

**EVALUATION OF THE EFFECT OF PLATELET RICH
PLASMA (PRP) ON THE ESTHETIC OUTCOME AND SCAR
FORMATION OF UNILATERAL CLEFT LIP REPAIR BY
MODIFIED MILLARD CHEILOPLASTY
(A RANDOMIZED CONTROLLED TRAIL)**

Submitted to the Faculty of Dentistry, Cairo University
In Partial Fulfillment of the Requirement of the Doctor Degree
In Oral and Maxillofacial Surgery

By

Shaimaa Mohsen Refahee

B.D.S (Faculty of Dentistry- Cairo University; 2006)
M.D.S (Faculty of Dentistry-Cairo University; 2013)

2018

Supervisors

Dr. Basma Gamal Moussa

Professor of Oral and Maxillofacial Surgery,
Faculty of Dentistry,
Cairo University.

Dr. Omnia Mohamed Abd Elaziz

Lecturer in Oral and Maxillofacial Surgery,
Faculty of Dentistry,
Cairo University.

Dr. Dawlat Emara Gomaa

Associate Professor of Plastic Surgery,
Faculty of Medicine,
Cairo University.

Dr. Hadeel Mohamed Saif Eldin Aly

Professor of Radio-diagnosis,
Faculty of Medicine,
Cairo University.

Judgment committee

Prof. Dr .Ragia Mohamed Mounir

Professor of Oral and Maxillofacial Surgery,
Faculty of Dentistry,
Cairo University.

Dr. Abd Elmonem Abd Allah Abd Elghaffar

Professor of Oral and Maxillofacial Surgery,
Faculty of Dentistry,
El Azhar University.

Dr. Basma Gamal Moussa

Professor of Oral and Maxillofacial Surgery,
Faculty of Dentistry,
Cairo University.

Dedication

This work is especially dedicated

To

*My family whom gave me love, care, and
support to be the best. From them I learned
“where there is a will, there is a way”.*

ACKNOWLEDGEMENT

*First of all, I am deeply thankful to **ALLAH** who gave me the strength and patience to accomplish this work. Words do fail to express my deepest gratitude to **HIS MIGHTY** who granted me with my Angels, i.e. Supervisors.*

*Really I don't find words to express my grateful appreciation and respect to my mentor **Prof. Dr. Basma Gamal Moussa**, Professor of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, for her great effort, continuous guidance, expert touches and instructions without which I would have never been able to fulfill this work.*

*From the depth of my heart, I would like to express all my deepest thank to **Dr. Omnia Mohamed Abd Elaziz**, Lecturer in Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, for her kind supervision, valuable advices and continuous encouragement throughout the study.*

*Words can never express my deep gratitude and sincere consideration to **Dr. Dawlat Emara Gomaa**. Assistant Professor of Plastic Surgery, Faculty of Medicine, Cairo University, for her grand efforts, times and patience in accomplishing this work with great accuracy.*

*My sincere thanks to **Prof. Dr. Hadeel Mohamed Saif Eldin Aly**. Professor of Radio-diagnosis, Faculty of Medicine, Cairo University, for her effort, guidance, and meticulous supervision.*

My deepest thanks to Prof. Dr. Mamdouh Ahmed Aboul Hassan Professor of Pediatric Plastic Surgery, Faculty of Medicine, Cairo University, for his kindness and support during clinical work of my thesis.

My sincere thanks to Prof. Dr. Kamal Hassan Ghallab Professor of Statistics and Plant Breeding, Institute for Research and Strategic Studies of Nile basin countries, Fayoum University, for helping me, his support, and kindness

*My great thanks to all **staff members** of Oral and Maxillofacial Surgery, Faculty of Dentistry, and Pediatric plastic surgery, faculty of medicine, Cairo University for helping me and giving me their experience throughout my work, their efforts will always be remembered.*

I would like to thank the children's parents for their cooperation, concern about their children, and their commitment.

Last but not least, my love and respect goes to my colleagues who helped me throughout my work,

CONTENTS

Title	Page
List of abbreviation	i
List of figures	iii
List of tables	vii
Abstract	Viii
Introduction	1
Review Of Literature	3
Aim Of The Study	31
Patients And Methods	32
Results	54
Discussion	67
Summary And Conclusions	74
References	77
Appendices	94
Arabic Summary	----

LIST OF ABBREVIATIONS

Abbreviation	Meaning
BM	Prof. Dr. Basma Mousa
CL	Cleft lip
CL/P	Cleft lip or palate
CL \pm P	Cleft lip with/without primary palate
CLP	Cleft lip and palate
CP	Cleft palate
CPLA	Computerized photogrammetric lip analysis
CT	Computer tomography
CTGF	Connective tissue growth factor
ECM	Extracellular matrix
EGF	Epidermal growth factor
FGF	Fibroblast growth factor
g or (RCF)	Gravitational force or (Relative centrifugal force)
GFs	Growth factors
HS	Prof. Dr. Hadeel Mohamed Saif Eldin
IL-10	Interleukin-10
IL-6	Interleukin-6
INR	International normalized ratio
min	Minutes
MRI	Magnetic resonance Image
MSS	Manchester scar scale
OA	Dr. Omnia Abd Elaziz
PDGF	Platelet derived growth factor
PH.L	Philtrum length
POSAS	Patient and observer scar assessment scale
PPP	Platelet poor plasma

PRP	Platelet rich plasma
PT	Prothrombin time
PTT	Partial thromboplastin time
RAE	Right angle endotracheal tube
RBCs	Red blood cells
SBSES	Stony Brook scar evaluation scale
SCs	Satellite cells
SM	Shaimaa Mohsen
SW	Scar width
TGF- β	Transforming growth factor- β
TNF α	Tumor necrosis factor- α
UCLP	Unilateral cleft lip and palate
VEGF	Vascular endothelial growth factor
VPI	Velopharyngeal incompetence
VSS	Vancouver scar scale
WB	Whole blood
WBCs	White blood cells

LIST OF FIGURES

NO	Figure	Page
(1)	The embryologic basis of a complete unilateral cleft lip	4
(2)	A photograph showing the normal upper lip anatomy	6
(3)	A drawing showing Orbicularis oris muscle fibers	6
(4)	(A) A schematic representation of the lower lateral cartilages demonstrating symmetry. (B) A schematic representation of the lower lateral cartilages demonstrating asymmetry: a short medial crus, an obtuse genu, and a lateral crus that is longer and drawn into an S-shaped fold on the cleft side	8
(5)	(A) A schematic representation of the orbicularis oris, demonstrating symmetry and continuity. (B) A schematic representation of the orbicularis oris affected by a cleft, demonstrating asymmetry and discontinuity	8
(6)	A diagram illustrating Kernahan's classification system	11
(7)	A diagram illustrating Elsayh's classification system	11
(8)	A diagram illustrating Friedman's classification system	12
(9)	A diagram illustrating Smith's classification system	12
(10)	A drawing showing unilateral cleft lip repair with Straight line technique	14
(11)	(A,B) A diagram showing unilateral cleft lip repair with. A. Quadrangular techniques. B. Triangular techniques	15
(12)	A diagram showing unilateral cleft lip repair with Rotation advancement technique	16
(13)	A diagram illustrating main phases and factors of the wound healing process	18

(14)	Schematic representation of basic steps of cutaneous wound healing which overlap in time	18
(15)	A diagram illustrating the role of growth factors and cytokines involved in the wound healing process	24
(16)	Vancouver Scar Scale (VSS)	27
(17)	Screenshot of randomization process by Researcher Randomizer	35
(18)	A photograph showing the surgical tray	37
(19)	Flow chart describing the preparation of PRP	39
(20)	A photograph of thermo scientific centrifuge	40
(21)	A photograph of automatic hematology analyzer	40
(22)	(A,B) Show counting of different cells in. A) Whole blood. B) Resultant PRP	40
(23)	Clinical preoperative photograph showing the surgical markings for unilateral cleft lip repair with modified rotation advancement technique	42
(24)	Clinical preoperative photograph showing landmarks and cutting design for modified rotation advancement technique: (A) advancement flap, (B) rotational flap, (C) C-flap.	42
(25)	A photograph showing all incisions complete	44
(26)	(A,B)A photograh showing the release of the skin from the underlying Orbicularis oris muscle	44
(27)	A photograph showing closure of orbicularis oris muscle fibers and nasal floor	45
(28)	A photograph showing PRP injection along suture line of the muscle	46
(29)	A photograph showing the dermis layer closure	46

(30)	(A-B) A photograph showing PRP injection along suture line of dermis layer	46
(31)	Intraoperative clinical photograph after PRP injection	47
(32)	A photograph showing of medical ultrasound system	51
(33)	A diagram showing the transducer application during scar width measurement	51
(34)	An ultrasound view demonstrating the measurement of scar width through the muscle layer	51
(35)	(A-C) Steps of anthropometric analysis using Image J Software	52
(36)	A photograph showing philtrum length (PHL) and scar width (SW) assessment using image J software	53
(37)	(A,B) Pie charts showing (A) Gender distribution (B) Cleft side distribution	55
(38)	A photograph showing wound dehiscence at 1week	55
(39)	A photograph showing hypertrophic scar after 3months	55
(40)	Bar chart showing the mean PLT count in WB and PRP	56
(41)	Bar chart showing the mean WBCs count in WB and PRP	56
(42)	Bar chart showing the mean scar width by ultrasound	57
(43)	Bar chart showing the mean scar width by photograph	58
(44)	Bar chart showing the mean of Vancouver scar scale	60
(45)	Linear char represent the mean change of VSS in both group through the different follow up intervals.	61
(46)	Bar chart representing the mean of philtrum ridge length	62
(47)	Bar chart representing the mean of philtrum ridge symmetry value.	62
(48)	Group (A), case I presentation A: Preoperative photograph. B: One month postoperative photograph	63

	C:Three months postoperative photograph D: Six months postoperative photograph E: Six months postoperative ultrasound view	
(49)	Group (A), case II presentation A: Preoperative photograph. B: One month postoperative photograph C:Three months postoperative photograph D: Six months postoperative photograph E: Six months postoperative ultrasound view	64
(50)	Group (B), case I presentation A: Preoperative photograph. B: One month postoperative photograph C:Three months postoperative photograph D: Six months postoperative photograph E: Six months postoperative ultrasound view	65
(51)	Group (B), case II presentation A: Preoperative photograph. B: One month postoperative photograph C:Three months postoperative photograph D: Six months postoperative photograph E: Six months postoperative ultrasound view	66

LIST OF TABLES

NO	Table	Page
(1)	Demographic data description regarding sex, age, cleft side, and gap width.	54
(2)	Descriptive statistics of PLTs and WBCs count in PRP and WB	56
(3)	Descriptive statistics of scar width assessment by ultrasound	57
(4)	Descriptive statistics of scar width assessment by photograph	58
(5)	Descriptive statistics of Vancouver scar scale	59
(6)	The mean, standard deviation (SD) values and P value of VSS through the different follow up intervals	60
(7)	The mean, standard deviation (SD) and P-value of Philtrum ridge length	61
(8)	Descriptive statistics of Philtral ridge symmetry value%	62

Abstract

Objective: To evaluate and analyze the effect of platelet-rich plasma (PRP) injection on the scar formed after unilateral complete cleft lip scar repair using a modified Millard technique.

Hypothesis: An unavoidable cheiloplasty scar is a result of the wound healing process that not only influences patient self-esteem for life but also affects muscle function.

Design: Blind, randomized, controlled clinical trial.

Patients: From December 2016 to February 2018, 24 patients with unilateral complete cleft lip undergoing primary cheiloplasties were equally assigned to study and control groups.

Intervention: All patients were treated by modified Millard cheiloplasty. In the study group, PRP was injected into the muscle and skin layers immediately after wound closure, while the control group patients were treated with no PRP injection.

Outcomes Measures: Scar width was assessed after 6 months through the muscle using ultrasonography and at the skin surface via photographs.

Results: Scar width showed a significant improvement in the study group.

Conclusions: Injection of autologous PRP provides effective improvement of cutaneous and muscular wound healing and decreases scar tissue formation.

Keywords: Cleft lip, platelet rich plasma, cheiloplasty, growth factors