The Effect of stem cell application on bone Regenerate during distraction osteogensis An Experimental Study

Thesis Submitted for partial fulfillment of the requirements for master degree in oral and maxillofacial surgery

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2015

“This thesis was a part of an experimental project conducted on distraction osteogenesis to assess the effect of Mesenchymal Stem Cell application on bone quality during distraction osteogenesis and assessment the effect of rate pattern alteration on bone quality and quantity. This project included thesis of dear colleagues Alaa Hanaa, Alaa Jamal, Fatma Wageeh and Kamal Alhadama.”

“For the one who believes in me

My Mother”

“In The Memory of Dear Friend

Abdu Allah Abd El Razek Hussain El Hawary”

“When I saw the embryo, I suddenly realized there was such a small difference between it and my daughters. I thought we can’t keep destroying embryos for our research. There must be another way”

Shinya Yamanaka, Noble prize laureate in 2012 for his achievements in stem cell research

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Acknowledgment

I would like to express my special thanks and gratitude to

- Dr/ Maram Obeid, lecturer of Endodontics, Faculty of Dentistry, Ain Shams University, for proposing the research idea of use of mesenchymal stem cells and providing priceless data which helped a lot in writing the thesis protocol.
- Pancreatic Transplant Unit, Ain Shams University Staff, especially Mr. AlaaEdris (technical supervisor of the laboratory of the unit) for their valuable support in hosting the animals and providing the technical laboratory support for the current research.
- Professor Dr/ Nahed Khamis Head of Pathology department, Faculty of Medicine, Ain Shams University, for her sincere help during histological assessment of the results of this research.
- Last, but not the least the distraction osteogensis project team (2011 master degree of Oral and Maxillofacial Surgery Faculty of Dentistry, Ain Shams University post graduate students) Alaa Hanna, Alaa Jamal, FatmaWageh and Kamal Alhadama for valuable assistance in conducting this research.

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DO: DistractionOsteogenesis.

BMP: Bone Morphogenic Protein.

NGF: Nerve Growth Factor.

MSCs: Mesenchymal Stem Cells.

BMSSCs: Bone Marrow Stromal Stem Cells.

DPSCs: Dental Pulp Stem Cells.

bFGF: basic Fibroblast Growth Factor.

MMP: Matrix Metalloproteinase.

SDF: Stromal Derived Factor.

PDL: Periodontal ligaments.

TMJ: Tempromandibular Joint.

BBM: Bovine Bone Mineral.

PBS: Phosphate Buffer Saline.

CBCT: Cone Beam Computed Tomography.

EDAX: Energy Dispersive X-Ray.

SEM: Scanning Electron Microscope.

H&E: Haematoxylin and Eosin

Introduction

Bone reconstruction procedures in the craniofacial region are considered a complicated condition, which usually require skeletal correction to overcome psychological, breathing and eating problems by reconstructing both soft and hard tissues. Grafting from distant sites to regenerate and reconstruct missing bony segments carries the risk of donor site morbidity, the risk of rejection, infection or low bone quality. Distraction osteogenesis is a surgical process used in reconstruction of skeletal deformities and lengthening of the long bones. Distraction technology was used mainly in orthopedics, and is currently used in the oral and maxillofacial region to correct deformities of the facial skeleton without grafting risks [(1)].

Distraction osteogenesis refers to a surgical technique designed to address defects and deficiencies in the skeleton. Distraction osteogenesis originally was first mentioned by Hippocrates, Ilizarov introduced the distraction osteogenesis 40 years ago and the orthopedic community has employed distraction techniques to lengthen and reconstruct arms and legs [(2)].

Distraction surgery was first reported to treat defects of the oral and facial region in 1992. Since then, the surgical and technological advances made in the field of distraction osteogenesis provided oral and maxillofacial surgeons

with a safe and predictable method to treat selected deformities of the oral and facial skeleton [3].

Maksimov in 1908 was the first scientist to introduce the term stem cells. Becker *et al.* in 1963 were the first to prove the existence of self reproducible cells in the bone marrow of rats. Stem cell therapy was used in many fields of regenerative medicine. Generally, the clinical use of mesenchymal stem cells remains a controversial issue. However, the use of mesenchymal stem cells use carries great hope in enhancing the healing and regenerative power of newly formed tissues [4].

Distraction osteogenesis is a useful technique in regeneration of new bone, but has the drawback of decreased bone quality and quantity [5].

The advantage of using mesenchymal stem cells combined with distraction osteogenesis might aid in improving the bone quality and quantity of the distracted bone regenerate.

Grafting from distant sites to regenerate and reconstruct missing bony segments carries the risk of donor site morbidity, the risk of rejection, infection or low bone quality. Those disadvantages supported the use of distraction osteogenesis. Distraction osteogenesis is a surgical process used in reconstruction of skeletal deformities and lengthening of the long bones. Distraction technology is used in orthopedics and in the oral and maxillofacial region. These techniques are now utilized extensively by the maxillofacial surgeons for the correction of congenital and acquired defects. Distraction osteogenesis is used to correct congenital defects as micrognathia, midface hypoplasia and fronto-orbital hypoplasia and acquired defect as craniofacial deformities following trauma, pathological defects and surgical defects [(1)].

Distraction osteogenesis originally was first mentioned by Hippocrates [(2)]. Codivilla in 1905 [(6)] was the first to introduce surgical distraction for lengthening of the lower limbs, but his early cases suffered plenty of complications especially during healing due to failure and infection. Putti in 1921 [(7)] designed a unilateral external fixation device to lengthen the femur and reduce trauma of the osteotomy by constant control of the traction process. Abbott in1924 [(8)] conducted an application of bilateral external