DIETARY MANAGEMENT OF GALACTOSEMIA

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Abstract. Galactosemia is detected by newborn screening in New South Wales and managed by the metabolic team at the Children's Hospital at Westmead. Infants with the Duarte variant are not treated. Management is based on the Handbook for Galactosemia prepared in 1998. This handbook provides information for the family on the dietary management, inheritance and ovarian function. The major dietary sources of galactose are milk and milk products. Breastfeeding must be ceased and replaced with a soy formula. Once solid foods are commenced certain foods should be avoided. Other foods, which may contain some free galactose are recommended in limited quantities only. There is no restriction on other fruits and vegetables. An ongoing issue with dietary management is adequate nutrient intake, particularly of calcium. Intake of milk substitutes and calcium supplements is often inadequate.

INTRODUCTION

Galactosemia is a defect in utilisation of galactose-1-phosphate via galactose-1-phosphate uridyltransferase (GALT; EC2.7.7.10). Galactosemia, with an incidence of 1:40,000, is diagnosed by newborn screening in New South Wales and managed by the metabolic team at the Children's Hospital at Westmead. Infants with the Duarte variant (expressed erythrocyte GALT activity at 50% of the normal level) are not treated. Management is based on the Handbook for Galactosemia, which provides information for the family on dietary management, inheritance and ovarian function (Working Party of Australasian Society for Inborn Errors of Metabolism, 1998). The galactose free diet which has been the basis of therapy since 1935, reverses the acute toxicity in infancy but has not prevented the later emergence of long term complications (Segal, 1998; Widhalm *et al*, 1997) of developmental delay, speech defects, ovarian function and ataxia syndromes, despite treatment beginning from day 1 in some groups. Suggested mechanisms are toxicity in utero, endogenous production of galactose and daily intake of small amounts of galactose (Widhalm *et al*, 1997; Acosta).

The major dietary sources of galactose are milk and milk products. Breastmilk contains 3.7 g galactose per 100 ml so breastfeeding must be ceased and replaced with a soy formula. Although casein hydrolysate formulas were originally the formulas of choice, these were found to contain traces of free galactose (2.5-17 mg galactose per 100 ml) (Acosta, manufacturers information). Soy

Table 1. Estimate of potential galactose intake.

*Food	Galactose content
Cows milk 250 ml	5.8 g free galactose
3 fruits (apple, banana, orange) and 3 vegetables (potato, pumpkin, French beans)	0.039 g free galactose
100 g tomato	0.5 g free and bound (availability unknown), 0.023 free galactose
100 g cooked soy beans	0.043 g free galactose
100 g soy flour	2.93 g free and bound (availability unknown)
100 g cooked chick peas (garbanzo beans)	0.444 g free galactose
1 egg	0.03 g bound (availability unknown)
20 g Cheddar cheese matured for 78 days	0.008 - 0.01 g free (more mature cheese contains less)

formula contains some bound galactose (eg Isomil 1.4 mg/100 ml). The availability of this bound galactose is under question (see below). Once solid foods are started there are further issues concerning galactose sources. Table 1 gives estimates of potential intake.

Once solid foods are commenced the Handbook for Galactosemia (Working Group for Australasia Society of Inborn Errors of Metabolism, 1998) recommends that the following foods be avoided:

- Milk and milk products, except for mature cheese in which the galactose has been broken down during the production process. These foods are major sources of lactose, which consists of a unit of glucose and a unit of galactose. It is important for patients and their families to understand that low lactose or lactose reduced products may still contain their full quota of galactose. During the maturing process of cheese, however, the majority of galactose is broken down. In view of the usefulness of cheese as a contributor of calcium in the diet, cheeses with less than 0.1% galactose (100 mg per 100 g cheese) may be included.
- Lactose, used as an ingredient and carrier for flavour in foods, as well as in some medications. Lactose is used as a carrier of flavourings and salt in foods. In Australia, The Smith's Snackfood Company has provided data to show that the flavour can contain between 8.8% and 42% lactose. This can result in a product with up to 11.3% lactose (2.8 g lactose per 25 g packet of extruded cheese snacks, 0.55 g lactose per 25 g packet flavoured potato chips). Families also need to check the use of lactose as a flavour carrier in take-away foods.
- Chickpeas (garbanzo beans), beans or gram flour, hommos, dahl and felafel made on chickpeas.
- Fermented soy products eg miso, tempeh, some soy sauce where bound galactose may be released.

Other foods which may contain some free galactose, such as Lima beans, kidney beans and lentils, and organ meats (liver, kidney, and brains) are recommended in limited quantities only. There is no restriction on other fruits and vegetables. Galactose may be present in some other foods in its free or bound form. Bound forms (Gross and Acosta, 1991) include:

- The oligosaccharides raffinose and stacchyose in cereals, beans, some vegetables
- Alpha galactosides in acacia (gum arabic), agar, carageenan and tragacanth
- Galactans and galactolipids in plant cell walls and chloroplasts
- With protein in egg
- With carbohydrate (D-galactosamine, cerebrosides and gangliosides) in shell fish
- Galactosides in organ meats (brain, liver, kidney, pancreas)

The availability from bound galactose in these foods is not known. For example it is disputed as to whether breakdown of galactans and galactolipids by beta galactosidase occurs in the gut (Knight, 1992; Acosta and Gross, 1995). Acosta (Acosta and Gross, 1995) raises the issue that fermentation, eg in the preparation of miso, some soy sauces, sauerkraut, releases galactose. Measurements of soluble galactose in fruit range from 1 to 35 mg per 100 mg, and in vegetables from 0-11 mg / 100 mg (Gross and Acosta, 1991). The problems in considering these issues for Australian patients are that there are no Australian analyses and the American analyses are of limited sample size. A wide variation can be expected with reports that galactose increases 4-6 times in the ripening of tomatoes. In light of the role that fruit and vegetables play in nutrition, it is important not to restrict them unnecessarily. Two studies question the need to be concerned about these smaller amounts of galactose. A study (Berry *et al*, 1995) in 1995 measured, for the first time, endogenous galactose production. Subjects were 3 adults without galactosemia and 3 with galactosemia, who were given isotopically labelled galactose in a continuous intravenous infusion. The galactose production rate was 1.1, 2, and 2.1 g per day in controls and 1.1, 1.2 and 1.3 in subjects with galactosemia. The authors hypothesize that the results may represent a minimal rate of synthesis because some of the isotopically labelled galactose may be recycled. On the basis of these observations, the authors suggest that minute dietary galactose manipulations may have no substantial effects on galactosemic patients. An earlier study (Berry *et al*, 1993), also reported that adding 200 mg galactose to the baseline low lactose diet of two patients with galactosemia had no effect on red blood cell galactose-1-phosphate levels.

ENSURING NUTRITIONAL ADEQUACY

An ongoing issue in dietary management is adequate nutrient intake, particularly calcium. Intake of milk substitutes and calcium supplements is often inadequate in galactosemia patients and others on milk free diets (Thompson, 2000a,b; Kaufman *et al*, 1993). In a group of children and adults with galactosemia from our own clinic, 13 of the 15 drank soy drink with a mean intake of only 154 ml per day, only 5 consumed soy yoghurts or custard and 5, mature cheese. Even with encouragement to take calcium supplements if intake of soy products was low, only 4 did so. Families therefore need advice on

optimising intake from foods and on appropriate supplements if dietary intake is inadequate.

REFERENCES

Acosta PB. Future clinical research: Nutrition support for the patient with galactosaemia B. In Galactosaemia : new frontiers for research. Washington: NIH, pp. 41-52.

Acosta PB, Gross KC. Hidden sources of galactose in the environment. *Eur J Pediatr* 1995; 154 7 (suppl 2): S87-S92.

Berry GT, Nissim I, Lin Z, Mazur A, Gibson J, Segal S. Endogenous synthesis of galactose in normal men and patients with hereditary galactosaemia. *Lancet* 1995; 346:1073-4.

Berry GT, Palmieri M, Gross MC, *et al.* The effect of dietary fruits and vegetables on urinary galactitol excretion in galactose - I phosphate uridyltransferase deficiency. *J Inher Metab Dis* 1993; 16: 91-100.

Gross KC, Acosta PB. Fruits and vegetables are a source of galactose: Implications in planning the diets of patients with galactosaemia. *J Inher Metab Dis* 1991; 14: 253-8.

Kaufmàn F, Loro M, Azen C, Wenz E, Gilsanz V. Effect of hypogonadism and deficient calcium intake on bone density in patients with galactosaemia. *J Pediatr* 1993; 123: 365-70.

Knight A. Diet in galactosaemia: a review. *Aust J Nutr Diet* 1992; 49: 87-9.

Segal S. Galactosaemia today: the enigma and the challenge. *J Inher Metab Dis* 1998; 21: 455-71.

Thompson S. Nutritional pitfalls of milk-free diets. New Zealand Dietetic Assoc Proceedings 2000a; 96-98.

Thompson S, Arrowsmith F, Allen J. Nutritional intake of patients with galactosaemia. Proceedings Human Genetics Society of Australia 2000b.

Widhalm K, da Cruz MB, Koch M. Diet does not ensure normal development in galactosaemia. *J Am Coll Nutri* 1997; 16: 204-8.

Working Party of Australasian Society for Inborn Errors of Metabolism. "Handbook for galactosaemia". Human Genetics Society of Australia, 1998.