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Dietary practices in isovaleric acidemia: A European survey

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ABSTRACT

Background: In Europe, dietary management of isovaleric acidemia (IVA) may vary widely. There is limited collective information about dietetic management.
Aim: To describe European practice regarding the dietary management of IVA, prior to the availability of the E-IMD IVA guidelines (E-IMD 2014).
Methods: A cross-sectional questionnaire was sent to all European dietitians who were either members of the Society for the Study of Inborn Errors of Metabolism Dietitians Group (SSIEM-DG) or whom had responded to previous questionnaires on dietetic practice (n = 53). The questionnaire comprised 27 questions about the dietary management of IVA.
Results: Information on 140 patients with IVA from 39 centres was reported. 133 patients (38 centres) were given a protein restricted diet. Leucine-free amino acid supplements (LFAA) were routinely used to supplement protein intake in 58% of centres. The median total protein intake prescribed achieved the WHO/FAO/UNU [2007] safe levels of protein intake in all age groups. Centres that prescribed LFAA had lower natural protein intakes in most age groups except 1 to 10 y. In contrast, when centres were not using LFAA, the median natural protein intake met WHO/FAO/UNU [2007] safe levels of protein intake in all age groups. Enteral tube feeding was rarely prescribed.
Conclusions: This survey demonstrates wide differences in dietary practice in the management of IVA across European centres. It provides unique dietary data collectively representing European practices in IVA which can be used as a foundation to compare dietary management changes as a consequence of the first E-IMD IVA guidelines availability.

1. Introduction

Isovaleric acidemia (IVA) (McKusick 243500) is a rare inherited condition, caused by a deficiency of the mitochondrial enzyme isovaleryl-CoA dehydrogenase (EC 1.3.99.10), leading to accumulation of isovaleryl-CoA and its metabolites including free isovaleric acid, 3-hydroxyisovalerate and *N*-isovalerylglycine [1]. The major goal of IVA management is to reduce the production and increase excretion of isovaleryl-CoA. This is achieved by: 1) limiting leucine intake via protein restriction [2–4]; 2) enhancement of alternative metabolic pathways using carnitine [5,6] and glycine [7,8] which conjugate with isovaleryl-CoA to produce the non-toxic compounds isovalerylglycine and isovalerylcarnitine; and 3) application of an emergency management protocol at times of metabolic stress (e.g. illness and fasting). However, partly due to IVA's heterogeneity, its rarity, shortage of large, multi-centre longitudinal studies and long-term outcome data, there is disagreement regarding optimal dietary management. Almost all reports are from case studies or small case series only.

The first case studies of IVA reported signs of dietary protein intolerance typically with episodes of vomiting, lethargy and acidosis with ketonuria after increased intake of protein-rich foods [9,10]. Many patients maintain long term metabolic stability on dietary protein restriction only [1,11–18]. In fact, the majority of IVA case studies advise some protein restriction [1–7,9,11,14–16,19–30] but with wide differences in the amount of natural protein given. Some centres prescribe less than the WHO/FAO/UNU 2007 safe levels of protein intake [31] and may specifically calculate and control leucine intake supplemented with leucine-free L-amino acid supplements (LFAA) [3,5,22,23,26–29,32–35].

In September 2014, the web based E-IMD IVA guidelines [36] advocated that natural protein intake be restricted to reduce the isovaleric acid burden but should supply at least the WHO/FAO/UNU 2007 safe levels of protein intake [31]. The use of LFAA was not discussed [36] and some considered they may provide little clinical benefit and thus provide extra burden to patients and families and unnecessary expense to health services.

This paper aims to describe European practice regarding the dietary management of IVA prior to the introduction of the E-IMD IVA guidelines in 2014.

2. Material and methods

A cross-sectional questionnaire was sent to all European dietitians who were either members of the Society for the Study of Inborn Errors of Metabolism Dietitians Group (SSIEM-DG) or whom had responded to previous questionnaires on dietetic practice (n = 53) [37]. We requested dietitians cascade the questionnaire to other dietitians and/or physicians within their own country between July and August 2014. The questionnaire consisted of 27 multiple choice and short answer questions. The questions were aimed at patients on dietary treatment. The following data were collected by age group: total protein intake prescribed, amount of natural protein and use of LFAA. Specific questions were asked about: special low protein foods, energy, vitamin and mineral supplements, use of enteral feeding, monitoring, treatment criteria and treatment drugs. The results were divided into geographical regions to examine trends in protein prescription. The groupings were: Western Europe Group A (Netherlands, Belgium, France), Western Europe Group