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ORIGINAL ARTICLE

Adverse Physiological and Biochemical Effects of Synthetic Human Insulin in Diabetic Type-2 Patients, A Comparative Clinical Study

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ABSTRACT

Background: The use of Synthetic human insulin in diabetic individuals may develop number of serious medical complications in population like Hypoglycemia, Weight gain, Little Skin Depression and Dementia.

Aims and Objectives: The aims and objects of current study were to provide awareness about the recent Biochemical and Physiological side effects of Artificial Insulin Therapy for Type 2 Diabetes Mellitus to the people.

Study Design: A comparative clinical study.

Place and Duration: Present study was conducted in Lahore Medical & Dental College Lahore, The university of Lahore, Lahore, Suleman Roshan medical college Tando Adam Sindh and Allama Iqbal Medical College Lahore Pakistan from March 2021 June 2022.

Methodology: Total 450 diabetic type- 2 patients of age 40-60 years were selected for present study and they were divided into three different groups regarding injected units of synthetic insulin. In Group-A 100 male and 50 female were taking 20 units twice a day, whereas 100 male and 50 female individuals with diabetes type-2 of Group-B were injected 30 units twice a day while 80 male and 40 female of Group-C were taking 45 units twice a day respectively. Fasting and Random glucose levels, Body mass index (BMI), levels of Dementia and Skin Depression parameters of each individual were measured and compared group wise.

Results: A remarkable significant changes (P≤0.05) in Fasting glucose levels, Random glucose levels after 2 hour of meal, Random glucose levels after 3 hour of meal, Random glucose levels after 4 hour of meal, Body mass index, body mass index after 6 month, body mass index after 12 month, Incidence of severe hypoglycemia of male and female were concluded in group-B and group-C as compared with group-A, because 20 units of insulin created less hypoglycemic effects as compared with 30 and 45 units which were injected in Group-B and Group-C comparatively.

Practical implication: Awareness about side effects of artificial Insulin therapy for Type 2 Diabetes Mellitus to the people is so important and helpful for quality of life and safety.

Conclusion: The findings of present study were indicated that long term insulin therapy develop hypoglycemia and significant changes (P≤0.05) in BMI in patients with diabetes type-2. It was concluded that a significant (P≤0.05) weight gain in regular user of synthetic insulin diabetic type-2 patients was very common.

Keywords: Hypoglycemia, Synthetic insulin, Body mass index, Diabetes Mellitus

INTRODUCTION

Research is shifting toward the creation of new therapies that can enhance overall management of the disease, particularly new insulins with unique pharmacologic profiles, as the prevalence of diabetes continues to rise globally[1]. One of these is the recently created basal insulin degludec[7]. Insulin degludec creates an ultra-long pharmacokinetic absorption profile when administered subcutaneously thanks to a special pharmacological mechanism1, which translates into a very long duration of action that has been demonstrated to last more than 42 hours in the majority of patients[1,5,7].

In order to make insulin therapy accessible to people all around the world, recombinant human insulin was come into being and it replaced the use of animal insulins and semisynthetic human insulin derived from different animals[2,13]. Recombinant human insulin is a synthetic form mostly synthesised with the help of a bacteria i.e. E.coli and its two peptide chain structure is similar to human natural insulin[10,13,17]. Recombinant human insulin injected under the skin and it cannot work as natural insulin because injected recombinant human insulin clumps together and it takes much time in absorption. A human gene could be inserted into the genetic code of a common bacterium thanks to a technique called recombinant DNA[15]. The protein encoded by the human gene might now be produced by this "recombinant" microorganism[3,4,9].

The human insulin gene is created in a laboratory. The human insulin gene is then inserted into a plasmid, a loop of bacterial DNA that has been removed[2,5,17]. The plasmid is returned to the bacteria, and the "recombinant" bacteria are then placed in huge fermentation tanks. There, the gene is used by the recombinant bacteria to start making human insulin[5]. The insulin is extracted from the bacteria by scientists, who then purify it so that it may be used as a human treatment. The insulin concentration is the main distinction between insulin intended for human use (glargine, NPH, and detemir) and insulin intended for use in animals (PZI, lente)[6]. U-40 insulin is accessible for PZI and lente insulin, but NPH, glargine, and detemir are only available as U-100 insulin [1,4,8].

Short-acting, intermediate-acting, and long-acting insulin preparations are the three categories that are available[7,9]. The treatment of diabetic ketoacidosis, hyperglycemic hyperosmolar diabetes, or anorexic, sick diabetic animals is often reserved for short-acting insulin products. Contrarily, as it can take several days for full insulin action to emerge, the insulin dose shouldn't be changed if blood glucose levels stay high[17]. It is also possible to start insulin therapy on an outpatient basis, with the owner receiving training on how to keep an eye out for hypoglycemia symptoms at home[19,20].

Significance of study: Present study has number of benefits for our community because awareness about side effects of artificial Insulin therapy for Type 2 Diabetes Mellitus to the people is so important and helpful for quality of life and safety.

Research Gap: Current study has some limitations rewarding synthetic insulin brands which were available in the market

because patients do not use same brands for the treatment of diabetes type-2.

Rationale of study: Chronic insulin administration may slow the rate of apoptosis in β-cell. The aims and objects of current study were to provide awareness about the recent Biochemical and Physiological side effects of Artificial Insulin Therapy for Type 2 Diabetes Mellitus to the people.

MATERIAL AND METHODS

Research Design: Current comparative clinical study was conducted Lahore Medical & Dental College Lahore, Suleman Roshan medical college Tando Adam Sindh and Allama Iqbal Medical College Lahore Pakistan from March 2021 June 2022.

Population Sampling: Male and female diabetic type-2 patients how were taking synthetic insulin as a treatment in different strength of units selected for present study.

Sample size: Collectively 450 diabetic type- 2 patients of age 40-60 years were selected for present study and all individuals were divided into three different groups regarding injected units of synthetic insulin. In Group-A 100 male and 50 female were taking 20 units twice a day, whereas 100 male and 50 female individuals with diabetes type-2 of Group-B were injected 30 units twice a day while 80 male and 40 female of Group-C were taking 45 units twice a day respectively

Sample Collection Method: Total 450 diabetic type- 2 patients of age 40-60 years were selected for present study and they were divided into three different groups regarding injected units of synthetic insulin. In Group-A 100 male and 50 female were taking 20 units twice a day, whereas 100 male and 50 female individuals with diabetes type-2 of Group-B were injected 30 units twice a day while 80 male and 40 female of Group-C were taking 45 units twice a day respectively. The Fasting and Random glucose levels, Body mass index (BMI) and percentage levels of Dementia parameters of each individual were measured and compared group wise. Blood samples were collected for the measurement of glucose levels.

Exclusion and Inclusion Criterial: Within 15 minutes, rapid-acting insulin enters the bloodstream and continues to function for up to 4 hours. Insulin with a short half-life reaches the bloodstream in just 30 minutes and functions for up to 6 hours. Insulin with an intermediate half-life enters your system in 2 to 4 hours and remains active for about 18 hours. Long-acting insulin starts functioning within a few hours and keeps glucose levels even for roughly 24 hours. Tiredness, sweating, pale skin, feeling weak and loss of consciousness were observed but not included as markers of present research.

Biochemical Analysis: Collected raw data of each parameter were presented in results after applying the Bio-statistical version 2020 in which Mean standard deviation (Mean±SD) were considered as a significant (P≤0.05) for each group respectively.

RESULTS

It was previously believed that people with type 2 diabetes who were receiving insulin therapy rarely had severe hypoglycemia. The prevalence of severe hypoglycemia is rising, according to recent long-term clinical trials in which patients with type 2 diabetes were given oral anti-hyperglycemic medications along with rigorous insulin therapy. In current study intensive glycemic control significantly increased the incidence of severe hypoglycemia. The risk ratio for mortality during the investigations rose when either intensively moderately managed individuals or uncontrolled patients experienced one or more severe hypoglycemia episodes

Table-1: Group-A:

Group-A individuals with diabetes type-2	
Male	100
Female	50
Insulin taking (BD)	20 units
Age (years)	40-60

Table-2: Group-A Male individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	94.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	160.02 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	140.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	110.02 ± 0.01	0.01
Body mass index	kg/m^2.	25.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	26.01± 0.01	0.01
Body mass index After 12 month	kg/m^2.	26.50 ± 0.04	0.04
Incidence of severe hypoglycemia	%	10.01± 0.01	0.01

Table-3: Group-A Female individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	90.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	151.02 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	130.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	100.02 ± 0.01	0.01
Body mass index	kg/m^2.	27.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	28.01± 0.01	0.01
Body mass index After 12 month	kg/m^2.	29.50 ± 0.04	0.04
Incidence of severe hypoglycemia	%	10.51± 0.01	0.01

In Group-A, Fasting glucose levels, Random glucose levels after 2 hour of meal, Random glucose levels after 3 hour of meal, Random glucose levels after 4 hour of meal, Body mass index, body mass index after 6 month, body mass index after 12 month, Incidence of severe hypoglycemia of male and female presented in Table-2 and Table-3 were seen (94.01± 0.02, 160.02 ± 0.01, 140.02 ± 0.03, 110.02 ± 0.01, 25.01± 0.04, 26.01± 0.01, 26.50 ± 0.04, 10.01± 0.01) (90.01± 0.02, 151.02 ± 0.01, 130.02 ± 0.03, 100.02 ± 0.01, 27.01± 0.04, 28.01± 0.01, 29.50 ± 0.04, 10.51± 0.01).

Table-4: Group-B

Group-B individuals with diabetes type-2	
Male	100
Female	50
Insulin taking (BD)	30 units
Age (years)	40-60

Table-5: Group-B Male individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	90.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	150.02 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	130.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	120.02 ± 0.01	0.01
Body mass index	kg/m^2.	25.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	26.50 ± 0.01	0.01
Body mass index After 12 month	kg/m^2.	27.03 ± 0.04	0.04
Incidence of severe hypoglycemia	%	11.01± 0.01	0.01

whereas In Group-B, Fasting glucose levels, Random glucose levels after 2 hour of meal, Random glucose levels after 3 hour of meal, Random glucose levels after 4 hour of meal, Body mass index, body mass index after 6 month, body mass index after 12 month, Incidence of severe hypoglycemia of male and female presented in Table-5 and Table-6 were (90.01± 0.02, 150.02 ±

0.01, 130.02 ± 0.03, 120.02 ± 0.01, 25.01± 0.04, 26.50 ± 0.01, 27.03 ± 0.04, 11.01± 0.01), (90.01± 0.02, 152.01 ± 0.01, 125.02 ± 0.03, 120.02 ± 0.01, 25.01± 0.04, 25.50 ± 0.01, 26.53 ± 0.01, 11.01± 0.01).

Table-6: Group-B Female individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	90.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	152.01 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	125.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	120.02 ± 0.01	0.01
Body mass index	kg/m^2.	25.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	25.50 ± 0.01	0.01
Body mass index After 12 month	kg/m^2.	26.53 ± 0.01	0.01
Incidence of severe hypoglycemia	%	11.01± 0.01	0.01

Table-7: Group-C

Group-C individuals with diabetes type-2	
Male	80
Female	40
Insulin taking (BD)	45 units
Age (years)	40-60

Table-8: Group-C Male individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	80.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	140.02 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	120.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	100.02 ± 0.01	0.01
Body mass index	kg/m^2.	25.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	25.50 ± 0.01	0.01
Body mass index After 12 month	kg/m^2.	26.50 ± 0.04	0.04
Incidence of severe hypoglycemia	%	12.01± 0.01	0.01

Table-9: Group-C Female individuals with diabetes type-2

Parameters	Units	Mean ± SD	P value
Fasting glucose levels	mg/dl	83.01± 0.02	0.02
Random glucose levels after 2 hour of meal	mg/dl	145.02 ± 0.01	0.01
Random glucose levels after 3 hour of meal	mg/dl	110.02 ± 0.03	0.03
Random glucose levels after 4 hour of meal	mg/dl	100.01 ± 0.01	0.01
Body mass index	kg/m^2.	25.01± 0.04	0.04
Body mass index After 6 month	kg/m^2.	24.50 ± 0.01	0.01
Body mass index After 12 month	kg/m^2.	26.01 ± 0.04	0.04
Incidence of severe hypoglycemia	%	11.03± 0.01	0.01

Group-C presented in Table-8 and Table-9 (80.01± 0.02, 140.02 ± 0.01, 120.02 ± 0.03, 100.02 ± 0.01, 25.01± 0.04, 25.50 ± 0.01, 26.50 ± 0.04, 12.01± 0.01), (83.01± 0.02, 145.02 ± 0.01, 110.02 ± 0.03, 100.01 ± 0.01, 25.01± 0.04, 24.50 ± 0.01, 26.01 ± 0.04, 11.03± 0.01) respectively. A remarkable significant changes (P≤0.05) were concluded in group-B and group-C as compared with group-A because 20 units of insulin created less hypoglycemic effects as compared with 30 and 45 units which were injected in Group-B and Group-C comparatively.

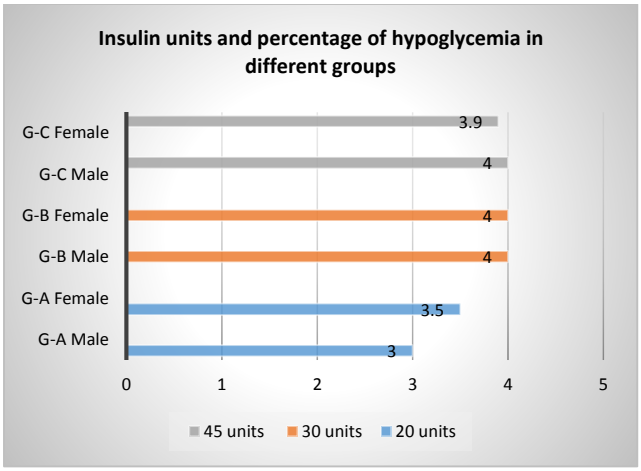

Figure-1: Insulin units and percentage of hypoglycemia in different groups

DISCUSSION

The current study was closely correlated with previous studies by different researchers. The findings of present study indicated that long term insulin therapy develop hypoglycemia in patients with diabetes type-2[20], it was previously believed that people with type 2 diabetes who were receiving insulin therapy rarely had severe hypoglycemia[12]. However, long-term clinical trials recently conducted where Diabetes type 2 patients have been treated with rigorous insulin therapy in addition to oral medication to reach a target HbA1c of 7% As the HbA1c is decreased to #7.0%, ant-hyperglycemic medications exhibit an increased prevalence of severe hypoglycemia[14]. In another study a remarkable growth was seen in intensive glycemic control which created severe hypoglycemia. According to different researchers the frequency of severe hypoglycemia related to insulin therapy concluded in recent retrospective review of the U.K. General Practice Research Database[13].

While it has been noted that hypoglycemia puts the brain at danger, other organs, including the heart, may also be affected possibly more so in type 2 DM[17,19]. Possible changes in heart ventricular repolarization that could cause sudden death are among the effects of hypoglycemia [16]. According to Desouza and colleagues' study, which included a combined assessment of a continuous glucose monitoring system and Holter monitors, hypoglycemia induces a prothrombotic state and may increase the risk of acute myocardial ischemia[15,17]. Hypoglycemia is generally believed to be less common and less severe in type 2 DM29 than in type 1 DM. This may be due in part to type 2 diabetes mellitus relative resistance to the effects of insulin, increased endogenous insulin production, and better-preserved counter regulation with protective responses at higher glucose levels [14]

In this study it was concluded that a significant (P≤0.05) weight gain in regular user of synthetic insulin diabetic type-2 patients was very common [9,11,13]. The rapid insulin intensification needed to reach normoglycemia has been linked to a considerable increase in weight. In one study, the introduction of insulin and its augmentation over the course of four weeks led to a rise in body weight from 92.5 kg to 101.2 kg (P 0.001) (15,20). Weight increase was linked with both the mean daily blood insulin levels (r=0.67, P0.01) and the total exogenous insulin dose (r=0.72, P0.02). People with type 2 diabetes who have tried and failed alternative treatments and have become insulin-deficient typically utilize insulin therapy. About 25% of all persons with type 2 diabetes belong to this group [4,7,13]. The majority of people with type 2 diabetes who begin or increase their insulin therapy gain weight, which could potentially reduce the prognostic benefit of increased glycaemia[12]. All currently published guidelines emphasize both achieving glycated hemoglobin (HbA1c) goals and controlling weight without telling the doctor which is more important[5,8,16].

CONCLUSION

The findings of present study were indicated that long term insulin therapy develop hypoglycemia and significant changes (P≤0.05) in BMI in patients with diabetes type-2. It was concluded that a significant (P≤0.05) weight gain in regular user of synthetic insulin diabetic type-2 patients was very common.

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