Central Manchester and Manchester Children's University Hospitals NHS Trust

Cambridge University Hospitals NHS Foundation Trust

Dietary intervention in children receiving substrate reduction therapy with miglustat (Zavesca®▼)

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Introduction

The iminosugar miglustat, inhibits glucosylceramide synthase, the initial enzyme in the formation of glycosphingolipids, offering a therapeutic approach to the treatment of Type 1 Gaucher disease and investigation into related lysosomal storage disorders. Reported side effects include watery diarrhoea, flatulence, abdominal cramps, nausea, weight loss and poor appetite. Miglustat inhibits sucrase-isomaltase and other disaccharidases in the small intestinal mucosa, to which its unwanted abdominal effects are attributed. A diet low in lactose or low in all disaccharides could be beneficial in alleviating gastrointestinal side effects and preventing associated weight loss. The neurological outcome of these patients is not discussed herein.

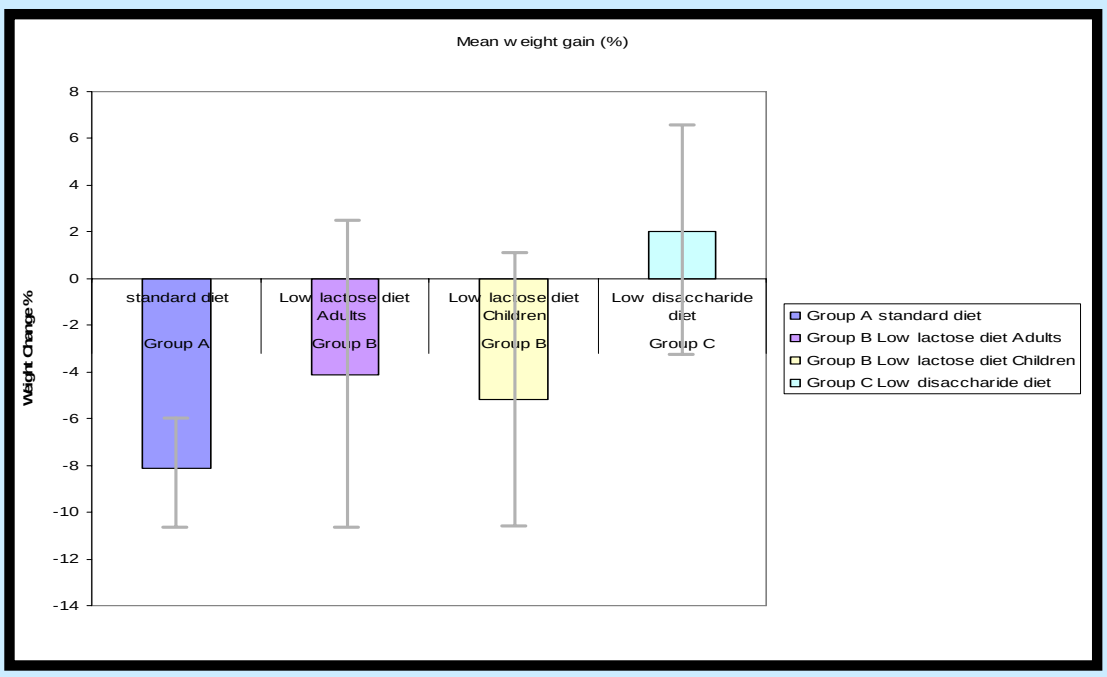
Methods

- We performed retrospective analysis on the effect of dietary modification over a six month period on 29 patients with related lipidosis treated with miglustat (Sandhoff's Disease, GM1 Gangliosidosis, Niemann-Pick Disease Type C).
- The age range was 1-39 years. Patients aged 0-20 years were defined as children/young adults and >20 years as adults.
- Group A were supported with a standard unmodified diet with milk-based supplements containing lactose to increase energy provision (n=5).
- Group B received a diet low in lactose but containing other disaccharides and refined carbohydrates (n=19).
- Group C received a modified diet, low in disaccharides but containing complex carbohydrate and maltodextrins (n=5).

	Group A Standard Diet Children n=5	**Group B** Low Lactose Diet Adults n=8	**Group B** Low Lactose Diet Children n=11	**Group C** Low Disaccharide Diet Children n=5
Mean age (years)	13.5	30.5	12.5	10.2
Mean weight gain (%) (SD shown in brackets)	-8.1 (± 2.2)	-4.1 (± 6.7)	-5.2 (± 6.1)	+2 (± 4.8)

Results

- All patients in Group A experienced loose stools resulting in missed schooling despite the use of loperamide, an anti gut motility agent used to control episodes of diarrhoea. These symptoms were experienced but controlled with loperamide in Group B. Gastrointestinal disturbance was not generally experienced in Group C.
- Weight loss: Patients on the standard diet experienced the greatest weight loss. Almost all patients on the low lactose diet experienced weight loss. Patients on the diet low in disaccharides had a mean weight gain.
- The range of weight variation for the patients on a low disaccharide diet (Group C) was large, however the trend seen was to improved body weight.



Conclusion

Retrospective analysis of the data from 29 patients receiving therapy with miglustat shows that with dietary modification, weight gain during treatment can be maintained in line with weight gain potential, and most episodes of gastrointestinal disturbances can be avoided. A diet low in disaccharides was most effective in maintaining expected weight gain in children/young adults, and commencing dietary intervention prior to starting miglustat provided best results. Adequate provision of energy can be obtained from fats, maltodextrins and proteins, and can be successfully used to maintain predicted weight gain.

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