

# Pancreatic Glucagon secretion is severely impaired and Somatostatin secretion unchanged in patients with Hyperinsulinaemic Hypoglycaemia

## BACKGROUND

- Hyperinsulinaemic hypoglycaemia (HH) is a common cause of hypoglycaemia in children.
- The interactions between blood glucose (BG),  $\beta$ -,  $\alpha$ -, and  $\delta$ -cells: Somatostatin (or more generally the  $\delta$ -cells) is stimulated by Glucagon ( $\alpha$ -cells) and BG; Glucagon ( $\alpha$ -cells) is inhibited by the  $\delta$ -cells (by Somatostatin) and by  $\beta$ -cell signals; and BG stimulates the  $\beta$ -cells. This network could easily explain the glucose counter regulation response to hypoglycaemia.
- Hypoglycaemia would decrease both  $\beta$ - and  $\delta$ -cell activity, which would entail increased release of Glucagon from  $\alpha$ -cells after the suppression from the neighbouring  $\beta$ - and  $\delta$ -cells is removed. However, it is not apparent whether this network can explain the defect in glucose counter regulation observed in  $\beta$ -cell deficiency or HH.
- Glucagon is an important counter-regulatory hormone and the role of somatostatin is not known in children with HH.

## RESULTS

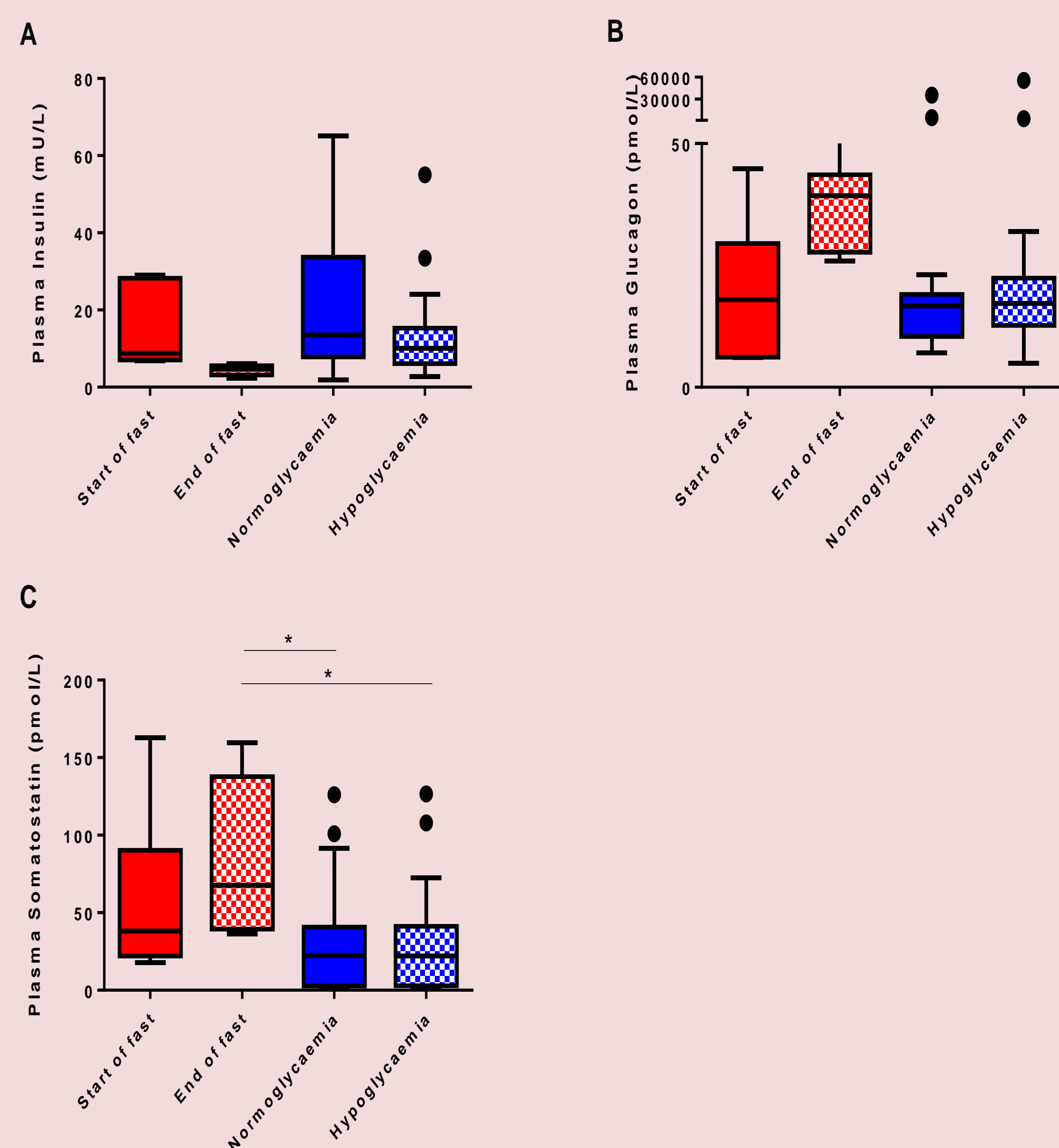
- There were 26 children with HH and 7 children as controls included in the study.
- The Median age was 2 months in HH group and 5 months in normal group.
- The ratio of M: F - 12:14 in HH group and 4:3 in normal group.
- Both mean and median were different and hence 50<sup>th</sup> centile (Q2 or median) is considered for calculation.
- The median insulin (mU/L), Glucagon (pmol/L) and Somatostatin (pmol/L) concentration at the start and at the end of the fast were 12.75 and 7.75; 16.8 and 16.05; 24.0 and 22.45 respectively.
- In the normal group, the median insulin (mU/L), Glucagon (pmol/L) and Somatostatin (pmol/L) concentration at the start and at the end of the fast were 8.6 and 4.1; 18.0 and 39.3; 38.1 and 67.8 respectively.
- Among HH patients, median insulin concentration was significantly increased at the start of fast compared to end of fast (p-value = 0.001). There was no significant change in glucagon and somatostatin concentration at the start and at the end of the fast (at the time of hypoglycaemia) (p-value >0.05).
- Among control group, median insulin concentration was significantly decreased and glucagon concentration was significantly increased (p-value < 0.05) at the end of the fast respectively. However, there was no significant change in somatostatin concentration at the start and end of the fast (p-value >0.05).

## OBJECTIVE

To understand the roles of glucagon and somatostatin in children with HH.

## METHODS

- Children admitted for management of HH had plasma insulin, glucagon and somatostatin collected at the start (normoglycaemia) and end of the fast or at the time of hypoglycaemia.
- Glucagon and somatostatin were measured by radioimmunoassay.
- Descriptive statistics mean, standard deviation (SD) and three quartiles (Q1, Q2 & Q3) were obtained to check normality assumptions for patients with HH and control group respectively.
- Ethical and R&D approval was obtained.



## CONCLUSION

- This study suggests that in HH Glucagon secretion is severely impaired from the  $\alpha$ -cell whereas Somatostatin secretion from the delta-cell is unaffected.
- The mechanisms that lead to impaired Glucagon secretion in HH are not clearly understood. Blunted Glucagon response may be related to prolonged hyperinsulinemia, causing a selective blunting of the plasma Glucagon response to hypoglycaemia, intra-islet hyperinsulinaemia, or defects in  $\alpha$ -/ $\beta$ -cell communication secondary to loss of SUR1/Kir6.2 type  $K_{ATP}$  channels at least in those patients with diffuse disease.
- HH is therefore associated not only with unregulated insulin secretion but also with impaired Glucagon counter regulation. Thus, relative deficiency of serum Glucagon counter regulation is another factor that predisposes these children to severe hypoglycaemia.
- Somatostatin does not seem to have any significant role as a gluco-regulatory hormone in patients with HH.

## REFERENCES

HUSSAIN, K., BRYAN, J., CHRISTESEN, H. T., BRUSGAARD, K. & AGUILAR-BRYAN, L. 2005. Serum Glucagon counterregulatory hormonal response to hypoglycemia is blunted in congenital hyperinsulinism. *Diabetes*, 54, 2946-51.