World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 7, Issue 10, 2018 ISSN: 2319-5622 USA CODEN: JPROK3

Research Article

HUMAN INSULIN AND INSULIN ANALOGUES IN MANAGEMENT OF DIABETES MELLITUS

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Received on: 01-10-2018; Revised and Accepted on: 22-10-2018

ABSTRACT

The aim of the study was to determine the outcomes of human insulin and insulin analogues in the management of diabetes mellitus. Since good glycemic control is needed for diabetic insulin analogues are having faster onset and shorter duration of action when compared to human insulin. Insulin analogues show improvements in clinical outcomes, medication adherence and patient satisfaction. When compared with human insulin, insulin analogues are having lesser episodes of hypoglycemia. Premixed insulin analogues show little benefits than Rapid and long acting insulin patients, Insulins are used widely for the treatment of diabetes mellitus. Most of the articles show analogues. This review indicates that the introduction of insulin analogues could be safe and effective approach for better glycemic control and to prevent long term complications in diabetes mellitus.

KEYWORDS: *Diabetes Mellitus, Insulin Analogues and Human Insulin.*

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases which results in hyperglycemia either because cells do not respond to insulin or the pancreas does not produce enough insulin [1]. Type 1 Diabetes mellitus is also called as insulin dependent diabetes mellitus, which results from body's failure to produce insulin. Type2 Diabetes mellitus, which results from failure of the cells to use insulin properly, sometimes it is combined with absolute insulin deficiency and it is also called as non-insulin dependent diabetes mellitus [2]. Insulin is indicated for patients with diabetes mellitus who were unable to achieve adequate glycemic control by exercise, diet or oral antidiabetic drugs [3, 6].

Insulin was first used in 1920s. Recombinant DNA technology enabled the synthesis of human insulin.[4]Human insulin and insulin analogues are insulin agents used for the treatment for diabetes mellitus [5].

Insulin analogues available include:

Rapid Acting : Insulin Lispro
Insulin Aspart

Long Acting : Insulin Glargine
Insulin Detemir

Premixed analogues: Insulin Aspart 70/30
Insulin Lispro 75/25
Insulin Lispro 50/50

Human insulin available includes:

Rapid Acting : Regular human insulin

Intermediate Acting: NPH Insulin

Premixed insulin : 30%/70% regular/NPH
50%/50% regular/NPH [7, 8]

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DOI: https://doi.org/10.5281/zenodo.1468476

Rapid acting analogues show shorter duration and faster onset of action than human insulin [9, 10] and Long acting insulin analogues shows a broad peak which lasts from 8 to 16 hrs with duration of action ranging from 20 to 36 hrs (Table 1).

NPH insulin shows unfavorable pharmacokinetic profile and short duration of action(less than 24 hour) [11] (Table 1) another important disadvantage is that it shows large variability in glucose lowering effect from injection to injection [12] Premixed insulin have to be injected once or twice daily regimen with or without oral antidiabetic drugs and it will also provide more options for physicians to achieve optimal control with greater flexibility of dosing [13, 14].

Insulin will bind to α subunits and activates GLUT 4 and helps in uptake of glucose to muscles and fat cells. It will also inhibit glycogenolysis and gluconeogenesis [45]. Glycemic control is the essential treatment strategy for type 1 diabetes mellitus patients to a substantial reduction of both microvascular and macrovascular complication [40]. Type-1 diabetes patients requires multiple injections to attain HbA1c level less than 7% [14]. Dietary restriction fails to achieve normal glucose level the insulin therapy is needed in GDM women. Newer insulin analogues are beneficial that they can reduce postprandial glucose level and can also reduce some maternal and fetal outcomes [42, 43].

How insulin can be used early or late in the disease process and how it complements other agents, for this physician need to understand the central role of insulin in pathophysiologic profile of diabetes [32]. Modern insulin analogues were designed to aid achievement of better glycemic control while addressing concerns about hypoglycemia and body weight gain [20]. Many type 2 diabetic patients could benefit greatly from insulin therapy. Delaying initiation of insulin therapy is due to the lack of awareness of disease progression, aversion to injection and patients and physicians concerns about weight gain and hypoglycemia [15, 17].

METHODOLOGY

Systematically reviewed articles based on Insulin analogues compared with human insulin in management of type 2 diabetes mellitus from 2000-2013.Study was a randomized one. Main search concepts were diabetes mellitus, insulin analogues and Human insulin. Various databases such as MEDLINE, EMBASE, and MEDSCAPE were searched and literatures were collected for this study. Articles were also

collected from various associations such as Diabetes and endocrine association, medical association and their associated sites. In this study 45 citations were reviewed regarding management of type 2 diabetes mellitus using insulin analogues compared with human Insulins.

Table No. 1: Pharmacokinetic Profile of Insulin [35-38]

Insulin Type	Onset of Action	Peak	Duration of Action
Rapid Acting			
Lispro	5-15 minutes	30-60 minutes	3-4 hours
Aspart	10-20 minutes	40-50 minutes	3-5 hours
Glulisine	20 minutes	1hour	4 hours
Short Acting			
Regular	30 minutes	60-120 minutes	6-8 hours
Intermediate Acting			
NPH	1-2hours	3-8 hours	12-15 hours
Long Acting			
Glargine	1-2 hours	Flat	~24 hours
Detemir	1.6 hours	Flat	Up to 24hours

RESULT

A meta-analysis in type 2 diabetes mellitus showed that the use of short acting insulin analogues in type 2 diabetes patients provide a better control of post prandial glucose and HbA1c in comparison with human insulin.[18]Several clinical studies have shown that rapid acting insulin analogues under various clinical situations provide superior glycemic control with more convenience and flexibility making them a patient friendly option. They have associated with improved hospital outcomes with or without critical illness and managing emergencies like diabetic ketoacidosis. Some studies which compare insulin lispro immediately before meal and regular human insulin 30 minutes prior to meal showed a decrease in HbA1c by 0.3-0.8 % without increase in hypoglycemic episodes. Apparently insulin aspart has longer duration of action than insulin lispro [21, 22]. The study on IDDM patients indicated that insulin lispro improves postprandial glucose control and it also reduces frequency of hypoglycemia in patients with IDDM [40]. In the study to assess the short term efficacy of insulin aspart in women with gestational diabetes it was found that insulin aspart was very effective in reducing peak post prandial glucose concentration when compared with regular insulin [39]. Studies showed that the rapid acting insulin analogues, such as insulin aspart used in basal bolus regimen have the ability to reduce hypoglycemia in patients with type1 diabetes mellitus [41]. Studies on Gestational diabetic patients showed that rapid acting insulin analogues (Insulin lispro and Insulin aspart) are novel treatments for improving glycemic control by reducing postprandial glycemia [44].

Study on long acting insulins concluded that, insulin glargine given once daily reduces the risk of hypoglycemia when compared to NPH insulin, which can facilitate more aggressive insulin treatment in patient with type2 diabetes mellitus to an HbA1c target of ≤7.0% [23]. Evidence supports that compared to NPH insulin, basal insulin analogues (glargine and detemir) offer improved pharmacodynamic and pharmacokinetic profiles. They also offers improved quality of life, better patient adherence, treatment satisfaction and improved glycemic control in patients with type2 diabetes mellitus poorly controlled with oral antidiabetic drugs in combination or not with NPH insulin [24-26]. In a comparative study of two treatment algorithm, with longstanding type 2 diabetes mellitus insulin glargine was found to be safe and effective in improving glycemic control [27]. It has been demonstrated that to achieve the same hypoglycemic potential insulin detemir needs to be given in four equimolar doses to NPH insulin [28].

From the studies it is confirmed that the use of premixed insulin analogues resulted in better postprandial plasma glucose control without increase in hypoglycemic episodes in general or exercise induced [30]. In a study on Premixed Insulin Analogue therapy in type 2 diabetes patients, it was concluded that the newly introduced premixed insulin aspart is an effective, safe and convenient option in insulin requiring patients [16]. Studies concluded that although premixed insulin analogues and premixed human insulins showed similar HbA1c control, premixed analogues showed lower risk of hypoglycemia when compared with premixed human insulins [30, 31].

CONCLUSION

The result indicates that insulin analogues have a few clinical advantages than human insulin in the treatment of diabetes mellitus. Studies reported better glycemic control, patient satisfaction and improved quality of life on treatment with insulin analogues. In type 2 and type 1 diabetes mellitus Rapid acting insulin analogues showed better control of Post Prandial Glucose (PPG) level so it can be replaced for regular human insulin. The NPH insulin can be replaced with the long acting insulin analogues for better HbA1c control. Premixed insulin analogues have more advantage than rapid acting and long acting insulin analogues. So furthermore investigation has to be done on the safety and efficacy of insulin analogues. In case of GDM better glycemic control can be achieved by rapid acting insulin analogues and long acting insulin analogues needed further more studies on safety issues before they can be prescribed.

ACKNOWLEDGEMENT

We thank PSG Hospitals for granting us permission to assess all required medical resources database, We also wish to express our sincere gratitude to Dr. M. Ramanathan, principal of PSG College of Pharmacy for encouragement and providing necessary facilities and Dr. ANDHUVAN, for her valuable feedback and constant encouragement, we also thank all the friends and colleagues for their comments that greatly improved the manuscript

ABBREVIATIONS:

DNA : Deoxyribo Nucleic Acid,
NPH : Neutral protamine Hagedorn,
GLUT4 : Glucose transporter type 4,
HBA1c : Glycated haemoglobin,
GDM : Gestational diabetes mellitus,
IDDM : Insulin-dependent diabetes mellitus

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How to cite this article:

Ndayishimye Samuel, Prudence A. Rodrigues. HUMAN INSULIN AND INSULIN ANALOGUES IN MANAGEMENT OF DIABETES MELLITUS. J Pharm Res 2018;7(10):224-226. **DOI: https://doi.org/10.5281/zenodo.1468476**

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil