

Electronic Supplementary Material

Drugs & Aging

A Comparison of Pharmacokinetic and Pharmacodynamic Properties Between Faster-Acting Insulin Aspart and Insulin Aspart in Elderly Subjects with Type 1 Diabetes Mellitus

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Table S1 Clamp quality for faster aspart and insulin aspart

	Faster aspart ^a Mean±SD	Insulin aspart ^a Mean±SD
Precision^b (%)		
Elderly	5.5±3.2	5.3±4.4
Younger adults	5.1±2.7	6.6±4.2
Control deviation^c (mmol/L)		
Elderly	0.04±0.12	0.02±0.11
Younger adults	0.04±0.10	0.04±0.13

^a Data are calculated between the timepoints $t_{10\% \text{ AUC}_{\text{GIR},0-t}}$ and $t_{90\% \text{ AUC}_{\text{GIR},0-t}}$ to exclude intentional blood glucose deviations from target at the beginning and end of the clamp (at the beginning of the clamp, the clamp design to determine onset of action implied blood glucose deviations from target, while at the end of the clamp, escape of blood glucose from target occurs due to a decreasing insulin action).

^b The coefficient of variation of the ClampArt blood glucose measurements.

^c The mean difference between the ClampArt blood glucose measurements and the target blood glucose level.

Data are based on the 44 subjects (22 in each age group) included in the pharmacodynamic analysis.

$\text{AUC}_{\text{GIR},0-t}$, total glucose-lowering effect; GIR, glucose infusion rate; SD, standard deviation; t, time of last GIR observation > 0; $t_{10\% \text{ AUC}_{\text{GIR},0-t}}$, time to 10% of $\text{AUC}_{\text{GIR},0-t}$; $t_{90\% \text{ AUC}_{\text{GIR},0-t}}$, time to 90% of $\text{AUC}_{\text{GIR},0-t}$.

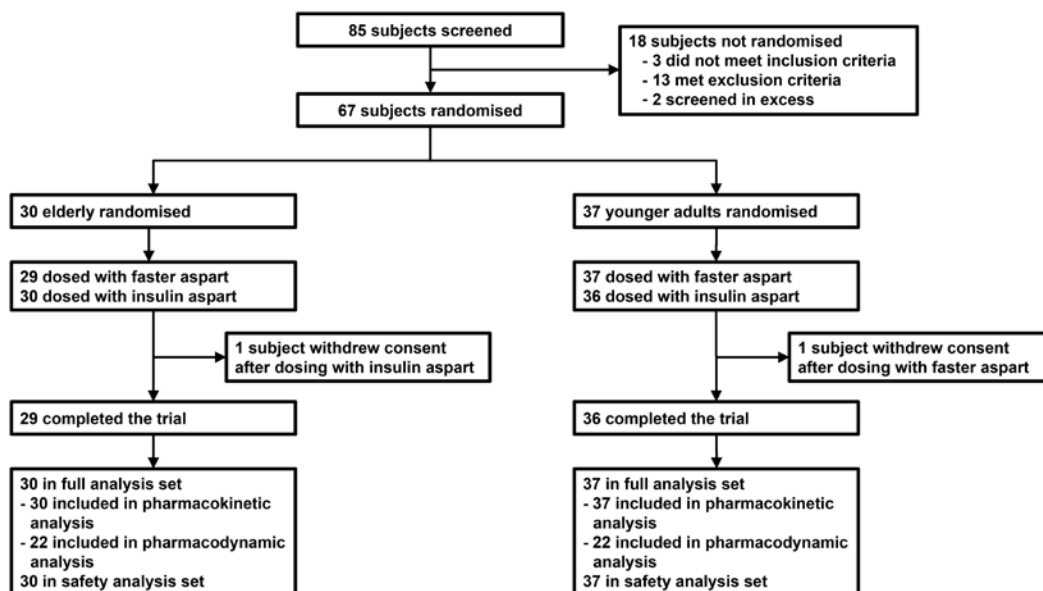


Fig. S1 Subject disposition

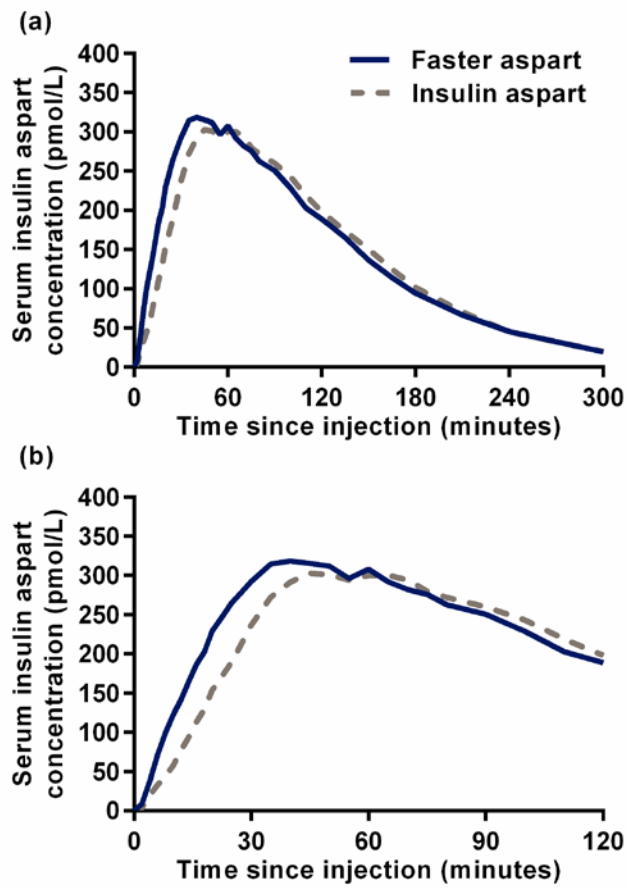


Fig. S2 Mean serum insulin aspart concentration-time profiles for 5 hours (a) and 2 hours (b) after administration of faster aspart and insulin aspart (0.2 U/kg) in younger adults with type 1 diabetes mellitus

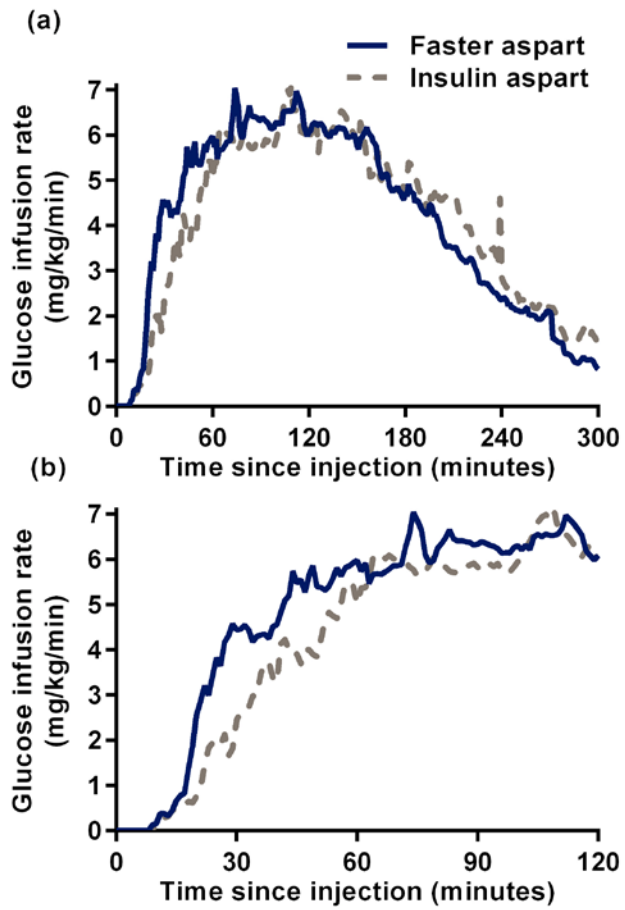


Fig. S3 Mean glucose-lowering effect-time profiles for 5 hours (a) and 2 hours (b) after administration of faster aspart and insulin aspart (0.2 U/kg) in younger adults with type 1 diabetes mellitus

Table S2 Onset of exposure and glucose-lowering effect after administration of faster aspart versus insulin aspart (0.2 U/kg) in younger adults with type 1 diabetes mellitus

	Faster aspart ^a	Insulin aspart ^a	Treatment ratio ^b [95% CI]	Treatment difference ^c [95% CI]	P-value ^d
Onset of exposure					
Onset of appearance (min)	3.1	5.9	0.53 [0.34;0.74]	-2.8 [-4.2;-1.4]	<0.001
t _{Early 50% C_{max}} (min)	18.9	26.6	0.71 [0.62;0.81]	-7.7 [-10.7;-4.7]	<0.001
t _{max} (min)	54.2	59.0	0.92 [0.77;1.09]	-4.8 [-14.6; 4.9]	0.321
Onset of glucose-lowering effect					
Onset of action (min)	17.6	26.3	0.67 [0.49;0.89]	-8.7 [-15.1;-2.3]	0.010
t _{Early 50% GIR_{max}} (min)	31.0	41.3	0.75 [0.65;0.86]	-10.3 [-15.4;-5.1]	<0.001
t _{GIR_{max}} (min)	113.8	124.6	0.91 [0.72;1.15]	-10.8 [-38.8; 17.3]	0.433

^a Data are least square means.

^b Faster aspart/insulin aspart (calculated using Fieller's method).

^c Faster aspart - insulin aspart.

^d For treatment comparison of faster aspart versus insulin aspart.

CI, confidence interval; t_{Early 50% C_{max}}, time to 50% of maximum insulin aspart concentration in the early part of the pharmacokinetic profile; t_{Early 50% GIR_{max}}, time to 50% of maximum glucose infusion rate in the early part of the glucose infusion rate profile; t_{GIR_{max}}, time to maximum glucose infusion rate; t_{max}, time to maximum insulin aspart concentration.

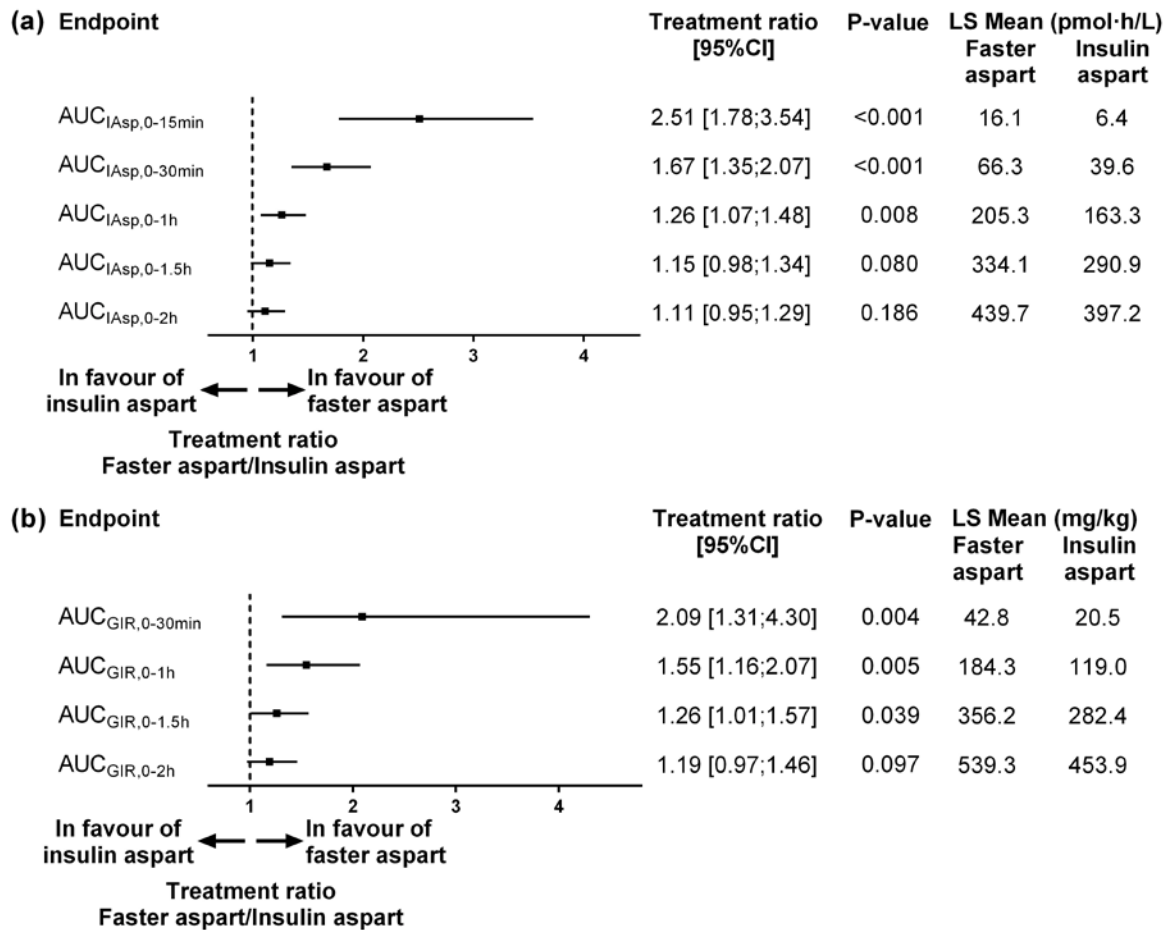


Fig. S4 Early exposure (a) and glucose-lowering effect (b) after administration of faster aspart versus insulin aspart (0.2 U/kg) in younger adults with type 1 diabetes mellitus. AUC, area under the curve; CI, confidence interval; GIR, glucose infusion rate; IAsp, insulin aspart; LS Mean, least square mean; P-value, treatment comparison of faster aspart versus insulin aspart.

Table S3 Overall exposure and glucose-lowering effect after administration of faster aspart versus insulin aspart (0.2 U/kg) in younger adults with type 1 diabetes mellitus

	Faster aspart ^a	Insulin aspart ^a	Treatment ratio ^b [95% CI]	P-value ^c
Overall exposure				
AUC _{IAsp,0-t} (pmol·h/L)	715.6	669.0	1.07 [0.92;1.25]	0.378
C _{max} (pmol/L)	317.3	306.1	1.04 [0.91;1.18]	0.582
Overall glucose-lowering effect				
AUC _{GIR,0-t} (mg/kg)	1227.5	1196.2	1.03 [0.90;1.17]	0.677
GIR _{max} (mg/kg/min)	6.5	6.3	1.04 [0.88;1.22]	0.660

^a Data are least square means.

^b Faster aspart/insulin aspart.

^c For treatment comparison of faster aspart versus insulin aspart.

AUC_{GIR,0-t}, total glucose-lowering effect; AUC_{IAsp,0-t}, total insulin aspart exposure; CI, confidence interval; C_{max}, maximum insulin aspart concentration; GIR_{max}, maximum glucose infusion rate.