Pharmacokinetics of Intravenous Glucagon in Children with Hyperinsulinaemic Hypoglycaemia

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Background

- Hyperinsulinaemic hypoglycaemia (HH) causes severe hypoglycaemia in children.
- Diazoxide is the first-line treatment for HH. Glucagon infusion is used to achieve normoglycaemia if children are unresponsive to diazoxide.

Aims

- To evaluate the efficacy, safety and pharmacokinetics of intravenous (IV) glucagon therapy in children with HH.

Results

- There were 13 children included in the study (1 excluded as had very high glucagon concentration)
- Mean log glucagon (LnGlucagon) concentration at glucagon dose 1mcg/kg/hour (4 patients), 2.5mcg/kg/hour (4 patients) and 5mcg/kg/hour (4 patients) were 3.296±0.448, 4.446±1.426 and 3.928±1.018 respectively (table 1). Overall mean LnGlucagon concentration is 3.88 ± 1.12.
- Significant difference seen between dose of 1 mcg/kg/hour with 2.5 and 5 mcg/kg/hour whereas no significant difference seen between 2.5 and 5 mcg/kg/hour dose (table 2).
- LnGlucagon concentration has significantly increased with doses 1mcg/kg/hour, 2.5mcg/kg/hour and 5mcg/kg/hour (figure 1) (p-value <0.001) . There is strong positive correlation (r=0.619, p-value=0.011) between glucagon dose 5mcg/kg/hour and blood glucose concentration.
- All patients were responsive to 2.5mcg/kg/hour of IV glucagon (except 1 who had dose increased to 5 mcg/kg/hour but had little effect on blood glucose concentration).

Table 2 - Post Hoc test for multiple comparisons between glucagon dose

Glucagon Dose (mcg/kg/hour)		Mean Difference	Std. Error	p-value	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2.5	-1.1498	0.25178	<0.001	-1.7660	-0.5336
	5	-0.6311	0.24768	0.040	-1.2373	-0.0250
2.5	5	0.5187	0.25178	0.113	-0.0975	1.1348

Methods

- Children admitted for management of HH were included in the study.
- Plasma glucagon concentrations measured by radioimmunoassay (in pmol/l) were collected at times 0min, +30min, +60min, +90min after initiation of IV glucagon infusion (at 1mcg/kg/hour; 2.5mcg/kg/hour and 5mcg/kg/hour respectively). Also, capillary blood glucose was measured at the same times.
- Glucagon concentrations were checked for normality assumptions. As the data is skewed and more variable, log transformation was done to analyse it.

Figure 1 – This figure shows marginal means of LnGlucagon concentration at doses of 1 mcg/kg/hour (blue), 2.5 mcg/kg/hour (green) and 5 mcg/kg/hour (yellow) at time points 0 min, 30 min, 60 min, 90 min

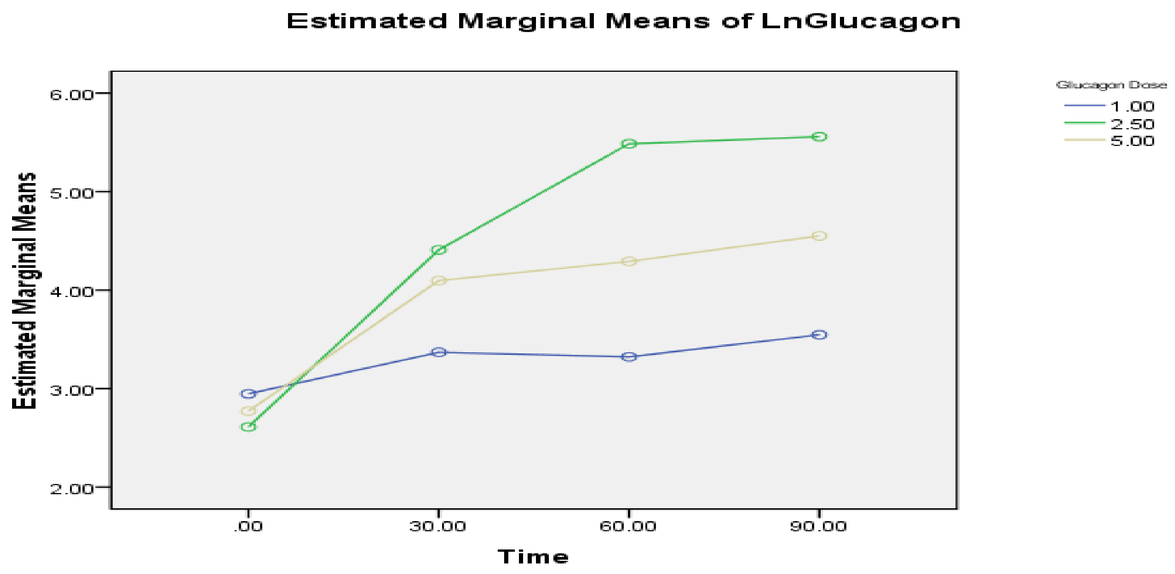

Table 1 - Mean and SD glucagon for 1, 2.5 and 5 mcg/kg/hour at 0, 30, 60 and 90 minutes. Mean glucagon concentration increases at each time period. Hence interaction effect (combined effect) of glucagon dose and time had significant effect on outcome (*very high glucagon concentration)

Glucagon Dose (mcg/kg/hour)	Time (min)	Mean LnGlucagon	N	Std. Deviation
1	0	2.9475	4	0.14305
	30	3.3690	4	0.20139
	60	3.3228	4	0.44099
	90	3.5469	4	0.70151
2.5	0	2.6111	4	0.16090
	30	4.4089	4	1.33382
	60	5.4858	4	0.61811
	90	5.5574	3*	0.43959
5	0	2.7715	4	0.24422
	30	4.0966	4	0.88449
	60	4.2916	4	1.04529
	90	4.5510	4	0.85299

Conclusion

- This study shows that 2.5-5mcg/kg/hour of IV glucagon can significantly increase blood glucose concentration. Glucagon concentration is significantly increased in first 30 minutes of starting IV infusion.
- These data will aid clinicians in the management of HH.

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Authors have nothing to disclose

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