

Role of Stem Cells of the Chondro-Osseous Graft in the Growth of the Condyle of the Temporomandibular Joint

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Abstract

Objective: To evaluate the role of mesenchymal stem cells in the growth and remodeling of the chondro-osseous graft used for Temporomandibular Joint (TMJ) reconstruction.

Methods: Experimental studies were conducted on eleven-week-old male rabbits. Condylar excision was performed followed by immediate reconstruction using a chondro-osseous graft.

Results: Histopathological evaluation demonstrated organized fibrocartilage, proliferative mesenchymal layers, hypertrophic chondrocytes and osteoid formation with marrow spaces.

Conclusion: Mesenchymal stem cells may contribute to graft growth, integration, and functional reconstruction of the temporomandibular joint.

The Temporomandibular Joint (TMJ) is a synovial joint and is unique among the joints of the human body, as it represents the only mobile articulation in the cranio-mandibular region where the mandible articulates with the bones of the skull base. These joint plays a crucial role in essential functions such as mastication, speech, and swallowing.

The TMJ is a highly specialized joint composed of two distinct compartments: The superior (upper) and inferior (lower) joint spaces, which are separated by an articular disc. Unlike most synovial joints, where the articular surfaces are covered by hyaline cartilage, the articular surface of the mandibular condyle and the temporal bone in the TMJ are covered by fibrocartilage, which provides greater resistance to mechanical stress and functional loading.

Both temporomandibular joints function in a coordinated and synchronized manner, similar to the conjugate movements observed in ocular activity. The functional movements of the TMJ are regulated by a complex neuromuscular control system involving reflex mechanisms that coordinate the muscles of mastication.

The role of the mandibular condyle as a growth center has been the subject of considerable debate. However, several experimental investigations have demonstrated that the condyle possesses significant growth potential and contributes to mandibular development. Mesenchymal stem cells play a critical role in the growth and remodeling of chondro-osseous grafts, contributing to the regenerative capacity of the joint.

Experimental studies conducted on rabbits have provided supporting evidence for the viability and growth potential of the TMJ condyle, thereby reinforcing the concept of its involvement in craniofacial growth and development.

Keywords: Stem cells; Chondro-osseous graft; Temporomandibular joint; Condyle growth; Mesenchymal stem cells

Introduction

Stem cells are undifferentiated cells that have the ability to develop into many different types of cells during early life and growth. They also function as a repair system in the body by replenishing damaged tissues.

In recent years, stem cells have played an increasingly important role in regenerative medicine. They are particularly significant in procedures such as bone grafting and distraction osteogenesis for bone elongation in children suffering from conditions such as poliomyelitis [1,2].

The therapeutic potential of stem cells has been widely investigated in the treatment of several diseases, including Type 1 diabetes, Parkinson's disease, Amyotrophic Lateral Sclerosis (ALS), heart failure, and osteoarthritis. Stem cells have also been used in the treatment of various blood disorders.

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Furthermore, stem cells possess the potential to be developed into new tissues for transplantation and regenerative therapies. In adults, stem cells can be obtained from several sources, including bone marrow, adipose tissue (fat), and peripheral blood.

Several types of stem cells have been reported in the literature, including embryonic stem cells, adult stem cells, adipose-derived stem cells, and undifferentiated somatic stem cells.

Despite their promising therapeutic applications, the use of stem cells carries certain risks. Potential complications include infection, particularly in patients with compromised immune systems or low white blood cell counts. In addition, viral and fungal infections may occur as adverse effects in some cases.

Stem cells can also be defined as undifferentiated cells in multicellular organisms that have the capacity for self-renewal and the ability to differentiate into specialized cell types.

Stem cells play a crucial role in the healing and regeneration of bone following bone grafting procedures and distraction osteogenesis, as described by Ilizarov, an orthopedic surgeon from Russia. Stem cells also contribute to the growth and development of the jaws and the Temporomandibular Joint (TMJ). In reconstructive procedures, the TMJ may be replaced using chondro-osseous grafts for the management of temporomandibular joint ankylosis and other joint defects.

Chondro-osseous grafts have also been used in the reconstruction and management of condylar hypoplasia and First Arch Syndrome [1-3].

The introduction of chondro-osseous grafts represented a significant advancement in the reconstructive surgery of the facial skeleton. Previously, costochondral grafts were widely used; however, their popularity has decreased due to several complications. These include dislodgement of cartilage during surgery, the requirement for prolonged intermaxillary fixation (5–6 weeks), the possibility of pleural perforation, and the unpredictable growth pattern of the graft, which may also affect the psychological well-being of the child.

Growth of the Condyle

There has been considerable controversy regarding the growth of the mandibular condyle and the mandible. According to John Hunter (1772–1773), the condyle acts as a primary growth center for mandibular development.

To investigate this theory, experimental studies were conducted on newborn rabbits. In these experiments, the head of the condyle was surgically resected. After three months, a significant jaw deformity was observed in the rabbits, with the mandible deviating toward the side where the condyle had been removed. These findings support the theory that the condyle functions as a growth center (Figure 1A).

In contrast, Moss (1962) proposed an alternative concept known as the Functional Matrix Theory, which challenges the idea of the condyle as the primary growth center. According to Moss, the growth of the mandible and midface occurs as a response to functional demands of the surrounding soft tissues and periosteal matrix.

Based on extensive clinical and experimental experience, it is reasonable to suggest that both theories may play a role in craniofacial growth. Therefore, the development of the mandible and midface is likely influenced by both intrinsic growth centers and functional environmental factors, rather than by a single mechanism alone (Figure 2A-2D).

Materials, Methods and Results

The aim of this research and the major scientific and methodological objectives were to evaluate the role of mesenchymal stem cells in the growth of the chondro-osseous graft used in Temporomandibular Joint (TMJ) reconstruction, as well as the role of stem cells in the growth, remodeling, and repair of the head of the chondro-osseous graft acting as a new condyle.

In this study, we used a novel technique for reconstruction of damaged or underdeveloped TMJ in several pediatric cases associated with different diseases. These included ankylosis of the joint with severe facial deformity on the affected side, accompanied by the inability of the child to open the mouth for chewing food.

The chondro-osseous graft was harvested from the iliac crest of children aged 5 to 7 years. The osteoid portion measured approximately 5 cm in length, with a cartilage cap of 1 cm height consisting of a bicortical graft.

This chondro-osseous graft was also used in children with condylar hypoplasia and in First Arch Syndrome, which occurs due to early occlusion of the stapodial artery, the main nutrient vessel supplying the first and second pharyngeal arches during embryonic development.

Experimental Studies

In this experiment, eight growing male rabbits aged eleven weeks and weighing approximately 1.5 kg were used. The condyle of each rabbit was surgically excised, and immediate TMJ reconstruction was performed using a chondro-osseous graft harvested from the iliac crest. The animals were kept in the colony and were able to masticate food normally after surgery.

All rabbits remained healthy postoperatively. Antibiotic therapy consisting of Ampicillin (250 mg intramuscularly, twice daily) was administered. One rabbit developed an infection, which was successfully controlled.

The rabbits were sacrificed after three months (Figure 1B). Specimens of the TMJ were immersed in 10% buffered formalin with a decalcification agent for two weeks, after which histopathological slides were prepared.

Histopathological Studies

Histological examination of the chondro-osseous graft revealed four distinct layers:

1. First layer: Dense fibrocartilage, which appeared thick due to the strong mastication activity of the rabbits.
2. Second layer: Several layers of small, round mesenchymal stem cells, representing the proliferative layer.
3. Third layer: Chondrocytes undergoing a sequence of hypertrophic changes.
4. Fourth layer: Osteoid tissue with bone marrow spaces in between.

G-protein-coupled receptor CXCR4 expression was observed in hypertrophic chondrocytes, while the chemokine stromal cell-derived factor SDF-1 was expressed in the bone marrow adjacent to the hypertrophic chondrocytes (Figure 1C).

Biological Reconstruction of the TMJ

There are two main techniques for biological reconstruction of the Temporomandibular Joint (TMJ):

1. Costo-chondral graft, which consists of rib bone with cartilage. However, the cartilage is not firmly attached to the rib.
2. Kummoona chondro-osseous graft, which consists of osteoid bone with a cartilage cap harvested from the iliac crest of children aged 5 to 6 years.

The graft consists of approximately 4 cm to 5 cm of osteoid tissue with a cartilage cap of about 1 cm, harvested from the child's iliac crest [4,5].

Our graft has become more widely used because the Costo-chondral graft consists of rib osteoid tissue with cartilage that is not firmly attached to the rib, and the cartilage may dislodge during surgical reconstruction of the TMJ. In addition, perforation of the pleura may occur during rib harvesting, particularly when performed by an inexperienced surgeon (Figure 3A, 3B).

Intermaxillary fixation following the use of a Costo-chondral graft may extend for up to five weeks, which can lead to spasms of the muscles of mastication. Furthermore, the growth pattern of the Costo-chondral graft is often uncontrolled and unpredictable.

Role of Stem Cells

Stem cells play an important role in the growth of the chondro-osseous graft and also contribute significantly to the healing process of the graft when rigid fixation with the bone of the ascending ramus is achieved.

Healing begins after decortication of both the graft and the ascending ramus followed by rigid fixation. Platelet aggregation occurs, resulting in the release of Platelet Growth Factor (PGF). Within the first twenty-four hours, small blood vessels invade the bone and graft through a creeping substitution mechanism.

Mesenchymal stem cells are derived from bone marrow, periosteum, and surrounding muscles.

Stem cells are undifferentiated cells with the capacity to both multiply and differentiate into more than 100 different cell types. Another important characteristic of stem cells is their ability either to remain as stem cells or to differentiate into specialized cells such as blood cells or nerve cells. They also possess a strong regenerative capacity.

In recent years, stem cells have become an important component of therapeutic medicine and are widely used in regenerative medicine to promote repair responses in diseased or dysfunctional tissues.

Clinical Application

The application of the Kummoona chondro-osseous graft in reconstruction of the temporomandibular joint represents a significant advancement in reconstructive surgery.

Recently, mesenchymal stem cells have also been used in immediate reconstruction with bone grafts following radical resection of malignant tumors. These studies were supported by experimental research in rabbits with subsequent clinical applications.

This approach has been considered part of therapeutic medicine because the technique has also been successfully applied in malignant cases [6].

References

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Figure 1A: Photo of deformed face of the Rabbit after resection of the head of condyle.

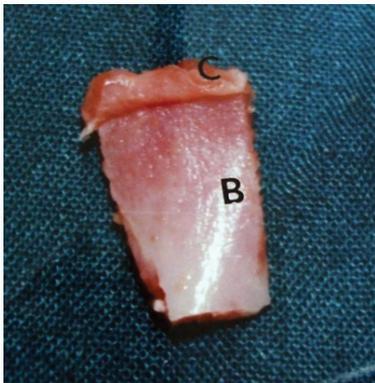


Figure 1B: Showing the chondro-osseous graft of rabbit.

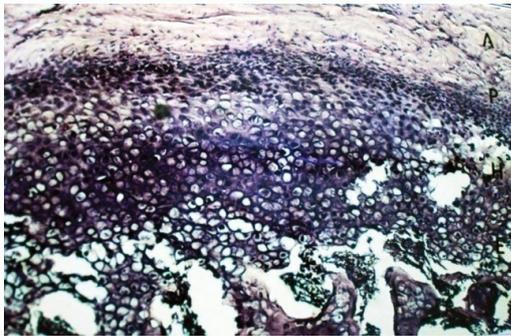


Figure 1C: Histopathological studies of Rabbit condyle showed 4 layers, first layer showing thick fibrocartilage, second layers showed many layers of small round mesenchymal stem layers, third layer showing hypertrophic chondrocyte and fourth layer were consist from bone marrow with osteoid tissue.

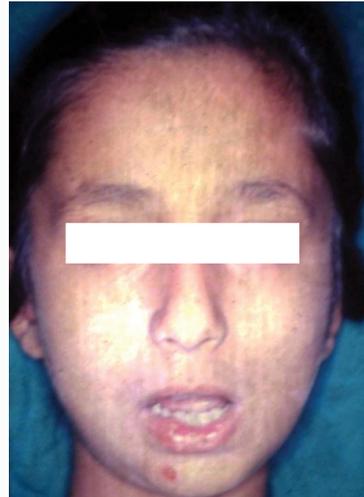


Figure 2A: Six years child with ankylosis of the mandible in the left side and deformity of lower jaw.



Figure 2B: Tomography of the Temporomandibular Joint (TMJ) showing ankylosed joint.



Figure 2C: One-year post-operative photo after reconstruction of the TMJ by chondro-osseous graft.



Figure 2D: Tomography of the left TMJ with full functional activity of TMJ that replaced by chondro-osseous graft.

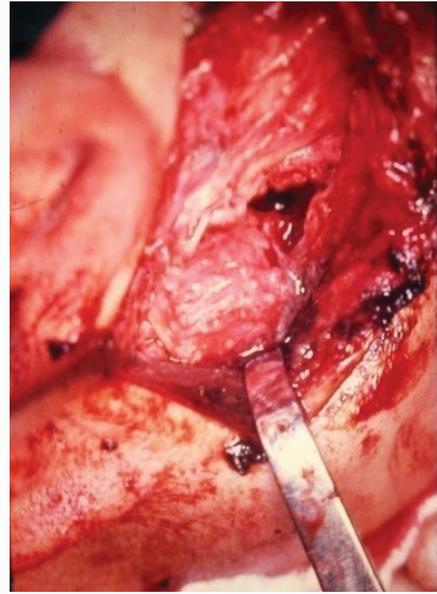


Figure 3B: Photo of Chondro-osseous graft after reconstruction was cited in the temporomandibular joint capsule replacing head of condyle.



Figure 3A: Photo showing the chondro-osseous graft of human child of 6 years, consist from osteoid tissue of about 4 cm length with cup of cartilage of about 1 cm.