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Metabolic Diet App Suite for inborn errors of amino acid metabolism

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ABSTRACT

Background: An increasing number of rare inborn errors of metabolism (IEMs) are amenable to targeted metabolic nutrition therapy. Daily adherence is important to attain metabolic control and prevent organ damage. This is challenging however, given the lack of information of disorder specific nutrient content of foods, the limited availability and cost of specialty products as well as difficulties in reliable calculation and tracking of dietary intake and targets.
Objectives: To develop apps for all inborn errors of amino acid metabolism for which the mainstay of treatment is a medical diet, and obtain patient and family feedback throughout the process to incorporate this into subsequent versions.
Methods & results: The Metabolic Diet App Suite was created with input from health care professionals as a free, user-friendly, online tool for both mobile devices and desktop computers (http://www.metabolicdietapp.org) for 15 different IEMs. General information is provided for each IEM with links to useful online resources. Nutrient information is based on the MetabolicPro™, a North American food database compiled by the Genetic Metabolic Dietitians International (GMDI) Technology committee. After user registration, a personalized dashboard and management plan including specific nutrient goals are created. Each Diet App has a user-friendly interface and the functions include: nutrient intake counts, adding your own foods and homemade recipes and, managing a daily food diary. Patient and family feedback was overall positive and specific suggestions were used to further improve the App Suite.
Discussion: The Metabolic Diet App Suite aids individuals affected by IEMs to track and plan their meals. Future research should evaluate its impact on patient adherence, metabolic control, quality of life and health-related outcomes. The Suite will be updated and expanded to Apps for other categories of IEMs. Finally, this Suite is a support tool only, and does not replace medical/metabolic nutrition professional advice.

1. Introduction

Inborn errors of metabolism (IEMs) although individually rare, form the largest group of monogenic disorders amenable to therapies targeting pathophysiology, often a lifelong dietary restriction combined with supplements and medications [1]. Examples include urea cycle defects, which require a protein restricted diet, arginine supplementation and emergency protocols with extra calories and fluids, to prevent hyperammonemia and accumulation of other toxic metabolites [2]. Expanded newborn screening (NBS) programs, increased awareness among clinicians, systematic evaluation of symptomatic patients (e.g. intellectual disability) and advances in diagnostic technologies (e.g. genome-wide sequencing) combined with discoveries of novel diseases and treatment approaches result in increased patient numbers. Consequently, physicians and dietitians are increasingly involved to counsel individuals affected by an IEM [3,4].

Strict adherence to disorder specific metabolic nutrition therapy (MNT) and medications can reduce the morbidity and improve patient outcomes [5]. Early and precise treatment can prevent complications such as severe neurological and other organ damage. In the best scenario, patients can develop at par with their peers [5,6]. Adherence to metabolic diets often interferes with social and cultural traditions, posing a burden for the patient and (extended) family alike [7]. Palatability issues as well as social, economic, educational, and motivational factors all challenge compliancy, and therefore impact metabolic control [8,9].

Phenylketonuria (PKU; OMIM# 261600) is the most common treatable IEM with an incidence of 1 in 10,000 births [10] and a Phenylalanine (Phe) restricted diet is the mainstay of treatment. Walter et al.

Abbreviations: DHT, digital health technology; GMDI, Genetic Metabolic Dietitians International; IEMs, inborn errors of metabolism; Leu, leucine; Lys, lysine; MSUD, maple syrup urine disease; MNT, metabolic nutrition therapy; Phe, phenylalanine; PKU, phenylketonuria; PDE, pyridoxine dependent epilepsy; NBS, newborn screening.

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(2002) found that blood Phe concentrations exceeded treatment ranges in 30% of children younger than 10 years of age and in 80% of adolescents (aged 15–19 years old) [11]. Poor metabolic control poses the risk of organ damage and negatively impacts health and overall functioning in patients with IEMs [11].

Tracking daily dietary intake of disorder specific amino acids is difficult since this information is not readily displayed on food labels. Patients and their caregivers are at risk of under- or over-estimating amino acid content of foods, and threatening metabolic control. To enhance availability of nutrient information and to simplify the task of diet tracking and meal planning, we developed a digital tool for patients and their caregivers. With mobile digital health technology (DHT) integrated in our daily lives, we expect that this Metabolic Diet App Suite will fill a useful gap and facilitate varied meal planning and treatment adherence for this growing group of rare disease patients.

2. Methods

2.1. Ethics board approval

The University of British Columbia regional ethics board approved the current survey study (H14-00,818.)

2.2. Parameters

For inclusion in this App Suite, we selected inborn errors of amino acid metabolism for which a dietary therapy is deemed 'standard of care'. In total, 15 different IEM disorder specific apps were created plus one general protein restriction diet app. The target user groups of this tool were defined as IEM patients and their caregivers as well as their health care professionals. This tool does not replace management and follow up visits with their physician and/or registered dietitian. It cannot be used as a replacement for complete diet assessments done using comprehensive tools such as GMDI's Metabolic Pro™ nutrient analysis program.

2.3. Access

This App Suite can be accessed free of charge online via http://www.metabolicdietapp.org (or the shortened URL http://mdapp.org). The App Suite can be viewed and used in the latest versions of all browsers (with a recommendation for Chrome, Firefox and Safari). Users are required to create a login to access and personalize the diet app on their desktop computers. Subsequently, based on the IEM chosen in the sign-up process, the user has access to his/her own digital database with food items on both their desktop computers and handheld devices (smartphones, tablets etc). All information entered into the App Suite is de-identified and encrypted via secure sockets layer (SSL) technology.

2.4. Data source

The nutrient values of foods were sourced from the Genetic Metabolic Dietitians International (GMDI) MetabolicPro™ food database accessed in 2014. MetabolicPro™ is a diet analysis program widely used by North American metabolic dietitians. The database contains nutrient information on over 100,000 food products. It is based on the U.S. Department of Agriculture's National Nutrient Databank for Standard Reference food composition database, with additional nutrient information on medical formulas and specialty low protein foods.

2.5. Survey methods

In phase 1, an online feedback survey (see supplementary materials for details) was developed for parents after testing the Diet App for pyridoxine-dependent epilepsy(due to *ALDH7A1* deficiency; OMIM# 266100). The feedback obtained was integrated to generate the second version of the PDE App and a first version of the PKU App. An additional feedback function was added to these Apps, which encouraged users to submit comments and questions to the developers (RH, JJ), allowing development of the model for cloning all 15 Diet Apps in the suite.

2.6. Design

Metabolic dietitians (KU, BC, AG), a metabolic diseases specialist physician (CvK), a nutrition sciences undergraduate student (GH), and two developers (RH, JJ) collaborated on the design and content of the tool.

Phase 1: Initially, we had compiled information from the USDA nutrient file version 26 [12]. In addition, nutrient values for low protein food items distributed to IEM patients in our province by the British Columbia Metabolic Nutrition Program (BCMNP) were manually added to the database. Once the database was complete, Health2Media translated it into the first version of the Diet App for Pyridoxine Dependent Epilepsy (PDE due to *ALDH7A1* deficiency) for mobile devices and subsequently for desktops. Physicians, registered dietitians and researchers at our tertiary care centre (BC Children's Hospital, Vancouver, Canada) tested the Diet App and parents of PDE patients were given access to pilot test the PDE diet app. Feedback was used to develop the next versions of the PDE Diet App.

Phase 2: After receiving feedback from the parents and health care providers, it was clear that the raw USDA foods database was not detailed enough for families on specialized metabolic diets counting daily amino acid dietary intakes, nor did it contain the many special foods and formulas required by these diets. We acquired a food composition database from GMDI used for their Metabolic Pro diet analysis program, which included food composition data for specialty low-protein foods and metabolic formulas in addition to the USDA food database selections. Once the GMDI database was implemented, the updated PDE Diet App and the new PKU Diet App were tested by physicians, metabolic dietitians and researchers, prior to being sent out to patients for beta-testing. An additional feedback function was added to the Apps, which allowed users to submit comments and questions to the developers, who subsequently used this to further improved the tools.

Phase 3: The Diet Apps for thirteen other IEM's were created based on the final versions for PDE and PKU. The functional design of each App is similar, but as its content is IEM-specific it displays only nutrients that are relevant to the selected IEM. Each Diet App has its own specific logo and color pattern, making it easily recognizable for users.

3. Results

3.1. General

The available functions were designed to aid users in the task of food counting and thereby improve dietary adherence. The diet app was devised to be user friendly with the use of lay language and distinctive icons. In total, diet apps were developed for 15 different IEMs: pyridoxine dependent epilepsy (MIM:266100), phenylketonuria (MIM 261600), maple syrup urine disease (MIM248600), methylmalonic acidemia (MIM 251000), glutaric acidemia type 1 (MIM 231670), homocystinuria (MIM 236200), propionic Acidemia (MIM 606054), isovaleric Acidemia (MIM 243500), argininemia (OMIM 207800), argininosuccinic aciduria (OMIM 207900), carbamoyl phosphate synthetase I (MIM 608307), tyrosinemia (MIM 276700), ornithine transcarbamoylase deficiency (MIM 311250), N-acetylglutamate Synthetase Deficiency (OMIM#:237310), & argininosuccinate Synthetase Deficiency/citrullinemia I (OMIM 215700) [13]. An introduction with basic information about the IEM along with links to internationally recognized digital resources including the Genetics Home Reference [14] and Gene Reviews are included [15]. We added an additional app, which may be useful for other IEMs requiring a protein-free diet.