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A Retrospective Study of Insulin and Insulin Analogues in Type I and Type II Diabetic Patients

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ABSTRACT

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Study was carried out to compare and estimate the safety, efficacy and quality of life of insulin and insulin analogue in Type I and Type II Diabetic patients. A retrospective observational study was conducted on 50 patients in which 30 patients were on conventional insulin and 20 patients on analogues. Safety was measured based on number of hypoglycemic events and the efficacy by comparing FBS and HbA_1c levels in both groups. QoL was assessed by using EQ-5D questionnaire and EQ Visual Analogue Scale (EQ-VAS). Percentage of hypoglycemic events in conventional insulin group was 53.3% (n=16) and 20% (n=4) in analogue group. Risk of hypoglycemia has been estimated by using Fisher's exact Test (p=0.02). The mean value of FBS for conventional insulin and insulin analogue subjects was 176.85 ± 1.58 and 162.36±2.01 respectively whereas the mean value of HbA1c was found to be 8.72 ± 0.04 and 8.67 ± 0.07 respectively. The percentage of patients reported 'no problem' was considered as they have better quality of life. Analogues have low risk of hypoglycemia as number of hypoglycemic events are reduced in those patients but these benefits are not reliable across insulin types. For glycaemic control, analogues and conventional insulins do not constitute statistically vital differences. And there was no significant impact of treatment in diabetic patients even though analogue group reported better QoL. Out of all dimensions majority of them are anxious and depressed among the study population.

Keywords: Insulin analogs, hypoglycemia, efficacy, safety, quality of life.

INTRODUCTION

Diabetes Mellitus is a metabolic disorder which is expected to persist as a most important health problem owing to its severe complications. Insulin is indicated for type 1 diabetes patients and for patients with type 2 diabetes if glycemic control cannot be achieved satisfactorily in the course of oral hypoglycemic therapy[1].

Insulin:

Insulin is a polypeptide of 51 aminoacids. Insulin has been used since 1922 as monotherapy in patients with type I disease and since the late 1950's in combination or monotherapy in patients with type II diabetes. Insulin regimen should be personalized to each patient's individual needs, desired metabolic control and age. Each patient may experience variations in clinical response to various particular class of insulin.[2]

Types of Insulin:

Insulin is categorised in to Conventional insulin agents and insulin analogues.

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Conventional Insulin Agents:

Human insulin and intermediate acting Neutral Protamine Hagedorn Insulin (NPH).

There is variation in insulin absorption with the basal formulations such as NPH due to their low and relatively constant levels between meals[3].

Insulin Analogs:

Modifications have been made in the amino acid sequence of the insulin molecule to overcome the pharmacokinetic shortcomings of human insulins.

These alterations produced different types of analogs such as:

- Rapid acting analogues for controlling post prandial hyperglycemia.
- Long acting insulin analogues have more physiologic substitution than NPH in glycemic control[4].
- Analogues have low risk of hypoglycemia with prolonged duration of action and greater consistency than NPH[5]. They offer patients greater flexibility and more convenience in administration compared with human insulins[6]. But more expensive than conventional insulins.

Safety: Insulin analog, Lispro, showed improved glycemic control with less hypoglycemic events[7].

- Basal biphasic formulations are associated with a higher

incidence of nocturnal hypoglycaemia compared with biphasicanalogues[8].

- Major ADR (Adverse Drug Reaction) of insulin treatment is hypoglycemia. Nocturnal hypoglycemia is a particular problem because the early warning symptoms are not recognized.
- Weight gain is common after starting insulin therapy. In type I DM it is caused by the reversal of the catabolic state of insulin deficiency, in type II is partly caused by gain of the calories previously last through glycosuria, but also because of increased hunger from mild hypoglycemia and continued excess intake of calories.
- Allergy- some patients have an allergic reaction to insulin injections, which appears as redness around the injection site and generalised itching, this allergy is usually triggered by components of the preservatives in the insulin solution and is often solved by changing the brand of insulin used.
- DKA (Diabetic Ketoacidosis) is the leading cause of death in patients with type I DM under the age of 20 years[9].

Quality of Life: It can be improved in diabetic children and their families by insulinanalogues due to their structural modifications, low risk of nocturnal hypoglycaemia[10].

- Rapid –acting insulinanalogue improved quality of life in the majority of patients[11].
- And also the long acting Insulinanalog- glargine showed improved quality of life than NPH[12].

Efficacy: Hyperglycemia is a common end point for all types of diabetes mellitus and is the parameter that is measured to evaluate and manage the efficacy of diabetes therapy.HbA1c is considered as the gold standard for measuring long term glycemic control[13].

- The rapid-acting and pre-mixed analogues can provide improved glycemic control, particularly after meals, compared with human insulin along with more convenient dosing.
- Insulin analogues have been shown to have less pharmacologic variability, lower hypoglycemic risk, greater impact on quality of life when compared with traditional insulin formulations, all of which would be expected to improve adherence.
- Treatment with the analogues provides an improved balance between glycemic control and the risk for hypoglycaemia, together with greater flexibility in timing of dosing and thus increased convenience for patients.
- Switching from human insulin to analogues, there was a significant decrease in hypoglycaemic episodes accompanied by a significant increase in treatment satisfaction[14].
- Health Related Quality of Life is seemed to be increased when insulin therapy is beginning with or switching to insulin analogue[15].

So this influenced us to compare and evaluate clinical benefits of human insulin and analogues in a group of diabetic population who are on insulin therapy in KMCH hospital in the department of diabetology.

In this study we are going to assess:

1. Safety based on number of hypoglycaemic episodes
2. Effectiveness based on their blood sugar levels
3. Q.O.L is estimated by using EOQ-5D questionnaire.

MATERIAL AND METHODS

Objective:

To compare and estimate the safety, efficacy and quality of life of insulin and insulin analogue in Type I and Type II Diabetic patients.

Study Design:

A retrospective observational study was conducted over a period of six months. The data was collected from various sources such as patient's case sheet, treatment chart, laboratory reports and also through direct patient interview.

Study Procedure:

A 50 patients who are diagnosed with Type I and II Diabetes mellitus are included. The patients who do not wish to complete the questionnaire and those with cognitive impairment, visual or hearing loss are excluded. Both inpatients and out patients are included. The laboratory values such as FBS and HbA_1c, number of hypoglycemic events and medications were noted from the patient's chart.

Data are collected by providing the EQ-5D questionnaire which consists of EQ- 5D descriptive system and EQ Visual Analogue Scale (EQ-VAS) to assess the quality of life from the patients.

The patients were interviewed on a structured questionnaire after their verbal consent. The EQ-5D descriptive system comprises the following 5 dimensions:

- Mobility
- Self care
- Usual activities
- Pain /discomfort.
- Anxiety /depression.

Each has three levels which describes "no problem", " some problem", " severe problem" and then patients were asked to indicate his/her health state by ticking in the box against the most appropriate statement in each of the 5 dimensions .The EQ-5D levels were dichotomised into "no problems" (level 1) and "problems"(level 2 and 3) Visual Analogue Scale used to help people say how god or bad their health state . The patients were asked to draw a line from the box below to whichever point on the scale indicates their current health state. The EQ-VAS scores however are anchored on 100 = best imaginable health and 0= worst imaginable health.

Data Analysis:

Data is analyzed by using Graph Pad Prism (5.01) software .Unpaired t-test and Fisher exact test are used to assess the Safety, Efficay and QoL among conventional insulin and insulin analogue patients. The 'p' value less than 0.05 is considered statistically significant.

RESULT

Among 50 study group, 30 patients were on conventional insulins and 20 patients were on insulin analogues. The mean age of subjects using conventional insulin and insulin analogue were 44.7 ± 0.79 and 40.2 ± 1.18 respectively.

It was found that percentage of patients who had events of hypoglycemia was 53.3% (n=16) and 20% (n=4) among two groups. The percentage of patients who never had events among insulin and insulin analogue were 46.6% (n=14) and 80% (n=16) respectively. Risk of hypoglycemia has been estimated by using Fisher's exact Test. (Table 1).

The efficacy was measured by comparing FBS and HbA_1c levels in both groups. The mean value of FBS for conventional insulin and insulin analogue subjects was 176.85 ± 1.58 and 162.36±2.01 respectively whereas the mean value of HbA1c was found to be 8.72 ± 0.04 and 8.67 ± 0.07 respectively. An Unpaired t test has been applied to compare the FBS and HbA1c levels among the two groups (Table 2).

The Quality of life of the subjects was evaluated based on EQ-5D questionnaire .In the questionnaire given, 5 dimensions were used which involves mobility, self care, activity, pain and anxiety. The rating given was 'no problem', 'moderate problem' and 'severe problem' Fisher's exact test was used for comparison. (Table3).

Table 2: Comparison of the Study between two groups

Efficacy	Insulin	Insulin analogue	P Value
FBS	176.85	162.36	0.8757
HbA_1c	8.72%	8.6%	0.7641

Table 1: Impact of therapy between two groups on safety level.

Safety (hypoglycemic events)	Insulin	Insulin analogue	OR	95%CI	RR	95%CI	P Value
Yes	53.3%(n=16)	20%(n=4)					
			4.571	1.234 to 1.694	1.714	1.103 to 2.664	0.0221*
No	46.6%(n=14)	80%(n=16)					

**P*<0.05 OR, Odds Ratio; CI, Confidence interval; RR, Relative risk

Table 3: Characteristics of subjects based on EQ-5D Questionnaire

Variables	Insulin	Insulin analogue	OR	95%CI	RR	95%CI	P Value
Mobility							
No Problem	22	17	0.48	0.11 to 2.11	0.77	0.49 to 1.22	0.48
Problem	8	3					
Self care							
No Problem	21	16	0.58	0.15 to 2.24	0.81	0.51 to 1.29	0.52
Problem	9	4					
Usual activity							
No Problem	14	13	0.47	0.14 to 1.51	0.74	0.47 to 1.17	0.25
Problem	16	7					
Pain							
No Problem	21	15	0.77	0.21 to 2.79	0.90	0.56 to 1.46	0.75
Problem	9	5					
Anxiety							
No Problem	15	16	0.66	0.21 to 2.09	0.85	0.54 to 1.33	0.56
Problem	15	8					

OR,Odds Ratio; CI, Confidence interval; RR, Relative risk

Table 4: Comparsion of QOL among two groups	
Types	**EQ-5D VAS**
Insulin	70.9
Insulin Analogue	90.75

A rating scale (VAS) was given ranging from 0-100 in which the mean score points gained by conventional insulin patients and by insulin analogue group is determined (Table 4).The p value obtained for Qol was 0.998 which is not statistically significant.

DISCUSSION

A study conducted by Arturo Rolla, reported that therapy with the analogues provides an improved balance between glycemic control and the risk for hypoglycemia, together with greater flexibility in timing of dosing and thus increased convenience for patients.

Our results suggest that difference between the conventional insulin and insulin analogues are minimal in management of Type I and Type II.

In a study conducted by Andreia Cristina et al., suggests that there is no significant difference between long acting insulin and NPH insulin in efficacy and safety. But in our study we found statistically significant difference (p=0.021) in safety between conventional insulin and insulin analogue patients in terms of hypoglycemia.

For hypoglycaemic events, there were statistically significant advantages for analogue insulins for both Type 1 and Type 2 patients for nocturnal hypoglycaemia, although results were not consistent across insulins

A study conducted by Arturo Rolla reports that rapid-acting and premixed analogues offer better control of post prandial glucose excursions than regular human insulin, resulting in similar or lower HbA1c levels. In our study we found that most estimates of differences in HbA1c (p=0.76) and FBS (p=0.87) between the treatment groups were not statistically significant.

A study conducted by Siddharth Shah et al., assessed 66,726 people by the validated EQ-5D questionnaire reported that HQoL increased significantly by 13.8 points (p=0.001) and determined that beginning insulin with, or switching to , insulin analogue therapies are associated with increased health related Quality of Life. This study suggests that analogues had its own influence in enhancing the quality of life. In contrast to this literature, our study shows that there is no statistically significant difference in QoL between the two treatment groups, even though the overall percentage of quality of life based on five dimensions was more for analogue group (73%) than the conventional group(63.98%). Because VAS score and percentage of patients reported 'no problem' in five dimensions was not statistically differed significantly. As far concerned to QoLolder people reported more problems on all dimensions. Out of all dimensions majority of them are anxious and depressed among the study population.

CONCLUSION

Insulin Analogues have low risk of hypoglycemia as numbers of hypoglycemic events are reduced in those patients. but these benefits are not reliable across insulin types.For glycaemic control, analogues and conventional insulins do not constitute statistically vital difference indicate that analogue insulins have no advantage over conventional insulins in efficacy and there was no significant impact of treatment in diabetic patients even though analogue group reported better QoL More studies are considered necessary to comprehend better the impact of insulin analogues on quality of life, efficacy and safety.

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