

Age at onset of weight gain in Prader-Willi syndrome is often between 1 and 2 years, preceding the hyperphagic phase; implications for management

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Introduction

The classic 2-stage model of nutritional status in Prader-Willi syndrome (PWS) – initial failure to thrive due to hypotonia and poor feeding, followed by hyperphagic obesity (Figure 1) – has been replaced by a more complex 7-stage concept which includes a period aged 20-31 months during which weight increases without an obvious change in appetite (Miller et al, 2011)

Aim of study

To examine trends in body mass index (BMI) in order to determine a particular age zone at which inappropriate weight gain begins in preschool children with PWS.

Methods

BMI was plotted for each clinic visit in patients attending the PWS clinic at the Royal Hospital for Sick Children, Glasgow, over a 20-year period. BMI trends were categorised as showing a) no inappropriate increase in BMI (Fig 2); b) no definable age for BMI increase since child obese at referral (Fig 3); a definable age at which BMI increased (Figs 4 and 5).

Results

The case sheets of 76 patients were studied of which 36 had insufficient data for analysis, leaving 40 subjects (24M:16F) in whom onset of BMI increase could be categorised. Aetiology of PWS was: 15q deletion in 24 patients; maternal isodisomy in 15 patients; and imprinting centre mutation in one patient.

- No inappropriate weight gain had occurred in 10 patients by the time of study (see Figure 2). Seven were still young at 1.5-3.8 (median 2.8) years, with three patients aged 6.6, 11.5 and 15.2 years at last data point.
- Age at BMI increase was indeterminate in 9 patients, all of whom were obese at age of first data point (see Figure 3). Median (range) age at presentation in this group was 3.2 (2.4-5.0) years.
- Age at onset of BMI increase could be ascertained in 21 patients (see Figures 4 and 5).
- While their median (range) age was 2.0 (0.5-3.8) years, nine patients showed onset of BMI increase at ≤ 1.5 years; with onset 1.8 – 2.0 years in four patients, and ≥ 2.3 years (2.3, 2.5, 2.5, 2.6, 2.8, 2.8, 3.8 and 3.8 years) in the remaining eight patients.

No significant correlation could be found between age at onset of BMI increase and either gender or genotype.

Discussion

- Our data support the observation that weight gain in PWS may start **before** hyperphagia has become an obvious behavioural feature (e.g. 2-4 years).
- The median age at onset of BMI increase in our series was 24 months, which is within the 20-31 month range described by Miller et al.
- However, nine of 21 patients in whom age at BMI increase could be ascertained were aged 18 months or younger.

Figure 1 At what age did the trend towards weight gain start in this boy with Prader-Willi syndrome?

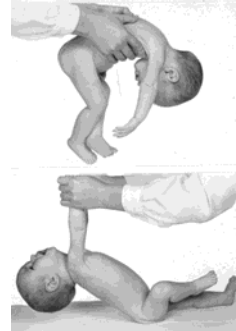


Figure 2 No inappropriate increase in BMI trend

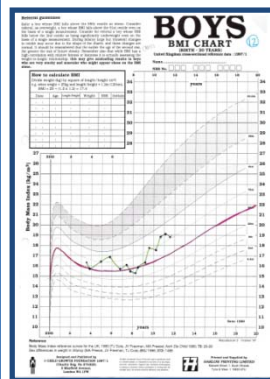


Figure 4 Age at BMI ascertainable boy becoming obese

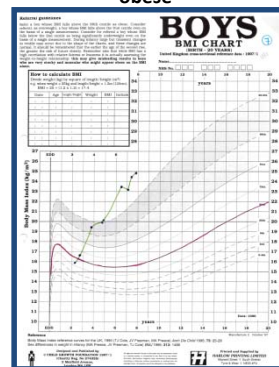


Figure 3 Age at BMI increase not ascertainable (obese at presentation)

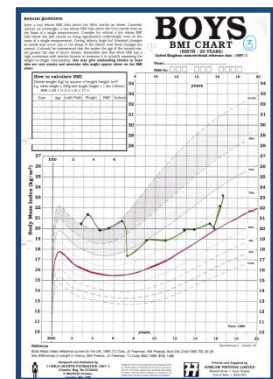


Figure 5 Age at BMI increase ascertainable in patient responding to diet

Conclusion

- The phenomenon of weight gain preceding hyperphagia in PWS is attributable a decrease in energy expenditure due to hypotonia, which is particularly marked in the early years.
- A dual approach to management is needed from an early age:
 - giving a diet which is appropriate to age and body size
 - increasing energy expenditure to reach that of normal children (rather than reducing intake to offset the effect of the hypotonia)
- Practical measures to increase activity in infants and preschool children with PWS, including regular swimming, should be explored with the family.