Incretins and the anaesthetist: a systematic review

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Introduction

Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulintropic peptide (GIP) are incretin hormones. By lowering blood glucose in a glucose-dependent manner, incretin-based therapies represent a novel and promising intervention to treat hyperglycaemia in hospital settings. We performed a systematic review of the literature for a full scope of current applications of incretin-based therapies in the perioperative and critical care setting.

Methods

We searched MEDLINE, the Cochrane Library, and EMBASE databases for all randomised controlled trials using exogenous glucagon-like peptide 1 (GLP-1), GLP-1 receptor agonists, exogenous glucose-dependent insulintropic polypeptide (GIP), and dipeptidyl peptidase-IV inhibitors in patients during surgery or critical illness. Outcomes of interest included blood glucose, frequency of hypoglycaemia and insulin administration.

Results

Of the 1190 articles identified during the initial literature search, 38 fulfilled criteria for full text review and 19 single-centre studies were subsequently included in the qualitative review. Of the 18 studies reporting glycaemic control, improvement was reported in 15, defined as lower glucose concentrations in 12 and as reduced insulin administration (with similar glucose concentrations) in 3 studies. Due to heterogeneity, meta-analysis was only possible for the outcome of hypoglycaemia. This revealed an incidence of 7.4% in those receiving incretin-based therapies and 6.8% in comparator groups ($p = 0.94$).

Study (Author, year)	Effect of Intervention		Threshold hypoglycaemia	Incidence hypoglycaemia				Weight	Odds Ratio M-H, Random, 95% CI	p value	Odds Ratio M-H, Random, 95% CI
	Glycaemia	Insulin given		Incretin		Comparator					
				n	group	n	group				
Besch, 2017	No effect	Lower	3.3 mmol l ⁻¹	2	53	1	51	8.1%	1.96 [0.17, 22.32]	.58
Brackbill, 2012	No effect	No effect	3.3 mmol l ⁻¹	5	30	2	32	12.9%	3.00 [0.54, 16.81]	.06	
Deane, 2010	Lower	-	3.0 mmol l ⁻¹	0	25	0	25		Not estimable	1	
Galiatsatos, 2014	No effect	No effect	2.8 mmol l ⁻¹	1	9	3	9	7.8%	0.25 [0.02, 3.04]	.58	
Garg, 2017	Similar	Lower	3.9 mmol l ⁻¹	1	33	1	33	5.7%	1.00 [0.06, 16.69]	1	
Holmberg, 2014	-	-	4.0 mmol l ⁻¹	8	21	0	41	6.1%	52.26 [2.83, 966.6]	.003	
Kar, 2015	No effect	-	Not stated	0	24	0	24		Not estimable	1	
Kohl, 2014	Lower	-	3.8 mmol l ⁻¹	0	37	0	40		Not estimable	1	
Lips, 2017	Lower	-	3.3 mmol l ⁻¹	2	19	4	19	11.9%	0.44 [0.07, 2.76]	.12	
Meier, 2004	Lower	-	4.0 mmol l ⁻¹	0	8	0	8		Not estimable	1	
Mussig, 2008	Similar	Lower	Not stated	0	10	0	10		Not estimable	1	
Pasquel, 2017	Similar	Lower	3.9 mmol l ⁻¹	13	138	17	139	24.7%	0.75 [0.35, 1.60]	.45	
Polderman, 2014	Lower	Lower	4.0 mmol l ⁻¹	1	44	5	106	9.5%	0.47 [0.05, 4.14]	.26	
Sokos, 2007	Lower	Lower	3.3 mmol l ⁻¹	1	10	2	10	7.4%	0.44 [0.03, 5.88]	.39	
Umpierrez, 2014	Similar	Lower	3.9 mmol l ⁻¹	3	56	2	26	11.8%	0.68 [0.11, 4.33]	.86	
Total (95% CI)					484		540	100%	0.97 [0.47, 2.02]	.94	
Total events				37		37					

Heterogeneity: Tau² = 0.39 Chi²=12.94, df = 9 (p = 0.17); I² = 30% Test for overall effect: Z = 0.08 (p = 0.94)

favours comparator favours incretin

Conclusion

In small single-centre studies, incretin-based therapies lowered blood glucose, and reduced insulin administration without increasing the incidence of hypoglycaemia.