The effect of stem cell application on bone regenerate during rapid distraction osteogenesis (an experimental study)

Thesis

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Dedication

This work is dedicated to

My Dear parents
My brothers and sister

The light that leads my way

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DO : Distraction osteogenesis

TMJ : Temporomandibular joint

PEMF : Pulsed electromagnetic field

MSCs : Mesenchymal stem cells

ASCs : Adult stem cells

ESCs : Embryonic stem cells

BMSCs : Bone marrow stromal cells

FACS : Fluorescence-activated cell-sorting

MACS : Magnetic-activated cell-sorting

BBM : Bovine bone mineral

CT : computed tomography

CBCT : Cone beam computed tomography

DEXA : (**DXA**) Dual-energy X-ray absorptiometry (Bone Densitometry)

cm : Centimeters

HU : Hounsfield unit

H&E : Hematoxylin and Eosin

SD : Standard deviation

List of abbreviations

Kv. : Kilo Volt.

mA. : Milliampere

mm : Millimeter

µm : Micrometer

Kg : Kilograms

Mg : Milligram

Ml : Milliliter

3D : Three dimensions

IAN : Inferior alveolar nerve

PDL : Periodontal ligament

The craniofacial region is a complex tissue, consisting of bone, cartilage, soft tissue, nerves, and blood vessels. A number of conditions, such as cancer surgeries, trauma, congenital malformations, and progressively deforming skeletal diseases, can cause damage to these structures, leading to deformity.(1)

The only solution for extensive injuries is a reconstructive procedure. The bones of the craniofacial region provide the support for other elements, their successful regeneration and reconstruction are of the greatest importance to restore normal function of the craniofacial unit. The optimal bone constructed for the repair should be able to replicate the lost structure and completely restores its function and easily replaceable through the body's physiologic processes, harmless for the patients and reliable in defects where the tissue is compromised because of infection, radiation, scarring, or extensive trauma.(2)

Although traditional orthognathic surgery and craniofacial reconstruction have gained a generalized acceptance and experienced widespread success, several limitations are associated with acute advancement of osteotomized bone segments. (3-5) One of the major limitations is the inability of the soft tissues to be acutely stretched. (6-9) Moreover, many of the congenital deformities require such large skeletal movements that the surrounding soft tissues cannot adapt to their new position, resulting in degenerative changes, relapse, and compromised function and aesthetics. (10-12)

In light of these limitations, alternative approaches have been developed to correct severe anteroposterior, transverse and vertical deformities of the craniofacial skeleton. One of these alternative approaches is the method of gradual bone distraction known as Distraction Osteogenesis (DO). Distraction osteogenesis is a biologic process that promotes bone formation between cut osseous surfaces that are gradually separated by incremental traction.(13) The technique of bone lengthening by DO was first described in 1905 by Codvila,[14] but it remained undeveloped until Ilizarov, [13,15,16] a Russian physician, further developed the technique in the 1950s in Kurgan in West Siberia. For more than 35 years he successfully applied the technique of DO to the endochondral bone of the upper and lower extremities. A unique feature of the distraction technique is that bone regeneration by DO is accompanied by simultaneous expansion of the functional soft tissue matrix, including blood vessels, nerves, muscles, skin, mucosa, fascia, ligaments, cartilage and periosteum. These adaptive changes of the surrounding soft tissues through the tension that is generated by the distraction forces applied on the bone, is called distraction histogenesis. [17]

Distraction osteogenesis begins with the development of a reparative callus between the edges of two bone segments divided by a low-energy osteotomy. After the callus has initially formed, a distraction force is applied to these bone segments and gradually pulls them apart. Gradual incremental separation of bone segments places the callus under tension, this aligns the inter-segmentary gap tissues parallel to the direction of distraction. After the desired amount of bone length is achieved, the distraction force is discontinued. The newly formed bone (distraction regenerate) then undergoes maturation and remodeling until it becomes undistinguishable from the residual host bone. (18)

Regardless of the surgical site, adherence to Ilizarov principles is the key to surgical success. (15) Ilizarov principles are first osteotomy of the bone site with minimal periosteal stripping, followed by latency period 3, 5, or 7 days depending on the surgical sit, then Distraction rate of 1.0 mm per day. Distraction rhythm continuous force application is best.

Last, consolidation until a cortical outline can be seen radiographically across the distraction gap, usually 6 weeks.

Osteotomy is the surgical separation of an intact bone into two segments. It results in a loss of continuity and mechanical integrity, which triggers the process of fracture healing. A reparative callus begins to form within and around the ends of the fractured bone segments. (15)

Latency phase is the time between performance of the osteotomy and activation of the device. This phase generally lasts 5 to 7 days and allows for the development of an adequate hematoma with granulation tissue plug within the distraction gap at the osteotomy site. The intervening granulation tissue exhibits activity of inflammatory cells, proliferation of fibroblasts that provide a collagen network, the development of vascular channels, and invasion of