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Comparative Study between the Glycemic Control of Human Insulin and Insulin analogue In Sample of Iraqi Type 1 Diabetic Children and Adolescents

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Abstract:

Insulin analogue introduced to offer insulin replacement therapy mimic to normal human physiology. The aim of this study is to compare between the glycemic control of insulin analogue and conventional human insulin in a sample of type 1 diabetic Iraqi children and adolescents. Forty type 1 diabetic Iraqi children and adolescents age between (6-18) years enrolled in this study and divided into two groups. Group 1 contains 20 patients switched from human insulin to insulin analogue. Group 2 contain 20 patients continued with conventional human insulin. The results showed that both therapies reduced fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c %) but insulin analogue treated group had highly significant reduction. Both therapies did not affect on blood urea nitrogen and serum creatinine. Human insulin reduced triglyceride (TG) and very low-density lipoprotein (VLDL) significantly. The parameters measures at baseline and after three months of treatments. In conclusion insulin analogue is superior over conventional human insulin in reducing glycemic indices in a sample of type 1 diabetic Iraqi children and adolescents.

Key words: Insulin analogue, Conventional Human insulin, Glycemic control

دراسة مقارنة بين الفعالية لخفض مستوى السكري للانسولين البشري والانسولين المشابه للبشري لدى عينة من المرضى العراقيين الاطفال والمراهقين المصابين بداء السكري من النوع الاول

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الخلاصة:

الانسولين المشابه للانسولين البشري(insulin analogue) ظهر ليوفر تعويض للانسولين بشكل مشابه للافراز الطبيعي. الهدف من الدراسة هو المقارنة بين الفعالية في خفض مؤشر السكر في الدم لدى عينة من المرضى العراقيين الاطفال والمراهقين المصابين بالسكري من النوع الاول.اربعون مريضا انضموا الى الدراسة وتم تقسيمهم الى مجموعتين.المجموعة الاولى ضمت عشرون مريض تم تحويلهم من الانسولين البشري الى الانسولين المشابه للبشري . المجموعة الثانية ضمت عشرون مريض استمروا العلاج بالانسولين البشري. اظهرت النتائج ان العلاج في المجموعتين خفض مستوى السكر في الدم (FPG)ومستوى السكر المرتبط بالهيموغلوبين (HbA1c) لكن الانخفاض في المجموعة الاولى كان ملحوظا بشكل كبير . العلاج في المجموعتين لم يؤثر على مستوى اليوريا في الدم وعلى الكرياتنين. المجموعة الثانية اظهرت انخفاض في مستوى الدهون الثلاثية (TG)بشكل ملحوظ . كل التحاليل اجريت عند بدء الدراسة وبعد ثلاثة اشهر من العلاج. الاستنتاج من الدراسة تبين ان الانسولين المشابه للبشري افضل من الانسولين البشري في خفض مؤشر السكري عند عينة من المرضى العراقيين الاطفال والمراهقين المصابين بالسكري من النوع الاول .

الكلمات المفتاحية : الانسولين البشري،الانسولين المشابه للبشري،السيطرة على ارتفاع السكري

Introduction:

Type 1 diabetes mellitus (T1DM) is a chronic metabolic disease characterized by deficiency in insulin secretion due to destruction of pancreatic beta-cells, leading to disturbances in glucose metabolism [1]. Exogenous insulin is given to compensate the deficiency and avoid severe diabetic complications. This type of diabetes appears mainly in childhood (between 7-15 years old) [2]. The rate of occurrence is rising globally its about 90,000 children diagnosed annually and exogenous insulin is needed to replace the endogenous loss after β cells destruction [3]The need to improve the physiological profile of insulin to mimic endogenous insulin secretion and improved knowledge of the amino acid sequencing of the insulin molecule has prompted the emergence of bioengineered analogues insulin and has indicated an exciting new era in insulin therapeutics [4]. Analogue insulin is similar to human insulin with a slight variation in amino acid composition and structure but with improved pharmaco-kinetics [4].

Patients and methods:

The study was conducted on 40 Iraqi children and adolescents age range (6-18) year, already diagnosed as type 1 diabetic patients, have been selected during attending the Child Consultant Clinic at National Diabetic Center. The patients chosen to participate in this study were devided into two groups according to type of insulin used, and an informed agreement was taken from the patient's parents to make the study. The patients were educated to continue their regular drug treatment schedule, also medical and drug history was taken from the selected patients.

Patients groups:

Patients in the study were devided into two groups: First group includes 20 patients receive insulin analogue Novorapid® (insulin aspart) at meal times and Lantus® (insulin glargine) at night. Second group includes 20 patients receive Human insulin (soluble insulin at meal time) and (Neutral Protamine Hagedorn (NPH) insulin twice daily). Patients received insulin dose according to their weight or body mass index. Patients in each group were followed up for 3 months. Fasting Plasma Glucose (FPG), Glycated Hemoglobin (HbA1C%), Blood Urea Nitrogen (BUN), Serum Creatinine (S.Cr.), Lipid profile, Weight (Wt.), Height (Ht.) and Body Mass Index (BMI) were measured before, and after three months of therapy.

Statistical analysis:

SPSS 20.0.0, Minitab 17.1.0 software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05

Results:

Demographic data: There was no significant difference in the age, duration of disease and gender between both groups.as shown in table (1).

Table (1): Demographic data

	Human insulin group	Insulin analogue group	P value
Number	20	20	-
Age (years)	12.05 ± 4.06	12.45 ± 3.65	0.745
BMI ($kg/m^{2)}$	20.00 ± 4.57	20.00 ± 3.49	0.908
Duration (years)	4.65 ± 3.21	3.78 ± 3.59	0.422
Gender			0.744
Female	12 (60%)	13 (65%)	
Male	8 (40%)	7 (35%)	
Independent t test, Chi square test, p value >0.05 non-significant, N (patients' number) = (40) Mean +_SD			

Insulin analogue reduced FPG significantly from baseline to 3 months, while human insulin reduced FPG however it was not statistically significant, overall human analogue was better that human insulin (p value of interaction = 0.041) as shown in figure1.Both human insulin and insulin analogue reduced HbA1c significantly, and there was significant difference between both treatment on HbA1c (p value of interaction = 0.051. As illustrated in figure 1. Both treatments did not affect urea and creatinine from baseline to 3 months. Human insulin reduced significantly serum triglyceride (TG) and very low-density lipoprotein (VLDL) from baseline to 3 months, while for the rest of the lipids panel there was no significant effect for both treatments (p value>0.05).

Table (2): Comparsion the effect of different insulin therapy on different biochemical parameters.

Variable		Baseline	3 months	P value
	Number	20	20	-
FPG (mg/dl)	Human insulin	279.55 ± 155.26	248.60 ± 101.75	0.305
	Insulin analogue	269.20 ± 116.63	182.75 ± 109.82	0.014*
HbA1c%	Human insulin	10.89 ± 1.74	9.72 ± 2.00	0.003**
	Insulin analogue	10.62 ± 2.04	8.58 ± 1.57	0.001**
Urea (mg/dl)	Human insulin	21.32 ± 5.42	20.29 ± 4.13	0.547
	Insulin analogue	23.04 ± 6.17	21.30 ± 7.10	0.245
Creatinine (mg/dl)	Human insulin	0.61 ± 0.15	0.67 ± 0.16	0.251
	Insulin analogue	0.68 ± 0.16	0.66 ± 0.12	0.547
Cholesterol (mg/dl)	Human insulin	165.80 ± 36.91	168.30 ± 55.50	0.865
	Insulin analogue	190± 46.46	170.00 ± 43.78	0.063
TG (mg/dl)	Human insulin	77.5(57-101)	55.5 (45.3-66.3)	0.003**
	Insulin analogue	55 (42.5-95.3)	70 (41.3-90.8)	0.723
HDL (mg/dl)	Human insulin	47.67 ± 17.10	47.38 ± 16.17	0.928
	Insulin analogue	53.54 ± 9.28	48.60 ± 13.10	0.068
LDL (mg/dl)	Human insulin	103.63 ± 33.82	98.26 ± 26.63	0.402
	Insulin analogue	121.73 ± 46.21	103.95 ± 40.81	0.133
VLDL (mg/dl)	Human insulin	16.00 ± 7.19	11.21 ± 3.57	0.013*
	Insulin analogue	17.50 ± 23.62	13.70 ± 7.83	0.446

FPG: fasting plasma glucose, HbA1c% glycated hemoglobin, TG: triglyceride, HDL: High density lipoprotein, LDL: low density lipoprotein, VLDL: very low density lipoprotein, Paired t test used for analysis , TG analyzed using Wilcoxon rank test .
P value >o. o5 non-significant
P value <0.05 significant
Significant =*
Highly significant =**

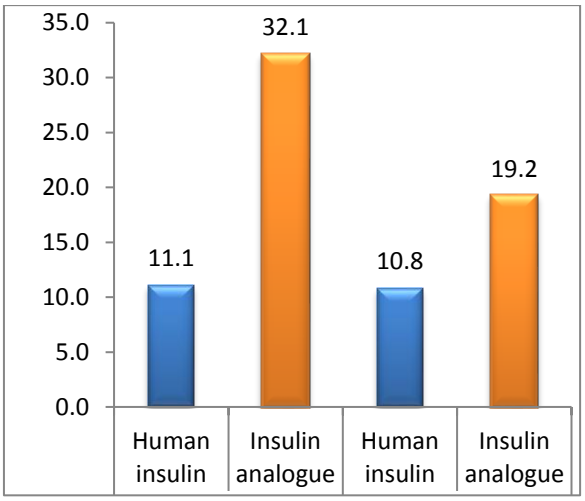

Figure (1): percentage change from baseline to 3 months for each group

FPG (P value of interaction=0.041)
HbA1c % (p value of interaction =0.051)

Discussion:

The current results compatible with Chapman TM.et al (2002) who concluded that insulin aspart better than regular human insulin in lowering mean glycosylated hemoglobin and manages hyperglycemia in type 1 diabetic patients (5) In type 1 diabetes, compared with human insulin, the rapid-acting analogues generally reduced hypoglycemia and postprandial glucose, whereas the basal analogues tended to reduce hypoglycemia particularly nocturnal hypoglycemia(6,7,8) the results also compatible with
Siebenhofer A.et al (2004) assessed the effects of short acting insulin analogues against regular human insulin and they found that insulin analogue favorable than human insulin in HbA1c reduction (9) Warren E et al (2004) found that insulin glargine seemed to be more effective than neutral protamine Hagedorn (NPH) in reducing FPG and there were some signs that both insulins are as effective as each other in both FPG and HbA1c control (10). Glargine is superior to NPH for enhancing HbA1c and FPG levels through insulin therapy in patients with type 1 diabetes and is linked with less night-time hypoglycemia (11). Siebenhofer A.et al (2004) found a slight advantage to hemoglobin A(1c) values in patients with T1DM (9) There is no effect on renal function test since the current study showed not significant differences in (BUN and S.Cr.) in the different types of insulin treated groups at baseline and after three months of therapy. Human insulin reduced significantly serum triglyceride TG and VLDL from baseline to 3 months, while for the rest of the lipids panel there was no significant effect for both treatments in the present study insulin analogue did not reduce lipid profile to a significant degree this might be because of insulin resistance might be associated with T1DM this may be emphasize by the study done be Bulum T. et al (2013) they found that though insulin resistance is frequently related with the T2DM, it can also be related to T1DM. Insulin resistance has been recognized in type 1 diabetes and may contribute to the great danger of cardiovascular illness in those people (12).
Insulin replacement may correct the irregularities, and fine controlled diabetics may improve triglyceride (13).

Conclusion:

In the present study, insulin analogue is superior over conventional human insulin in reducing glycemic indices in a sample of type 1 Iraqi diabetic children and adolescents.

References:

1- Ganjali S, Dallinga-Thie GM, Simental-Mendía LE, et al. HDL functionality in type 1 diabetes. Atherosclerosis.267:99-109.
2- Klinegman RM BR, Jenson HB, Stanton BF, et al. Nelson Text book of Pediatrics. 18th edition Philadelphia: Elsevier; 2007.
3- Chisholm-Burns MA WB, Schwing Hammer TL, Malone PM, et al. Pharmacotherapy principle and practice. 4th edition ed. USA: TheMcGraw-Hill Companies; 2016. Chapter 40, DM; PP. 643-653.
4- Brange J, Ribel U, Hansen J, et al. Monomeric insulins obtained by protein engineering and their medical implications. Nature.1988;333(6174): 679.
5- Chapman TM, Noble S, Goa KL. Insulin aspart: a review of its use in the management of type 1 and 2 diabetes mellitus. Drugs. 2002;62 (13):1945-81.
6- Raskin P, Guthrie RA, Leiter L, et al. Use of insulin aspart, a fast-acting insulin analogue, as the mealtime insulin in the management of patients with type 1 diabetes. Diabetes Care. 2000; 23(5):583-8.
7- Liu S, Hempe JM, McCarter RJ, et al. Association between Inflammation and Biological Variation in Hemoglobin A1c in U.S. Nondiabetic Adults. The Journal of Clinical Endocrinology and Metabolism. 2015 Jun; 100(6):2364–71.
8- Bardini G, Rotella CM, Giannini S. Dyslipidemia and Diabetes: Reciprocal Impact of Impaired Lipid Metabolism and Beta-Cell Dysfunction on Micro- and Macrovascular Complications. The Review of Diabetic Studies: RDS. 2012; 9(2-3):82-93.
9- Siebenhofer A., Plank J, Berghold A. et al. Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus. Cochrane Database Syst. Rev., n.2, CD003287, 2004.
10- Warren E, Weatherley-Jones E, Chilcott J, et al. Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine. Health Technol Assess 2004;8(45)
11- Fullerton B, Siebenhofer A, Jeitler K, et al. Short-acting insulin analogues versus regular human insulin for adults with type 1 diabetes mellitus. Cochrane Database Syst Rev. 2016 Jun 30; (6):CD012161. Epub 2016 Jun 30.
12- Bulum T, Duvnjak L. Insulin resistan]’ce in patients with type 1 diabetes: relationship with metabolic and inflammatory parameters. Acta clinica Croatica. 2013; 52(1):43-51.
13- Goldberg IJ. Diabetic Dyslipidemia: Causes and Consequences.The Journal of Clinical Endocrinology& Metabolism. 2001; 86(3):965-71.