

## Use Of HAM In Surgical Treatment Of TMJ

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### Summary

Surgery to correct disorders of the TMJ has been performed and documented since the mid-nineteenth century. Facts shows that reversible non-surgical treatment can improve the situation of patients with internal pathological conditions of the joint, but still some patients require surgical intervention. We have several techniques to treat TMJ derangements of which is TMJ arthroplasty with the interposition of autograft (e.g. dermis, temporal fascia, or cartilage). Recently, with the inception of the 21<sup>st</sup> century, HAM is observed to be a promising material used in treatment of different surgical fields. The HAM is the inner layer of the placenta which surrounds the baby during pregnancy. The HAM has been shown to have anti-fibrotic, anti-inflammatory, anti-angiogenic and anti-microbial properties. Also, it is considered encouraging because of its transplant structure and the ability to provide an excellent substrate for growth, migration, and adhesion of cells. This project was triggered by a study to demonstrate whether the HAM could prevent TMJ reankylosis in randomized rabbit models (2010). Case Report: A severe TMJ degeneration was diagnosed with a 48-years old woman and surgical treatment was necessary. Cryopreserved HAM patch was applied within the joint space as a disc-replacing film. The patient reported an overall improvement in chewing as well as the absence of pain. The aim of this article is to be regarded as initial spadework and should motivate other institutions to intensify their clinical research in this field. As to prevent recurrence of TMDs.

**Abbreviations:** TMJ- Temporomandibular Joint, HAM- Human Amniotic Membrane, TMDs- Temporomandibular Disorders, MRI- Magnetic Resonance Imaging.

**Key Words:** TMJ, HAM, TMJ derangements, TMJ arthroplasty, Cryopreserved HAM, TMDs.

### Introduction

Patients frequently consult a dentist because of pain or dysfunction in the temporomandibular region. the most common causes of TMDs are muscular disorders, which are commonly referred to as myofascial pain and dysfunction. These muscular disorders are generally managed with a variety of reversible nonsurgical treatment methods.

Other causes of temporomandibular pain or dysfunction originate primarily within the TMJ. These causes include internal derangement, osteoarthritis, rheumatoid arthritis, chronic recurrent dislocation, ankylosis, neoplasia, and infection. Although most of these disorders respond to non-surgical therapy, some patients may eventually require surgical treatment. If a successful result is to be achieved, management of these patients requires a coordinated plan that includes the general dentist, the oral-maxillofacial surgeon, and other health care providers. <sup>[1-1]</sup>

One of most disorders that require surgical intervention is

usually either TMJ ankylosis or anterior disk derangement. These two are best to be treated by arthroplasty which refers to a group of TMJ surgical procedures approached with an incision directly into the joint itself.

It's a minimally invasive technique and is indicated for those patients with progressively debilitating internal derangement refractory. Gap arthroplasty and interpositional arthroplasty are the most regularly used therapeutic options to treat TMJ ankylosis. The real complication of the two intervention is the recurrence of ankylosis. Until this point, no surgical or nonsurgical method can ensure nonrecurrence; in this manner, the effective treatment of HAM will post a clinical challenge based on the unacceptable outcomes experienced with the current treatment choices. <sup>[2]</sup>

Furthermore, discectomy, the closest surgical treatment to arthroplasty, is the removal of disk due to having a severely damaged disk. It was one of the earliest surgical procedures described for treatment of severe TMJ internal derangements. After new technologies, the discectomy procedure can be performed through arthroscopic techniques to minimize scar tissue formation and preserve lubrication provided by the synovium. Although this technique has been widely used, a wide variation seems to exist in clinical results; some joints showing minimal anatomic changes, significant clinical improvement, and demonstrating severe degenerative changes with continued symptoms of pain and dysfunction. <sup>[3]</sup>

Therefore, HAM gives the best prognosis and results in such surgical treatments with many variations. It reduces inflammation, provide a matrix highly rich in protein, and thereby facilitate migration of cells at the area of defect. Common applications of HAM include chemical or thermal burns, correction of corneal epithelial defects, neurotrophic corneal ulcers, leaking blebs after glaucoma surgery, reconstruction of conjunctival and ocular surfaces, ocular cicatricial pemphigoid or Stevens-Johnson syndrome, and bullous keratopathy.

### Overview

The objective of this review is to clearly show the effectiveness of HAM as an interpositional material in the temporomandibular space. This all is proved by 3 case reports that escalates the experimentations of the HAM on TMJs starting from animals. It is a traumatic and dangerous intervention, but as Hippocrates says, "The life so short, the craft so long to learn".

### Human Amniotic Membrane

The study of Human Amniotic membrane use in TMJ refers to 3 applications:

First, in 2010, a study of applying the HAM as an interpositional material to prevent TMJ reankylosis in randomized rabbit model. The experiment was on 24 New Zealand white rabbits that were used, and all right joints were operated. The rabbits were isolated into 2 gatherings. The primary gathering was determined as the demonstration gathering (n = 8). In this gathering, fibrous ankylosis was developed. The rabbits in the second gathering, the treatment gathering (n = 16), were separated into 2 subgroups: gap arthroplasty, performed in gathering A (n = 8); and HAM,

utilized as an interpositional arthroplasty material in gathering B (n = 8).

In all rabbits, the scope of jaw movements and weight diminished after induction of ankylosis. After careful surgical treatment of fibrous ankylosis, the vertical, right, and left movements of the jaw and weights of rabbits increased right away. The outcomes were assessed clinically, macroscopically, histologically, and radiologically. There was a measurably huge distinction in the jaw movements between gatherings A and B ( $P < .05$ ). All operated joints in gathering A indicated fibrous adhesions across the gap and the articular surface was unpredictable with osteophytes and hard bony islands on the joint surface. In gathering B, no fibrous adhesions were observed. This proved that interpositional arthroplasty with HAM was superior to gap arthroplasty in the rabbit model in preventing ankylosis.<sup>[4]</sup>

Second, a case reports the usage of HAM combined with a costochondral graft as an interpositional material in TMJ reconstruction for the first time in humans. A 53-year-old, otherwise healthy woman presented herself because of pain in the left TMJ region and an insufficient mouth opening. Clinical examination revealed a maximum interincisal opening of 15 mm. In preliminary investigations, radiographic, computed tomographic, and magnet tomographic analysis were performed and a neoplasm at the left condylar process, involving the whole joint cavity, was detected. To clarify the finding, a biopsy of the suspicious mass was performed, and a giant cell tumor was diagnosed. After careful evaluation of the diagnosis, risks, and benefits of all possible treatment options, the woman was assessed to undergo radical excision of the tumor including total resection of the condylar process plus the articular disk. Based on the positive outcome of the previously performed animal experiments and the informed consent of the patient, a costochondral graft combined with an allogeneic HAM, it was chosen to reconstruct the joint head. For this intention, ethical approval of the independent ethics committee was obtained.

Beginning the operation, the occlusion was fixed with wire splints. In the following stage, the costochondral graft was harvested with no difficulty from the right ninth rib and kept in a moist bandage during the extraction of the neoplasm. Through a submandibular and a preauricular approach, the tumor and the condylar process were completely resected. The edges of every single frozen segment were clear. The collected autologous costochondral rib graft was arranged and shaped before transplantation. Osteosynthesis of the cleaned, shaped, and adjusted rib graft to the mandibular ramus was ensured with 2 mini plates. The chondral part of the rib graft was set facing the articular fossa of the temporal bone, framing another condyle that guaranteed articular functions. The cryopreserved and moist allogeneic amniotic layer was mounted onto the condylar piece of the new joint head. Accordingly, the epithelial side of the film was balanced toward the joint cavity. Before closing the operation site, the patient's occlusion was evaluated and balanced. Intraoperatively, no surgical inconveniences were seen and furthermore the anesthesia was all around endured by the patient.

As a result, the postoperative treatment included intensive physiotherapy and regular follow-up appointments. Wound healing, mouth opening, and her general condition were evaluated on the 1st, 3rd, 5th, 7th, 14th, and 30th day and then every month postoperatively. A 20-month follow-up of the patient showed uneventful wound healing without complication. Ankylosis of the TMJ was avoided by long-term observation and the patient presented a maximum interincisal opening of 32 mm, 8 months postoperatively. The redness of the ankylosis must be considered as the result of an ideal interchange of the resection of the tumor, the effective reconstruction, forceful physiotherapy, and great consistency by the patient.

The aim of this case was to build on the encouraging outcome of the animal study and to prove these findings. Because we used HAM combined with a costochondral graft, the results cannot be directly linked to HAM. Based on our experience, the outcome was better than in our conventionally treated cases, but no solid evidence exists. Although no fibrotic intergrowth, an uneventful integration of HAM, and recovery of a normal mouth opening range can be reported in this case, this innovative therapy option must be compared to the currently applied interventions. As this case describes the usage of HAM combined with a costochondral graft in TMJ reconstruction for the first time, it must be considered as an approach bringing to light the great potential of amniotic membrane in this indication. Beyond a doubt, one case makes it hard to accept efficacy and safety. Nevertheless, the reported antiadhesive effect, preventing TMJ ankylosis 20 months postoperatively, gives hope to finding a proper interpositional material preventing TMJ ankylosis. In any event, further clinical studies with high validity need to be performed to verify these findings.<sup>[5]</sup>

Third, after many positive potential effects of HAM on surgical conditions including the interpositional arthroplasty for TMJ ankylosis, the positioning within the intra-articular space of arthritic TMJs has never been investigated. This case reports HAM positioning within the intra-articular space of TMJs with severe inflammatory-degenerative disorders. As this patient have diagnosis of TMD and underwent major surgery with the application of a cryopreserved HAM patch.

A 48-year-old female came to observation due to a limitation in mouth opening range. She also reported crepitus sounds at the left TMJ as well as pain, exacerbated by function (e.g., chewing) and increasing in intensity over the past three months. Clinical assessment showed a limited mouth opening (i.e., 22 mm) and pain with palpation at the left joint and all the main masticatory muscles, more severe on the left side. At the first appointment (T0), mandible manipulation was performed to achieve a forced opening of about 40 mm. A MRI was prescribed to assess the disc-condyle relationship as the possible source of limitation in mouth opening and to gather some pictorial evaluation of the presence of joint effusion. Despite the clinical suspicion of TMJ arthritis, computerized tomography was not prescribed at this stage due to the expected low impact on treatment planning decisions. MRI showed a regularly

shaped condyle, with an anteriorized disc at closed mouth.

At the maximum mouth opening, the condylar translation is reduced and the disc is not recaptured. Joint effusion of severe entity is also present. A conservative approach to provide pain relief and to manage muscle tension was provided, based on counseling, a home program of self-exercise and a stabilization appliance to wear at night. After three months, symptoms improved only partially, with a reduction of pain with muscle palpation but a steady pain at the left joint.

Based on that, a cycle of five arthrocentesis plus viscosupplementation with hyaluronic acid (Synovial, IBSA) has been performed weekly. Clinical data has been recorded at each time point before each injection and 15 days after the last one. After one month from the last arthrocentesis plus visco-supplementation, the patient still showed some pain and, more important, still felt a limitation in the unassisted mouth opening and right laterotrusion. A diagnosis of TMJ intermittent locking on the left side was thus performed, and given the difficulties to stabilize clinical symptoms and mouth opening with the usual conservative approaches, the patient was planned for a surgical removal of the TMJ disc with concurrent HAM positioning TMJ surgery provided condyle remodeling and discectomy after which a HAM patch is positioned within the intra-articular space. Then stratified stitching is performed to avoid postoperative scars. Three months after the intervention, the patient showed no negative exclusions or postsurgical side effects. Jaw range of motion was increasing, both as for unassisted mouth opening (38 mm) and right laterotrusion (8 mm). The patient reported an overall improvement in chewing efficiency as well as the absence of pain.

Five months after surgery, a new MRI was performed. The images showed the physiological excursion of the TMJ condyle during mouth opening. This situation record demonstrates that inside the surgical treatment of TMJ arthrosis, the interposition of HAM in the intra-articular space due to an arthroplasty intervention represents a promising solution. In truth, three months after the intervention, the patient mentioned the absence of pain, an expanded masticatory potential, and development of variety mouth opening.<sup>[6]</sup>

## Properties Of HAM

### *Biomechanical properties*

An important property of amniotic membrane is its resistance to various proteolytic factors owing to the presence of interstitial collagens. Elastin found in amnion is chargeable for offering elasticity. It has a couple of metabolic functions consisting of its role in water and soluble material transportation and manufacturing of bioactive peptides, growth factors, and cytokines. Thickness of normal amniotic membrane lies between 0.02 and 0.5mm, which includes around 6–8 layers of cells. An average surface area of this membrane is about 1600 square centimeters.

### *Promotion of epithelization*

Amniotic membrane facilitates migration of epithelial cells, reinforces basal cell adhesion, promotes epithelial differentiation, prevents epithelial apoptosis, and promotes epitheli-

zation in healing of wounds. Various growth factors produced by amniotic membrane can stimulate epithelialization. It can also promote expansion and maintenance of epithelial progenitor cells in vivo and can produce endothelin-1 and parathyroid hormone related protein. Brain natriuretic peptide and corticotrophin releasing hormone are also produced by membrane epithelial cells which play roles in increasing cellular proliferation and calcium metabolism. Expression of mRNA for epidermal growth factor, hepatocyte growth factor receptor, and keratocyte growth factor receptor was demonstrated by Koizumi et al. in 2000 in cryopreserved amniotic membrane. Its basement membrane serves as a safe and suitable bed for the growth of epithelial cells. Sufficient oxygenation for epithelial cells is provided by its good permeability in contrast to other synthetic materials. Thus, amniotic membrane is an ideal tissue which facilitates the growth of epithelial cells, helping in their migration and differentiation.

### *Inhibition of fibrosis*

The amniotic membrane possesses antifibrosis properties. Fibroblasts are evidently chargeable for scar formation in the course of wound restoration and are activated by transforming growth factor  $\beta$ .

Amniotic membrane reduces the risk of fibrosis by down-regulation of transforming growth factor  $\beta$  and its receptor expression by fibroblasts. Therefore, scaffold of an amniotic membrane modulates wound healing by promoting reconstruction of tissues rather than promoting formation of scar tissue

### *Anti-microbial and Anti-viral properties (interferon $\alpha$ , $\beta$ , and $\gamma$ )*

The risk of infection is reduced by amniotic membrane due to its antimicrobial and antiviral properties. Microorganisms upon their entry into the body are eliminated by our immune system through an adaptive immune response,  $\beta$ -defensins, a major group of antimicrobial peptides and an integral part of the innate immune system, which are expressed at surfaces of mucosa by epithelial cells and leukocytes. Amniotic membranes also have the ability to produce  $\beta$ -defensins with the predominant type present in amniotic epithelium being  $\beta$ 3-defensin. Amniotic membrane may prevent infiltration and adhesion of microorganisms to wound surfaces by acting as a barrier. The hemostatic property of collagen fibers of amniotic basement membrane prevents hematoma formation in clean surgical wounds. This reduces bacterial load and risk of infection by preventing accumulation of microbes. Another mechanism of action against infection by membranes is through their adhesion to the wound surface. This attachment prevents formation of dead space and accumulation of serous discharge. Furthermore, bacterial entrapment and stimulation of migration of phagocytes also occur by fibrin filaments formed during wound healing. These filaments cause adhesion of the wound bed to amniotic membrane collagens. There is a report that bacterial proliferation is reduced even in contaminated wounds by amniotic membrane.

### Cell differentiation properties

The fetal placental tissues have the potential to transform into different cell lineages. The hematopoietic lineage is found in the chorion, allantois, and yolk sac; and the mesenchymal lineage is found in both the chorion and amnion. The cells isolated from the chorion are good sources of cells of hematopoietic and mesenchymal lineages as they possess these properties. It is considered that the amniotic membrane can maintain pluripotent stem cell potential for cell differentiation.

### Lack of immunogenicity

Occurrence of acute rejection after transplantation of amniotic membranes is negated by the fact that amniotic epithelial cells do not express HLA-A, HLA-B, HLA-D, and HLA-DR antigens but express HLA-G on their surfaces. Presence of interferon  $\gamma$  and other immunologic factors has also been observed in the amniotic membrane. It seems that amniotic membrane may induce immunologic reactions in the presence of viable epithelial cells. One study revealed that transplantation of fresh amniotic membrane is associated with a mild inflammatory response. This could be probably due to expression of HLA-I antigens by viable epithelial cells. However, immunogenicity of cryopreserved amniotic membrane is less than that of fresh amniotic membrane as epithelial cells are lost in cryopreservation. T lymphocytes in allografted limbus cells are suppressed by amniotic membrane. This implies immunosuppressive properties of amniotic membrane which can increase the chances of successful grafting. As tissue grafts of placental membrane materials present a low risk of immune rejection, they are bestowed with "immune privilege".<sup>[7]</sup>

### Results

This research is a promising suggestion concerning the use of HAM for TMJ surgery. Case series providing a longer follow-up should be encouraged, as well as the assessment of less invasive strategies for HAM positioning. Specifically, future scientific trials would possibly aim at comparing the effectiveness of HAM with respect to conventional interpositional surgical intervention. In addition, thanks to its properties, it has been validated that the utility of HAM to wounds markedly reduces patients' experienced pain intensity. Furthermore, amniotic membrane can reduce postoperative adhesion.

### Discussion

Alloplastic materials, such as silicone or Teflon, achieve a preservation of the vertical height of the ramus, though allergic and foreign body reactions have been reported. The facts that alloplastic materials are very expensive and must not be used in children and limits their utilization. Other interpositional material could be biological materials such as fascia lata and fat graft but they cannot preserve the vertical height of the mandibular ramus and in consequence, functional problems are common.

At present, the most frequently used interpositional materials are bone grafts such as metatarsal, sternoclavicular, or costochondral grafts. Among these, the costochondral graft interposition has been extremely popularized. In consequence, the use of an autologous costochondral graft combined with free fat graft, as it is reported to have the best

long-term outcome, is considered the criterion standard. Nevertheless, costochondral grafts have an unpredictable growth potential and their extraction is always accompanied by donor site morbidity.<sup>[8]</sup>

### Conclusion

The aim of this research is to recognize the best material to promote healing of the TMJ after surgical intervention, without any recurrence of disease. All this information is gathered to encourage institutions to publish more researches about this material and motivate future clinical trials to aim at the comparison of the effectiveness of HAM with respect to standard interpositional surgical intervention. Longer follow-up should be encouraged, as well as, imaging techniques trying to assess the intra-articular changes associated with the use of human membrane. This will help in defining their overall scope and further applications in the field of oral and maxillofacial surgery.

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