

Functional Approaches to Oral-Maxillo-facial Restoration

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Abstract

Several lesions or pathologies alter the symmetry, anatomical morphology and facial physiology of the patient affecting their quality of life; therefore they need to be adequately repaired.

Customized prosthetic devices allow proper correction of these alterations through surgical interventions. Thus it is important to develop protocols aimed to design the prosthesis considering the anatomical parameters of the patient, its placement and the comprehensive approach to each case.

Tissue engineering proposes new strategies for regeneration or replacement of tissues or organs, restoring the shape and function to the affected area. Many therapeutic approaches are based on stem cells since they could make the difference in promoting tissue acceleration and regeneration in clinical practice.

With the prospect of being implemented in the field of oral-maxillofacial reconstruction, these developments could have positive effects on patient's care, impacting on population health.

Keywords: Regenerative dentistry; Pulp cells; Surgical protocol

Introduction

Some vital functions depend on the correct functioning of the oral-maxillofacial area of the human organism, such as speech ability, food intake, or breathing. On this matter, it is relevant that the stomatognathic system preserves its functional integrity, since its deterioration could be invalidating due to different causes. Therefore, new therapeutic approaches are required for the repair of the region, in order to return patients their oral health status.

In dental practice one of the most important challenges is the replacement of tissues that may be affected, which is done using different materials and reconstructive surgical techniques, with the aim to repair anatomically and functionally the damaged area.

Some surgical treatments turn to the placement of standard prostheses with variable outcomes. Nowadays, personalized prosthetic devices designed for these surgeries allow the restoration of the impaired function to the patient. In order to optimize the generation and placement of the aforementioned devices, it is necessary to develop protocols aimed to perform a comprehensive surgical reconstruction.

In recent decades, tissue engineering has proposed therapies for tissue or organ replacement through different strategies, many of them based on stem cell developments that may have multiple possible applications in clinical practice.

The aim of the present study is to gather recent advances made in both types of therapeutic approaches aimed at oral-maxillofacial reconstruction.

Development

Malformations, traumas, or pathologies that cause alterations of the oral-maxillofacial region substantially modify the symmetry, the normal anatomical morphology and the facial physiology. As consequence, the treatment of these conditions represents a great challenge for the health team, and requires deploying strategies aimed at restoring the well being of the patients.

In these cases, when the damaged tissues are bone or cartilage,

reconstructive dentistry resorts to its substitution, by placing prosthetic devices using surgical procedures, in order to seek the functional repair of the affected area.

In order to carry out these surgeries, standard prostheses are frequently used, which often fail to correct the impairments. The use of this type of prosthetic devices requires the adjustment of the implant piece to the anatomy of the patient in situ, prolonging the surgical length. Due to the difficulties implicit in these adjustments, patients may suffer sequelae such as decreased speech ability or difficulties to swallow, and must undergo successive surgical procedures as to restore these functions.

On the other hand, the surgical reconstruction approach that involves placing personalized prostheses to the patients allows the surgeon to restore their facial symmetry and normal oral-maxillofacial functioning. These devices must be designed taking into consideration the anatomical parameters of the patient related to shape, size, weight and other features from preoperative computerized and imaging studies. An anatomic model with the defect is then used to create the implant for reconstruction and surgical placement. Customized designs may improve not only the aesthetic conditions, but also morphological and functional issues regarding the movements of the area under treatment. As it has been described, this method of reconstruction is rapid, exact and reduces operative time significantly in these defects [1].

The development of surgical protocols aimed to improve the approach and rehabilitation of patients suffering from these health

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problems are strategies focused on minimizing the sequelae of the surgical intervention. The protocols applied for the diagnosis of a certain pathology, a treatment or a surgical procedure are practice guidelines that may be adopted to encourage the use of the most scientifically acceptable materials and methods, but they are not meant to tell dental providers how to perform procedures of their own practice which is done by their professional education. So, these practice guidelines are defined as "descriptive tools of standardized specifications for care of the typical individual in the typical situation, developed through a formal process that incorporates the best scientific evidence of effectiveness with expert opinion" [2].

Over the past decades, dentistry has begun to incorporate more evidence-based practice guidelines rather than empirical observations to make decisions related to treatments for different conditions. Scientific-professional organizations periodically review the scientific literature covering selected dental topics and make recommendations for diagnosis and treatment, which intent to help colleagues choose the most effective mode to perform these procedures supported by scientific evidence. They are neither statutory nor regulatory documents aimed to improve results [2].

In this way, an adequate protocol is based on the interdisciplinary contribution of the work team which is made up of oral-maxillofacial, oncology and plastic surgeons, other professionals belonging to health sciences and biomedical engineers. By means of joint work the surgical approach projection is made, the necessary materials are designed and produced, and the procedure in question is carried out. In this way, the protocol developed is intended to provide surgeons with the tools to enhance the surgical planning and results of the procedure, in order to improve the quality of life of the patients under treatment [3].

The surgical act demands the surgeon's disposition to engage in the preparation of the patient and the environment for the surgery [4]. A protocol includes not only medical and surgical aspects of the treatment applied to the patient, but also describes the procedures used for the design of specific instruments or implants for him.

It should be highlighted that the protocol must begin when the patient makes the first consultation with the surgeon, including the diagnostic process, the surgical act, finalising with the actions undertaken for the follow-up and integral rehabilitation of the individual. In order to define a protocol, a careful preoperative study must be started to assess the surgical risk, for which the clinical history is a reliable parameter in order to detect certain patient risk factor [4].

In the treatment of pathologies that require bone repair and regeneration autografts, allografts, xenografts to alloplastic grafts have been used. Among them, the autograft is considered "gold standard" of bone grafting to induce bone formation and regeneration through osteogenesis, osteoinduction and osteoconduction, but the application of autografts may be limited by the insufficient donor bone tissue supply and additional surgical wounds. On the other hand, alloplasts are synthetic materials that can be designed with different shape, chemical composition, and varied surface configurations for the repair bone defects and promotion of bone growth [5].

The restorative materials in dentistry for implants manufacture are diverse, including non-metallic materials such as plastic, carbon and apatite compounds. Among these materials the Hard Tissue Replacement (HTR) is a synthetic polymer created as an implant material for bony reconstruction and maintenance, that has been clinically used in a large number of patients for a variety of reconstructive procedures including alveolar ridge augmentation, as space-occupying material for

periodontal pockets and extraction sockets, mandibular repair, among others [6,7]. The ideal nonresorbable synthetic bone include biological compatibility, microporosity that provides a scaffold for formation of new bone, radiopacity, nonmigratory particles, osteogenicity or the ability to facilitate new bone formation [6]. It has polymeric composition (polymethylmethacrylate core) and outer layer of calcium hydroxide, porous dimension is suitable for fibrovascular and bone internal growth, and it was observed that patients remained infection-free during the follow-up period [1,8].

Some metals are used as passive substitutes for hard tissue replacement such as total hip and knee joints, for fracture healing aids as bone plates and screws, spinal fixation devices and dental implants. Metallic biomaterials include stainless steel, cobalt-chrome-molybdenum alloys, and titanium, pure or alloyed. In this technological development, titanium was found the only metal biomaterial to osseointegrate, and has become important as a biomaterial, given its extreme chemical passivity and, therefore, excellent biocompatibility, in addition to gathering adequate physical properties for good long-term biomechanical behaviour [9].

In the last decades, tissue engineering has proposed new therapies that imply the replacement of tissues through three-dimensional constructs, which restore the shape and function to the affected body area. The constructs involve the patient's own cells, in conjunction with biomaterials and biomolecules. It should be noted that regenerative therapy is aimed at the repair or replacement of cells, tissues or organs in order to restore altered functions due to diverse causes. Because stem cells underpin many of the therapeutic approaches of regenerative medicine, they are becoming increasingly important [10-12].

Tissue engineering strategies involve three main elements: cells, molecular signals and natural or artificial scaffolds. These scaffolds provide the base for the repopulation and specialization of stem cells, blood vessels and extracellular matrices, and their surface morphology strongly affect the attachment of surrounding cells and tissues after implantation. They have been developed for use in different tissues such as bone and cartilage [13]. In connection with this, an important concept for promoting the repair and regeneration of bone tissue is to combine scaffolds of different biomaterials with living cells to form tissue-engineering constructs. The cells that are often used in such constructs are the mesenchymal stem cells (MSC) due to its abilities to proliferate and differentiate toward bone-forming cells [5].

Despite new advances in orthopaedic surgery that enhanced fracture healing and surgical outcomes, there are a subset of fractures deficient in bone repair and culminate in nonunion. There are four elements integral to bone repair: an osteoconductive matrix, osteoinductive signals, osteogenic cells capable of responding to these signals, and a sufficient blood supply [14]. Since the use of autologous bone-graft provides many of these elements but there are morbidities associated to limited supply among other factors, progress in the utilization of stem cells have been made in promoting the fusion of long bones in nonunion treatment and fracture-healing in the clinical settings [14].

The treatment of invalidating knee injuries such as osteoarthritis by intra-articular injection of autologous MSCs obtained from the patient's bone marrow has given good results in a pilot study [15]. It has been created in vitro entire bone condyles containing viable cells, human MSCs, at physiologic density and well-developed bone matrix, acellularized bone scaffold, which has tremendous potential to provide patient-specific bone grafts for craniofacial reconstruction after congenital defects, cancer, resections and traumas [16].

Recently, a new nanomaterial called graphene has begun to be used, which provides a promising biocompatible scaffold that does not hamper the proliferation of human MSC and accelerates their specific differentiation into bone cells [17]. Materials coated with graphene or even 3D graphene foam were capable to guarantee viability and to induce osteogenic differentiation compared with traditional substrates or scaffolds and have effects on stem cells commitment [18]. Graphene-modified substrates and materials are biocompatible, allow cell adhesion and proliferation, and increase differentiation of stem cells into osteogenic lineage. As graphene and its derivatives present properties such as high surface area, high mechanical strength, and ease of functionalization, they hold great potential for biomedical applications [19].

Restoration of tooth tissue, whether from disease or trauma, represents a significant proportion of daily routine for many practicing clinicians, so moving toward the tissue engineering of teeth are of great interest since they provide potential for restoration of the structural integrity of dental tissues with positive impact on treatments for the patients [20]. The potential of clinical application of the stem cells in the orofacial complex is in the biological regeneration of affected structures or tissues by hereditary conditions, traumas neoplastic diseases or infections, and for those missing in hypodontia [20,21]. It should be remembered that deficiency in the alveolar bone due to loss of teeth, infection or trauma is the main limiting factor for dental implant-supported prosthetic therapies [5].

In the oral cavity numerous types of human dental tissue-derived mesenchymal stem cells have been isolated and characterized such as dental pulp stem cells (DPSCs), those derived from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs), dental follicle progenitor cell (DFPC), alveolar bone derived MSCs (ABMSCs), stem cells from apical papilla (SCAP), tooth germ progenitor cells (TGPCs), and gingival MSCs (GMSCs) [22]. These post-natal populations have mesenchymal-stem-cell-like qualities, including the capacity for self-renewal and multilineage differentiation potential, they can be isolated from the extracted specialized dental tissues by enzymatic digestion. These stem cells have the niches that provide specific signals that modulate cell fate decisions, were found to express several surface markers, and have the capacity to differentiate into adipocytes and osteocytes, among other lineages. Since multipotent derived from teeth are easily accessible this new source of stem cells could be of benefit in cellular therapy with clinical applications [23-25].

The main source of adult stem cells of permanent teeth are molars, showing their DPSCs the highest osteogenic potential compared to cells obtained from other body locations, resulting in satisfactory bone regeneration in animal models [26].

Stem cells derived from various tissues have different patterns in relation to proliferation, clonogenicity, and differentiation abilities *in vitro* and *in vivo*. Tooth-derived stem cells that have been obtained from various tooth-derived tissues show heterogeneity, particularly those obtained from permanent third molars were more proliferative *in vitro* than those from other sources [27].

Stem cells can be used in biomedical research as a model to study different diseases, but their relevance would be even more outstanding in relation to regenerative medicine [12]. Undoubtedly the frontier of knowledge in this matter is in full expansion, biologic and clinical interest in MSC has risen dramatically in the last decades, seeking for the development of novel cellular therapies, but the methods to isolate and expand the cells may be significantly different among laboratories,

raising the need to define their characteristics. The International Society for Cellular Therapy stated that 'multipotent mesenchymal stromal cells' is the currently recommended designation and proposes minimal criteria to define human MSCs [28].

The potential of stem cells for tissue repair and regenerative dentistry applications refers to clinical therapies for different types of tissues, with multiple body locations, related to important functions of the human body [24,29].

Scientists put great effort in the understanding, identification, and characterization of the various differentiation processes stem cells may undergo, which opens doors to the development of cell-based therapies to treat disease, with two different strategies for application, on one hand, the injection of cell suspension into the blood circulation or the target tissue (cell therapy) and, on the other, the implantation of tissue-like construct consisting of a 3D matrix colonized by cells into the tissue defect of the recipient. From the point of view of trauma and joint surgery, the use of stem cells in dentistry could make a difference in the promotion of tissue acceleration and regeneration, and have multiple applications in clinical practice [30].

Conclusion

The placement of personalized prosthetic devices for the surgical treatment of oral-maxillofacial disorders is put into practice within the framework of comprehensive patient management protocols. Although it requires careful planning, including the preparation of the patient along with the design of the implant device, it has several advantages. Among them are issues specific to the procedure, such as safety conditions and better expected results in the reconstruction of the affected area.

In turn, the use of stem cells in dentistry is in full progress and the application of these cells would be a great contribution to existing therapies, with the perspective of being implemented in the future, with benefits for human oral health.

Both types of therapeutic approach aimed at oral-maxillofacial reconstruction could have a positive impact on the health of the population.

Conflict of Interests

There is no conflict of interest between authors.

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