ISSN No:-2456-2165

Regeneration of Temporomandibular Joint – A Review

Rohit Raghavan[1], Shajahan P A[2], Neha joe[3]
[1] Head of the Department, [2] Professor, [3] Post Graduate Student
Department of Prosthodontics and Crown and Bridge, Royal Dental College; Chalissery.

Abstract:- Temporomandibular joint is a giglymoarthroidal joint which is composed of a synovial cavity, capsule and an articular cartilage. It's a very sensitive joint that it can easily undergo degenerative changes which in turn compromise the quality of life of the patients. There are several invasive and non-invasive treatments for the rehabilitation of disc degeneration. With regenerative medicine, the treatment planning can be done efficiently utilising minimally invasive and non-invasive methods which can improve ease and comfort of the patient. Tissue engineered implants, prolotherapy, intra articular injections of growth factors are novel approaches in establishing a better treatment outcome.

Keywords:- *Temporomandibular joint, regenerative medicine, tissue engineering, implants, Prolotherapy, Intra articular injections.*

I. INTRODUCTION

Temporomandibular joint is a synovial joint of condylar variety with essential functions of chewing and talking. The damage of tmj causes pain and dysfunction in 20-25% of adults. The temporomandibular joint disc is a fibro cartilaginous structure within the joint that can facilitate load bearing, congruity, and smooth movement between the mandibular condyle and skull base.

TMJD shows characteristics of malocclusion, pain, limited range of motion, deviation, clenching and joint clicking.
Pain is the main symptom and the primary factor why patien ts are referred to receive healthcare from practitioners.

The Treatments for temporomandibular joint (TMJ) disc perforation and thinning conditions are prevalent in TMJ pathologies and these are palliative but not reparative. Based on severity the treatment of internal derangement can differ, and for early stages of diseases non-invasive or minimally invasive options are used.

For complex situations like progressive stages of internal derangement more aggressive treatments are performed like complete disc removal or Prosthetic total joint replacements. Minimally invasive treatments do not repair any damages discs but can offer a relief. To this day, there is an unmet need for therapies to repair damaged discs in order to avoid further growth into serious degeneration.

We humans are made of cells not drugs or plastics. TMJ rehabilitation is the zone in prosthodontics where we need more research to bridge the gap between a prosthetics and biologics.

Tissue engineering and regenerative medicine opens a door of hope in every practitioner who is having an empathy to every patient who is suffering.

Temporomandibular joint disorder prevalence is 52 per cent.Features of TMJ degeneration are: displacement, thicke ning, and/or perforation of discs There is a finding that disc deformation contributes to disc displacement and is often accompanied by pain and inflammation.

But there are cases where patients experience inflammation and disc degeneration without disc displacement. whole destruction of articular fibrocartilage and critical alterations of bone remodeling such as sclerosis or peri articular osteophyte formation [4,5]. The ultimate degeneration results in the replacement of TMJ by a block of fibrous and bony tissue, namely, ankyloses

The embryonic origin of mandibular articular surface is still debatable as blastemal or periosteal. As we all know TMJ disc has a concave configuration which follows the surface of condyle and temporal bone.it is a synovial joint of condylar variety, unlike other synovial joints in human's temporomandibular joint is covered by a fibrous tissue rather than hyaline cartilage[6]

In fig 1, it shows a freshly extracted TMJ disc from an animal model in a study conducted by D.F.Angelo et al ,he also managed to exhibit fresh disc with and without attachments.

The circular or oval, biconcave, avascular fibrocartilag e between the condyle and the glenoid fossa is the articular d isk.

In the intermediate region, the disk is significantly thin ner. The thickness of the triangular anterior band is about 2 mm and blends with the capsule of the joint.The anterior tria ngular band has a thickness of around 2 mm and blends with the capsule of the joint. The posterior band is approximately 3 mm thick and continues as a bilaminar zone consisting of a superior fibro elastic layer (also known as temporal lamina) that binds to PGP and an inferior fibrous layer (also known as retrodiscal area and posterior attachment) that attaches to

ISSN No:-2456-2165

PGP and an inferior fibrous layer (also known as the inferior lamina) that attaches to the posterior condylar neck.

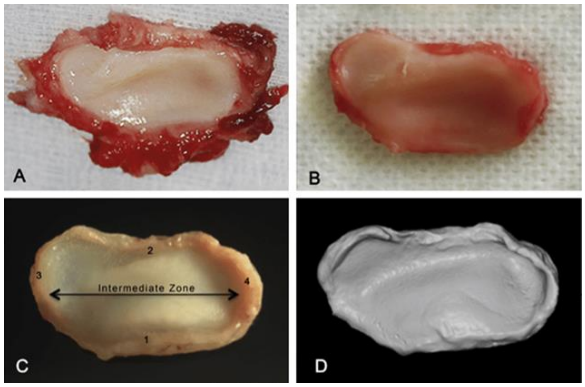

FIG 1 (A) fresh disc with attachments. (B). Fresh disc without attachments. (C). TMJ disc submitted to Color Bond treatment: (1) anterior band, (2) posterior band, (3) medial band, (4) lateral band.D). TMJ disc 3D virtual model

II. ROLE OF COLLAGENS

In a study conducted by sheng jei cui et al they are making a hypothesis that chronic inflammation contributes to the deterioration of the Nano mechanical properties and ultrastructure of collagen fibres in temporomandibular joint discs.

Collagen is the structural component of TMJ disc, it is often affected by inflammation of the disc. Chronic inflammation leads to the deterioration of micromechanical properties of collagen.

Collagen type I is predominant, although there are othe r collagen types: II, III, VI, IX, and XII. Collagens are predo minantly anisotropic in the disc.

Tissue engineering and tmj regeneration

Even when innovative biomaterials are in action, the implementation is crucial as it is an invasive procedure. Due to its limited healing capacity TMJ is one of the difficult tissues to regenerate.

An ideal approach to TMJ regeneration is the special o steochondral molecular gradient scaffold functionality comp rising a single population of stem cells such as BMSCs, AD SCs, or DPSCs that can be osteogenic.

The functionalization with active molecules such as IGF-1, TGF-_1 or BFGF is the key for this complex regeneration. Regeneration can be limited by Nano/micro-assisted functionalization and by spatiotemporal drug delivery systems orchestrating the 3D formation of TMJ tissues.

Hurdles of tmj regeneration

As we discussed earlier TMJ is a very complex structure which is narrow, dense and with limited blood supply leading to complexity in its healing capabilities.

Tissue engineering and regenerative medicine has to be improved in such a way that it can overcome all these mentioned hurdles to keep the system in harmony.

Figure 2 represents the limitations in reconstruction of temporomandibular joint with tissue engineering and regenerative medicine.

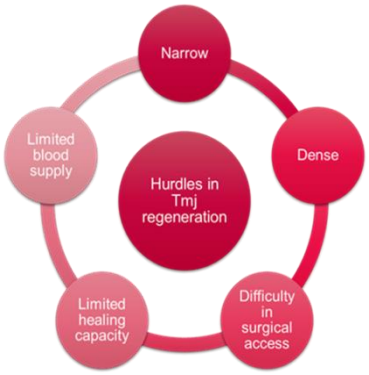

Fig 2 Limitations in reconstruction of TMJ

The ultimate ambition in temporomandibular regeneration is

- To match the mechanical and structural properties of mandibular condyle implants with anatomic condyle.
- Implanted tissue engineered mandibular condyle must have rapid and adequate remodelling potential allowing oral functions

III. INGREDIANTS OF TISSUE ENGINEERING

Tissue engineering can only come into life with these three golden elements.

Figure 3 represents the mandatory ingredients for tissue engineering which includes cells , growth factors and scaffold

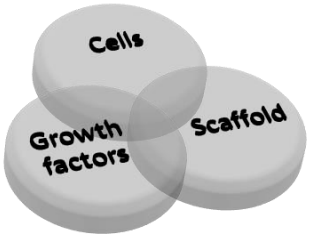

Fig 3: Ingredients of tissue engineering

Cell strategies

The role of cells in regenerative medicine is commendable as it acts as the mother of the all results we get. Only a cell which has the potential to regenerate will support and get us the exact output which we desire for [8].

- Fibro chondrocytes
- Bone marrow mesenchymal stem cells (BMSCs)[10]
- Adipose stem cells (ADSCs)

- Periodontal ligament stem cells (PDLSCs)
- Stem cells from apical papilla (SCAPs)
- Dental follicle progenitor cells (DFPCs)
- Dental pulp stem cells (DPSCs)
- Dermal fibroblasts

SCAFFOLDS

Scaffolds are those materials that have been engineered to promote a desirable cellular interaction so that it can contribute the formation of new functional tissues for medical purposes.

Scaffolds for TMJ Cartilage Regeneration

- Hyaluronic acid (HA)
- Agarose
- Poly-vinyl alcohol (PVA)
- Poly-L-lactic-co glycolic acid (PLGA)-FDA approved

Scaffold for TMJ disc Regeneration

- Poly glycolic acid
- Poly L lactic acid
- Collagen
- Composite
- Gelatine

Based on incorporation of cells, temporomandibular regeneration can be conducted in both in situ and ex vivo [21]

In in situ working condition there is incorporation of an extra cellular scaffold matrix attracting local cells (cell homing) guiding the process of regeneration

In ex vivo there is cell seeding on the scaffold which provides enough competent cells to orchestrate the regenerative mechanism.

These scaffolds need certain condition to replicate the environment for regenerative potential and those are

- Low intensity pulsing ultrasound
- Spinner flask or bioreactor

GROWTH FACTORS

Growth factors are those elements that can provide a spark for the division of these cells.

A.FOR DISC

- Transforming growth factor-β1 (TGF-β1)
- Basic fibroblast growth factor (bFGF)
- Platelet derived growth factor(PDGF)

B. FOR CONDYLE

- Transforming growth factor-β1 (TGF-β1)
- Insulin-like growth factor 1 (IGF-1)

FUNCTIONS OF GROWTH FACTORS

- They can promote the differentiation and proliferation of cells.
- They can support extracellular matrix synthesis and its mineralization.
- In order to be selflimited, they can also biologically mod ulate regeneration and avoid ossification and fibrousadhe sion.
- They are able to maintain disc-like tissue in culture and to induce BMSCs differentiation into fibroblast-like cells, synthesizing disc matrix of type I collagen and glycosaminoglycan's (GAGS)[11,12,13].

Drug Delivery Systems

- Scaffold immersion in a solution of growth factors allow s for a random distribution of snappy release.
- Covalent binding to the scaffold of growth factors increa se the control of the release.

And this timely release is mandatory for the final result to be success and this system which helps for this timely release is called drug delivery system in regenerative medicine.

IV. FUNCTIONALIZATION

It is also possible to perform gene transfer via viral or non-viral transduction.

For tissue regeneration, retroviruses, adenoviruses or a denoassociated viruses are often used as most effective tool for gene transfer.

Through nanotechnology, this functionalization is strea mlined.

The concentration of various active molecules permitte d by nanotechnology is also very helpful for the orchestratio n of different sstages of TMJ regeneration and for synergetic action of growth factors.

INTRA ATICULAR INJECTIONS IN TMJ ION

- Pain management
- Regenerative strategies
- Prior to implantation for favourable environment

Medium used

- Hydrogels
- polymeric micro particles
- liposomes

PROLOTHERAPY

Prolotherapy facilitates longterm pain relief, often lasti ng, by enhancing the ability of the body to heal itself. To all eviate pain, it requires injecting an irritant solution into a joi nt space, damaged ligament, or tendon insertion[17].

Hyperosmolar dextrose, glycerin, lidocaine, phenol an d sodium morrhuate are widely used agents (a derivative of cod liver oil extract). The injection is applied to the joints or tendons where the bo ne is attached.

The overall appointment time, including planning, cou nseling and recovery time, takes approximately 30 minutes.

ROLE OF 3D BIOPRINTING

Personalized TMJ prosthesis can be designed for each patient with the help of 3D printing. This type of prosthesis has the advantage of better biomechanical and clinical outcomes.

The positioning of implant becomes lot easier during the surgery as it has its optimal shape and to the opportunity to have an optimal 3D surgical guide.

In a study conducted by Natalia vaprinarsky she concluded that the tissue engineered implants are durable after implantation. They dint dislodge, and got partially fused after an evaluation for 2-8 weeks.

The step by step method of tissue engineering using 3D prin ting is shown in Figure 4.

A CT scan image of the recipient is first obtained here and then the image is submitted for design using CAD CAM . The designed image is used for 3 D printing of the desired form of the scaffold.

In cell culture, stem cells isolated from the recipient ar e used, and then cell seeding is performed on the scaffold. Cell seeded scaffold is transferred to the bioreactor for tissue regeneration.

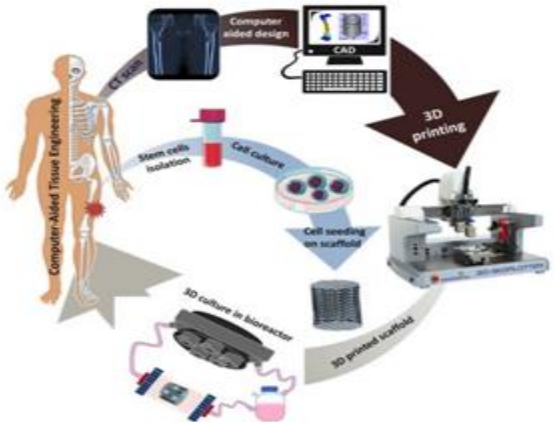

Fig 4 Step by step procedure of tissue engineering with 3D

Remaining Hurdles For Tissue Engineering

- Increase the dimension of TMJ disc construction
- it should be constructed with larger area and also increased thickness
- Perform translational studies in suitable animal models
- Develop novel surgical procedures and strategies
- Examine the systemic and local responses of the body after implantation

V. CONCLUSION

There are yet sides of regenerative medicines that is to be discovered and if we can overcome the hurdles in this area, it can surely solve all the difficulties which we are facing now and can give rise to an era with almost all solution to the people who are suffering with these difficulties.

REFERENCES

[1]. Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. J Dent Res. 2008;87(4):296–307.
[2]. Aryaei A, Vapniarsky N, Hu JC, Athanasiou KA. Recent tissue engineering advances for the treatment of temporomandibular joint disorders. Curr Osteoporos Rep. 2016;14(6):269–79.
[3]. Zarb GA, Carlsson GE. Temporomandibular disorders: osteoarthritis. J Orofac Pain. 1999 Autumn;13(4):295–306.
[4]. Kalpakci KN, Willard VP, Wong ME, Athanasiou KA. An interspecies comparison of the temporomandibular joint disc. J Dent Res. 2011;90(2):193–8.
[5]. Detamore MS, Hegde JN, Wagle RR, Almarza AJ, Montufar-Solis D, Duke PJ, et al. Cell type and distribution in the porcine temporomandibular joint disc. J Oral Maxillofac Surg. 2006;64(2):243–8.
[6]. Wong GB, Weinberg S, Symington JM. Morphology of the developing articular disc of the human temporomandibular joint. J Oral Maxillofac Surg. 1985;43(8):565–9.
[7]. Kinoshita Y, Maeda H. Recent developments of functional scaffolds for craniomaxillofacial bone tissue engineering applications. ScientificWorldJournal. 2013;2013:863157.
[8]. El-Bialy T, Uludag H, Jomha N, Badylak SF. In vivo ultrasound-assisted tissue-engineered mandibular condyle: a pilot study in rabbits. Tissue Eng Part C Methods. 2010;16(6):1315–23.
[9]. Detamore MS, Athanasiou KA. Use of a rotating bioreactor toward tissue engineering the temporomandibular joint disc. Tissue Eng. 2005;11(7–8):1188–97.
[10]. Almarza AJ, Athanasiou KA. Evaluation of three growth factors in combinations of two for temporomandibular joint disc tissue engineering. Arch Oral Biol. 2006;51(3):215–21.
[11]. Detamore MS, Athanasiou KA. Evaluation of three growth factors for TMJ disc tissue engineering. Ann Biomed Eng. 2005;33(3):383–90.
[12]. Su X, Bao G, Kang H. Effects of basic fibroblast growth factor on bone marrow mesenchymal stem cell differentiation into temporomandibular joint disc cells. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2012;29(4):732–6.

[13]. Murphy MK, MacBarb RF, Wong ME, Athanasiou KA. Temporomandibular disorders: a review of etiology, clinical management, and tissue engineering strategies. Int J Oral Maxillofac Implants. 2013;28(6):e393-414.
[14]. Tissue Engineering: Applications in Oral and Maxillofacial Surgery and Periodontics.
[15]. Donahue RP, Hu JC, Athanasiou KA. Remaining hurdles for tissue-engineering the temporomandibular joint disc. Trends Mol Med. 2019;25(3):241–56.
[16]. Vapniarsky N, Huwe LW, Arzi B, Houghton MK, Wong ME, Wilson JW, et al. Tissue engineering toward temporomandibular joint disc regeneration. Sci Transl Med. 2018;10(446):eaaq1802.
[17]. Prolotherapy [Internet]. Orlandopainandspine.com. 2015 [cited 2021 Jan 8]. Available from: https://www.orlandopainandspine.com/procedures/prolotherapy/
[18]. Reeves KD, Lyftogt J. Prolotherapy. In: Pain Management. Elsevier; 2011. p. 1027–44.
[19]. The glossary of prosthodontic terms: Ninth edition. J Prosthet Dent. 2017;117(5S):e1–105.
[20]. Van Bellinghen X, Idoux-Gillet Y, Pugliano M, Strub M, Bornert F, Clauss F, et al. Temporomandibular joint regenerative medicine. Int J Mol Sci [Internet]. 2018;19(2). Available from: http://dx.doi.org/10.3390/ijms19020446