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Variation in 24 hour basal insulin requirements with age in children and young people (CYP) with type 1 diabetes mellitus (T1DM)

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Introduction

- Insulin requirements in children and young people with type 1 diabetes change with age. This is reflected in basal insulin requirements which are independent of dietary intake and will be influenced by growth hormone secretion as well as pubertal hormones in the adolescent age group.
- The central circadian clock controls many biological rhythms including the light-dark cycle and energy metabolism. There is evidence that insulin itself can modulate the central circadian clock[1].
- Little is known of the impact of age on the circadian variation in insulin secretion.
- We have studied changes in insulin basal rates as a proxy for insulin sensitivity in CYP with well controlled T1DM.
- Understanding this circadian variation is important in advising children and young people with type 1 diabetes on changes to basal rates with age. When the nocturnal basal rates change, young people and their families may be more anxious about the risk of undetected hypo or hyperglycaemia.
- Many centres will use basal rate time blocks to determine starting basal rates. Others will hourly rate changes determined by pump software packages using data extrapolated from adult studies to determine an hourly basal rate profile [2].
- Most insulin pumps will allow up to 48 basal rate changes per 24 hour clock.

Methods

- We examined routine pump download data from Children and Young people attending diabetes clinics at University College London Hospital.
- Insulin pump settings for total daily dose (TDD) and sensitivity ratio were obtained from 22 children and young people with type 1 diabetes and documented good glycaemic control.
- There were 9 males/13 females aged 4-14.5 years.
- Height and weight data from the time of pump download were used to calculate BMI.
- Basal insulin requirements were calculated for 4 time blocks 00:00-06:00h, 06:00-12:00h, 12:00-18:00h and 18:00-24:00h.
- Insulin settings were related to age, sex and body mass index (BMI).
- We compared the differences in insulin requirements across the four time blocks for age, gender, BMI and HbA1c
- Linear regression was used to compare the relationship between the basal rates and age at different time blocks and slopes and intersects of the equation compared
- We also used linear regression to evaluate the effect of age on sensitivity ratio and HbA1c

Results

- For the 22 children and young people studied:
- The total daily dose was 0.9Units/kg for males and 0.7Units/kg for females (P=0.03).
- There were no differences between the sexes for age, BMI or HbA1c.
- For every 1 year increase in age HbA1c declined by 0.13% (P=0.02).
- The sensitivity ratio was inversely related with age (r= -0.65; P=0.006) with no effect of sex or BMI.
- The Total basal insulin increased with age.
- The coefficient for this increase was highest (0.11) for the time period 00:00-06:00h compared to the other time periods; 06:00-12:00h (0.09), 12:00-18:00h (0.03) and 18:00-24:00h (0.05).

	00:00-06:00h	06:00-12:00h	12:00-18:00h	18:00-24:00h
Coefficient beta	0.11	0.09	0.03	0.05
P value	<0.001	<0.001	P =0.04	P = 0.001
Mean Basal insulin rate (units/hr)	0.53 (0.4)	0.58 (0.46)	0.52 (0.45)	0.66 (0.49)

Discussion

- These data suggest that there is an age effect on the circadian variation in insulin sensitivity as reflected in basal insulin delivery rates.
- This change is most evident between 00:00-06:00
- The change in insulin sensitivity decreases with age across the whole study population and is not influenced by sex or BMI.
- Although Growth Hormone has been implicated in the pubertal alterations these data would suggest that other factors, either intrinsic or extrinsic, may influence insulin sensitivity through childhood and adolescence.
- Establishing circadian profiles in the context of age, may help with setting the pump basal rates more accurately.
- Understanding the insulin sensitivity in the context of the circadian profile, may also guide to the setting of the insulin sensitivity ratios.

References

[1] Challet, E. Keeping circadian time with hormones. Diabetes, Obesity and Metabolism17 (Suppl. 1): 76–83, 2015

[2] Bachran et al. Basal rates and ciracdian profiles in continuous cubcutaneous insulin infusion (CSII) differ in preschool children, prepubertal children, adolescents and young adults.