Gluten-free diet in children with recent onset type 1 diabetes: a 12 months intervention trial

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Background

- Gluten is considered a possible islet autoimmunity trigger since its pro-inflammatory effects have been observed in animal studies [1,2] the introduction of gluten after 9 months of age was associated with higher risk of autoantibodies occurrence [3] and its higher dose in pregnant women was associated with higher risk of type 1 diabetes (T1D) development in their offspring [4].
- Gluten-free diet (GFD) is a well established and safe intervention for coeliac disease yet its effect on T1D was not fully studied as of yet.

Aim

- We aimed to investigate the effect of GFD on the progression of T1D in non-coeliac children during the first year after the disease onset.

Methods

- 46 children with new onset T1D were recruited throughout the period of 2 years at two tertiary pediatric diabetes centres into this self-selected intervention trial (**Figure 1).**
- 26 subjects started with strict GFD while 20 remained on the standard diet at mean ± SD 37.8 ± 9.2 days after the diagnosis. The intervention assignment was decided by their their parents.
- The participants followed study protocol as detailed in **Figure 2**.
- At 6 and 12 months the subjects provided a detailed three-day food record and their daily nutrients intake was measured.
- At 12 months the standard quality of life (QoL) questionnaires [5] were filled out by the subjects and their parents.
- Intervention adherence was tested for all subjects based on gluten immunogenic peptides (GIP) presence in stool samples provided at each visit. The GIP positivity in one or more samples led to the subjects exclusion from statistical analysis.
- Data from 39 subjects (20 GFD, 19 controls) were subject to analysis at 12 months. Linear and longitudinal regression models adjusted for baseline values were used for the analysis of the outcomes.

Figure 1 - Study flowchart

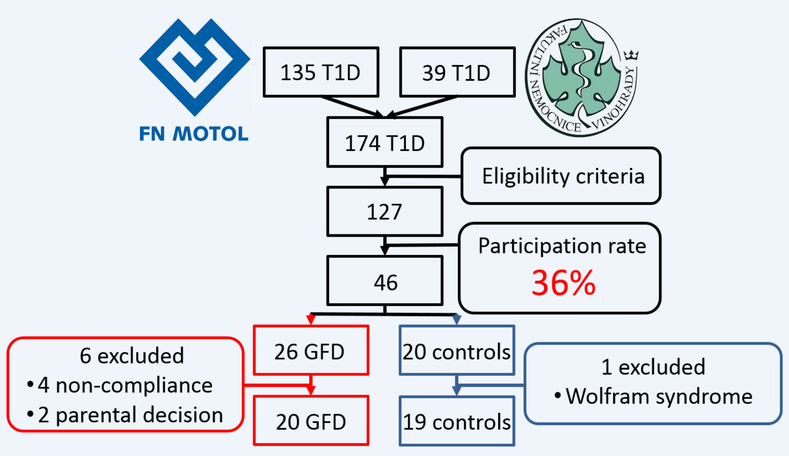
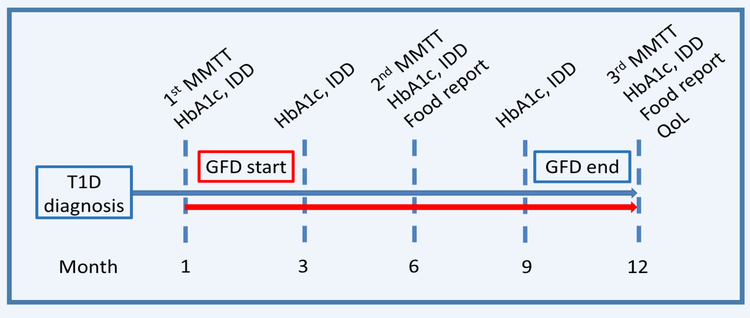


Figure 2 - Study protocol



Results

- At 12 months the groups did not differ significantly in their mean decrease of C-peptide AUC (p=0.34) (**Figure 4**) nor their insulin dose (p=0.07) (**Figure 5**).
- The GFD group achieved a significantly lower HbA1c 7.8 mmol/mol (p=0.02) (**Figure 6**) and lower IDAA1c by 1.4 (p=0.01) (**Figure 7**) at 12 months.
- In a longitudinal analysis of all three time points, C-peptide declined more slowly in the GFD group than in controls, with the difference in trends being 409 pmol/l/year (p = 0.04).
- Partial clinical remission as defined by IDAA1c<9 [6] was achieved in 71.4% GFD as compared to 31.6% control subjects (p=0.03).
- The GIP were found in the stool of four subjects which were subsequently excluded from the analysis. Stools of the control group subjects were all positive for GIP.
- The groups did not differ significantly in their carbohydrate, fat nor protein intake per day at 6 and at 12 months (**Table 1**).
- There was no observable difference in the QoL between the subjects (p=0.70) nor their parents (p=0.60).

Figure 4 - Comparison of C-peptide AUC between the groups (p=0.34).

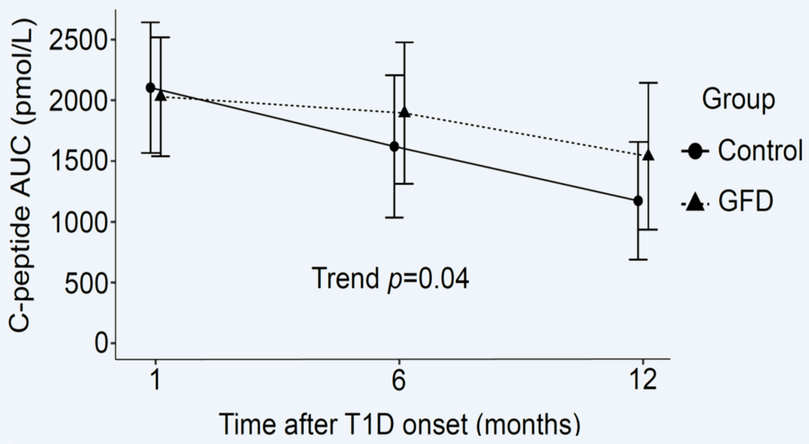


Figure 5 - Comparison of daily insulin dose between the groups (p=0.08).

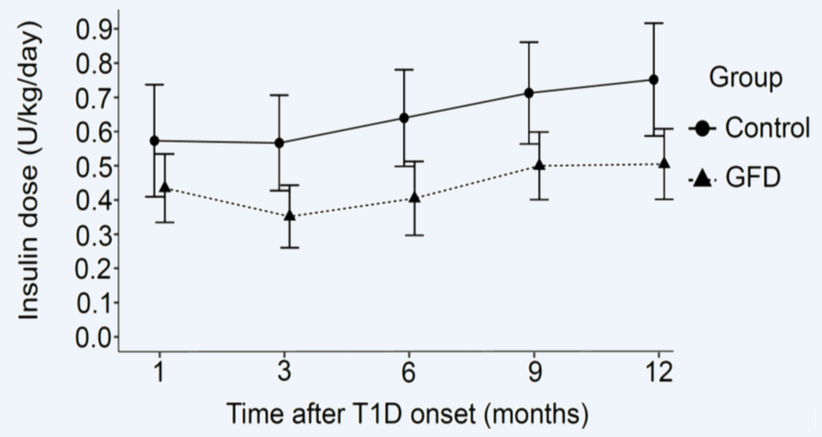


Figure 6 - Comparison of HbA1c between the groups. *p=0.02

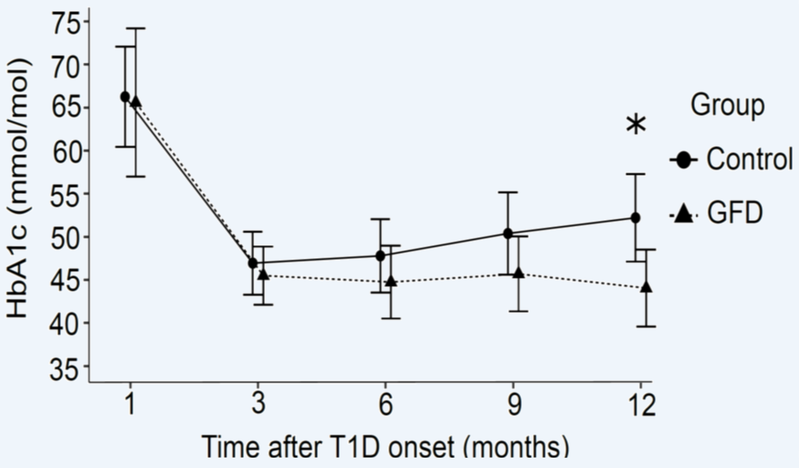


Figure 7 - Comparison of insulin dose adjusted A1c between the groups. *p=0.01

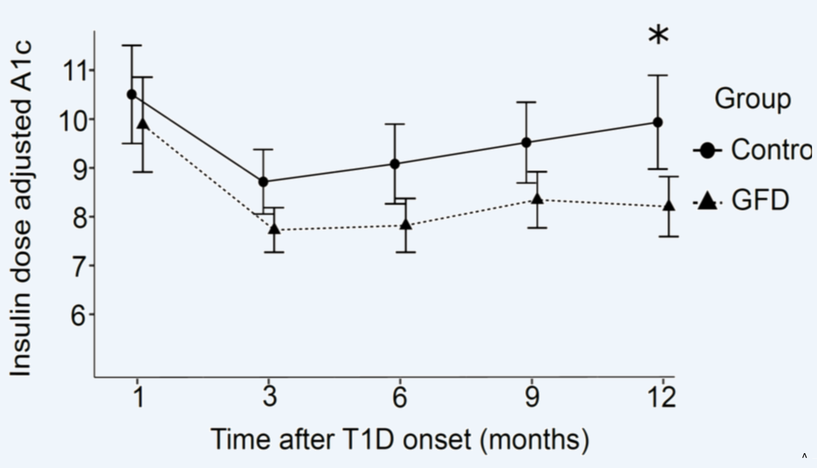


Table 1 - Comparison of major nutrients intake between the groups

	Gluten-free diet (6 months)	Standard diet (6 months)	p-value	Gluten-free diet (12 months)	Standard diet (12 months)	p-value
Carbohydrates (g/day)	210.7	214.1	0.86	220.9	208.1	0.49
Fats (g/day)	83.6	84.2	0.93	82.3	78.6	0.67
Proteins (g/day)	79.6	79.9	0.95	77.5	76.5	0.90

Conclusions

- Our results indicate that GFD is associated with slower pace in the decline of beta-cell capacity, better metabolic control and longer and more pronounced partial remission period without negatively influencing the quality of life.
- The physiological pathways through which such an effect might be exerted as well as the therapeutic potential of GFD remains to be studied.

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Photography encouraged

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Diabetes and insulin

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