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Evaluation of the Use of Sirolimus in Treatment of Complex Vascular Malformation and Tissue Overgrowth Syndromes

Thesis

For Partial Fulfilment of MD Degree
in Pediatric Surgery

BY

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2021

سورة البقرة الآية: ٣٢

Acknowledgment

First of all, all gratitude is due to **God** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

Really I can hardly find the words to express my gratitude to my dear professors **Prof. Drs. Hatem Saafan, Iman Rageb, Amr Zaky,Mohamed Elsherbeeny and Mohamed Mousa**, *for their supervision, continuous help, encouragement throughout this work and tremendous effort they have done in the meticulous revision of the whole work. It is a great honor to work under their guidance and supervision.*

I would like also to express my sincere appreciation and gratitude to **Prof. Drs. Osama Elnagar and Shimaa Abdelsattar,** *for their continuous directions and support throughout the whole work.*

Really I can hardly find the words to express my gratitude to our dear professors **Prof Drs. Alaa Fayez (may God have mercy upon him) and Hesham Abdelkader** *the founders of vascular anomalies multidisciplinary clinic which provides unique and great care to our patients*

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Mohamed Aly Abdelhamid Abdelbaky

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List of Abbreviations

Abb.	Full term
Avf	*Arteriovenous Fistula*
AVM	*Arteriovenous Malformation*
AVMs	*Arteriovenous Malformations*
BRBNS	*blue rubber bleb nevus syndrome*
CH	*Congenital hemangioma*
CLOVES	*congenital lipomatous overgrowth with vascular, epidermal, and skeletal anomalies*
CLM	*Capillary Lymphatic Malformation*
CM	*Capillary Malformation*
CT	*Computed Tomography*
CTA	*Computed Tomographic Angiography*
CVM	*Congenital Vascular Malformation*
CVMs	*Congenital Vascular Malformations*
DIC	*Disseminated intravascular coagulopathy*
ISSVA	*International society for the study of vascular anomalies*
KHE	*Kaposiform hemangioendothelioma*
KTS	*Klipple-trenaunay syndrome*
LFVM	*Low-flow vascular malformations*
LIC	*Local intravascular coagulation*
LM	*Lymphatic malformation*
LMWH	*Low molecular weight heparin*
MRA	*Magnetic resonance angiography*
MRI	*Magnetic resonance imaging*
mTOR	*Mammalian target of rapamycin*
NGS	*Next-generation sequencing*
NICH	*Non-involuting congenital hemangioma*
PICH	*Partially involuting congenital hemangioma*
PI3K	*Phosphatidylinositol 3 kinase*
PedsQL	*Pediatric quality of life*

List of Abbreviations (Cont...)

Abb.	Full term
PWS	*Parkes-weber syndrome*
RICH	*Rapidly involuting congenital hemangioma*
SCORAD Index	*('Severity Scoring of Atopic Dermatitis: The SCORAD Index', 1993)*
US	*Ultrasound*
VA	*Vascular anomaly*
VEGF	*Vascular endothelial growth factor*
VM	*Venous malformation*

Abstract

BACKGROUND AND OBJECTIVES: Management of complex vascular malformations and overgrowth syndromes is challenging. They usually present at birth and have different complications including bleeding, pain, cosmetic disfigurement and functional impairment. This study was to done to determine symptomatic relief and quality of life improvement after sirolimus.

METHODS: The intervention phase included sirolimus administered orally on a continuous dosing schedule at a starting dose of 0.8 mg/m2, and its level to be maintained between 4-12 ng/ml. Dose was rounded to the nearest 1mg tablet form.

Assessment of response to sirolimus was done (usually 2 weeks after start of sirolimus) clinically by assessment of clinical improvement of the main complaint of the patient e.g. bleeding, pain, cosmetic disfigurement. Laboratory Improvement of patients labs after start of sirolimus e.g elevation of hemoglobin and Mean cell volume. Arabic translation of pediatric quality of life PedsQL 4.0 was done again 6 months after start of sirolimus. Assessment of safety of sirolimus was done clinically by surveillance for incidence of any complications e.g chest infections, diarrhoea, mucositis. and laboratory assessment after 2 weeks and after every 6 months including blood picture, liver function test (Alanine transferase) , kidney function test (creatinine), fasting lipid profile :cholesterol and triglycerides and sirolimus trough level.

RESULTS: 33patients were enrolled, Age of the patient during start of sirolimus ranged from 5 months to 13 years with median age 3 years. Bleeding stopped in 15 patients (93.8%), cosmetic Disfigurement improved in 21 patients (80%) and perception of pain improved in 8 patients (72.7%). Also, mean pediatric quality of life score rase from 65.18 to 78 after sirolimus. 10 (30%)patients had adverse effects from sirolimus including infections 15.2% ,,mucositis 12.1% and diarrhea 1%.

CONCLUSIONS: Patients with complex vascular malformation require multidisciplinary team for diagnosis and management. Symptomatic relief in patients after sirolimus is evident with better quality of life.

KEYWORDS: Sirolimus _Vascular malformation_ Overgrowth syndromes