Diabetes Research and Metabolism: Open Access
Received: Nov16, 2015, Accepted: Nov 27, 2015, Published: Nov 30, 2015
Diabetes Res Metab, Volume 1, Issue 1
http://crescopublications.org/drmoa/DRMOA-1-003.pdf
Article Number: DRMOA-1-003

Research Article Open Access

Improved Glycemic Control with Lesser Daily Dose with Insulin Glargine on Retransition from Insulin Detemir

Roshni Narurkar[1] and Udaya M Kabadi[2]*

[1]Broadlawns Medical Center, Des Moines, Iowa, USA

[2]University of Iowa, Iowa City, IA, USA

***Corresponding Author**: Udaya M Kabadi, University of Iowa, Iowa City, IA 52242, USA; Tel: 3195948575; E-mail: ukabadi@gmail.com

Citation: Roshni Narurkar and Udaya M Kabadi (2015) Improved Glycemic Control with Lesser Daily Dose with Insulin Glargine on Retransition from Insulin Detemir. Diabetes Res Metab 1: 003.

Abstract

Background: We documented lapse of glycemic control, despite higher daily insulin dose, 2 SC injections, and increased number of daily blood glucose monitoring with less convenience on switching from Insulin Glargine (GI) to Insulin Detemir (DI) in subjects with Type 1 and type 2 DM.

Objective: Assess impact of retransition from DI to GI in subjects with Type 1 and Type 2 DM.

Subjects and Methods: 14 subjects, 8 men and 6 women with Type 1 (36 ± 3 years) and 24 subjects, 12 men and 10 women with type 2 DM (62 ± 5 years). Duration of DM (years) was 15 ± 2 in type 1 and 12±3 years. DI was discontinued in both groups. Insulin Aspart (AI) was continued premeal 3 times daily in type 1 and Metformin and Glimepiride were continued in same daily dose in type 2. GI was reinitiated at 0700-0800 AM in the same daily dose as DI. Daily dose of insulin DI, GI and AI, no of injections, HbA1c, body weight (BW) and hypoglycemia (Hypo) were assessed.

Results: In subjects with type 1 DM, daily insulin dose, 58±6 and DI, 31±6 declined to 48±6 and GI, 23±5 units respectively ($p<0.05$). AI daily dose was not significantly altered. No of injections with DI, 4.6±0.3 declined to 4.0 ±0 with GI. HbA1c, BW and Hypo were not significantly different (GI: HbA1C, 7.2 ± 0.2; BW, 70 ± 4; Hypo, 0.5 ± 0.2) vs. DI: HbA1c, 7.4 ± 0.3; BW, 71 ± 5 Kg; Hypo, 0.6 ± 0.2). In subjects with type 2 DM, on transition to GI, daily DI dose,70±11 units, no. of injections,1.4±0.2 and HbA1c, 7.6±0.3 declined to 56±6 units, 1±0, and 7.1±0.2 respectively ($p<0.01$). No significant changes occurred in BW (93±5 with DI vs. 91±3 with GI) and hypo (0.2±0.1 with DI vs. 0±0 with GI).

Conclusion: Insulin Glargine is more cost effective than Insulin Detemir due to lower daily dose, less equipment, (syringes, needles, alcohol pads) needed for once daily administration (more convenient with better quality of life) in type1 and type 2 Once daily blood sugar testing may further lower cost in type 2. Thus, Insulin Glargine and Detemir are not bioequivalent and transition from one to another may be detrimental.

Introduction

In 2006, State of Iowa in USA made a decision to lower costs by an abrupt transition from insulin glargine to insulin detemir in all subjects with diabetes mellitus irrespective of the type or the glycemic control against the recommendations by experts and providers. Therefore, we conducted studies to assess the impact of this practice in subjects with both type 1 and type 2 diabetes mellitus. We documented a lapse of glycemic control despite using a significantly higher daily dose of insulin detemir divided and administered subcutaneously in 2 daily injections on switching from insulin glargine administered once daily in the morning in subjects with type 1 diabetes mellitus [1]. The glycemic control also deteriorated in subjects with type 2 diabetes mellitus following transition to insulin detemir administered at bed time in the same daily dose as insulin glargine administered once daily in AM[2].Moreover, the quality of life declined in subjects with type 1 diabetes due to increase in number of daily injections as well as number of times of daily blood glucose monitoring and ensuing symptoms due to lapse of glycemic control expressed by rises in HbA1c and daily blood sugars noted on home blood sugar monitoring records [1]. Subjects with type 2 diabetes also reported inconvenience and decreased quality of life because of onset of symptoms, e.g. polyuria, nocturia, polydypsia etc caused by rising blood sugars. The costs escalated as well due to needed increase in supplies e.g. syringes and needles, alcohol pads, lancets etc. required for higher number of daily injections as well as number of times of daily blood glucose monitoring and recurrent need to contact providers or other ancillary personell, e. g. diabetes educators to adjust treatment [1, 2]. These studies finally resulted in the reversal of the policy by Iowa Medicaid. Therefore, we examined the impact of retransition from Insulin type 2 diabetes mellitus.

Subjects and Methods

14 subjects with Type 1 diabetes,8 men and 6 women(age, 36 ± 3 years) and 22 subjects with type 2 diabetes, 12men and 10 women (age,62 ± 5 years) attending Diabetes clinic during 01/2013 to 06/2013 participated after obtaining informed consent. The study was approved by Investigational review board at the institution. The duration of diabetes was 15 ± 2 years in subjects with type 1 and 12± 3 years in subjects.

In both groups, Insulin detemir was discontinued and insulin glargine was reinitiated to be administered SC at 0700-0800 AM in the same daily dose as insulin detemir. Subjects were instructed to adjust the daily dose of insulin glargine by 2 units at interval of 3 days until AM blood sugar 80- 120 mg/dl as per self blood sugar monitoring was attained. Insulin glargine was then continued for 6 months with readjustment of the dose as required to maintain fasting blood sugar 80-120 mg/ dl. In subjects with type 1 diabetes, insulin aspart was continued premeal 3 times daily with adjustment as required by a correction dose scale as shown in Table 1. Oral agents in the same daily dose metformin, 2000 mg. and glimepiride, 8 mg. were continued in subjects with type 2 diabetes. Comparisons were conducted in both Individual groups with type 1 and type 2 diabetes between HbA1c, body weight, the daily dose of insulin, number of daily injections lipids and number of hypoglycemic events during the last 4 weeks of therapy with insulin detemir prior to initiation of insulin glargine and at 6 months while using insulin glargine. The comparison was also performed between the daily dose of insulin aspart used with insulin detemir and insulin glargine at 6 months in subjects with type 1 diabetes. Statistical methods used for these comparisons were Students't' test and analysis of variance. All values are reported as Mean +-SEM.

Table 1

Aspart Insulin Regimen with Correction Dose According to Pre Meal Blood Sugar level

Pre Meal Blood Sugar (mg/dl)	Correction Dose (Units)
< 50	Minus 2
50 - 100	Minus 1
101 - 150	Scheduled dose
151 - 200	Plus 1
201 - 250	Plus 2
251 - 300	Plus 3
< 300	Plus 4

Results

In subjects with Type 1 diabetes, the total daily insulin dose declined significantly on switching from insulin detemir to insulin glargine (Table 2). The daily dose of insulin glargine was significantly lower when compared to insulin detemir as well whereas daily dose of insulin aspart was not significantly altered on switching insulin detemir to insulin glargine (Table 2). Number of daily SC injections used during the regimen with insulin detemir also declined on changing over to insulin glargine (Table 2). HbA1c, body weight and number of hypoglycemic events were not significantly altered (Table 2). Severe hypoglycemic episodes were not reported in either of the regimens. Finally, serum lipid pattern showed a significant lowering of LDL cholesterol without significant changes in total cholesterol, HDL cholesterol and triglyceride levels (Table 3).

Table 2

Daily Insulin Dose; Total, Basal and Aspart as well as Number of Daily Injections in Type 1 Diabetes Mellitus.

Subjects	DI*+NI†	GI‡+NI	P
Total Daily Dose (units)	58±6	48±6	< 0.05
Basal Daily Dose (units)	DI 31±6	GI 23±5	< 0.05
NI Daily Dose (units)	28±8	25±6	NS
No of Injections	4.6±0.3	4±0	<0.05

*** Detemir,† Aspart, ‡ Glargine**

Table 3

HbA1c, Serum Lipid Concentrations, Body Weight and Hypoglycemic Events in Type1 Diabetes Mellitus

Subjects	DI* + NI†	GI‡ + NI	P
HBOS A1C (%)	7.4 ± 0.3	7.2 ± 0.2	NS
Cholesterol (mg/dl)	132 ± 13	123 ± 11	NS
Triglyceride (mg/dl)	133 ± 23	138 ± 14	NS
LDLCholesterol (mg/dl)	83 ± 7	68 ± 8	<0.05
HDLCholesterol (mg/dl)	41 ± 5	44 ± 4	NS
Body Weight (KG)	71 ± 5	70 ± 4	NS
Hypoglycemic Events#	0.6 ±0.2(0)€	0.5 ± 0.2(0) €	NS

*Detemir; † OAD (Metformin, SU); ‡ Glargine

No. of Events/Subject in the last 4 weeks, € No. of severe hypogjycemic events

In subjects with type 2 Diabetes, transition from insulin detemir to insulin glargine resulted in a significant lowering of the daily insulin dose, number of SC injections and serum concentrations of HbA1c, total and LDL cholesterol and triglyceride while no significant changes occurred in body weight, HDL cholesterol level and number of hypoglycemic events (Table 4). Severe hypoglycemic episodes were not reported during either regimens.

Table 4

Daily Insulin Dose, Number of Daily Injections,Body Weight, HbA1c, Serum Lipid Concentrations and Number of Hypoglycemic Events in Subjects with Type 2 Diabetes Mellitus.

Subjects	DI* +OAD	GI‡+OAD	P
Daily Dose (units)	70±11	56±6	< 0.01
No of Injections	1.4±0.2	1±0	<0.05
Body Weight (KG)	93±5	1±3	NS
Hb A1C (%)	7.6±0.3	7.1±0.2	<0.05
Cholesterol (mg/dl)	146±13	133±11	NS
Triglyceride (mg/dl)	171±23	138±14	<0.05
LDLCholesterol (mg/dl)	83±7	68±8	<0.05
HDLCholesterol (mg/dl)	41±5	44±4	NS
Hypoglycemic Events#	0.2±0.01 (0) €	0(0) €	NS

*Detemir; † OAD (Metformin, SU); ‡ Glargine
No. of Events/Subject in the last 4 weeks, € No. of severe hypogjycemic events

Discussion

This study demonstrates that in subjects with type 1 diabetes mellitus, the daily dose of insulin glargine is significantly lower on transition from insulin detemir while maintaining comparable glycemic control. Moreover, it is apparent that lower dose of insulin glargine is responsible for the smaller total daily insulin dose as well since the daily dose of insulin aspart remained unchanged during both regimens. Finally, the majority of subjects were receiving 2 daily doses of insulin detemir prior to transition whereas insulin glargine was administered once daily in all subjects thus providing better quality of life and lesser costs required for injection equipment e.g. syringes, needles, alcohol pads etc.

These findings are consistent with data in previous studies which documented lower daily dose of insulin glargine as compared to insulin detemir in either randomized clinical trials individually or in meta analysis or in comparison conducted on transition from insulin glargine to insulin detemir [3 – 12]. Our study is the first documentation of a similar finding in a clinical trial conducting transition from insulin detemir to insulin glargine.

Several previous clinical trials have been conducted providing comparative data between insulin glargine and insulin detemir in subjects with type 2 diabetes Mellitus [5, 7-11, 13-19]. Many of these studies have documented the lower daily dose of insulin glargine when compared with insulin detemir required to attain comparable glycemic control [8-11, 13, 15, 17-19]. Also, the majority of subjects required twice daily administration of insulin detemir while Insulin glargine was injected once daily [5, 8-11, 13-19]. We also have documented lapse of glycemic control as expressed by a significant rise in HbA1c levels following transition of insulin glargine to insulin detemir with the same daily dose while both being administered once daily [2].

This study demonstrates that administration of insulin glargine improved glycemic control with a significantly lesser daily dose on transition from insulin detemir in subjects with type 2 diabetes Mellitus. Moreover, in all subjects following transition, insulin glargine was administered once daily where as insulin detemir was required to be injected twice daily in majority of subjects. Again, this observation is the first documentation in a clinical trial using a protocol involving the transition from insulin detemir to insulin glargine in subjects with type 2 diabetes Mellitus. Another interesting finding in this study documented declines in serum cholesterol and triglyceride concentrations on transition from insulin detemir to insulin glargine (Table3). The improvement in lipid profile may be attributed to attainment of a better glycemic control as expressed by lowering of HbA1c levels as documented by us previously [20-22].

Finally, this study confirms once again that insulin glargine administered once daily helps attain better glycemic control with lesser daily dose in comparison to insulin detemir injected once or twice daily in subjects with both type 1 and type 2 diabetes mellitus. The lower dose of insulin glargine and its once daily administration in attaining comparable or superior glycemic control as compared to insulin detemir in subjects with both type 1 and type 2 diabetes mellitus may be attributed to the peak less profile as well as a longer duration of insulin glargine in comparison to insulin detemir documented in euglycemic clamp studies [23, 24]. Therefore, Insulin glargine is more cost effective than Insulin detemir due to lower daily dose and, less equipment, (syringes, needles, alcohol pads) needed for once daily administration. Moreover, once daily blood sugar testing required while using insulin glargine may further lower costs in subjects with type 2 diabetes mellitus. Finally, insulin glargine may provide a better quality of life because of once daily administration and one daily self blood sugar monitoring in contrast to twice daily administration and twice daily self blood sugar monitoring required for insulin detemir in subjects with type 2 diabetes mellitus. Thus, Insulin glargine and detemir are not bioequivalent and transition from one to another is likely to be detrimental to well being of subjects.

References

1. Kabadi UM (2008) Deleterious Outcomes after Abrupt Transition from Insulin Glargine to Insulin Determir in Patients with Type 1 Diabetes Mellitus. Clin Drug Invest 28: 697-701.

2. Udaya Kabadi (2011) Iowa Medicaid 2: Lapse of Glycemic Control on Abrupt Transition from Insulin Glargine to Insulin Detemir in Type 2 Diabetes Mellitus. Journal of Diabetes Mellitus 1: 124-128.

3. Bott S, Tusek C, Jacobsen LV, Endahl L, Draeger E, et al. (2006) Insulin detemir under steady-state conditions: No accumulation and constant metabolic effect over time with twice daily administration in subjects with type 1 diabetes. Diabetic Medicine 23: 522-528.

4. Pieber TR, Treichel HC, Hompesch B, Philotheou A, Mordhorst L, et al. (2007) Comparison of insulin detemir and insulin glargine in subjects with type 1 diabetes using intensive insulin therapy. Diabetic Medicine 24: 635-642.

5. Dornhorst A, Luddeke HJ, Sreenan S, Koenen C, Hansen JB, et al. (2007) Safety and efficacy of insulin detemir in clinical practice: 14-week follow-up data from type 1 and type 2 diabetes patients in the predictive European cohort. International Journal of Clinical Practice 61: 523-528.

6. Heller S, Koenen C, Bode B (2009) Comparison of insulin detemir and insulin glargine in a basal-bolus regimen, with insulin aspart as the mealtime insulin, in patients with type 1 diabetes: a 52-week, multinational, randomized open-label, parallel-group, and treat-to-target noninferiority trial. Clin Ther 31: 2086-2097.

7. Kato T, Tokubuchi I, Muraishi K, Sato S, Kato T, et al. (2010) Distinct pharmacodynamics of insulin glargine and insulin detemir: Crossover comparison in type 1 and type 2 diabetic patients on basal-bolus regimen. Diabetes Research and Clinical Practice 90: 64-66.

8. Abe S, Inoue G, Yamada S, Irie J, Nojima H, et al. (2011) Two-way crossover comparison of insulin glargine and insulin detemir in basal-bolus therapy using continuous glucose monitoring. Diabetes Metab Syndr Obes 4: 283-288.

9. Bryant GA, McDanel DL, Horner KE, Farris KB, Newkirk EN (2013) Evaluation of dosing and clinical outcomes in patients undergoing conversion of insulin glargine to insulin detemir. Pharmacotherapy 33: 56-62.

10. Wallace JP, Wallace JL, McFarland MS (2014) Comparing dosing of basal insulin analogues detemir and glargine: is it really unit-per-unit and dose-per-dose? Ann Pharmacother 48: 361-368.

11. Laubner K, Molz K, Kerner W, Karges W, Lang W, et al. (2014) Daily insulin doses and injection frequencies of Neutral Protamine Hagedorn (NPH) insulin, insulin detemir and insulin glargine in type 1 and type 2 diabetes: a multicenter analysis of 51 964 patients from the German/Austrian DPV-wiss database. Diabetes Metab Res Rev 30: 395-404.

12. Abalı S, Turan S, Atay Z, Güran T, Haliloğlu B, et al. (2015) Higher insulin detemir doses are required for the similar glycemic control: comparison of insulin detemir and glargine in children with type 1 diabetes mellitus. Pediatr Diabetes 16: 361-366.

13. Rosenstock J, Davies M, Home PD, Larsen J, Koenen C, et al. (2008) A randomized, 52- week, treat-to-target trial comparing insulin detemir with insulin glargine when administered as add-on to glucose lowering drugs in insulin-naive people with type 2 diabetes. Diabetologia 51: 408-416.
14. Hollander P, Cooper J, Bregnhøj J, Pedersen CB (2008) A 52-week, multinational, open-label, parallel group, noninferiority, treat-to-target trial comparing insulin detemir with insulin glargine in a basal-bolus regimen with mealtime insulin aspart in patients with type 2 diabetes. Clinical Therapeutics 30: 1976-1987.
15. Swinnen SG, De Vries JH (2009) Higher dose requirements with insulin detemir in type 2 diabetes - Three cases and a review of the literature. Diabetes Research and Clinical Practice 84: 24-26.
16. Raskin P, Gylvin T, Weng W, Chaykin L (2009) Comparison of insulin detemir and insulin glargine using a basal-bolus regimen in a randomized, controlled clinical study in patients with type 2 diabetes. Diabetes/Metabolism Research and Reviews 25: 542-548.
17. Johnson CK, Shimshi M (2009) When a unit of insulin is not a unit: Detemir dosing and insulin cost in type 2 diabetes mellitus. Insulin 4: 87-93.
18. Swinnen SG, Dain MP, Aronson R, Davies M, Gerstein HC, et al. (2010) 24-week, randomized, treat-to-target trial comparing initiation of insulin glargine once-daily with insulin detemir twice-daily in patients with type 2 diabetes inadequately controlled on oral glucoselowering drugs. Diabetes Care 33: 1176-1178.
19. Dailey G, Admane K, Mercier F, Owens D (2010) Relationship of insulin dose, A1c lowering, and weight in type 2 diabetes: Comparing insulin glargine and insulin detemir. Diabetes Technology & Therapeutics 12: 1019- 1027.
20. Erdman DM, Cook CB, Greenlund KJ, Giles WH, El-Kebbi I, et al. (2002) The impact of outpatient diabetes management on serum lipids in urban African-Americans with type 2 diabetes. Diabetes Care 25: 9-15.
21. Kabadi U (2004) Lipid Profiles in Type 2 Diabetes Mellitus: comparisons amongst treatment with oral antihyperglycemic drugs. 12th International Congress of Endocrinology, P142.
22. Palmer AJ, Roze S, Valentine WJ, Minshall ME, Hayes C, et al. (2004) Impact of changes in HbA1c, lipids and blood pressure on long-term outcomes in type 2 diabetes patients: an analysis using the CORE Diabetes Model. Curr Med Res Opin 20 Suppl 1: S53-S58.
23. Porcellati F, Rossetti P, Busciantella NR, Marzotti S, Lucidi P, et al. (2007) Comparison of pharmacokinetics and dynamics of the long-acting insulin analogs glargine and detemir at steady state in type 1 diabetes: a double-blind, randomized, crossover study. Diabetes Care 30: 2447-2452.
24. Lucidi P, Porcellati F, Rossetti P, Candeloro P, Cioli P, et al. (2011) Pharmacokinetics and pharmacodynamics of therapeutic doses of basal insulins NPH, glargine, and detemir after 1 week of daily administration at bedtime in type 2 diabetic subjects: A randomized cross-over study. Diabetes Care 34: 1312-1314.