Pakistan
Journal of Biological Sciences

Efficacy of Dongsulin (rDNA Human Insulin) in a Normal Clinical Practice Setting

[1]M.Y. Ahmedani, [2]A. Fawwad, [1]A. Basit and [3]A. Nawaz
[1]Department of Medicine,
[2]Research Department,
[3]National Diabetes and Diabetic Food Program, Baqai Institute of Diabetology and Endocrinology,
Baqai Medical University, Plot No. 1-2, II-B, Block 2, Nazimabad, Karachi-74600, Pakistan

Abstract: The aim of this study was to evaluate the effectiveness of Dongsulin (rDNA, insulin) in maintaining HbA1c level in a normal clinical practice setting and secondly to assess weight gain, episodes of hypoglycaemia, insulin dose change and its safety. Fifty two diabetic patients already on human insulin (rDNA) were enrolled to a 12 week of treatment. Patients with HbA1c level between 6-8% were switched to Dongsulin on same dosage. The compliance of the patient regarding dietary pattern, physical activity and insulin dosages were assessed. HbA1c was checked after 12 weeks. Patient known to have either of the noncompliance factors during the study period were grouped as group B (non compliant) while, patients who were compliant were grouped as group A (compliant). Thirty nine patients completed the study. No significant difference was found between the HbA1c of two visits in group A (p = 0.32) while, HbA1c in group B was significantly raised as compared to first visit (p = 0.000). In group B patients missed the doses, changes in their diets and decreased their physical activity significantly. The mean insulin dose and weight of the patient remained the same in both groups. No major episode of hypoglycemia was observed. This study has shown that patients who remained compliant during the study period, switched over to Dongsulin had no significant change in the glycaemic control as measured by HbA1c.

Key words: Insulin, glycaemic control, compliance

INTRODUCTION

About 194 million people worldwide, or 5.1%, in the age group 20-79 were estimated to have diabetes in 2003. This estimate is expected to increase to some 333 million, or 6.3% of the adult population, by 2025. The largest proportional and absolute increase will occur in developing countries, where the prevalence will rise from 4.2 to 5.6% (International Diabetes Federation, 2006).

The number of people with diabetes is increasing due to population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity (Sarah et al., 2004). It accounts for about one sixth of all expenditures for health care.

The mortality rate in patients with diabetes may be up to 11 times higher than in persons without the disease. Diabetes is a leading cause of blindness, renal failure and foot and leg amputations in adults. Managed care and budgeted resources challenge clinicians to provide comprehensive health care to patients with diabetes (Joe and Bryan, 1999).

The Health economic condition is not very healthy in a developing country like Pakistan. The monthly expenditure of an average Pakistani household in 2004-05 was 9,121 rupees (152 USD); only 3.8% i.e., 346 rupees (5.7 USD) is spent on health reflecting the fact that health care is a low priority for the majority of Pakistani households (Household Integrated Economic Survey, 2001-2002).

The Diabetes Control and Complications Trial and the UK Prospective Diabetes Study were benchmark studies that have shown that good glycaemic control can reduce the risk of diabetic complications and poor outcomes (Lynda et al., 2006).

Insulin therapy is often an important part of diabetes treatment since its discovery in 1921. This discovery meant that people with diabetes who were insulin-treated survived the acute effects of the disease (International Diabetes Federation, 2006).

The major problem today lies in the widespread long-term lack of access to insulin and diabetes supplies, which poses a serious threat to the lives of people with

Corresponding Author: Muhammad Yakoob Ahmedani, Department of Medicine,
Baqai Institute of Diabetology and Endocrinology, Baqai Medical University, Plot No. 1-2, II-B,
Block 2, Nazimabad, Karachi-74600, Pakistan
Tel: 92 21 6688897, 92 21 6608565, 92 21 6707179 Fax: 92 21 6608568

diabetes in developing countries. For proper delivery of diabetes care, insulin, insulin syringes and needles and other monitoring supplies should be available, accessible and affordable to all those who require them (International Diabetes Federation, 2006).

The World Health Organization (WHO) estimates that 40% of people with diabetes need oral medicines and 40% need insulin injections. However, it is estimated that only 3% of people with diabetes in developing countries are being treated. Insulin is particularly difficult to make available because of the need for daily injections and its relatively high cost. Insulin is difficult to manufacture to sufficiently consistent quality for therapeutic use (WHO, 1998).

Data published by IDF recorded that an estimated 150 million vials of insulin were produced yearly with the vast majority being used in developed countries. Seventy percent of all insulin was used in countries that comprised 16% of the world's population (Raab, 1999).

The price of insulin is influenced by many factors, including the original price from the manufacturer, transport and storage costs, size of market, the profit margins of distributors and retailers and government taxes. It is frequently those most in need who are most adversely affected by these factors-smaller countries with small markets and transport problems, multiple intermediaries, excessive bureaucracy, tariffs and sometimes corruption (Graham *et al.*, 2006).

In the developed world and some developing countries, insulin is provided free or at minimal cost by government health services or insurance arrangements. Where, this is not so and the drug is not provided by charitable organizations, insulin must be purchased at market or premium prices. A 10 mL vial of 100 U mL^{-1} insulin costs up to 1800 (30 USD). Assuming an average price of 900 rupees (15 USD), a person with type 1 diabetes using 50 U day^{-1} will use 18 vials/year-a cost of 16200 rupees (270 USD)/year. This may exceed the family's total annual income. The financial impact is compounded by other components of care-syringes and needles, blood glucose monitoring, consultation fees, travel expenses and missed work days (Garham *et al.*, 2006).

The majority of poor and even middle-class people in developing countries do not have health insurance and are forced to pay for medicines as they need them. Since diabetes is a lifelong condition, the cost of medicines can drive people living with diabetes into a downward spiral of debt and poverty (Mohga, 2003).

In 1982, the first genetically engineered product-human insulin using *E. coli* bacteria- was approved for use by diabetics (Biotechnology Institute, 2005). But in developing countries due to cost animal insulin was still in use. Animal insulin is 50% cheaper than recombinant human insulin.

There was a need of relatively low cost human insulin in Pakistan. Highnoon Laboratories, one of the leading National pharmaceutical company started to import recombinant human insulin from China to Pakistan with the name of Dongsulin in 2000. The price of Dongsulin was 13 to 31% lesser as compared to the Recombinant human insulin marketed by multinational companies in Pakistan.

The objective of this study was to evaluate the effectiveness of Dongsulin in maintaining HbA1c level over 3 months period in a normal clinical practice setting and secondly to assess weight gain, episodes of hypoglycaemia, insulin dose change and safety of dongsulin.

MATERIALS AND METHODS

It was an Open label phase 4 trial conducted at Baqai Institute of Diabetology and Endocrinology, Karachi Pakistan from May 2006 to September 2006. A written informed consent was obtained from all those patients who fulfilled the inclusion criteria. The protocol was approved by the Institutional Review Board (IRB) of BIDE. A total of 52 subjects with type 1 or type 2 diabetes already on commercially available (rDNA) human insulin at least from last six months, were enrolled to a 12 week of treatment. HbA1c was checked at the baseline visit and patients with HbA1c level between 6-8% were switched from their current (rDNA) human insulin to Dongsulin on same dosage. The patients were asked to check their blood glucose at home as they were checking before. They were also, asked to follow the same dietary and physical activity routine as they were following before. The compliance of the patient regarding dietary pattern, physical activity and insulin dosages were assessed at baseline and at the end of the study. Patients known to have either of the noncompliance factors at the start of the study was excluded from the study. After 12 weeks, the patients had their HbA1c checked again. There were no essential planned visits for the study; patients followed the clinic as they were doing previously in normal clinical practice setting. Doses of insulin were adjusted according to the blood glucose levels. Patients with pregnancy, hepatic or renal impairment and with known hypersensitivity to Dongsulin or any of its constituents were excluded from the study. Patients who were not compliant to insulin dosage prescribed, dietary guidelines and physical activity pattern during the study period were grouped as group B (non compliant) while, patients who were compliant to all those factors were grouped as group A (compliant).

RESULTS AND DISCUSSION

Out of 52 patients, 39 completed the study in which 64.1% (n = 25) were females. 82.05% (n = 32) were having type 2 diabetes. Mean age of the patients was 49±12 years (Table 1).

Group A (compliant) and B (non compliant) were consisting of 25 and 14 patients, respectively. No significant difference was found between the HbA1c of two visits in group A (compliant) (p = 0.32) while, HbA1c in group B (non compliant) was significantly raised as compared to first visit (p = 0.000) (Table 2). While looking at the factors affecting glycaemic control in group B (non compliant), it was found that 71.4% (n = 10) patients missed the doses, 78.5% (n = 11) patients made significant changes in their diets and (n = 10) 71.4% patients decreased their physical activity. The mean insulin dose and weight of the patients remained the same between first and second visits in both groups as shown in Fig. 1a and b. No major episode of hypoglycemia was observed while 8% patient suffered from minor episodes of hypoglycemia.

This study was carried out to assess the efficacy of newly available economical recombinant rDNA human insulin (Dongsulin) in normal clinical practice setting. It was observed that 25 out of 39 patients remained compliant to insulin dosage, dietary guidelines given and exercise pattern advice. These patients maintained their HbA1c at the end of study. While, 14 patients did not comply and hence, deterioration in their glycaemic control as measured by HbA1c was observed.

Several factors i.e., dose missing, change in quality and quantity of food and change in physical activity as shown by others in which glycaemic control was not achieved even by increasing the number of OHAs for

co-administration or by insulin use unless dietary/exercise therapy, a basic therapeutic option, was adequately used (Nippon, 2004).

Almost three fourth of the patient in group B (non compliant) were missing their insulin dose can lead to hyperglycemia (National Diabetes Information, 2004). Almost similar number of subjects (77%) were found to be inconsistent to their diet intake and studies have shown that diet is an important factor in glycemic control and variation to dietary guideline can lead to increase in blood glucose levels (Mary and Frank, 2006).

The reasons leading to non compliance of previously compliant patients would be many. Mango season, traveling as there were school summer vacation and frequent marriage ceremony in the month preceding Ramadan, all could contribute. This observational study has limitations. Moreover the information's collected at the time of the start of the study were subjective in nature. The subjects were not followed intensively and the same routine of blood sugar checking and follow-up was advised as they were doing before the start of the study to avoid any bias in the study.
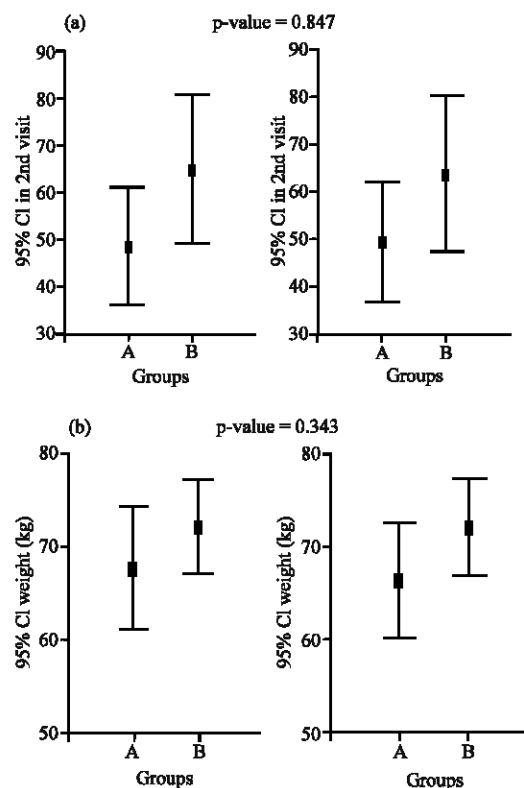

Fig. 1: (A) Comparison of insulin doses between 1st and 2nd visit [Group A (n = 25) and Group B (n = 14)] and (b) Comparison of weight between 1st and 2nd visits [Group A (n = 25), Group B (n = 14)]

Table 1: Basic characteristic of the sample

Variables	Mean±SD (n = 39)
Age (year)	49±12
BP (Systolic) mm Hg	128±18
BP (Diastolic) mm Hg	80±7
BMI (kg m^{-2})	22±4
Randam plasma glucose (mg dL^{-1})	166.73±47.2
Serum creatinine (mg dL^{-1})	0.97±0.22
SGPT (Iu mL^{-1})	29.4±17.2
Female*	64.1%
Male*	35.9%

* Percentage is reported

Table 2: Comparison of HbA1c between 1st and 2nd visits in group A and B

Groups	Mean±SD	p-value
A (n = 25)		
HbA1c (1st visit)	7.492±0.4663	0.320
HbA1c (2nd visit)	7.644±0.5959	
B (n = 14)		
HbA1c (1st visit)	7.214±0.4276	0.000
HbA1c (2nd visit)	8.764±0.9262	

No significant change in the units of insulin was observed in group B despite being poor glycaemic control, due to lack of blood glucose monitoring. Those patients who followed after blood glucose checking were advised to improve their compliance first.

CONCLUSION

This study has shown that patients who remained compliant during the study period, switched over to Dongsulin had no significant change in the glycaemic control as measured by HbA1c. Dongsulin was well tolerated with no significant hypoglycaemic events. No significant change in weight and dose requirement was noted. Since this study had limitations therefore further single or double blinded studies are required to give us more elaborated results.

ACKNOWLEDGMENT

We are thankful to Highnoon Laboratories Limited for their support in this study.

REFERENCES

Biotechnology Institute, 2005. Historical events in biotechnology web page. http://www. biotechinstitute.org/what_is/timeline.html.

Graham, O., B. David, R. Raab and D. Larry, 2006. Global access to and availability of insulin. Diabetes Voice, 51: 22-25.

Household Integrated Economic Survey, 2001-2002. Chapter 2, pp: 10. Http://www.statpak.gov.pk/depts/ fbs/statistics/hies0102/summary.pdf.

International Diabetes Federation, 2006. Prevalence of diabetes. IDF Atlas 3rd Edition.

Joe, A.F. and F.Y. Bryan, 1999. Treatment of type 2 diabetes mellitus. Am. Family Physician, 15: 2835-2348.

Lynda, K.F., M. Jerry, O. Susan, P. Jan and A.P. Margaret, 2006. Advancing the treatment of diabetes with insulin and technology. The Diabetes Educator, 32: 7S-8S.

Mary, C.G. and Q.N. Frank, 2006. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. Nut. Metabolism, 3: 16-16.

Mohga, K.S., 2003. Why developing countries need access to cheap treatments for diabetes. Diabetes voice, 48: 2 http://www.diabetesvoice.org/en/articles/ why-developing-countries-need-access-to-cheap-treatments-for-diabetes

National Diabetes Information, 2004. Diabetes monitor. Chapter 3. http://www.diabetesmonitor.com/ lowglucose.htm.

Nippon, J., 2004. The factors affecting glycemic control in Japanese adolescents with type 2 diabetes mellitus. Med. Sch., 71: 156-159.

Raab, R., 1999. The problem of access to insulin, test stripes and other diabetes supplies in many countries and how to improve it. Pract. Diab. Int., 16: 58-60.

Sarah, W., R. Gojka, G. Anders, S. Richard and K. Hilary, 2004. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care, 27: 1047-1053.

World Health Organization Press Release, 1998. Diabetes and human rights. www.who.int/inf-pr-1998/en/pr98-85.html.