Electronic supplementary material

ESM Table 1 Comparability of glucose clamp studies of long-acting insulin analogues

Clamp methodology	
Biostator vs manual clamp	Study [reference]
Manual	Lepore 2000 [7], Plank 2005 [15], Scholtz 2005 [8], Luzio 2006 [11], Porcellati 2007 [18], Porcellati 2007 [12]
Biostator	Heinemann 2000 [16], Heise 2004 [17], Klein 2007 [10]
Study design	
Study population	Study [reference]
Type 1 diabetes	Lepore 2000 [7], Heise 2004 [17], Plank 2005 [15], Porcellati 2007 [18], Porcellati 2007 [12]
Type 2 diabetes	Luzio 2006 [11], Klein 2007 [10]
Healthy volunteers	Heinemann 2000 [16], Scholtz 2005 [8]
Infusion (i.v.) of human regular insulin	Study [reference]
Started 4–6 h prior to study insulin administration	Lepore 2000 [7], Heise 2004 [17], Plank 2005 [15], Porcellati 2007 [18], Klein 2007 [10], Porcellati 2007 [12]
Gradually decreased after study insulin administration	Lepore 2000 [7], Plank 2005 [15], Porcellati 2007 [18], Porcellati 2007 [12]
Stopped before study insulin administration	Heise 2004 [17], Klein 2007 [10]
Continuous infusion throughout the clamp	Heinemann 2000 [16]
Not employed	Scholtz 2005 [8], Luzio 2006 [11]
Time of day of study insulin administration	Study [reference]
Morning	Heinemann 2000 [16], Scholtz 2005 [8], Luzio 2006 [11]
Noon	Heise 2004 [17], Klein 2007 [10]
Evening	Lepore 2000 [7], Plank 2005 [15], Porcellati 2007 [18], Porcellati 2007 [12]
Clamp duration	Study [reference]
24 h, or the time at which the glucose concentration	Porcellati 2007 [12]

reaches >10.0 mmol/l (180 mg/dl), after study insulin administration	
24 h, or the time at which the glucose concentration reaches >11.1 mmol/l (200 mg/dl), after study insulin administration	Lepore 2000 [7], Heise 2004 [17], Plank 2005 [15]
24 h after study insulin administration	Scholtz 2005 [8], Luzio 2006 [11], Klein 2007 [10]
30 h after study insulin administration	Heinemann 2000 [16]
32 h after study insulin administration	Porcellati 2007 [18]
Study insulin dose (U/kg)	Study [reference]
0.30	Lepore 2000 [7], Porcellati 2007 [18]
0.35	Porcellati 2007 [12]
0.40	Heinemann 2000 [16], Heise 2004 [17], Plank 2005 [15], Scholtz 2005 [8], Klein 2007 [10]
0.50	Luzio 2006 [11]
0.10, 0.20, 0.40, 0.80, 1.60	Plank 2005 [15]
0.40, 0.80, 1.40	Klein 2007 [10]
Single vs repeated study injections	Study [reference]
Single injection	Heinemann 2000 [16], Lepore 2000 [7], Heise 2004 [17], Plank 2005 [15], Scholtz 2005 [8], Luzio 2006 [11], Klein 2007 [10]
Repeated injections	Porcellati 2007 [18], Porcellati 2007 [12]
Site of injection	Study [reference]
Thigh	Lepore 2000 [7], Heise 2004 [17], Plank 2005 [15], Porcellati 2007 [18], Klein 2007 [10], Porcellati 2007 [12]
Abdomen	Heinemann 2000 [16], Scholtz 2005 [8], Luzio 2006 [11]
Clamp glucose target (mmol/l) [mg/dl]	Study [reference]
5.0 [90]	Heinemann 2000 [16], Klein 2007 [10]
5.6 [100]	Heise 2004 [17], Porcellati 2007 [12]
7.2 [130]	Lepore 2000 [7], Plank 2005 [15], Porcellati 2007 [18]
Baseline glucose concentration	Scholtz 2005 [8], Luzio 2006 [11]

Outcome measures	
GIR-AUC, GIR_{max}, t_{GIRmax}	Study [reference]
GIR-AUC, GIR_{max} and t_{GIRmax}	Heinemann 2000 [16], Heise 2004 [17], Plank 2005 [15], Scholtz 2005 [8], Luzio 2006 [11], Klein 2007 [10], Porcellati 2007 [12]
GIR-AUC	Porcellati 2007 [18]
Not specifically reported	Lepore 2000 [7]
Onset of action	Study [reference]
The time after study insulin administration at which the rate of i.v. insulin was reduced by 50%	Lepore 2000 [7], Plank 2005 [15], Porcellati 2007 [18]
The time after study insulin administration at which i.v. glucose was started	Porcellati 2007 [12]
The time of study insulin administration	Klein 2007 [10]
Not defined	Heinemann 2000 [16], Heise 2004 [17], Scholtz 2005 [8], Luzio 2006 [11]
End of action	Study [reference]
The time after study insulin administration at which the glucose concentration reached >8.3 mmol/l (150 mg/dl), or end of clamp	Lepore 2000 [7], Plank 2005 [15], Porcellati 2007 [18], Porcellati 2007 [12]
The time after study insulin administration at which GIR <0.00275 mmol kg^{-1} min^{-1} (0.5 mg kg^{-1} min^{-1}), or end of clamp	Klein 2007 [10]
Not defined	Heinemann 2000 [16], Heise 2004 [17], Scholtz 2005 [8], Luzio 2006 [11]
Statistical methods	
Averaging	Study [reference]
Mean time–action profile	Heinemann 2000 [16], Lepore 2000 [7], Plank 2005 [15], Scholtz 2005 [8], Luzio 2006 [11], Porcellati 2007 [18], Klein 2007 [10], Porcellati 2007 [12]
Individual time–action profiles	Heise 2004 [17]