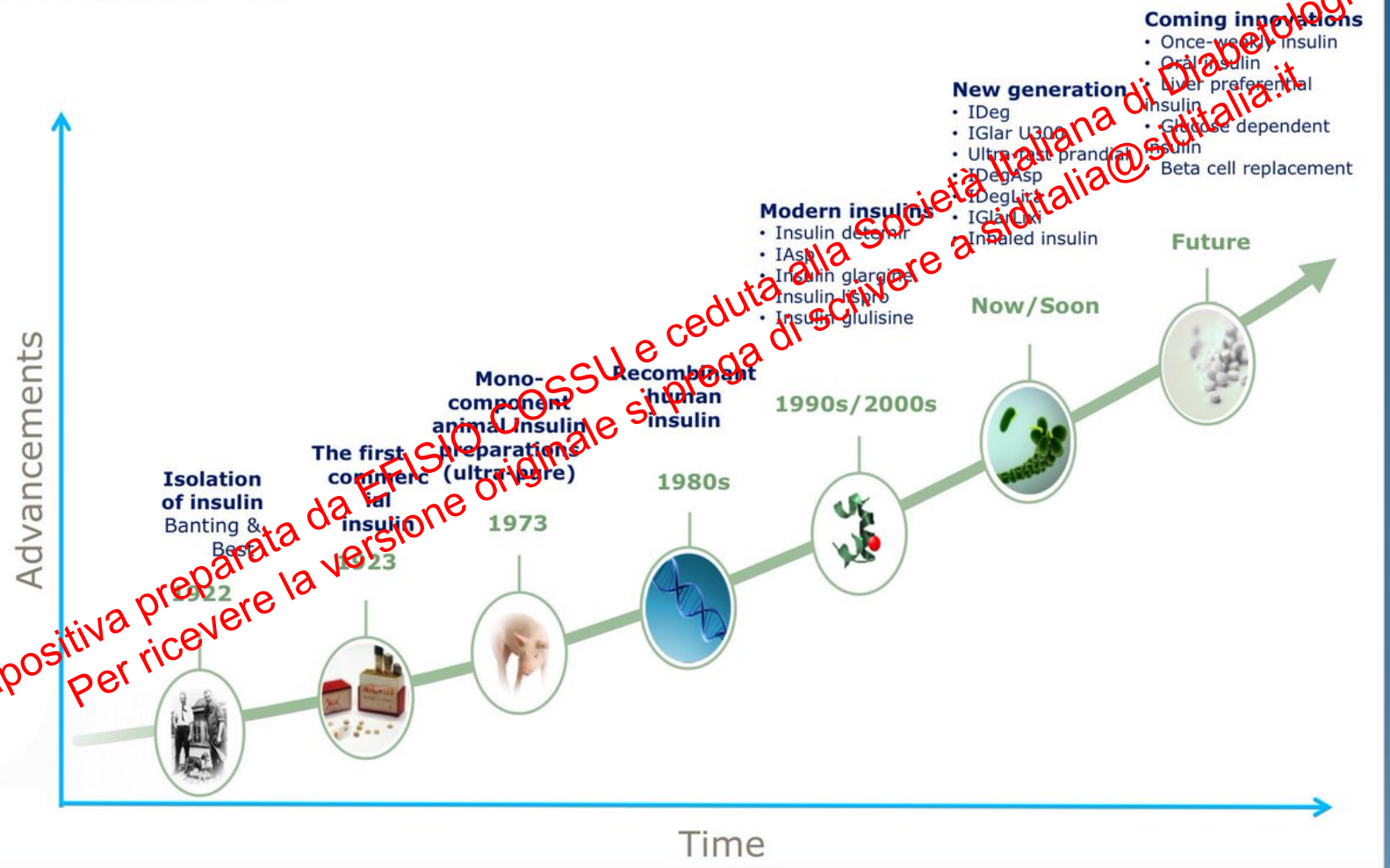
Basalizzazione efficace ed ottimizzazione dei boli prandiali

Efisio Cossu

Il Dott. Efisio Cossu dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

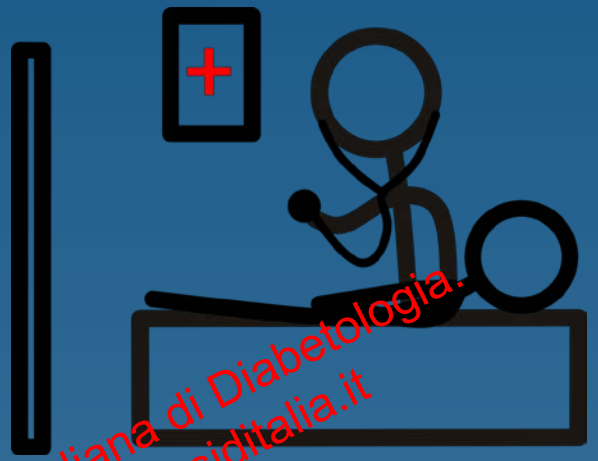
Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc).

Insulin therapy development: A rich history, a good present, a bright future



Oscar

51aa, imprenditore edile



T1DM da 31 anni

- Nessuna familiarità per patologie autoimmuni
- Scarso automonitoraggio
- Incremento del fabbisogno insulinico negli ultimi anni
- **Frequenti ipoglicemie sintomatiche con recente ipoglicemia grave e accesso in PS**

Comorbilità

- Retinopatia diabetica preproliferante
- Neuropatia diabetica con emg+

Automonitoraggio glicemico domiciliare

A digiuno	2 ore dopo colazione	Prima di pranzo	2 ore dopo pranzo	Prima di cena	2 ore dopo cena
182	197		194		277
272			305	64	280
127	72		227	132	215
	239	188			
297					383
132	210			179	197
		103	199		90

Glargine U100: 46UI
Glulisina: 18UI+25UI+22UI

Peso 97 kg
Altezza 172 cm
BMI 32,78 kg/m2
CV 106 cm

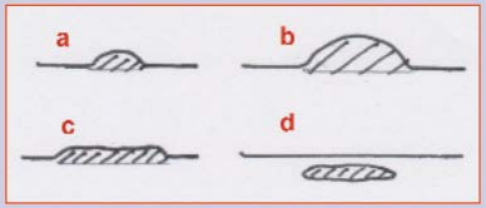
Esami di laboratorio	
HbA1c	78 mmol/mol (9,3 %)
eGFR	79 ml/min/1,73 mq
Microalbuminuria	40 mg/l

Esame obiettivo:

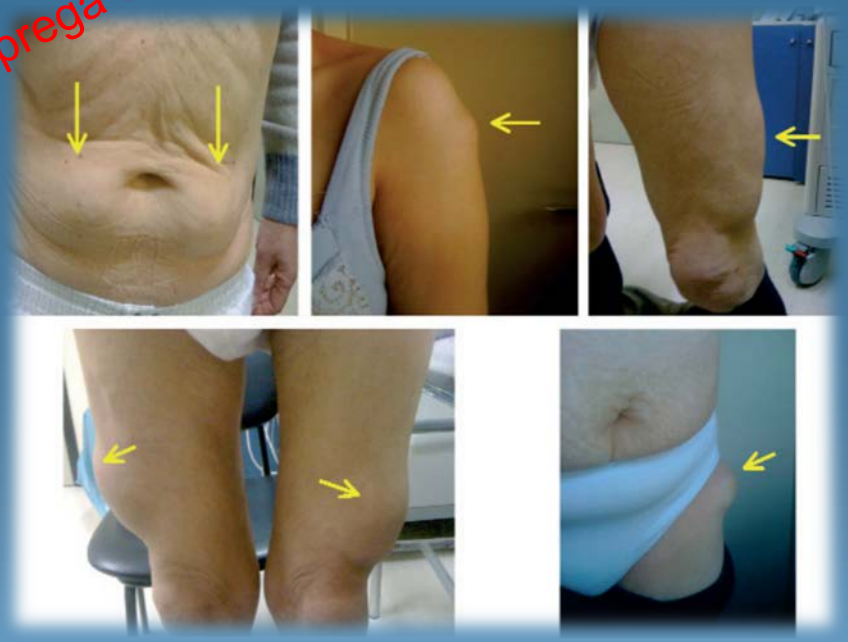
Presenti aree di lipoipertrofia
Epatomegalia
Micosi interdigitale

Terapia

Glargine U100: 46UI
Glulisina: 18UI+25UI+22UI



	Definizione	Visibile	Palpabile	Consistenza
a	Nodulo piccolo	Bene/meglio con luce tangenziale/di profilo	Bene	Duro-elastica
b	Nodulo grande	Bene/meglio con luce tangenziale/di profilo	Bene	Duro-elastica
c	Piastrone piano	Poco visibile	Non bene/ meglio pizzicando	Solitamente dura
d	Nodulo piano	Non visibile	Con difficoltà/ meglio palpazione profonda o con pizzicotto	Solitamente dura



Laviola L. et al, Lipodistrofie da iniezione di insulina: conoscerle, riconoscerle, prevenirle, G It Diabetol Metab 2016;36:32-36

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SciVerse ScienceDirect
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EM|consulte
www.em-consulte.com/en
ELSEVIER MASSON
Diabetes & Metabolism
Diabetes & Metabolism 39 (2013) 445–453

Original article

Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes

M. Blanco [a], M.T. Hernández [b], K.W. Strauss [c,*], M. Amaya [d]

Abstract

Introduction. – Our objective was to assess the frequency of lipohypertrophy (LH) and its relationship to site rotation, needle reuse, glucose variability, hypoglycaemia and use of insulin.

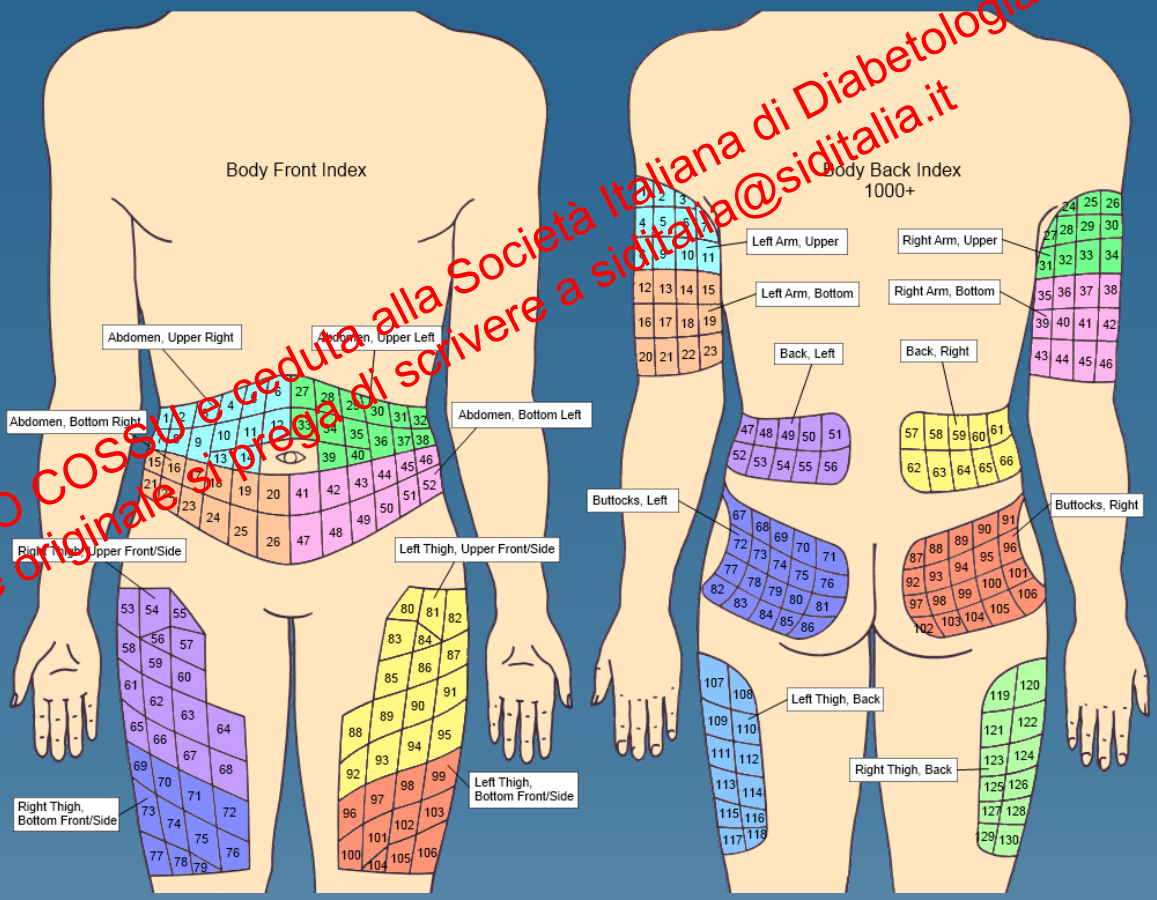
Methods. – The study included 430 outpatients injecting insulin who filled out a wide-ranging questionnaire regarding their injection technique. Then, a diabetes nurse examined their injection sites for the presence of LH.

Results. – Nearly two-thirds (64.4%) of patients had LH. There was a strong relationship between the presence of LH and non-rotation of sites, with correct rotation technique having the strongest predictive value against LH. Of the patients who correctly rotated sites, only 5% had LH while, of the patients with LH, 98% either did not rotate sites or rotated incorrectly. Also, 39.1% of patients with LH had unexplained hypoglycaemia and 49.1% had glycaemic variability compared with only 5.9% and 6.5%, respectively, in those without LH. LH was also related to needle reuse, with risk increasing significantly when needles were used > 5 times. Total daily insulin doses for patients with and without LH averaged 56 and 41 IU/day, respectively. This 15 IU difference equates to a total annual cost to the Spanish healthcare system of > €122 million. This was also the first study in which the use of ultrasound allowed the description of an "echo signature" for LH.

Conclusion. – Correct injection site rotation appears to be the critical factor in preventing LH, which is associated with reduced glucose variability, hypoglycaemia, insulin consumption and costs.

Standard di cura SID-AMD 2018

Siti di iniezione raccomandati



Standard di cura SID-AMD 2018

Siti di iniezione raccomandati

Uso di un ago da 4mm x 32 G, inserito perpendicolarmente

Standard di cura SID-AMD 2018

Siti di iniezione raccomandati

Uso di un ago da 4mm x 32 G, inserito perpendicolarmente

Gli analoghi ad azione rapida e gli analoghi basali possono essere iniettati in corrispondenza di qualunque sito, perché il loro assorbimento non è sito-dipendente

Standard di cura SID-AMD 2018

Siti di iniezione raccomandati

Uso di un ago da 4mm x 32 G, inserito perpendicolarmente

Gli analoghi ad azione rapida e gli analoghi basali possono essere iniettati in corrispondenza di qualunque sito, perché il loro assorbimento non è sito-dipendente

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Standard di cura SID-AMD 2018

Siti di iniezione raccomandati

Uso di un ago da 4mm x 32 G, inserito perpendicolarmente

Gli analoghi ad azione rapida e gli analoghi basali possono essere iniettati in corrispondenza di qualunque sito, perché il loro assorbimento non è sito-dipendente

La mancata rotazione delle sedi di iniezione, il riutilizzo dello stesso ago, l'iniezione di insulina fredda sono fattori predisponenti alla formazione di aree di lipoipertrofia

L'iniezione di insulina in aree lipoipertrofiche ne modifica la farmacocinetica e la farmacodinamica, provocando assorbimento variabile ed imprevedibile del farmaco.

Automonitoraggio glicemico domiciliare

A digiuno	2 ore dopo colazione	Prima di pranzo	2 ore dopo pranzo	Prima di cena	2 ore dopo cena
182	197		194		277
272			305	64	280
127	72		227	132	215
	239	188			
297					383
132	210			179	197
		103	199		90

Glargine U100: 46UI
Glulisina: 18UI+25UI+22UI

Algorithm : The Basal-Bolus Insulin Concept

Starting dose based on weight: 0.4-0.5 units/kg/day

Basal insulin
40-50% Total Daily Dose

+

Bolus insulin
50-60% Total Daily Dose

- Controls glucose production between meals and overnight
- Near-constant levels

- 10% to 20% of total daily insulin requirement at each meal
- Limits hyperglycemia after meals
- Immediate rise and sharp peak at 1 hour post-meal

- ❑ Higher TDI needed for obese patients, those with sedentary lifestyles, and during puberty.
- ❑ Dosage adjustment:
  - dosage must be titrated to achieve glucose control and avoid hypoglycemia;
  - adjust dose to maintain premeal and bedtime glucose in target range.

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87
ADA 2019
UpToDate 2019

PHARMACOLOGIC THERAPY FOR TYPE 1 DIABETES

Recommendations

9.1 Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion. **A**

9.2 Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk. **A**

9.3 Patients with type 1 diabetes should be trained to match prandial insulin doses to carbohydrate intake, premeal blood glucose, and anticipated physical activity. **C**

Lo schema di terapia raccomandato è quello basal-bolus da realizzare tramite terapia multiiniettiva o con microinfusore. ***I A***

Nella terapia basal-bolus multiiniettiva, si devono usare analoghi a breve durata d'azione per i boli prandiali e analoghi a lunga durata d'azione come insulina basale. ***I A***

Standards of Medical Care in Diabetes— ADA 2020
Standard di cura SID-AMD 2018

Glycemic targets for type 1 diabetes mellitus in adults

Glycemic targets	American Diabetes Association [8]	Linee guida SID-AMD 2018
HbA1c	< 7% (53 mmol/mol)[a] < 8% (64 mmol/mol) for patients with history of severe hypoglycemia or comorbid diseases[a] < 6.5% (48 mmol/mol) for selected patients (short duration of diabetes, long life expectancy, or no significant cardiovascular disease) if it can be achieved without significant hypoglycemia or adverse events[a]	< 6,5 % (48 mmol/mol) senza complicanze < 7 % (53 mmol/mol) con complicanze < 8 % (64 mmol/mol) con ipoglicemie gravi, età avanzata, comorbilità
FPG or preprandial PG	4–7.2 mmol/L (80–130 mg/dL)	80 – 130 mg/dl
Peak postprandial PG[b]	< 10 mmol/L (180 mg/dL)	< 160 mg/dl

Andrej Janez et al, "*Insulin Therapy in Adults with Type 1 Diabetes Mellitus: a Narrative Review*", Diabetes Ther, 4 january 2020

Pharmacokinetic and pharmacodynamic properties of insulins

Insulin type	Onset	Peak	Duration (h)	Molecular structure[a]
Basal				
Long acting				
Detemir U100	1–2 h	None[b]	< 24	Omission of B30 threonine; C14 fatty acid chain added to B29
Gla-100	~ 1 h	None[b]	24	A21 asparagine replaced with glycine; 2 arginines added to C-terminus of B chain
Gla-300	6 h	None	24–36	
Degludec U100 or U200	~ 1 h	None	Up to 42	Omission of B30 threonine; glutamic acid and C16 fatty acid chain added to C-terminus of B chain
Intermediate acting				
NPH insulin U100	1–2 h	4–14 h	4–16 h	
Bolus				
Rapid acting (lispro, aspart, glulisine)	5–15 min	0.5–1.5 h	3 to < 6	Lispro: B28 proline replaced with lysine; B29 lysine replaced with proline Aspart: B28 proline replaced with aspartic acid Glulisine: B3 asparagine replaced with lysine; B29 lysine replaced with glutamic acid
Faster-acting aspart	2.5–4 min	~ 1 h	3–5	Faster-acting aspart: B28 proline replaced with aspartic acid
Short acting (regular human)	30–60 min	2–4 h	6–12	

Andrej Janez et al, "Insulin Therapy in Adults with Type 1 Diabetes Mellitus: a Narrative Review", Diabetes Ther, 4 january 2020

A suggested treatment algorithm for T1DM

BASAL (MDI)

One of:

- **First choice:** Gla-300, subcutaneous injection once daily **or** degludec, subcutaneous injection once daily* **or**
- **Second choice:** Detemir, subcutaneous injection once or twice daily as appropriate **or** Gla-100, subcutaneous injection once daily† **or**
- **Third choice:** NPH, subcutaneous injection twice daily

and

PRANDIAL (MDI)

One of:

- **First choice:** Lispro, aspart, or glulisine, subcutaneous injection premeal
- **Second choice:** Faster-acting aspart, subcutaneous injection premeal‡
- **Third choice:** Regular human insulin, subcutaneous injection 2–3 times daily

or

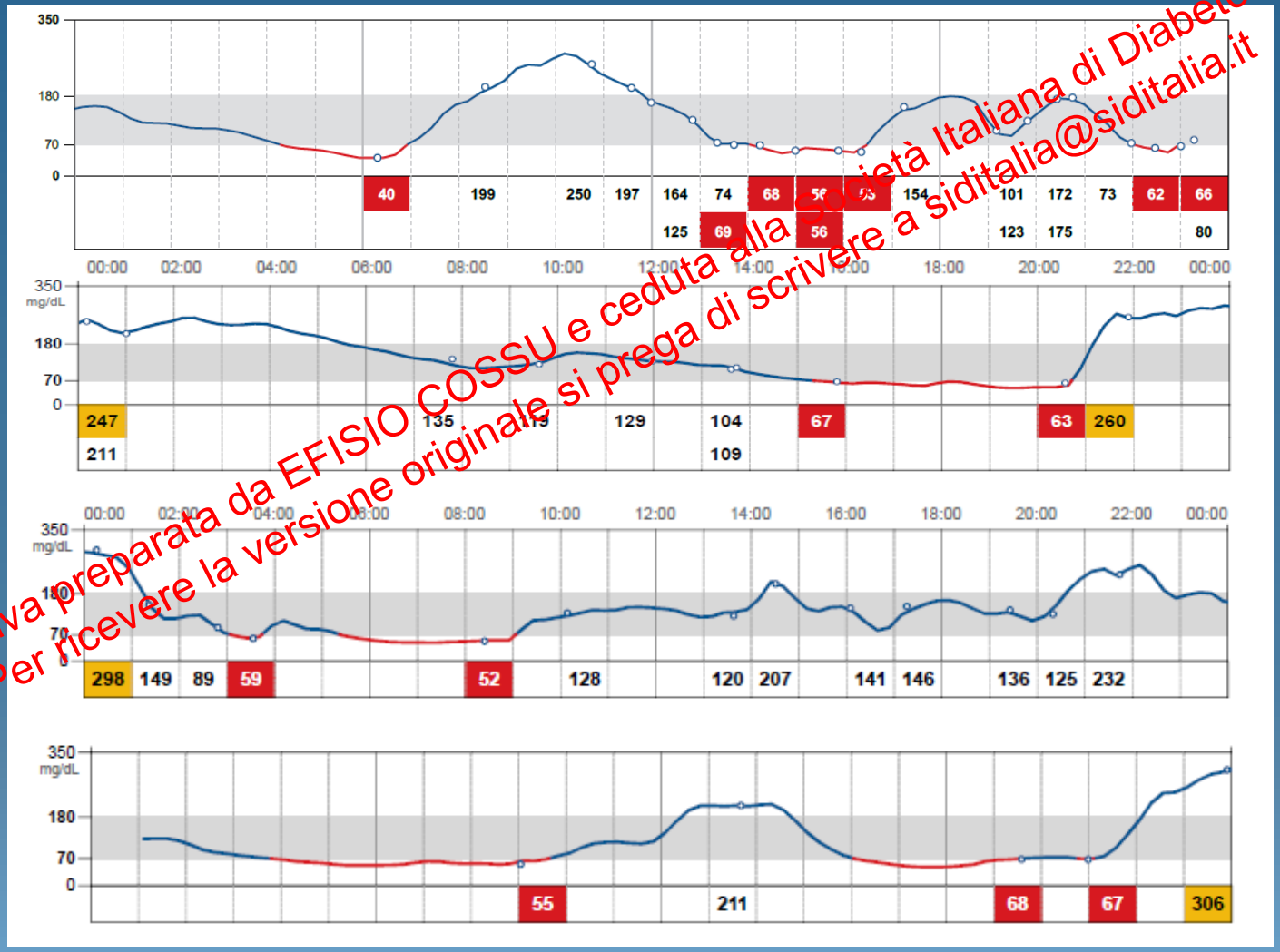
PRANDIAL (CSII)§

- Faster-acting aspart (first choice) or lispro, aspart, or glulisine (second choice) or regular human insulin (third choice)

Andrej Janez et al, "Insulin Therapy in Adults with Type 1 Diabetes Mellitus: a Narrative Review", Diabetes Ther, 4 january 2020

Grafici FGM con modifica della posologia insulinica

Glargine U100: 38 UI
Glulisina: 13 UI + 20 UI + 20 UI



Quale è il problema? Insulina o paziente?

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 12, Number 11, 2010

DOI: 10.1089/dia.2010.0135

Reviews

Clinical Experience with Insulin Glargine in Type 1 Diabetes

Satish Garg, M.D.,[1] Emily Moser, B.A.,[1] Marie-Paule Dain, M.D.,[2] and Anastasia Rodionova, B.A.[1]

Abstract

The Diabetes Control and Complications Trial (DCCT) demonstrated the importance of optimal glycemic control achieved through intensive insulin therapy in reducing the microvascular complications associated with type 1 diabetes. However, the DCCT, which was conducted prior to the availability of insulin analogs, also reported a significant increase in severe hypoglycemia with intensive versus conventional therapy. Insulin analogs were developed to aid patients in achieving better diabetes control by providing insulins with optimized pharmacokinetic and pharmacodynamic characteristics. Insulin glargine was the first long-acting insulin analog with a 24-h duration of action, offering once-daily injection, and has now been in clinical use for over 10 years. The authors performed a systematic search of EMBASE, MEDLINE, and Web of Science (Science Citation Index) to determine the efficacy of insulin glargine in type 1 diabetes in basal–bolus insulin regimens. Randomized controlled trials have demonstrated that glycemic control with insulin glargine is at least comparable to that with neutral protamine Hagedorn (NPH) insulin in adults and in children and adolescents, and with continuous subcutaneous insulin infusion in adults. However, these same trials show a significantly lower risk for hypoglycemia with insulin glargine compared with NPH insulin in adults.

Treatment Satisfaction and Quality of Life With Insulin Glargine Plus Insulin Lispro Compared With NPH Insulin Plus Unmodified Human Insulin in Individuals With Type 1 Diabetes

SIMON G. ASHWELL, MD[1]
CLARE BRADLEY, PHD[2]
JAMES W. STEPHENS, MS[3]
ELKE WITTHAUS, MD[4]
PHILIP D. HOME, DM, DPHIL[1]

OBJECTIVE — The purpose of this study was to compare quality of life (QoL) and treatment satisfaction using insulin glargine plus insulin lispro with that using NPH insulin plus unmodified human insulin in adults with type 1 diabetes managed with multiple injection regimens.

RESEARCH DESIGN AND METHODS — As part of a 32-week, five-center, two-way crossover study in 56 individuals with type 1 diabetes, randomized to evening insulin glargine plus mealtime insulin lispro or to NPH insulin (once or twice daily) plus mealtime unmodified human insulin, the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the Audit of Diabetes Dependent Quality of Life questionnaire were completed at baseline and at weeks 16 and 32, with additional interim DTSQ measurements.

RESULTS — For all patients combined, the mean baseline present QoL score was 1.3, reflecting "good" QoL. Present QoL improved with glargine + lispro but did not change with NPH + human insulin (1.6 ± 0.1 [mean ± SEM] vs. 1.3 ± 0.1, difference 0.3 [95% CI 0.1–0.6]; $P = 0.014$). Baseline mean average weighted impact score (AWI) of diabetes on QoL was −1.8, indicating a negative impact of diabetes on QoL. The AWI score at end point improved significantly with glargine + lispro but changed little with NPH + human insulin (−1.4 ± 0.1 vs. −1.7 ± 0.1, 0.3 [0.0–0.6]; $P = 0.033$). Treatment satisfaction (DTSQ 36-0 scale score) at end point was markedly greater with glargine plus lispro compared with that for NPH plus human insulin (32.2 ± 3.4 vs. 23.9 ± 7.2, 8.6 [6.5–10.6]; $P < 0.001$).

CONCLUSIONS — Insulin glargine plus insulin lispro improves treatment satisfaction, reduces the negative impact of diabetes on QoL, and improves QoL in comparison with NPH insulin plus unmodified human insulin in type 1 diabetes.

Diabetes Care 31:1112–1117, 2008

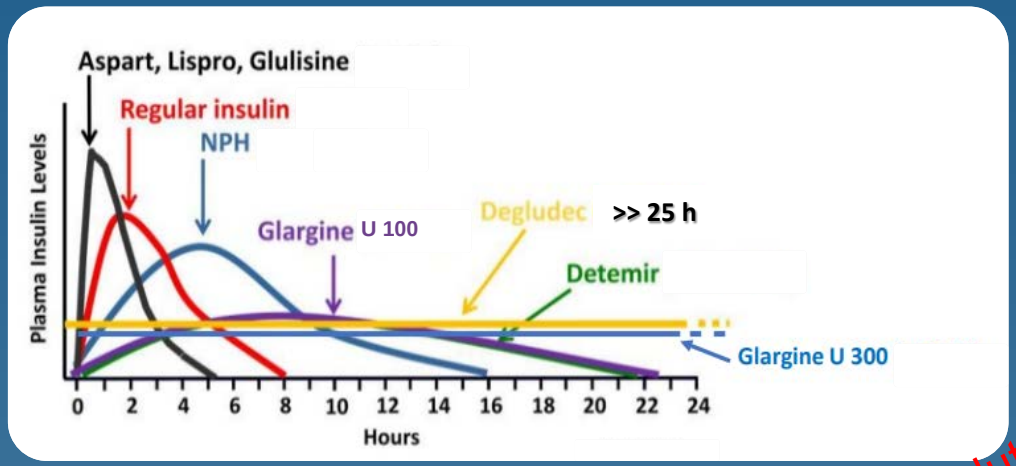
Reference	Design	No. patients	Trial Duration	Treatments	Change from baseline: A1c (%)	Change from baseline: FBG (mmol/L)	Frequency of hypoglycemia (episodes/patient–month, % patients): Symptomatic	Frequency of hypoglycemia (episodes/patient–month, % patients): Nocturnal	Comment
vs NPH insulin									
Ratner 2000[13] (Study 3004)	Open-label, multicenter, parallel-group study	534	28 weeks	Bedtime glargine NPH (od or bd)	−0.16% (baseline 7.7%) −0.21% (baseline 7.7%) $P = 0.44$	−1.67 (FPG) −0.33 (FPG) $P = 0.0145$	39.9% 49.2% $P = 0.0219$	18.2% 27.1% $P = 0.001$	Lower FPG levels with fewer episodes of hypoglycemia with glargine compared with od- or bd NPH as part of a basal–bolus regimen
Raskin 2000[12]	Open-label, multicenter, parallel-group study	619	16 weeks	Glargine + lispro (od) NPH (od or bd) + lispro	−0.1% (baseline 7.6%) −0.1% (baseline 7.7%) $P = NS$	−30.6 −10.8 $P = 0.0001$	90.6% 90.5% $P = 0.84$	69.0% 63.1% $P = 0.06$	Glargine appears to be as safe and at least as effective as using NPH as basal–bolus treatment with lispro
Rossetti 2003[10]	Open-label, parallel-group study	51	12 weeks	Dinnertime glargine Bedtime glargine NPH (od) + lispro	−0.4% (baseline 7.0%) −0.1% (baseline 6.8%) +0.1% (baseline 6.9%) $P < 0.04$	7.6 ± 0.1[a] 7.6 ± 0.2[a] 8.1 ± 0.2[a] $P < 0.03$	8.1 ± 0.8[b] 7.7 ± 0.9[b] 12.2 ± 1.3[b] $P < 0.04$ vs NPH	1.7 ± 0.2 2.0 ± 0.19 3.6 ± 0.4 $P < 0.05$	Decreased A1c and hypoglycemia with glargine. In contrast to NPH, which should be given at bedtime, glargine can be administered at dinner time without deteriorating BG control
Porcellati 2004[11]	Open-label, parallel-group study	121	52 weeks	Dinnertime glargine + lispro NPH (od) + lispro	−0.4% (baseline 7.0%) 0.0% (baseline 7.0%) $P < 0.05$	7.6 ± 0.11[a] 8.1 ± 0.22[a] $P < 0.05$[a]	7.2 ± 0.5[b] 13.2 ± 0.6[b] $P < 0.05$[b]	0.3[c] 2.1c $P < 0.05$[c]	Glargine decreased A1c and reduced the frequency of hypoglycemia versus NPH
Hershon 2004[18] (Study 3004)	Subgroup analysis of Raskin study (2000)[6] of patients treated with NPH bd	394	28 weeks	Glargine (od) NPH (bd)	−0.09% −0.19% $P = NS$	−1.17 −0.56 $P = 0.015$	73.3%[d] 81.7%[d] $P = 0.02$	Severe 36.6%[e] Severe 46.2%[e] $P = 0.003$	Glargine was at least as effective as NPH in improving FBG control with fewer symptomatic hypoglycemic events
Home 2005[14] (Study 3001)	Open-label, multicenter, parallel study	585	28 weeks	Glargine + lispro NPH (od or bd) + RHI	+0.21 ± 0.05% (baseline 7.9%) +0.10 ± 0.05% (baseline 8.0%) $P = NS$	−1.17 −0.89 $P = 0.07$	89.0%[g] 84.6%[g] $P = NS$	61.0%[g] 61.1%[g] $P = NS$	Bedtime, glargine was as least as effective as NPH, without an increased risk of hypoglycemia

Reference	Design	No. patients	Trial Duration	Treatments	Change from baseline: A1c (%)	Change from baseline: FBG (mmol/L)	Frequency of hypoglycemia (episodes/patient–month, % patients): Symptomatic	Frequency of hypoglycemia (episodes/patient–month, % patients): Nocturnal	Comment
Fulcher 2005[16] (Study 4010)	Single-blinded, multicenter, parallel-group study	125	30 weeks	Glargine (od) + lispro	−1.04% (baseline 9.2%)	−3.46[h]	Severe 0.87[i]	Severe: 0.23[i]	Significantly lower A1c and FBG levels and less severe nocturnal hypoglycemia with glargine
				NPH (od) + lispro	−0.5% (baseline 9.7%) $P < 0.01$	−2.34[h] $P = 0.032$	Severe 0.99[i] $P = NS$	Severe: 0.37[i] $P = 0.02$	
Chatterjee 2007[15] (Study 6004)	Open-label, single-center, two-period crossover study using a BBT regimen	53	36 weeks	Glargine + aspart	−0.46% (baseline 8.53%)	−3.08	80.8%[j]	NR	Lower A1c and mean FPG (–54 mg/dL, $P = 0.002$), and greater satisfaction with glargine compared with NPH (DTSQ, $P = 0.001$)
				NPH (bd) + aspart	−0.26% (baseline 8.53%) $P = 0.04$	−0.08 $P < 0.01$	77.2%[j] $P = 0.11$	NR	
Bolli 2009[17] (Study 4019)	Parallel, open-label, multicenter study of patients switched from NPH	175	4-week run-in, 24 weeks treatment	Dinnertime glargine + lispro	−0.56% (baseline 7.82%)	−28.8 mg/dL	+0.26[k]	Serious (42 mg/dL) −0.19[k]	Lower FBG, lower BG variability and reduced nocturnal hypoglycemia with glargine. Similar changes in A1c, FBG, PPBG and incidence of hypoglycemia. Greater satisfaction and lower cost with glargine
				NPH (bd) + lispro	−0.56% (baseline 7.82%) $P = NS$	−9.8 mg/dL $P = 0.0064$	+0.21[k] $P = 0.953$	−0.10 (<42 mg/dL)[k] $P = 0.383$	

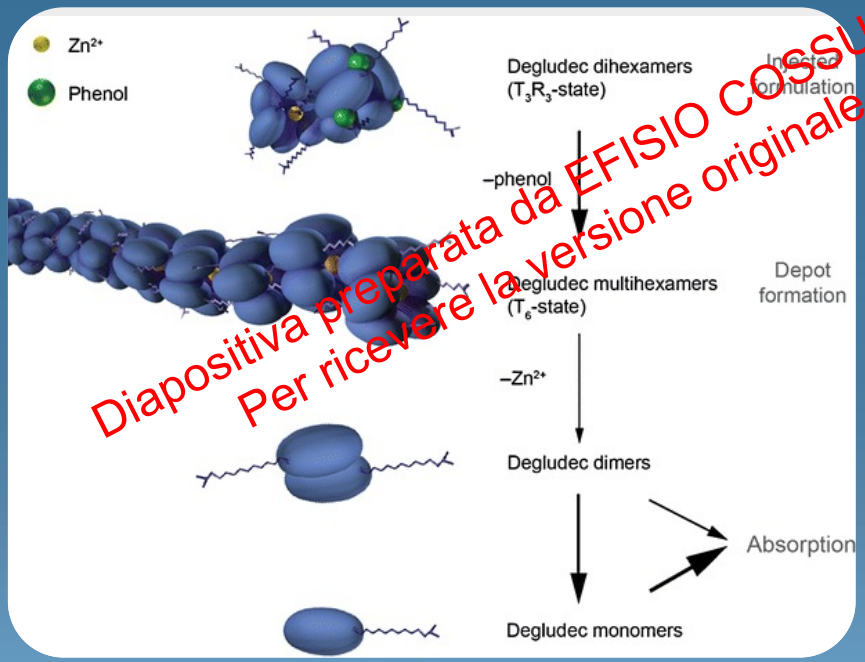
Reference	Design	No. pts	Trial duration	Treatments	A1c change from baseline (%)	24-h PG AUC (mmol/L/h)	PG AUC >7.0 mmol/L (mmol/L/h)	PPPG AUC	Frequency of nocturnal hypoglycemia (episodes/patient-month)	Comments
Ashwell 2006[30] (Study 4006)	Open-label, multicenter, two-way crossover study	56	32 weeks (two 16-week periods)	Glargine + lispro	−0.5% (baseline 8.0%)	187	47	75	0.66 episodes	Glargine + lispro improved A1c and 24-h PG monitoring compared with NPH + RHI, with a reduction in nocturnal hypoglycemia
				NPH (od or bid) + RHI	0.0% (baseline 8.0%)	203	62	88	1.18 episodes	
					$P < 0.001$	$P = 0.037$	$P = 0.017$	$P = 0.002$	$P < 0.001$	

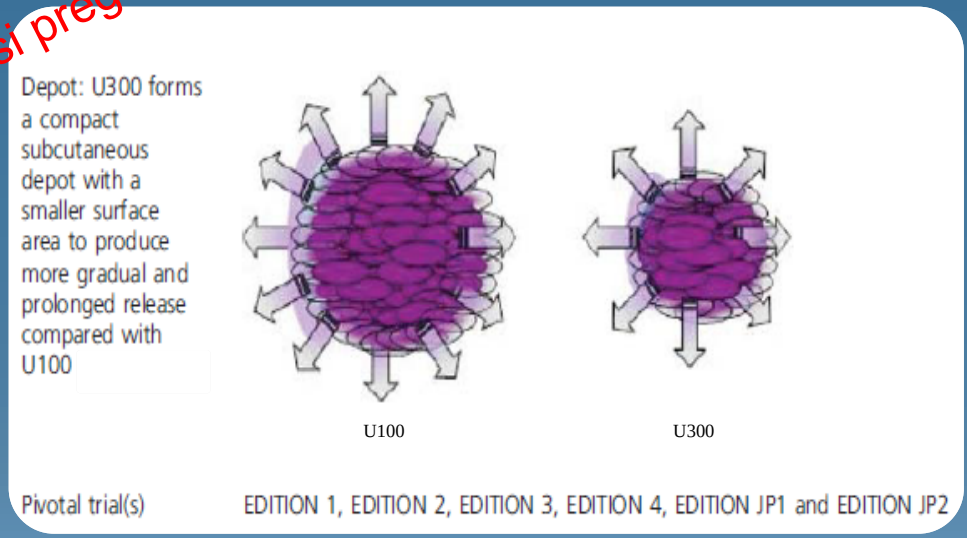
Satish Garg et al, Clinical Experience with Insulin Glargine in Type 1 Diabetes, Diabetes Technology & Therapeutics, vol 12, number 11, 2010

Insuline lente ed ultralente



Insulina lente ed ultralente	Steady state
Glargine U-100	2-4 gg
Glargine U-300	2-4 gg
Degludec	2-3 gg





Tim Heise et al, Steady state is reached within 2–3 days of once-daily administration of degludec, a basal insulin with an ultralong duration of action, Journal of Diabetes 8 (2016) 132–138
Chantal Mathieu et al, Efficacy and Safety of Insulin Degludec in a Flexible Dosing Regimen vs Insulin Glargine in Patients With Type 1 Diabetes (BEGIN: Flex T1): A 26-Week Randomized, Treat-to-Target Trial With a 26-Week Extension, J Clin Endocrinol Metab, March 2013, 98(3):1154–1162

New Insulin Glargine 300 Units/mL Versus Glargine 100 Units/mL in People With Type 1 Diabetes: A Randomized, Phase 3a, Open-Label Clinical Trial (EDITION 4)

DOI: 10.2337/dc15-0249

OBJECTIVE

Insulin therapy in type 1 diabetes still provides suboptimal outcomes. Insulin glargine 300 units/mL (Gla-300), with a flatter pharmacodynamic profile compared with insulin glargine 100 units/mL (Gla-100), is an approach to this problem.

RESEARCH DESIGN AND METHODS

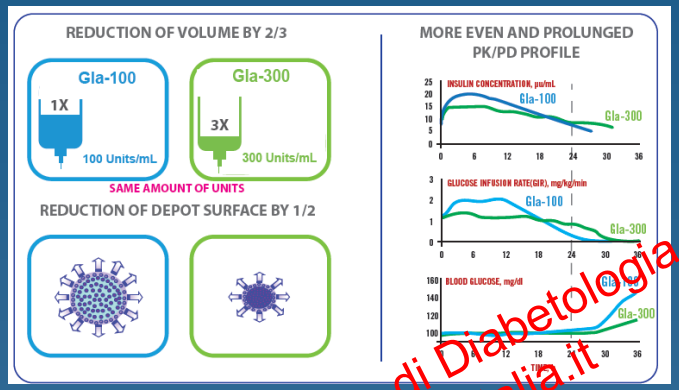
People with type 1 diabetes, using a mealtime and basal insulin regimen, were randomized open-label to Gla-300 or Gla-100 and to morning or evening injection, continuing the mealtime analog, and followed up for 6 months.

RESULTS

Participants (n = 549) were a mean age of 47 years, had a duration of diabetes of 21 years, and a BMI of 27.6 kg/m^2. The change in HbA_{1c} (primary end point; baseline 8.1%) was equivalent in the two treatment-groups (difference 0.04% [95% CI −0.10 to 0.19]) (0.4 mmol/mol [−1.1 to 2.1]), and Gla-300 was thus noninferior. Similar results with wider 95% CIs were found for morning and evening injection times and for prebreakfast self-measured plasma glucose (SMPG) overall. Results were also similar for Gla-300 when morning and evening injection time was compared, including overlapping 8-point SMPG profiles. Hypoglycemia did not differ, except for the first 8 weeks of the study, when nocturnal confirmed or severe hypoglycemia was lower with Gla-300 (risk ratio 0.69 [95% CI 0.53–0.91]). Hypoglycemia with Gla-300 did not differ by time of injection. The basal insulin dose was somewhat higher at 6 months for Gla-300. The adverse event profile did not differ and was independent of the Gla-300 time of injection. Weight gain was lower with Gla-300.

CONCLUSIONS

In long-duration type 1 diabetes, Gla-300 provides similar glucose control to Gla-100, with a lower risk of hypoglycemia after transfer from other insulins, independent of time of injection, and less weight gain.



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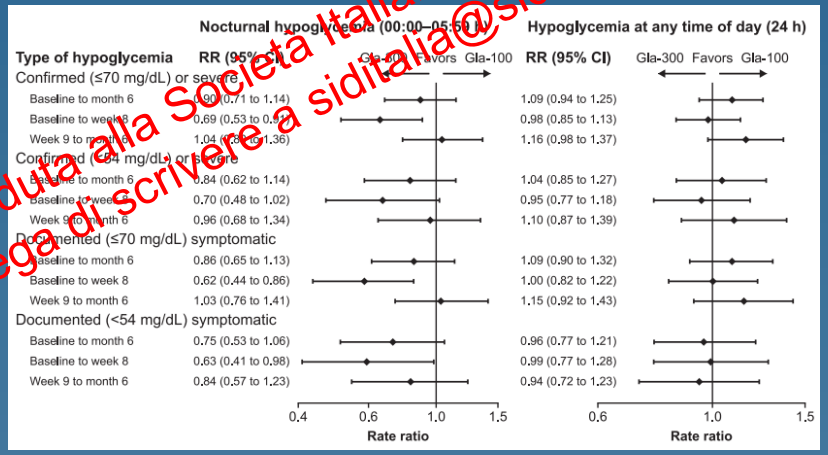
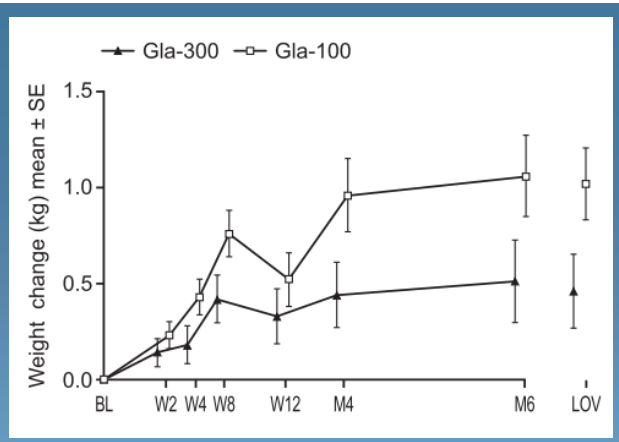
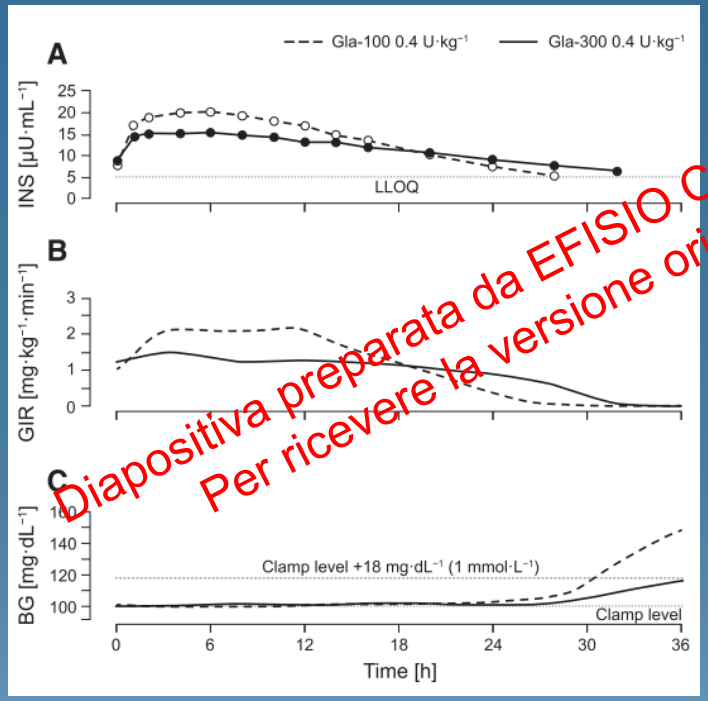




New Insulin Glargine 300 Units·mL^{-1} Provides a More Even Activity Profile and Prolonged Glycemic Control at Steady State Compared With Insulin Glargine 100 Units·mL^{-1}

Diabetes Care 2015;38:637–643 | DOI: 10.2337/dc14-0006



OBJECTIVE

To characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of a new insulin glargine comprising 300 units·mL^{-1} (Gla-300), compared with insulin glargine 100 units·mL^{-1} (Gla-100) at steady state in people with type 1 diabetes.

RESEARCH DESIGN AND METHODS

A randomized, double-blind, crossover study (N = 30) was conducted, applying the euglycemic clamp technique over a period of 36 h. In this multiple-dose to steady-state study, participants received once-daily subcutaneous administrations of either 0.4 (cohort 1) or 0.6 units·kg^{-1} (cohort 2) Gla-300 for 8 days in one treatment period and 0.4 units·kg^{-1} Gla-100 for 8 days in the other. Here we focus on the results of a direct comparison between 0.4 units·kg^{-1} of each treatment. PK and PD assessments performed on the last treatment day included serum insulin measurements using a radioimmunoassay and the automated euglycemic glucose clamp technique over 36 h.

RESULTS

At steady state, insulin concentration (INS) and glucose infusion rate (GIR) profiles of Gla-300 were more constant and more evenly distributed over 24 h compared with those of Gla-100 and lasted longer, as supported by the later time (~3 h) to 50% of the area under the serum INS and GIR time curves from time zero to 36 h post dosing. Tight blood glucose control (≤105 mg·dL^{-1}) was maintained for approximately 5 h longer (median of 30 h) with Gla-300 compared with Gla-100.

CONCLUSIONS

Gla-300 provides more even steady-state PK and PD profiles and a longer duration of action than Gla-100, extending blood glucose control well beyond 24 h.

Insulin degludec, an ultra-longacting basal insulin, versus insulin glargine in basal-bolus treatment with mealtime insulin aspart in type 1 diabetes (BEGIN Basal-Bolus Type 1): a phase 3, randomised, open-label, treat-to-target non-inferiority trial

*Simon Heller, John Buse, Miles Fisher, Satish Garg, Michel Marre, Ludwig Merker, Eric Renard, David Russell-Jones, Areti Philotheou, Ann Marie Ocampo Francisco, Huiling Pei, Bruce Bode, on behalf of the BEGIN Basal-Bolus Type 1 Trial Investigators**

Summary

Background Intensive basal-bolus insulin therapy has been shown to improve glycaemic control and reduce the risk of long-term complications that are associated with type 1 diabetes mellitus. Insulin degludec is a new ultra-longacting basal insulin. We therefore compared the efficacy and safety of insulin degludec and insulin glargine, both administered once daily with mealtime insulin aspart, in basal-bolus therapy for type 1 diabetes.

Methods In an open-label, treat-to-target, non-inferiority trial, undertaken at 79 sites (hospitals and centres) in six countries, adults (aged ≥18 years) with type 1 diabetes (glycated haemoglobin [HbA_{1c}] ≤10% [86 mmol/mol]), who had been treated with basal-bolus insulin for at least 1 year, were randomly assigned in a 3:1 ratio, with a computer-generated blocked allocation sequence, to insulin degludec or insulin glargine without stratification by use of a central interactive response system. The primary outcome was non-inferiority of degludec to glargine, assessed as a reduction in HbA_{1c} after 52 weeks with the intention-to-treat analysis. This trial is registered with ClinicalTrials.gov, number NCT00982228.

Findings Of 629 participants, 472 were randomly assigned to insulin degludec and 157 to insulin glargine; all were analysed in their respective treatment groups. At 1 year, HbA_{1c} had fallen by 0·40% points (SE 0·03) and 0·39% points (0·07), respectively, with insulin degludec and insulin glargine (estimated treatment difference –0·01% points [95% CI –0·14 to 0·11]; p<0·0001 for non-inferiority testing) and 188 (40%) and 67 (43%) participants achieved a target HbA_{1c} of less than 7% (<53 mmol/mol). Rates of overall confirmed hypoglycaemia (plasma glucose ≤3·1 mmol/L or severe) were similar in the insulin degludec and insulin glargine groups (42·54 *vs* 40·18 episodes per patient-year of exposure; estimated rate ratio [degludec to glargine] 1·07 [0·89 to 1·28]; p=0·48). The rate of nocturnal confirmed hypoglycaemia was 25% lower with degludec than with glargine (4·41 *vs* 5·86 episodes per patient-year of exposure; 0·75 [0·59 to 0·96]; p=0·021). Overall serious adverse event rates (14 *vs* 16 events per 100 patient-years of exposure) were similar for the insulin degludec and insulin glargine groups.

Interpretation Insulin degludec might be a useful basal insulin for patients with type 1 diabetes because it provides effective glycaemic control while lowering the risk of nocturnal hypoglycaemia, which is a major limitation of insulin therapy.

Simon Heller et al, Lancet 2012; 379: 1489–97

Insulin degludec: Lower day-to-day and within-day variability in pharmacodynamic response compared with insulin glargine 300 U/mL in type 1 diabetes

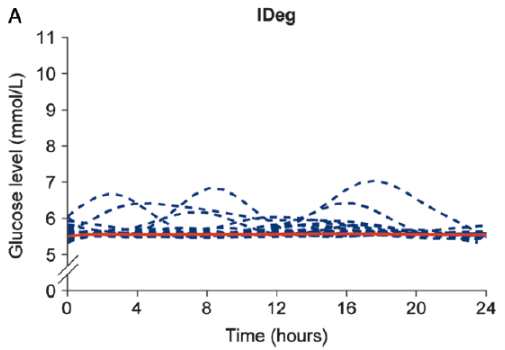
Tim Heise MD[1] | Marianne Nørskov[2] | Leszek Nosek MD[1] | Kadriye Kaplan[2] | Susanne Famulla PhD[1] | Hanne L. Haahr[2]

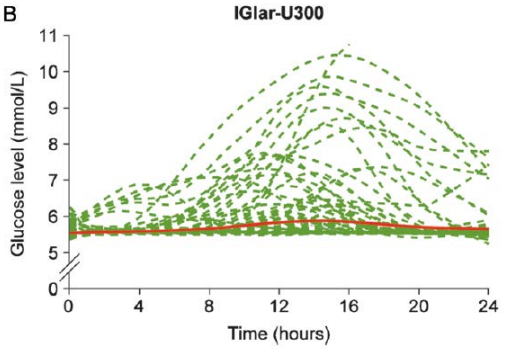
Aim: To compare day-to-day and within-day variability in glucose-lowering effect between insulin degludec (IDeg) and insulin glargine 300 U/mL (IGlar-U300) in type 1 diabetes.

Materials and methods: In this double-blind, crossover study, patients were randomly assigned to 0.4 U/kg of IDeg or IGlar-U300 once daily for two treatment periods lasting 12 days each. Pharmacodynamic variables were assessed at steady-state from the glucose infusion rate profiles of three 24-hour euglycaemic glucose clamps (days 6, 9 and 12) during each treatment period.

Results: Overall, 57 patients completed both treatment periods (342 clamps). The potency of IGlar-U300 was 30% lower than IDeg (estimated ratio 0.70, 95% confidence interval [CI] 0.61; 0.80; $P < .0001$). The distribution of glucose-lowering effect was stable across 6-hour intervals (24%-26%) for IDeg, while IGlar-U300 had greater effects in the first (35%) and last (28%) intervals compared with 6 to 12 hours (20%) and 12 to 18 hours (17%). Within-day variability (relative fluctuation) was 37% lower with IDeg than with IGlar-U300 (estimated ratio IDeg/IGlar-U300: 0.63, 95% CI 0.54; 0.73; $P < .0001$). The day-to-day variability in glucose-lowering effect with IDeg was approximately 4 times lower than IGlar-U300 (variance ratio IGlar-U300/IDeg 3.70, 95% CI 2.42; 5.67; $P < .0001$). The day-to-day variability in glucose-lowering effect assessed in 2-hour intervals was consistently low with IDeg over 24 hours, but steadily increased with IGlar-U300 to a maximum at 10 to 12 hours and 12 to 14 hours after dosing (variance ratios 12.4 and 11.4, respectively).

Conclusion: IDeg has lower day-to-day and within-day variability than IGlar-U300 and a more stable glucose-lowering effect, which might facilitate titration and enable tighter glycaemic control with a reduced risk of hypoglycaemia.





Diabetes Obes Metab. 2017 Jul;19(7):1032-1039

Morning administration of 0.4 U/kg/day insulin glargine 300 U/mL provides less fluctuating 24-hour pharmacodynamics and more even pharmacokinetic profiles compared with insulin degludec 100 U/mL in type 1 diabetes

T.S. Bailey [a,*], J. Pettus [b], R. Roussel [c,d,e], W. Schmider [f], M. Maroccia [g], N. Nassr [f], O. Klein [h], G.B. Bolli [i], R. Dahmen [f]

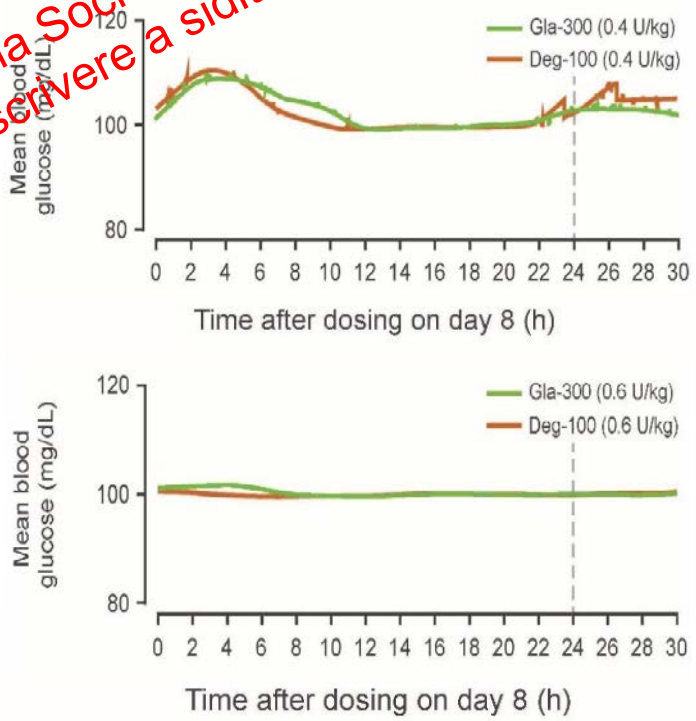
ABSTRACT

Aim. – To compare steady state pharmacodynamic and pharmacokinetic profiles of insulin glargine 300 U/mL (Gla-300) with insulin degludec 100 U/mL (Deg-100) in people with type 1 diabetes.

Methods. – This single-centre, randomized, double-blind crossover euglycaemic clamp study included two parallel cohorts with fixed once-daily morning dose regimens. For both insulins participants received 0.4 (n = 24) or 0.6 U/kg/day (n = 24), before breakfast, for 8 days prior to the clamp. The main endpoint was within-day variability (fluctuation) of the smoothed glucose infusion rate (GIR) over 24 hours (GIR-smFL$_{0-24}$).

Results. – Gla-300 provided 20% less fluctuation of steady state glucose infusion rate profiles than Deg-100 over 24 hours at 0.4 U/kg/day (GIR-smFL$_{0-24}$ treatment ratio 0.80 [90% confidence interval: 0.66 to 0.96], P = 0.047), while at the dose of 0.6 U/kg/day the difference between insulins was not statistically significant (treatment ratio 0.96 [0.83 to 1.11], P = 0.603). Serum insulin concentrations appeared more evenly distributed with both dose levels of Gla-300 versus the same doses of Deg-100, as assessed by relative 6-hour fractions of the area under the curve within 24 hours. Both insulins provided exposure and activity until 30 hours (end of clamp).

Conclusion. – Gla-300 provides less fluctuating steady state pharmacodynamic profiles (i.e. lower within-day variability) and more evenly distributed pharmacokinetic profiles, compared with Deg-100 in a once-daily morning dosing regimen of 0.4 U/kg/day.



Passaggio a Glargine U-300

Grafici FGM con modifica della posologia insulinica

U300: 41 UI

Glu: 13 UI + 20 UI + 20 UI

Counting dei carboidrati

Il counting dei carboidrati si conferma nel contesto della MNT, componente essenziale, e identifica la strategia più efficace per il controllo glicemico nel paziente con diabete in trattamento insulinico intensivo. **I B**

I pazienti devono:

- essere informati sull'indice glicemico dei vari cibi
- prediligere tra i carboidrati quelli a **minor indice glicemico**
- effettuare le dovute correzioni della dose di insulina nel caso consumino CHO ad alto indice glicemico

ADI-AMD-SID, 2014; Augustin et al, 2015; Linee guida SID-AMD 2018

Regola del 500

$$\frac{500}{\text{Fabbisogno Insulinico Giornaliero (FIG)}}$$

➔ quanti g di CHO vengono 'consumati' con 1 UI

Fattore di sensibilità

$$\frac{1800}{\text{Fabbisogno Insulinico Giornaliero (FIG)}}$$

➔ quanto si 'abbassa' la glicemia con 1 UI

Bolo di correzione

$$\frac{\text{Glicemia misurata} - \text{Glicemia desiderata}}{\text{Fattore di sensibilità}}$$

➔ quante UI dovete praticare

Agrusta et al., «Piccola guida al microinfusore e dintorni»

Il **bolo di correzione** è la quantità di insulina da somministrare per abbassare la glicemia fino ai valori obiettivo.

Bolo di correzione a digiuno

Come fare per calcolare il bolo di correzione a digiuno? Imparate ad applicare questa semplice formula:

$$\frac{\textbf{Glicemia misurata} - \textbf{Glicemia desiderata}}{\textbf{Fattore di sensibilità}}$$

La *glicemia desiderata* è la glicemia che ritenete accettabile in questa occasione.

ESEMPIO

$$\frac{\textbf{320} \text{ (glicemia misurata)} - \textbf{170} \text{ (glicemia desiderata)}}{\textbf{37,70} \text{ (fattore di sensibilità)}} = 4 \text{ UI}$$

➔ per correggere una glicemia di 320 e farla 'scendere' fino a 170 è necessario praticare **un bolo di 4 unità di insulina**

Bolo di correzione postprandiale

Se dopo pranzo vi ritrovate la glicemia alta potete praticare un bolo suppletivo tenendo presente che:

si consuma **ogni ora il 25%** dell'ultimo bolo effettuato

Cioè:

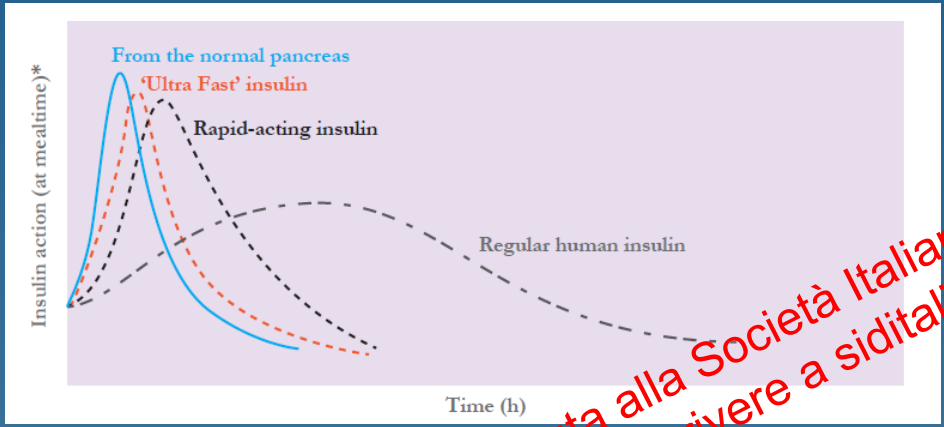
se avete praticato a pranzo	**10 UI** di Humalog
dopo **1 ora** se ne sono consumate	il **25%**
e quindi ne sono rimaste in funzione	**7,5 UI**
dopo **2 ore** ne consumate	il **50%**
quindi rimangono attive	**5 UI**

Dovendo praticare un bolo suppletivo, perché avete la glicemia alta, dovreste sottrarre al bolo di correzione le UI ancora in funzione.

bolo di correzione – UI ancora in funzione

Capirete bene che spesso ciò non è possibile in quanto **le UI del bolo di correzione sono inferiori alle UI ancora in funzione**, quindi, spesso il bolo di correzione postprandiale è utilizzabile solo a 3-4 ore dal pranzo.

Insuline rapide



Adattato da Home PD. Diabetes Obes Metab 2015

Inizio di azione più rapido, durata d'azione più breve e picco di concentrazione plasmatica più ampio e precoce rispetto all'insulina umana regolare, consentendo un miglior controllo glicemico in fase post-prandiale precoce e riducendo il rischio di ipoglicemia in fase post-prandiale tardiva (Home, 2012).

Somministrazione subito prima del pasto, anziché 20-30 minuti prima come l'insulina umana regolare; la rapidità di azione si traduce anche in una maggior maneggevolezza (Home, 2012).

Sebbene esistano piccole differenze cinetiche fra i tre analoghi disponibili, sul piano clinico non emergono differenze di rilievo (Siebenhofer et al., 2006; Home, 2012).

OPTIMIZED BASAL-BOLUS INSULIN REGIMENS IN TYPE 1 DIABETES: INSULIN GLULISINE VERSUS REGULAR HUMAN INSULIN IN COMBINATION WITH BASAL INSULIN GLARGINE

Satish K. Garg, MD,[1,2] Julio Rosenstock, MD, FACE,[3] and Kirk Ways, MD, PhD[4]

ABSTRACT

Objective: To compare the efficacy and safety of insulin glulisine (GLU), a new rapid-acting insulin analogue, injected 0 to 15 minutes before or immediately after meals, with regular human insulin (RHI), injected 30 to 45 minutes before meals.

Methods: Patients with type 1 diabetes (N = 860) received once-daily insulin glargine and subcutaneous injections of either GLU (premeal or postmeal) or premeal RHI in this open-label, randomized, controlled, multicenter, parallel-group, 12-week study.

Results: Baseline to endpoint changes in mean glycated hemoglobin (as A1c equivalents) (A1c) occurred in the premeal GLU, postmeal GLU, and premeal RHI groups (−0.26%, −0.11%, and −0.13%, respectively). The reduction in A1c was greater for the premeal GLU group in comparison with the RHI group ($P = 0.02$) and the postmeal GLU group ($P = 0.006$); no significant between-treatment difference was found for postmeal GLU versus RHI. Overall, blood glucose profiles were similar in all 3 treatment groups but were significantly lower for premeal GLU 2-hour postbreakfast measurements (premeal versus postmeal GLU, $P = 0.0017$; premeal GLU versus RHI, $P = 0.0001$) and 2-hour postdinner measurements (premeal GLU versus RHI, $P = 0.0001$; premeal versus postmeal GLU, $P = 0.0137$). Severe hypoglycemic episodes were comparable for premeal GLU, postmeal GLU, and premeal RHI groups (8.4%, 8.4%, and 9.0%, respectively). Body weight increased (+0.3 kg) in the RHI and premeal GLU groups; however, weight decreased in the postmeal GLU group (−0.5 kg; between-treatment difference, $P = 0.03$).

Conclusion: Better A1c reductions were obtained with premeal GLU, but postmeal administration of GLU was as safe and effective as premeal GLU or RHI in combination with insulin glargine and was not associated with weight gain. **(Endocr Pract. 2005;11:11-17)**

Abbreviations:
A1c = glycated hemoglobin as A1c equivalents; **CI** = confidence interval; **GLU** = insulin glulisine; **ITT** = intention-to-treat; **RHI** = regular human insulin; **TEAE** = treatment emergent adverse event

INTRODUCTION

The Diabetes Control and Complications Trial showed that intensified glycemic control reduces the risk of developing the late complications of diabetes (1,2). Traditionally, fasting plasma glucose and glycated hemoglobin (as A1c equivalents) (A1c) have been used to assess glycemic control; however, more recently, postprandial blood glucose excursions have been proposed as additional targets for further improvement of glycemic control (3). Better glycemic control can be achieved by using a regimen of short-acting (bolus) insulin together with long-acting (basal) insulin in a basal-bolus regimen. Optimization of such insulin regimens, however, is often hindered by the disadvantageous pharmacokinetics and variability of absorption of traditional insulin preparations after subcutaneous administration (4,5).

Regular human insulin (RHI) has been adapted for use as a bolus insulin, but when compared with endogenous insulin release, its onset of action is too slow (30 to 45 minutes after administration) and its duration of action is longer (6 to 8 hours) than desired to provide ideal physiologic prandial insulin requirements (6,7). The introduction of rapid-acting insulin analogues has provided bolus insulins with more appropriate time-action profiles, a feature that offers clinical advantages over RHI (8).

Insulin glulisine (GLU) is a new, rapid-acting insulin analogue that differs from RHI by the replacement of the amino acid asparagine with lysine at position 3, and the replacement of lysine with glutamic acid at position 29, on

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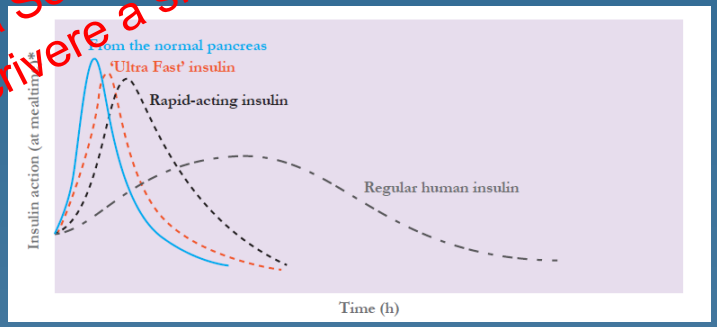
Address correspondence and reprint requests to Dr. Satish K. Garg, Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, 4200 East 9th Avenue, Box B-140, Denver, CO 80262.



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Short-acting insulin analogues versus regular human insulin on postprandial glucose and hypoglycemia in type 1 diabetes mellitus: a systematic review and meta-analysis

Karla F. S. Melo[1,2,3*], Luciana R. Bahia[2,4], Bruna Pasinato[5], Gustavo J. M. Porfirio[6], Ana Luiza Martimbianco[6], Rachel Riera[6,7], Luis E. P. Calliari[8], Walter J. Minicucci[2], Luiz A. A. Turatti[2], Hermelinda C. Pedrosa[2] and Beatriz D. Schaan[5,9]

Abstract

Introduction: Strict glucose control using multiple doses of insulin is the standard treatment for type 1 diabetes mellitus (T1DM), but increased risk of hypoglycemia is a frequent drawback. Regular insulin in multiple doses is important for achieving strict glycemic control for T1DM, but short-acting insulin analogues may be better in reducing hypoglycemia and postprandial glucose levels.

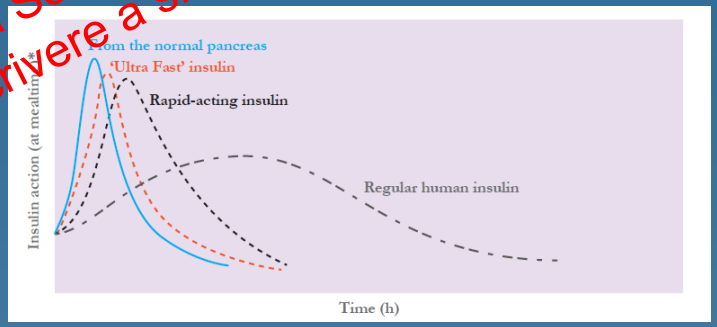
Objective: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to assess the effects of short-acting insulin analogues *vs* regular human insulin on hypoglycemia and postprandial glucose in patients with T1DM.

Methods: Searches were run on the electronic databases MEDLINE, Cochrane-CENTRAL, EMBASE, ClinicalTrials.gov, LILACS, and DARE for RCTs published until August 2017. To be included in the study, the RCTs had to cover a minimum period of 4 weeks and had to assess the effects of short-acting insulin analogues *vs* regular human insulin on hypoglycemia and postprandial glucose levels in patients with T1DM. Two independent reviewers extracted the data and assessed the quality of the selected studies. The primary outcomes analyzed were hypoglycemia (total episodes, nocturnal hypoglycemia, and severe hypoglycemia) and postprandial glucose at all times, after breakfast, after lunch, and after dinner). Glycated hemoglobin (HbA1c) levels and quality of life were considered secondary outcomes. The risk of bias of each RCT was assessed using the Cochrane Collaboration Risk of Bias table, while the quality of evidence for each outcome was assessed using the GRADEpro software. The pooled mean difference in the number of hypoglycemic episodes and postprandial glucose between short-acting insulin analogues vs. regular human insulin was calculated using the random-effects model.

Results: Of the 2897 studies retrieved, 14 (6235 patients) were included. Short-acting insulin analogues were associated with a decrease in total hypoglycemic episodes (risk rate 0.93, 95% CI 0.87–0.99; 6235 patients; $I^2 = 81\%$), nocturnal hypoglycemia (risk rate 0.55, 95% CI 0.40–0.76, 1995 patients, $I^2 = 84\%$), and severe hypoglycemia (risk rate 0.68, 95% CI 0.60–0.77; 5945 patients, $I^2 = 0\%$); and with lower postprandial glucose levels (mean difference/MD −19.44 mg/dL; 95% CI −21.49 to −17.39; 5031 patients, $I^2 = 69\%$) and lower HbA1c (MD −0,13%; IC 95% −0.16 to −0.10; 5204 patients; $I^2 = 73\%$) levels.

Conclusions: Short-acting insulin analogues are superior to regular human insulin in T1DM patients for the following outcomes: total hypoglycemic episodes, nocturnal hypoglycemia, severe hypoglycemia, postprandial glucose, and HbA1c.

Keywords: Diabetes mellitus, Type 1 diabetes, Insulin, Aspart insulin, Glulisine insulin, Lispro insulin, Systematic review, Meta-analysis



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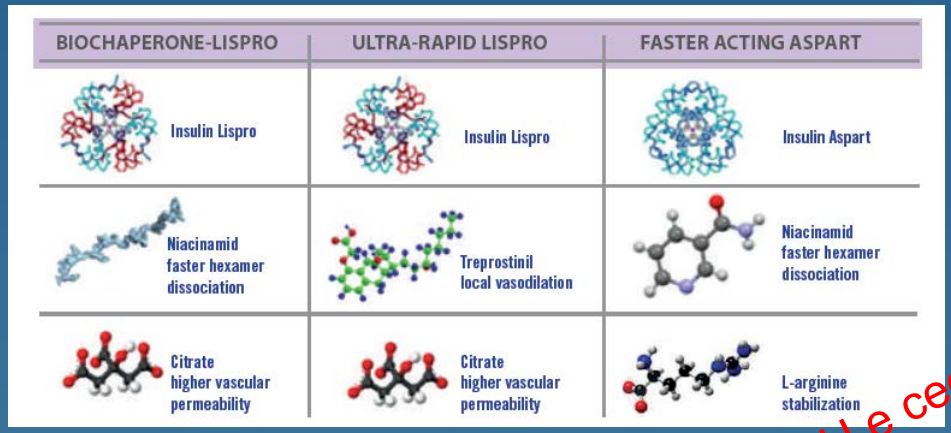
Insuline ultrarapide



Delle tre insuline ultrarapide messe a punto (Fast Insulin Aspart, Ultra-Rapid Lispro, BioChaperone Lispro), solo Fast-Aspart è attualmente disponibile in Italia

Adattato da Home PD. Diabetes Obes Metab 2015

Fast-Acting Insulin Aspart Improves Glycemic Control in Basal-Bolus Treatment for Type 1 Diabetes: Results of a 26-Week Multicenter, Active-Controlled, Treat-to-Target, Randomized, Parallel-Group Trial (onset 1)

Diabetes Care 2017;40:943–950 | https://doi.org/10.2337/dc16-1771

OBJECTIVE

This multicenter, treat-to-target, phase 3 trial evaluated the efficacy and safety of fast-acting insulin aspart (faster aspart) versus conventional insulin aspart (IAsp) in adults with type 1 diabetes.

RESEARCH DESIGN AND METHODS

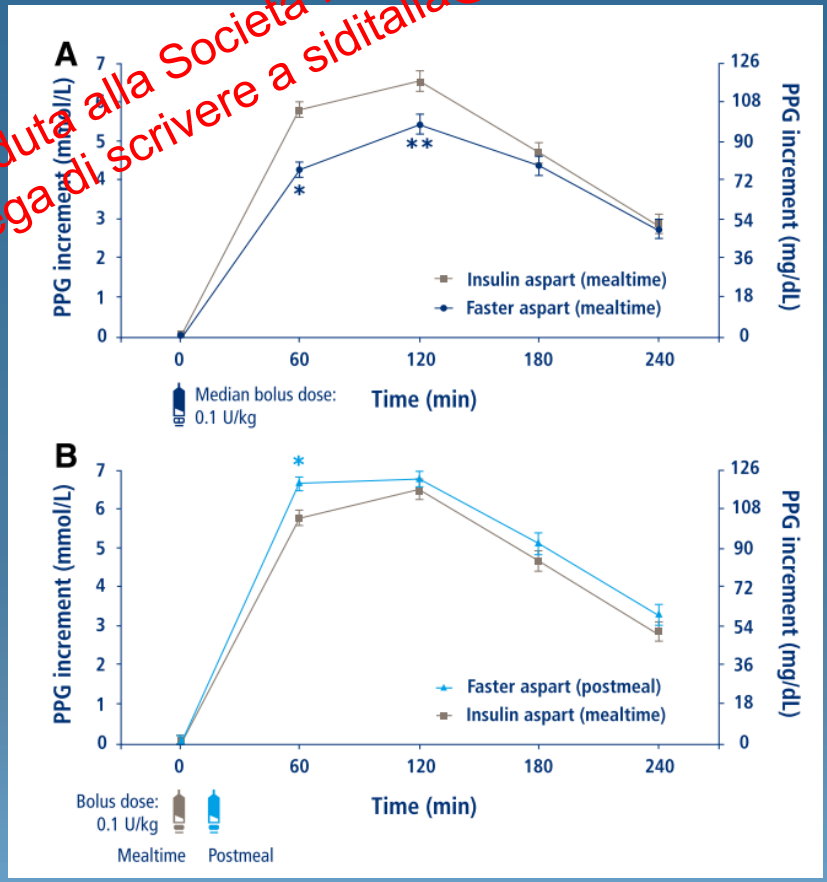
The primary end point was change from baseline in HbA_{1c} after 26 weeks. After an 8-week run-in, subjects were randomized (1:1:1) to double-blind mealtime faster aspart (n = 381), IAsp (n = 380), or open-label postmeal faster aspart (n = 382) — each with insulin detemir.

RESULTS

HbA_{1c} was reduced in both treatment groups, and noninferiority to IAsp was confirmed for both mealtime and postmeal faster aspart (estimated treatment difference [ETD] faster aspart–IAsp, mealtime, −0.15% [95% CI −0.23; −0.07], and postmeal, 0.04% [−0.04; 0.12]). Mealtime faster aspart statistically significantly reduced HbA_{1c} versus IAsp (P = 0.0002). Postprandial plasma glucose (PPG) increments were statistically significantly lower with mealtime faster aspart at 1 h (ETD −1.18 mmol/L [95% CI −1.65; −0.71], −21.21 mg/dL [−29.65; −12.77]; P < 0.0001) and 2 h (−0.67 mmol/L [−1.29; −0.04], −12.01 mg/dL [−23.33; −0.70]; P = 0.0375) after the meal test; superiority to IAsp for the 2-h PPG increment was confirmed. The overall rate of severe or blood glucose–confirmed (plasma glucose <3.1 mmol/L [56 mg/dL]) hypoglycemic episodes and safety profiles were similar between treatments.

CONCLUSIONS

Faster aspart effectively improved HbA_{1c}, and noninferiority to IAsp was confirmed, with superior PPG control for mealtime faster aspart versus IAsp. Subjects randomized to postmeal faster aspart for all meals maintained HbA_{1c} noninferior to that obtained with mealtime IAsp.



Fast-acting insulin aspart versus insulin aspart in the setting of insulin degludec-treated type 1 diabetes: Efficacy and safety from a randomized double-blind trial

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Aim: To evaluate the efficacy and safety of mealtime or post-meal fast-acting insulin aspart (faster aspart) vs mealtime insulin aspart (IAsp), both in combination with insulin degludec, in participants with type 1 diabetes (T1D).

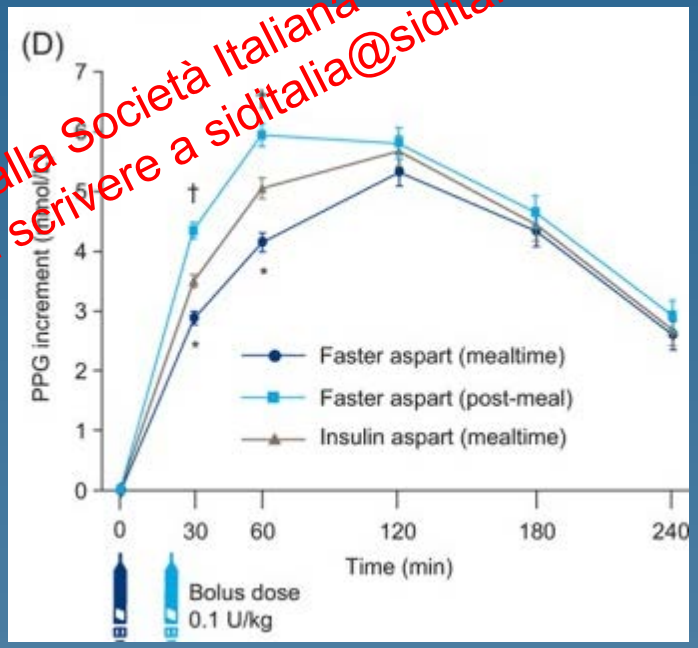
Methods: This multicentre, treat-to-target trial (Clinical trial registry: NCT02500706, ClinicalTrials.gov) randomized participants to double-blind mealtime faster aspart (n = 342) or IAsp (n = 342) or open-label post-meal faster aspart (n = 341). The primary endpoint was change from baseline in HbA1c 26 weeks post randomization. All available information, regardless of treatment discontinuation, was used for evaluation of the effect.

Results: Non-inferiority for the change from baseline in HbA1c was confirmed for mealtime and post-meal faster aspart vs IAsp (estimated treatment difference [ETD]: 95%CI; −0.02% [−0.11; 0.07] and 0.10% [0.004; 0.19], respectively). Mealtime faster aspart was superior to IAsp for 1-hour PPG increment using a meal test (ETD, −0.30 mmol/L [−0.36; −0.45]; P < 0.001). Self-monitored 1-hour PPG increment favoured faster aspart at breakfast (ETD, −0.58 mmol/L [−0.99; −0.17]; P = 0.006) and across all meals (−0.48 mmol/L [−0.74; −0.21]; P < 0.001). Safety profiles and overall rate of severe or blood glucose-confirmed hypoglycaemia were similar between treatments, but significantly less hypoglycaemia was seen 3 to 4 hours after meals with mealtime faster aspart.

Conclusion: Mealtime and post-meal faster aspart in conjunction with insulin degludec provided effective glycaemic control compared with IAsp, with no increased safety risk. Mealtime faster aspart provided PPG control superior to that of IAsp.

KEYWORDS

clinical trial, hypoglycaemia, insulin therapy, type 1 diabetes



John B. Buse et al., Fast-acting insulin aspart versus insulin aspart in the setting of insulin degludec-treated type 1 diabetes : Efficacy and safety from a randomized double-blind trial, Diabetes Obes Metab. 2018;20:2885–2893.

TAKE HOME MESSAGE

- Le insuline ultralente riducono la variabilità glicemica, le ipoglicemie, principalmente notturne, e l'incremento ponderale.

- Gli analoghi ultrarapidi rappresentano una soluzione terapeutica valida per la somministrazione post-prandiale in pazienti selezionati (anziani e ospedalizzati).

- Il counting dei carboidrati si conferma nel contesto della terapia medico-nutrizionale, componente essenziale, e identifica la strategia più efficace per il controllo glicemico nel paziente con diabete in trattamento insulinico intensivo.

GRAZIE PER L'ATTENZIONE