IAMGSD
International Association for Muscle Glycogen Storage Disease

Nutritional ketosis in McArdle Disease
A situation report

This statement is intended to assist clinicians and researchers by providing an insight into the knowledge gained from patients' own testing and development of nutritional ketosis.

This may inform formal research and help to speed the path to an eventual clarification of whether this is a suitable nutritional strategy for many McArdle patients.

Links to support documents are listed at the end.

Sources of anecdotal evidence	
Patient group	▪ Private Facebook group "Ketosis in McArdle's", >600 members worldwide. [1] ▪ Currently c200 patients regularly using Low Carbohydrate Ketogenic Diet (LCKD). ▪ Three years ago discussion centered on whether there was benefit – now very widely accepted. ▪ Today the posts are sharing experiences, tips, recipes and resources.
Survey results	▪ Over the last three years two surveys have been conducted (2015 n=38 and 2016 n=107). ▪ The report of the 2016 survey is available. [2] ▪ 79% reported improvement in ADLs, 69% felt as always in "second wind", and 76% reported improved exercise tolerance. ▪ Typical quotes "Transformed my life", "McArdle's not impacted on my life for six months."
Case series paper	▪ A case series of three patients "Can a Low-Carbohydrate Diet Improve Exercise Tolerance in McArdle Disease?", Journal of Rare Disorders: Diagnosis & Therapy, 2017. [3] ▪ One of the patients in the paper has been closely monitored medically and dietetically for over three years and all data is available on request.
Other GSDs	▪ People with GSD2, GSD3 and GSD7 have reported success with LCKD. ▪ Patient with GSD2 refused ERT on the basis of doing so well on LCKD.
Benefits reported	
Anecdotal reports	▪ Daily reports of newfound physical activity abilities with far less pain. ▪ Psychological benefit of being able to walk unimpeded with friends; no holding back, no excuses. ▪ Many report being able to lose weight, some as much as 100 lbs (45 kg), transforming their lives.
Documented quotes	▪ Typical quote "McArdle's no longer affects my normal day-to-day life". ▪ Extensive accounts of success with eliminated pain, increased performance and weight loss. ▪ Listing of anecdotal quotes from 35 patients. Report available here. [4]
Walking courses	▪ Patients taking part in walking courses in Wales and California on a LCKD have evidenced high performance – e.g. walking briskly uphill from a start with no issue of gaining "second wind".
Assessing the benefit of trials	
Impact on patients	▪ 95% of the day is NOT in "second wind" - hanging up laundry, drying hair, changing bed sheets, walking across the car park, keeping up with colleagues, etc. ▪ Ketosis increases the level of what can be done aerobically before the anaerobic threshold – perhaps by approx. 20% ▪ Patient feedback on ketosis – "It is like my whole body being in permanent second wind".
Assessment priorities	**1 Pre-second wind:** assessment should be on this critical period which has a major impact on lives. **2 Psychological:** also assessment of the psychological impact as the QoL benefit is potentially large. **3 Aerobic capacity:** a secondary effect through patients becoming encouraged to exercise more. Already well evidenced in McArdle's generally, but may be worth assessing in this group.
Weight loss	▪ LCKD and intermittent fasting (IF) serve to lower serum insulin and promote fat metabolism. **4 Weight loss:** worth assessing as it is a very valuable adjunct of LCKD for people with McArdle's.

Achieving ketosis	
Level of ketosis	▪ Plasma level of 0.5 mmol/L – significant amelioration of symptoms in ADLs. ▪ Plasma level of 1.5 mmol/L – almost total absence of symptoms in ADLs. ▪ Levels may vary slightly between individuals contingent upon CHO tolerance. ▪ Some people are going above 1.5 mmol/L if seeking significant athletic ability.
Types of ketogenic diet	▪ Most common in McArdle's – Standard Ketogenic Diet (SKD) – no more than 50 grams of CHO. ▪ Once fat-adapted, approx. 60% fat, 25% protein, 15% carbs works well. ▪ At least one patient on this for 5 years, dozens for 3 years, and many more for shorter periods. ▪ *Not suitable for us* – Cyclical, 2 days SAD, 5 days LCKD; & Targeted– CHO load prior to workouts. ▪ *We do not need the 90% fat* involved in the Therapeutic Ketogenic Diet used for epilepsy.
Alternatives being used successfully	▪ Some function well on one meal a day (OMAD), in the evening after activity has finished. ▪ Some use the "Modified Atkins" diet. ▪ Vegetarian and vegan LCKDs have been used successfully, although these are harder to maintain. ▪ The low-carb "1-2-3 Healthy Eating Approach" – 1 unit carbs, 2 protein, 3 vegetables has helped.
Ketosis achieved in under 24hrs	▪ Our inability to access muscle glycogen is equivalent to it being fully depleted. ▪ Muscle glycogen is 80% of the body's CHO so this is a major advantage for entering ketosis. ▪ It appears that the liver glycogen does not need to be fully depleted, only challenged. ▪ Exercise appears to be an important element in triggering ketosis quickly. ▪ Effective method – eat a low carb evening meal, fast overnight as usual, just coffee for breakfast, skip lunch, exercise for several hours – ketosis is achieved before the evening meal. ▪ Ketosis may then be maintained with three LCKD meals per day.
Monitoring	▪ At the start of a LCKD it is useful to check serum ketones with a lancet device. ▪ Ketone urine sticks are low cost and easy to use but may mislead as they measure waste ketones. ▪ After a while patients can assess their approx. ketosis level simply by the effect on their symptoms.
Breaks from LCKD	▪ Due to the ease of getting into ketosis it is not a problem if a patient takes a break for a child's birthday, a holiday weekend, etc. ▪ However, during the break symptoms are likely to return immediately.
Supplements used and tried	
Oils	▪ Patients can add oils such as olive oil and coconut oil to their food to help achieve the fat levels. ▪ MCT oil is also used, when a neutral taste is required.
Supplements	▪ LCT oils such as Nutricia's Calogen has been prescribed to several patients. We do not know of any patients who have continued with it. ▪ Exogenous ketones such as Ketōnd and Pruvit KetoOS drinks can raise serum ketones (BHB) to a therapeutic level. These may help when transitioning into ketosis or covering a lapse in diet.
Safety factors	
Anaerobic warning	▪ The only (early) reported incident involved a patient undertaking a major gym workout. ▪ Patients in ketosis can feel euphoric about the apparent elimination of symptoms. ▪ Warn that the benefit does not extend to isometric or significantly anaerobic activity.
Dropping off LCKD	▪ Patients need to be warned that when dropping off the LCKD they need to remember all their normal management techniques – second wind, six second rule, 30 for 80, etc.
Little risk of Ketoacidosis	▪ The therapeutic level of ketones in blood appears to be approx. 1.5 mmol/L. ▪ This is approx. 10% of the often quoted starting level for risks of ketoacidosis. ▪ In the absence of prior risk factors such as Type 1 Diabetes, there seems NO danger of ketoacidosis.
Improving cholesterol	▪ Some patients see a temporary rise in total cholesterol, but HDL usually rises more than LDL and the ratio is within range. ▪ LDL level can rise, but typically this consists of large "fluffy" type B particles. ▪ As patients become fully fat-adapted most are within range on all measures.
Resources for patients	
Web sites	▪ The most highly focused resource is the "Ketosis in McArdle's" Facebook group. [1] ▪ A myriad of free public web sites for LCKD are also of great assistance in McArdle's. ▪ Some are highly professional, and paid for, such as "Diet Doctor" by Dr Andreas Eenfeldt. ▪ There are regular on-line articles assisting with menu planning and recipes.
Apps	▪ There are apps for tracking your macronutrients, making it relatively simple to be compliant.
Books	▪ In addition to books for those following the diet, there are two books especially worthy of mention for professionals and others with a deeper interest: ▪ "Ketogenic Diet and Metabolic Therapies", [5]. ▪ "The Ketogenic Bible, the Authoritative Guide to Ketosis", [6]

Workshops and conferences

Workshops	▪ August 2015 – Ketosis in McArdle's Workshop, Columbia Medical Centre, New York. Report. [7] ▪ July 2016 – Low Carb USA, San Diego California. Report by Dr Richard Godfrey. [8]
IAMGSD presentations	▪ IGSD2017 International GSD Conference, Groningen, June 2017 (3 board members). [9] ▪ AGSD US Toronto, September 2016 and Chicago, September 2017 (2 board members). ▪ AGSD UK Bedfordshire, October 2016 and Nottingham, October 2017 (2 board members). ▪ Canadian Association of Physician Assistants, November 2017 (2 board members).

Overall health benefits of LCKD

Widely reported across the LCKD world	▪ Reduced serum insulin, improved insulin resistance. ▪ Weight loss, with all its known health benefits. (Approx. 3 out of 4 of McArdle patients are obese. Exercise becomes more attainable when carrying less weight.) ▪ Reduced risk of secondary conditions – type 2 diabetes, coronary heart disease, hypertension, obesity, atheroma, stroke, cancer, etc.

Links to support documents

Ref	Title	Type	Author/Source	URL to PDF or web site	Size
1	*Ketosis in McArdle's Facebook Group*	*Web site*	*Private group of >600 members*	*https://tinyurl.com/ydffpdoe*	*N/A*
2	*Patient-led Development of LCHF in Muscle GSDs – results of survey*	*PDF*	*Stacey L Reason*	*https://tinyurl.com/y8mdvcbm*	*1.2mb*
3	*Can a Low-Carbohydrate Diet Improve Exercise Tolerance in McArdle Disease? J Rare Disord Diagn Ther. 2017, 3:1.*	*PDF*	*Reason SL, Westman EC, Godfrey R, et al.*	*https://tinyurl.com/y9ns3qs2*	*270kb*
4	*Report of anecdotal quotes from 35 McArdle patients on LCKD*	*PDF*	*IAMGSD*	*https://tinyurl.com/ycusmca5*	*130kb*
5	*Ketogenic Diet and Metabolic Therapies*	*Book*	*Ed. Susan A Masino*	Oxford University Press, 2017	*408 pages*
6	*The Ketogenic Bible, the Authoritative Guide to Ketosis*	*Book*	*Dr Jacob Wilson and Ryan Lowery PhD*	Victory Belt Publishing, 2017	*384 pages*
7	*Report of "Ketosis in McArdle Disease" workshop, Columbia Medical Center, New York City, August 15-16, 2015*	*PDF*	*Andrew Wakelin*	*https://tinyurl.com/yah68vjs*	*250kb*
8	*Report on the 'Low Carb USA' Conference, San Diego CA, July 29-31 2016*	*PDF*	*Dr Richard Godfrey*	*https://tinyurl.com/y7tythqa*	*350kb*
9	*Ketosis in McArdle's and Tarui's, presentation at IGSD2017 conference, Netherlands, June 2017*	*PDF*	*Jeremy Michelson*	*https://tinyurl.com/y8k4pnlz*	*3.7mb*

Please read the anecdotal quotes from patients (Ref. 4 above)

These are two examples:

TT: "It has made a significant difference to me! Never felt better. I can do things that were virtually impossible before. I was a regular at the hospital last year, over 8 visits. I have only been once this year! I have NO sugar and feel invincible!"	**MB: "I have been keto for 5 years, lots of fat. I just had my yearly medical and all of my tests were beautiful he said. All of my markers for inflammation, heart health, diabetes, liver, and cholesterol were extremely good. My CPK was 73!"**

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