanism of action of these is still debatable.[6] TMDs are 30% more common in women receiving exogenous estrogen than those who are not concluding its increased risk in them.[7]

Role of female hormones on TMDs:

It has been stated that estrogen, progesterone and relaxin can modulate the remodelling activities of extracellular matrix and it may be one of the mechanisms of joint degeneration. Also that overexpression and overactivity of matrix metalloproteinases (MMP) in inflammatory processes result in TMJ destruction.[8]

a. Role of estrogen:

Processes of remodelling within the TMJ are affected by endogenous estrogen which occurs possibly by changing the extracellular matrix of the joint and by changing the bone volume. Such alterations can result in internal disc derangement of the TMJ.[9]

Beta estradiol, the most dominant and potent form of estrogen in women, affects the TMJ by binding of the estrogen receptor α (ERα) and estrogen receptor β (ERβ) to the DNA and/or by its

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*Correspondence Dr. Anukriti Vishwakarma.
Department of Oral Medicine and Radiology, Chhattisgarh Dental College and Research Institute, Rajnandgaon, India.
Email: anukriti.an23@gmail.com

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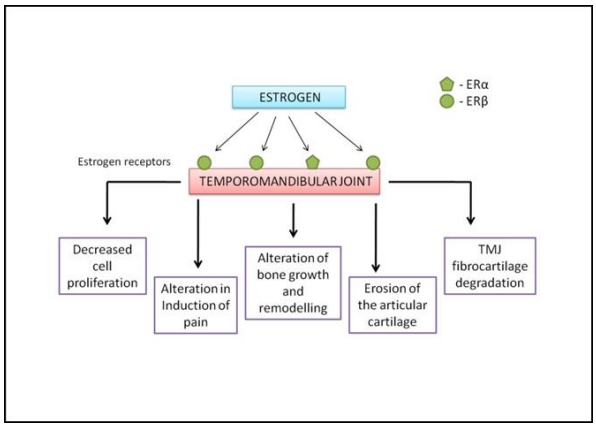

Fig 1: Role of estrogen on TMJ.

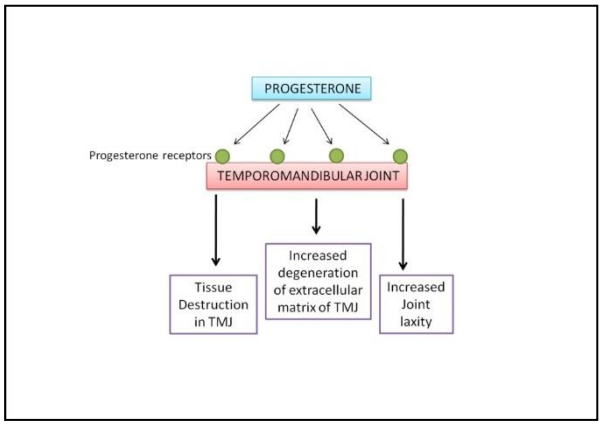

Fig 2: Role of progesterone on TMJ.

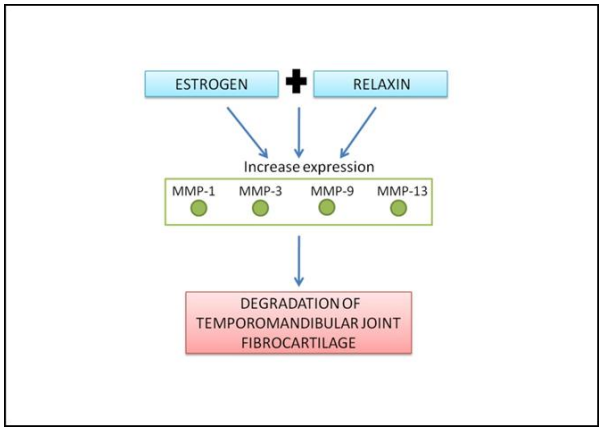

Fig 3: Role of estrogen and relaxin on TMJ.

interaction with various kinase.[10] The interaction of both the receptors with membrane associated molecule (G-protein coupled receptors & ion channels) may alter the cell physiology.[11]

The estrogen receptors are widely distributed in the thymus, bone marrow, and spleen which suggest its modulatory role in the immune system. Joint disorders may be caused as a result of altered immune response.[12,13] Estrogen receptors particularly ERα are present on the articular cartilage and subchondral bone of TMJ. This explains why alteration in the hormones would directly cause an impact over the TMJ.[9,14]

Estrogen decreases cell proliferation and regulates extracellular matrix expression thereby affecting osteoblastic differentiation. This explains the molecular mechanism of bone growth and remodelling affected by estrogen.[15] (Figure 1)

Some studies found that estradiol administration causes more erosion of the articular cartilage as compared with the controls.[16] It has been shown by various animal and human studies that administration of estrogen, either acute or chronic, can lead to induction of release of nitric oxide (a neurotransmitter) and its increase in fluid of TMJ is said to be related to pain onset.[17] There are evidences showing significantly increased levels of serum estrogen in TMD patients in contrast to controls.[18] These evidences clearly define the role of estrogen in causing TMDs.

b. Role of Progesterone:

Like estrogen, literature also suggest the presence of progesterone receptors over the TMJ.[19] Progesterone is known to cause decrease in MMP-9 expression (causes degeneration of extracellular matrix) which is dose dependent.[20] With increased levels of the progesterone there is an active tissue destruction in TMJ and mild degenerative changes which may be seen with inflammatory response manifesting as periods of pain.[8] (Figure 2) Increased joint laxity is seen during the phases when the levels of progesterone is increased.

Stress causes increase in production of cortisol which is a receptor site competitor with progesterone. By displacing the progesterone from its normal locus of action, it decreases the progesterone's activity level. Stress and anxiety are also linked with TMD. This may be due to the jaw grinding and clenching that often occurs subconsciously in patients suffering from anxiety. Also, the increased inflammatory load that is seen with stress contributes here, regardless of the clenching and grinding of the patient.[21]

c. Role of Relaxin:

Relaxin occurs in human body in three forms H1, H2 and H3. Type H2 causes alteration in organization and composition of matrix by modulating matrix-degrading enzymes and matrix molecule synthesis. It is thought to increase the expression of tissue degrading enzymes thereby causing muscle relaxation. It acts in co-ordination with estrogen to cause degradative remodelling of the articular disc. Laxity of the TMJ is said to develop TMDs.[22]

Estrogen and relaxin both cause TMJ degeneration by amplifying the expression of the tissue degrading enzymes of MMP family namely – MMP-1 (collagenase-1), MMP-3 (stromelysin-1), MMP- 9 (92kDa gelatinase) and MMP-13 (collagenase-3).[23,24] These basically act on collagen, proteoglycan and minor proteins present in the TMJ fibrocartilage.[25] Since degradation caused by MMPs is considered to be an important event in initiation and progression of the TMJ destruction, it suggests a role of relaxin and estrogen in causing TMDs. (Figure 3)

CONCLUSION

The etiology of TMDs is multifactorial and cause-effect relationship is still controversial. The endogenous and exogenous female hormones lead to specific changes in TMJ tissues. The female predilection to TMDs also has a pathophysiologic basis with its direct or indirect relation to hormones.

Various female hormones estrogen, progesterone and relaxin have their impact on the various joints in the body including temporomandibular joint which has been revealed by presence of the receptors of these hormones present over the TMJ. The exact mechanism that underlies the pathology is still not well understood thereby, stating a need to carry on studies regarding this issue.

A few of the mechanisms which have been explained are the effects of MMPs on the TMJ destruction induced by hormones such as estrogen and relaxin, effect of alteration of female hormone levels on TMJ and effect of adverse conditions like stress on TMJ in relation to female hormones.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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