

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

# بسم الله الرحمن الرحيم





MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

## جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



# Comparative Study of the Effectiveness of Long- and Intermediate-Acting Insulins in Children with Type 1 Diabetes Mellitus

#### Thesis

Submitted for Partial Fulfillment of Master Degree in **Pediatrics** 

### By

#### Eman Mohammed Ali Sakr

MB., B.Ch., Faculty of Medicine, Ain Shams University

Under Supervision of

## **Prof. Safinaz Adel Elhabashy**

Professor of Pediatrics Faculty of Medicine, Ain Shams University

#### Dr. Nouran Yousef Salah

Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Faculty of Medicine Ain Shams University 2021



سورة البقرة الآية: ٣٢

## Acknowledgments

First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Safinaz Adel Elhabashy**, Professor of Pediatrics, Ex-Head of Pediatric and Adolescent Diabetology Unit (PADU), Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.

Special thanks are due to **Dr. Mouran Yousef Salah**, Lecturer of Pediatrics, Faculty of

Medicine, Ain Shams University, for her sincere

efforts, fruitful encouragement.

I would like to express my hearty thanks to all my family and my husband for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients who participated in this study.

Eman Mohammed Ali Sakr

### رسالة الكلية

تقوم كلية طب جامعة عين شمس بإعداد طبيب مدرب ذو مهارة تنافسية على المستوى المحلي والإقليمي، وقادر على التعليم والتعلم والتدرب مدى الحياة وملتزم بمعايير الخدمة الطبية والأخلاق المهنية، وتدعم الكلية التطوير المستمر للبرامج والمقررات والبحث العلم مع الحرص على التوسع في الأبحاث العلمية التطبيقية وبرامج الرعاية الصحية لخدمة احتياجات المجتمع وتنمية البيئة

### **Faculty Mission**

The Faculty of Medicine of Ain Shams University prepares a trained doctor with competitive skill at the local and regional level, capable of teaching, learning and training for life and is committed to standards of medical service and professional ethics, and the college supports the continuous development of programs, courses and scientific research while keen to expand applied scientific research and health care programs To serve the needs of society and develop the environment.

#### **Abstract**

**Background:** Achieving glycemic control without risking hypoglycemia imposes a major challenge among young children with type 1 diabetes (T1D). **Objectives:** To compare the effectiveness of insulin degludec to insulin glargine and NPH insulin among toddlers and preschoolers with T1D in terms of glycosylated hemoglobin (HbA1c) and frequency of hypoglycemic episodes. **Methods:** This randomized-controlled trial included 60 toddlers and preschoolers with T1D aged 2-6 years, with disease-duration 0.07-6 months. They were 27 males (45%), 33 females (55%). According to basal insulin, they were randomly assigned into three groups; Group-A received insulin degludec, group-B insulin glargine and group-C NPH insulin. The three groups were followed-up for 6 months with assessment of insulin daily-dose (IDD), frequency of hypoglycemia and severe hypoglycemia/week and HbA1c. **Results:** The three groups were well-matched regarding baseline clinical and laboratory parameters (p>0.05). After 6 months, the insulin degludec group had significantly lower IDD (p=0.015), frequency of hypoglycemia (p=0.006) and severe hypoglycemia (p=0.029), and HbA1c (p=0.002) than the other two groups. The frequency of hospital admissions was significantly higher in the NPH group than the other two groups

(p=0.034). Insulin degludec and insulin glargine resulted in significant decrease of HbA1c than baseline (p=0.001 and p=0.024, respectively). Moreover, insulin degludec resulted in significant decrease in the frequency of hypoglycemia (p=0.003) and severe hypoglycemia (p=0.017). The insulin glargine group showed significantly lower IDD at the end of the study than baseline (P=0.032). No significant difference was found between toddlers and preschoolers as regards IDD, frequency of hypoglycemia and HbA1c. **Conclusion:** The use of insulin degludec and insulin glargine significantly improves glycemic control and reduces the risk of hypoglycemia with a lower insulin dosage among toddlers and preschoolers with T1D.

**Keywords:** Insulin glargine; insulin degludec; NPH insulin; toddlers; preschool children; type 1 diabetes.

## Tist of Contents

Title	Page No.
List of Tables	i
List of Figures	iii
List of Abbreviations	iv
Protocol	1
Introduction	9
Aim of the Work	12
Review of Literature	
Type 1 Diabetes	13
Insulin Therapy	30
Insulin related Hypoglycemia	42
Subjects and Methods	50
Results	57
Discussion	72
Summary and Conclusion	78
Recommendations	81
References	82
Appendix	100
Appendix (1): Modified scale for socioeconomic sta	atus100
Appendix (2): Morisky Scale (Mercy Clinics, Inc.)	101
Appendix (3): Medical examination sheet	102
Master Sheet	103
Arabic Summary	

## Tist of Tables

Table No.	Title	Page No.
Table 1:	Criteria for the diagnosis of diabet	es mellitus18
Table 2:	Clinical characteristics at present 1 diabetes	· -
Table 3:	Screening recommendations and for vascular complications	
Table 4:	Pharmacodynamics of currentl injectable insulin analogues	•
Table 5:	Baseline demographic and clinic toddlers and preschool children (n=60)	with T1D
Table 6:	Comparison of baseline clinica glycated hemoglobin of the three g	
Table 7:	Comparison of the baseline daily and after 3, and 6 months follo three studied groups	w up of the
Table 8:	Frequency of documented hypoglyothe three groups after 6 months for	_
Table 9:	Frequency of significant has frequency and hospital admission study groups	n among the
Table 10:	Comparison between the the regarding HbA1c initially, at 3, and	~ -
Table 11:	Comparison between the the regarding adherence to treatment end point	at the study
Table 12:	Correlations of severe hypoglycem among 60 studied toddlers and children with T1D	nd preschool

## Tist of Tables cont...

Table No.	Title	Page No.
Table 13:	Clinical and laboratory data and and preschool children with type receiving NPH insulin, insulin to insulin Degludec at baseline and a	e 1 diabetes Glargine and
Table 14:	Comparison between toddlers a children with T1D at baseline and	-

## List of Figures

Fig. No.	Title	Page No.
Figure 1:	Comparison between toddlers preschoolers receiving insulin consulin Degludec and NPH insulin as insulin daily dose initially, at 3 months.	Glargine, s regards s and 6
Figure 2:	Comparison of types of basal inservere hypoglycemia at 6 months followed	
Figure 3:	Comparison between toddlers preschoolers receiving insulin of insulin Degludec and NPH insulin as HbA1c initially, at 3 months and at 6	Glargine, s regards
Figure 4:	Correlation between severe hypoglycoduration of diabetes at 6 months follows (265)	ow up; (r
Figure 5:	Correlation between severe hypoglycoinsulin dosage at 6 months; (r =0. 379)	

## Tist of Abbreviations

Abb.	Full term
Ana	Argining
Arg	
	Asparagme Anti-thymocyte globulin
	Autologous hematopoietic stem cell
A11501	transplant
BG	-
BI	
BMI	
	· · · · · · · · · · · · · · · · · · ·
Bp	Cluster of differentiation 3
	Continuous glucose monitoring
	Cytotoxic T-lymphocyte-associated protein 4
	Diabetes Control and Complications Trial
	Diabetic ketoacidosis
	European Nicotinamide Diabetes
ENDII	Intervention Trial
Figgn	Faster-acting insulin aspart
	Glutamic acid decarboxylase 65
	Granulocyte colony stimulation factor
	Glucagon-like peptide-1
Gly	
	Hemoglobin A1c (glycosylated hemoglobin)
	Human leukocyte antigen
	Insulinoma-associated 2
	Antibodies to insulin
	Islet cell cytoplasmic antibodies
IDD	
IDeg	
	International Diabetes Federation
IGlar	
	Australian intranasal insulin trial II
	Juvenile Diabetes Research Foundation
	Multiple daily injections
1,11,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1	

## Tist of Abbreviations cont...

Abb.	Full term
MODY	Maturity onset diabetes of the young
NDM	Neonatal diabetes mellitus
NGSP	National Glycohemoglobin Standardization
	Program
NPH	Neutral protamine Hagedorn insulin
OGTT	Oral glucose tolerance test
PADU	Pediatric and adolescents diabetes unit
PD	Pharmacodynamics
PG	Plasma glucose
Ph	Negative logarithm of the hydrogen ion
	concentration
PK	Pharmacokinetic
RCTs	Randomized controlled trials
SC	Subcutaneous
SMBG	Self-monitoring blood glucose
T1D	Type one diabetes
	Type two diabetes
	Turbidimetric inhibition immunoassay
	Zinc transporter8
	<del>-</del>