Intensive Care Med (2009) 35:181–182
DOI 10.1007/s00134-008-1233-2

Paul Lee
Jerry R. Greenfield
Jacqueline R. Center
Lesley V. Campbell

Plasma insulin concentration is useful to guide glucose supplement in insulin overdose

Accepted: 3 July 2008
Published online: 6 August 2008

Sir: Estimation of the amount and duration of glucose support is an imprecise science following insulin overdose. Under-replacement causes recurrent hypoglycaemia. Over-replacement may cause hepatic steatosis and lactic acidosis [1]. We present three cases of insulin overdose to highlight how plasma insulin concentrations may be helpful to guide management.

Case 1

A 28-year-old non-diabetic woman collapsed with hypoglycaemia (capillary glucose = 2 mmol/L) following an intentional subcutaneous injection of 1,800 Units of intermediate acting insulin (Protaphane®). Despite a 10% intravenous dextrose infusion (100 ml/h), she suffered continuing hypoglycaemia requiring 10–12 boluses of 50% dextrose (25–50 ml) per day. Plasma insulin concentration remained elevated for 3 days (Table 1).

Case 2

A 53-year-old non-diabetic man intentionally injected 300 Units of regular insulin (Actrapid®) and 600 Units of neutral insulin 30%, isophane insulin 70% (Mixtard 30/70®) subcutaneously. He suffered two hypoglycaemic episodes (capillary glucose = 2.2 mmol/L) while receiving an intravenous 10% glucose infusion (100 ml/h). Initial plasma insulin concentration was 2,576 mIU/L. Intravenous glucose supplementation was increased to 25% dextrose (150 ml/h), which maintained euglycaemia. Plasma insulin concentration was measured regularly to guide glucose infusion (Table 1).

Case 3

A 51-year-old man with type 1 diabetes (regime: Lantus® 35 Units daily; Novorapid® 10 Units thrice daily) developed recurrent hypoglycaemia despite intravenous 5% dextrose (80 ml/h), and raised the possibility of insulin overdose. Plasma insulin level was 296 mU/L. The patient eventually admitted intentional subcutaneous injection of 120 Units of insulin glargine (Lantus®) 18 h earlier. Glucose supplementation was increased to 10% dextrose (100 ml/h) and maintained euglycaemia. Glucose supplementation was titrated with plasma insulin concentrations (Table 1).

Using the hyperinsulinaemic euglycaemic glucose clamp technique, Kolterman et al. [2] demonstrated the in vivo dose-response relationship between plasma insulin concentration and rate of glucose disposal. The maximum disposal rate plateaued at 10 mg/kg/min, corresponding to a plasma insulin concentration ≥1,000 mU/L. Therefore, we underestimated the glucose requirement in Case 1 (administered = 5 mg/kg/min vs. calculated = 10 mg/kg/min), resulting in frequent hypoglycaemia despite glucose infusion. Total glucose boluses approximated 4 mg/kg/min, which represented the glucose deficit (Table 1).

Despite a higher plasma insulin concentration than Case 1, Case 2 did not experience further hypoglycaemia following commencement of 25%

Table 1 Glucose requirement in relation to plasma insulin concentrations

	Case 1	Case 2	Case 3
Body weight (kg)	55	70	86
Basal glucose infusion 1st 24 h (g)	397	900	240
Total glucose boluses 1st 24 h (g)	300	0	0
Total glucose administered 1st 24 h (g)	697	900	240
Glucose administered in basal infusion (mg/kg/min)	5.0	9.0	2
Calculated basal glucose infusion requirement (mg/kg/min)	10	10	2.5
Plasma insulin concentration (reference range: 0–17 mU/L)			
6–8 h after injection	1,281	2,743	–
18 h after injection	942	657	296
30 h after injection	–	68	112
36 h after injection	906	122	98
48 h after injection	–	67	73
54 h after injection	819	71	48
60 h after injection	166	54	42
72 h after injection	15	16	22

Glucose infusion rate used based on plasma insulin in Cases 2 and 3

Plasma insulin concentration (mU/L)	Glucose infusion rate	
>1,000	10 mg/kg/min	25% glucose 150 ml/h
600–800	8.75 mg/kg/min	25% glucose 100 ml/h
100–300	2 mg/kg/min	10% glucose 100 ml/h

dextrose infusion (150 ml/h = 9 mg/kg/min), as predicted by the in vivo dose-response relationship (10 mg/kg/min). Monitoring of plasma insulin concentrations also unmasked the "depot-effect" [3], with plasma insulin concentration reaching a "nadir" at 30 h post injection, but rebounded, presumably due to unpredictable release of insulin from subcutaneous tissues (Table 1). Premature cessation of glucose may therefore precipitate further hypoglycaemia.

While insulin sensitivity varies between individuals, it is unlikely to cause clinical differences at the supraphysiological insulin levels attained in overdose [4]. We, therefore, administered 10% dextrose (100 ml/h = 2 mg/kg/min) in Case 3, as predicted by his plasma insulin level (2.5 mg/kg/min).

In conclusion, plasma insulin concentrations help to determine basal glucose infusion rate, detect fluctuating hyperinsulinemia from the "depot" effect, and confirm unreported overdose. Demonstration of normalisation of insulin concentrations facilitates transfer to psychiatric services, thus reducing prolonged monitoring in acute wards.

References

1. Jolliet P, Leverve X, Pichard C (2001) Acute hepatic steatosis complicating massive insulin overdose and excessive glucose administration. Intensive Care Med 27:313–316
2. Kolterman OG, Gray RS, Griffin J, Burstein P, Insel J, Scarlett JA, Olefsky JM (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin dependent diabetes mellitus. J Clin Invest 68:957–969
3. Brvar M, Mozina M, Bunc M (2005) Prolonged hypoglycaemia after insulin lispro overdose. Eur J Emerg Med 12:234–235
4. Reaven GM, Chen YI, Coulston AM, Greenfield MS, Hollenbeck C, Lardinois C, Liu G, Schwartz H (1983) Insulin secretion and action in noninsulin-dependent diabetes mellitus. Is insulin resistance secondary to hypoinsulinemia? Am J Med 30:85–93

P. Lee · J. R. Greenfield · J. R. Center · L. V. Campbell
Department of Endocrinology, St Vincent's Hospital, Sydney, Australia

J. R. Greenfield · L. V. Campbell
Diabetes Centre, St Vincent's Hospital, Sydney, Australia

P. Lee (✉) · J. R. Greenfield · J. R. Center · L. V. Campbell
Garvan Institute of Medical Research, 384 Victoria Street, Sydney, NSW 2010, Australia
e-mail: p.lee@garvan.org.au
Tel.: +61-2-92958486
Fax: +61-2-92958481