ASSESSMENT OF THE ROLE OF BONE MARROW IN HEALING OF ALVEOLAR CLEFT GRAFTS

Thesis

Submitted for partial fulfillment of M.D. Degree in

Oral and maxillofacial surgery

By

Amr Amin Ibraheem Ghanem

B.D.S, ٢٠٠٣

M.D.S, ٢٠٠٩

Assisstant lecturer of Oral and Maxillofacial surgery

Faculty of Dentistry – Ain Shams University

Faculty of Dentistry
Ain Shams University
٢٠١٣

SUPERVISORS

Prof. Dr.
Abdel Fattah Sadakah

Professor of Oral and Maxillofacial surgery

Faculty of Dentistry – Tanta University

Dr.
Salah Abdel Fattah

Assistant professor of Oral and Maxillofacial surgery

Faculty of Dentistry – Ain Shams University

Dr.
Marawa El Kassaby

Assistant professor of Oral and Maxillofacial surgery

Faculty of Dentistry – Ain Shams University

Acknowledgment

This work would have never been possible without the effort of three exceptional supervisors who for almost four years worked hard and diligently to bring this work to light.

Professor Sadakah *provided academic and clinical support throughout this work. Professor Sadakah was there every step of the way during the clinical phases of this research as well as during the editing phase, his efforts and support could only be described as fatherly.*

Dr. Salah Abdel Fattah *provided potent support to the clinical work which was performed in the operating room of the oral and maxillofacial surgery department of Ain Shams University. Furthermore, he provided valuable information and teachings that enhanced the presentation of this work.*

Dr. Marwa El Kassaby *has always been a pillar on which not only this research received foundation but also my entire surgical training. She is both a mentor and a friend. I will continue to learn from Dr. Marwa and hopefully will pass on her legacy of teaching and ethics to my younger colleagues.*

I would like here to acknowledge the efforts of my younger colleagues in the cleft care clinic: Mahmoud Yehia, Ramy Gaber, Mahmoud Abd Al Azeez, Omnia Adel and Yasser El Hadidy. All these brilliant assistant lecturers' and residents invested much of their time and effort in this research.

Last but not least, I would like to thank my friends and colleagues in the department of oral and maxillofacial surgery in Nasser institute hospital for their support and inspiration during the period I was amongst them.

I would like to dedicate this thesis to my dear family, wife and daughter, I dedicate this work to you in gratitude for your unconditional love and support.

I would like to also dedicate this work to Prof. Dr. Dr. med. Helmut Von Domarus. He has taught me to love surgery, literature and philosophy. He has provided with an image of the teacher that I have always wished to become.

Finally, I would like to dedicate this work to Professor Sadakah, Ass. Prof. Salah Abd Al Fattah and Ass. Prof. Marwa el Kassaby. Working with them in this research as well as during my surgical training has been an honor. I will always be proud that they were my mentors.

LIST OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

UCLP ..... Unilateral Cleft Lip and Palate.

BCLP..... Bilateral Cleft Lip and Palate.

ACG ..... Alveolar Cleft Graft.

MBG..... Mandibular Bone Graft.

ICB ..... .Illiac Crest Graft.

r-Bmp٢ ..... Recombinant Bone Morophogenic Two.

PRP..... Platlet Rich Plasma.

PRF..... Platelet Rich Fibrin.

PDGF ..... Platelet Derived Growth Factor.

TGF-ß..... Transforming Growth Factor Beta.

IGF-١ ..... Insulin Growth Factor One.

WBCS..... White Blood Cell Count.

RBCS..... Red Blood Cell Count.

CBCT ..... Cone Beam Computerized Tomography.

CT..... Computerized Tomography.

INTRODUCTION

Clefts of the Oral and Maxillofacial regions can be considered one of the most common craniofacial anomalies as regards occurrence. A congenital cleft lip is a deformity affecting multiple elements that have significant physical and psychological impact. Successful repair of the cleft lip and its associated deformities is a challenging and rewarding task. [١]

Oro-Facial clefts have variable presentations. As regards their anatomical position they may be unilateral or bilateral. They may be isolated affecting either the lip or palate only or the complete form that combines the previous two sites together. Clefts of the lip and palate may also be associated with other congenital anomalies and may be a part of a genetic syndrome. [١]

The primary palate is formed during weeks four to seven of gestation by the median palatine process derived from the fronto-nasal prominence. The lip and hard palate anterior to the incisive foramen are formed during this developmental process. Variations from normal development during this period may result in clefting of the primary palate, manifesting as incomplete or complete and unilateral or bilateral cleft extending into the lip. It is important to realize that the alveolus lies within the primary palate; thus, an alveolar cleft is a result of divergence from normal development during fronto-nasal prominence growth, contact, and fusion. Therefore, alveolar clefts are associated with cleft lip but not with isolated cleft palate deformities. The cleft in the alveolus is typically

located between the lateral incisor and the canine, although it can also occur between the central and lateral incisors. [٢]

Facial disfigurement in a congenital cleft anomaly is frequently complicated by a disrupted dental arch. The anterior teeth may be malpositioned, malformed or congenitally missing [٣]. In this respect any patient born with a complete cleft should be considered for alveolar grafting. [٤]

The benefits of alveolar cleft grafting (ACG) include: stabilization of the maxillary arch, elimination of oro-nasal fistulae, creation of bony support for subsequent tooth eruption, and reconstruction of the hypoplastic pyriform aperture providing support to the nasal alar base[٤]. Furthermore; ACG provides bone for placement of dental implants in cases with congenitally missing teeth[٥] and allows improvement of the oral hygiene conditions. [٦]

Various protocols were suggested for grafting of the alveolar process. Primary bone grafting of alveolar cleft was defined as that which was performed at an age younger than two years. ACG performed between the ages of two and five years was termed early secondary bone grafting. Finally when ACG was performed at age greater than five years it was termed delayed secondary alveolar bone grafting.[٤]

There is a general consensus that autogenous bone grafting is the gold standard for ACG as it supplies osteogenic cells into the cleft area[٧]. However; controversy exists as regards the source

of autogenous bone. The anterior iliac crest graft (ICB) has for long been considered as the standard donor site for ACG[٨]. Alternative sources of autogenous bone have been employed such as: the calvarium, the mandibular symphyseal region (MBG) as well as the tibia. [٩, ١٠]

In concept there is an agreement amongst many surgeons that mesenchymal-derived bone (e.g., MBG) used as graft material is subjected to less bone resorption, compared with bone of endochondral origin (e.g., ICB). This physiological variation was attributed to a difference in bony architecture, with a greater fraction of cortical bone in the mesenchymal-derived graft. [١١]

Furthermore, the different autogenous bone donor sites provide different volumes of bone. The volume of bone that can be harvested from MBG was ٤,٧١ cc for the cortico-cancellous block (in average) and the largest cortical block that could be obtained was ٢٠,٩ x ٩,٩ x٦,٩ mm in dimension [٩]. On the other hands, the Anterior iliac crest provided ٥٠ cc of non compressed cortico cancellous graft or a cortical block ٣x٥ cm in dimensions. The posterior iliac crest provided ١٠٠-١٢٥cc of non compressed cortico-cancellous graft or a cortical block of ٥x٥cm dimensions[١٠]. The volumetric capacity of the ICB exceeds by far that of the MBG which suggests the need for volumetric support when using MBG in wide ACG procedures. [١٢]

Research into the field of allogeneic grafts stemmed from the concept of minimizing donor site morbidity without compromising the chances of graft success. Moreover; as

previously stated some donor sites needed augmentation when the operative procedure exceeded its volumetric requirement. Studies reporting successful ACG using allogeneic grafts have been reported [١٣,١٤]. These studies achieved a successful rate comparable to ACG using autogenous bone grafts.[١٣]

Alloplasts have also been suggested as an alternative source of bone to eliminate donor site morbidity but could not be used in ACG without a source of osteogenic cells as a supplement.[٨]

Reports of recombinant bone morphogenic protein type two (r-bmp٢) [١٥] as well as the use of stem cells with different carriers in ACG offered another promising alternative source of bone with minimal donor site morbidity.[١٦]

The use of platelet gel therapeutic concentrates and bone marrow aspirate have long been discussed in conjunction with grafting however they were seldom discussed in the field of ACG.

The use of bone marrow aspirate has long been advocated in orthopedic surgery. Centrifuged bone marrow aspirate is one of the most commonly used osteoinductors, in combination with synthetic osteoconductors (such as β-Tricalcium phosphates), due to their convenience, the technical ease with which they are obtained, intraoperative processing, lack of immunogenicity, non-transmissibility of diseases, and low cost [١٧]. Although in concept the use of centrifuged bone marrow would also be beneficial in ACG, however the literature lacks clinical trials that assess the use of bone marrow in ACG.

Moreover; ***Hak Jun Kim et al.*** in [١٨], attempted to prepare PRP form bone marrow aspirate. Their hypothesis was that PRP derived from bone marrow would contain more growth factors and mesenchymal stem cells. They combined this PRP with BMP-٢ and fibrin glue and used it for the repair of the achilles tendon –bone junction in rabbit model. They concluded that bone marrow derived PRP added to BMP-٢ improved significantly the mechanical strength of tendon bone junctions , accelerated the formation of fibrocartilage and new bone after tendon to bone junction injury.[١٨]

Since its introduction, PRP has been used in conjunction with different grafting materials in bone augmentation procedures. Several studies have supported the osteogenic capacity of PRP[١٩]. To date, the results from these studies are controversial and no conclusions can be drawn regarding the bone regenerative effect of PRP.[٢٠]

Platelet-rich fibrin (PRF) represents the second generation in the platelet gel therapeutic concept with simplified processing without the artificial biochemical modification[٢١]. Unlike other platelet concentrates, this technique requires neither anticoagulants nor bovine thrombin nor any other gelifying agent. Hence, it is no more than centrifuged natural blood without additives. [٢٢،٢٣]

Several reports support that, PRF will have a longer and more predictable positive effect on both hard and soft tissue healing while PRP will have a massively uncontrollable and short-term effect.[٢٤, ٢٥]

A myriad of postoperative assessment methods have been suggested following ACG procedures. Never the less, the highest accuracy in volumetric assessment has been associated with cone beam computed tomography (CBCT).[٢٦, ٢٧]

The previously discussed scientific reports were used to formulate the scientific hypothesis of this study. The study aims to provide a clinical appraisal of the bone marrow aspirate and its centrifuged product namely PRF on the healing phase following the ACG procedure. Furthermore, ACG using MBG combined with allogeneic bone was used as both the study control and as carrier in the study group in an effort to find a more conservative approach to ACG. The use of CBCT as the volumetric assessment method was selected due to the volumetric accuracy associated with this radiographic technique.