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Ketogenic diet therapy provision in the COVID-19 pandemic: Dual-center experience and recommendations

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1. Introduction

The past several months have dramatically affected the way neurologists care for patients with epilepsy. The current coronavirus disease (COVID-19) pandemic has led to stay-at-home orders and other measures to promote social distancing, keeping patients and their families at home with decreased direct access to physicians, electroencephalogram (EEG), and even antiseizure drugs (ASDs) [1,2]. However, refractory epilepsy does not stop in a pandemic, and patients need other options if their current regimen is not successfully reducing seizures. These options may include epilepsy surgery, neurostimulation, and new ASDs, which can be difficult or impossible to arrange or obtain in a pandemic situation.

Similarly, there are many reasons why neurologists would not offer ketogenic diet therapy (KDT) in a pandemic. Food availability is often a concern, and there may be shortages, especially of milk, eggs, fresh produce, and meat which are frequently used by those on KDT. Often, the classic ketogenic diet (KD) is started in the hospital and requires a team including a dietitian, which is certainly more time-intensive than trialing a new ASD [3]. It is an elective treatment, not required, or emergent in most cases (except perhaps in hospitalized patients with uncontrolled seizures and sedation from ASDs, status epilepticus, or infantile spasms). Not all centers have KDT services, and clinicians and dietitians may be redeployed to assist other services. There is also concern regarding potential risk of COVID-19 exposure in a hospital setting where infected individuals are being treated [2]. For these reasons and others, neurologists may incorrectly perceive that KDT initiation and even maintenance in this pandemic are not appropriate or practical.

However, this may be an erroneous assumption. There is precedent for starting KDT on an outpatient basis; the modified Atkins diet (MAD) is typically initiated in this manner, and studies have demonstrated that even the classic KD can be begun as an outpatient in select situations [3,4]. Many high-fat, low-carbohydrate foods (e.g., oil, nuts, avocados, tuna, mayonnaise, cheese) have not been difficult to obtain in this pandemic. Additionally, a change in diet compared with a new ASD may represent a feasible and lower risk option for patients and their care providers.

We present our combined experience with new KDT initiations in the COVID-19 pandemic with examples of varied methods to start a child or an adult on KDT. In addition, we discuss how our centers have been able to maintain outpatient follow-up clinics by telemedici.
Finally, some information received from other KDT centers, patients, and caregivers about problems and solutions for those on KDT is described.

2. Results

2.1. The Johns Hopkins Pediatric Ketogenic Diet Centers

2.1.1. Novel methods of ketogenic diet initiation

2.1.1.1. Case 1. A 3-year-old male presented with several tonic–clonic seizures in January 2020. Initial EEG and magnetic resonance imaging (MRI) results were normal, but within 6 weeks, he began having atonic seizures every 2–3 days despite levetiracetam 60 mg/kg/day. Video-EEG in early March 2020 revealed bursts of polyspike–wave activity associated with head drops, consistent with the diagnosis of epilepsy with myoclonic–atonic seizures (Doose syndrome). Valproate up to 30 mg/kg/day did not control seizures, and a decision was made to start the classic KD. Because of his young age as well as his family's unfamiliarity with dietary therapy, he was admitted for diet initiation on March 31, 2020, just as the pandemic was beginning to escalate in Maryland.

In order to expedite his initiation, he did not fast, and baseline labs were obtained the morning of his admission. He was started immediately on a 4:1 ratio KD with 50% of his caloric intake for 12 h (2 meals, initially as a formula), followed by full calories with solid foods the next day. Blood glucose was 85–89 mg/dl, and ketones were 40 mg/dl on day 1 and 160 mg/dl by dinner on day 2. Five educational classes were held over the 32-h admission period; he was discharged day 2 at 6 pm in good condition. Follow-up video visits were completed with his neurologist and dietitian at 2, 9, 20, and 40 days after discharge (Fig. 1); he is in moderate-large ketosis, and seizures are 90% improved at this time.

2.1.1.2. Case 2. A 6-year-old female with a history of seizures since age 4 presented for consideration of KDT. Electroencephalogram had shown multifocal discharges; MRI and genetic testing were unrevealing of an etiology; and seizures were atonic (1–2 per month), behavioral arrest (2–3 per day), and tonic–clonic (1–2 per month) despite trials of 7 ASDs and artisanal cannabidiol. In November 2019, the family tried a low-carbohydrate diet on their own without benefit but with documented negative urinary ketosis.

She was initially scheduled for a regular KD admission on April 6, 2020, but it was canceled because of the pandemic. Seizures stabilized temporarily with clobazam, valproate, and levetiracetam but then worsened. The family was contacted by email, and plans were made to initiate the classic KD as an outpatient with telemedicine. The consent form was signed and emailed back as a portable document format (PDF) file. Information was given regarding common ketogenic foods to buy (Table 1); her height/weight and a 3-day food record were provided by parents to calculate a 4:1 ratio KD (and 1650 cal/day); and food allergies and preferences were queried. April 23, 2020, we met the family in

Table 1

Ketogenic diet food “shopping list”.

| Essentials – choose 1–2 from each category, do not need to buy all |
|---|
| Fats: |
| Heavy whipping cream |
| Butter |
| Mayonnaise |
| Oil (any kind of oil – vegetable, canola, olive, coconut, ghee) |
| Protein: |
| Eggs |
| Bacon |
| Chicken, beef, pork, fish, shellfish (any of these products) |
| Tuna fish |
| Fruit: |
| Applesauce, blueberries |
| Vegetables: |
| Cauliflower, broccoli, carrots |
| Fruit or vegetable can be fresh, frozen, or canned |
| Snack foods: |
| Baby bell cheese, string cheese |
| Guacamole snack packs |
| Pork rinds |
| Beef jerky |
| Cheese crisps |
| Nuts |
| Raw whole nuts |
| Nut flours |
| Nut butters |
| Shelf stable nut milks |

Fig. 1. Follow-up visit by Zoom™ at 9-days post-KDT initiation.
the hospital entrance by car and provided them with a gram scale, digital video disc (DVD) of educational classes, a box of urine ketone strips, written teaching materials for educational classes, and Flintstones™ vitamins (Fig. 2). Baseline labs had been obtained one month prior so were deferred.

On the day of KDT initiation (April 27, 2020), the patient did not fast and received a normal breakfast at home. A video visit with the neurologist and dietitian occurred at 9 am followed by educational classes (by Zoom™) at 10 am, 11 am, and 1 pm (Fig. 3). She received a 2:1 ratio lunch, then 2:1 ratio dinner, which her parents created using precise recipes based on the child’s food preferences provided by the dietitian (ZT) by email. The dietitian was available for education regarding how to cook the ketogenic foods if necessary. On day 2 of the KDT initiation, another video visit with the child occurred at 9 am. By this point, she was in moderate urinary ketosis and doing well with fewer seizures. Blood glucose was not obtained. Classes continued by Zoom™ at 10 am, and a group support meeting with two established KDT families occurred at 11 am. Parents provided a 4:1 breakfast and lunch based on set recipes and then using the computer program KetoDietCalculator™ made their own recipes for dinner. On day 3, she was seen for a final video visit at 9 am and was in large urinary ketosis (Fig. 4). Breakfast foods created were also shared (Fig. 5).

The child has been seen two additional times via telemedicine and is doing well with a 90% reduction in seizures after 4 weeks of KDT. Her mother also reports improvement in cognition, with more precise coloring and reading. She will be seen by video visit again in one month.

2.1.1.3. Case 3. A 3-year-old male with the diagnosis of epilepsy with myoclonic–atonic seizures (Doose syndrome) was started on the MAD in February 2020 after failing to respond to 5 ASDs. Although seizures improved by more than 90% (from 6 convulsions per day to a seizure every 5–8 days) and blood beta-hydroxybutyrate ranged from 2.6 to 5.8 mmol/L, he was admitted on April 7, 2020 because of prolonged seizures requiring rectal diazepam twice for cessation.
A decision was made to transition him to the classic KD with a 3:1 ratio. The dietitian (SB) spent 30 min with his mother in the hospital room, providing education on weighing and calculating meals. He was discharged after a brief, 16-h admission in order to limit his time in the hospital. When his mother received the scale, SB provided 90 additional minutes of phone education as the family did not have access to video visit software at the time (Fig. 6). Since that time, there have been several phone and video visits, and he has continued to improve, with seizures decreasing in frequency and no longer requiring rescue medications (seizures are currently lasting 10–30 s maximum).

2.1.1.4. Case 4. A 5-year-old female with the diagnosis of refractory focal epilepsy secondary to neonatal meningoencephalitis and bilateral periventricular and subcortical white matter gliosis on brain MRI was referred by an outside epileptologist for a new patient appointment for the classic KD on March 31, 2020. Electroencephalogram revealed multifocal sharp waves. She had trialed 5 ASDs but continued to have focal seizures with impaired awareness 1–3 times per month.

During the COVID-19 pandemic, the hospital was limiting inpatient admissions unless emergent, and therefore, the parents were offered the MAD instead of waiting until KD admissions were resumed. A plan to transition to the classic KD later if needed was discussed. Educational information on the MAD was reviewed over telemedicine and then sent via email on the MAD diet (Fig. 7). Initial screening labs were combined with a serum-beta-hydroxybutyrate (3.3 mmol/L) when the family presented to a scheduled lab appointment at a satellite office 9 days later. One month later, she continues to have an appropriately high beta-hydroxybutyrate of 3.7 mmol/L, and she is seizure-free to date. In this case, an inpatient admission was avoided, and she has remained on the MAD. Despite never having any inperson office visits with either JA or SB, close communication and follow-up have been maintained.

2.1.2. Maintenance of pediatric KD during a pandemic

With the sudden elimination of inperson outpatient clinic visits, our centers rapidly transitioned to telemedicine for KD follow-up. In the Johns Hopkins Hospital Pediatric Ketogenic Diet Center, our April and May KD follow-up monthly clinics were converted to telemedicine. Prior to April, patients were seen for 60-min visits in which they were triaged by medical assistants, brought back to outpatient rooms, first evaluated by our pediatric ketogenic dietitian then presented and seen by the neurologist followed by prescriptions written, plans typed out, and the family walked back out to the waiting room. Approximately 8–10 children were scheduled per day, and appointments were made every 30 min (with 2 rooms running simultaneously).

On April 14, 2020, we were successful in seeing 8 children virtually over an 8-h period. Parents were emailed one week in advance and asked to install Zoom™ on their phones or computers with a camera, with a link to a single “room” attached. They were asked to obtain the following in advance: 1) recent height and weight, 2) updated list of medications and their preferred pharmacy, 3) any forms that needed completion including for ketogenic formula, and 4) a list of questions to be asked of the team. During each appointment, both the neurologist and dietitian together discussed care with the parents first for approximately 20 min, with a 10-min video-observed physical examination, followed by 15 min of planning dietary and medical changes, ordering medications, and arranging any tests and follow-up. On May 12, 2020, 8 different children were scheduled for shorter 45-min time slots based on previous experience. Most families were pleased with the experience and commented on appreciation for not having to travel and risk their health because of hospital COVID-19 exposure. Additionally, EK and ZT were able to engage in a KD second opinion video visit for a child in New York on the classic KD at another center on May 13, 2020, saving the family from travel costs.

2.2. The Johns Hopkins Adult Epilepsy Diet Center

2.2.1. Overall experience

When Maryland Governor Larry Hogan issued the stay-at-home order and cessation of outpatient office visits for the foreseeable future, the Adult Epilepsy Diet Center (AEDC) had been evaluating
approximately 10 new and 20 follow-up outpatients per month (typically on Fridays twice per month) [5]. New patients were usually started on the MAD unless primarily tube-fed, and follow-up patients were continued on the MAD unless they were already on a classic KD prior to their initial visit with adequate seizure control. Following the stay-at-home order, several patients immediately elected to postpone their clinic visits; however, the majority chose the option of having these converted to telemedicine visits with the adult epileptologist [MCC, TJWM] and dietician [BJB, DV] and were appreciative of the opportunity to continue rather than delay care without risking pandemic exposure. Approximately half of patients from the AEDC travel from out-of-state, so epileptologists obtained temporary emergency licenses for 8 additional states to provide telemedicine services or were granted waivers to do so.

New patient visits were conducted via live web and video conferencing platforms including Polycom™, Zoom™, or Doximity™ combined with either live or prerecorded (via Zoom™) virtual instructional sessions. These sessions were saved as a SharePoint (a Microsoft™ web-based platform for collaborations and documents) web link, which was password-protected with an expiration date and emailed to patients with instructions on how to access the link. The initial virtual visit lasted 60–120 min and occurred just prior to the instructional sessions. Thirty-minute follow-up visits with the epileptologist were lengthened to 45 min, and clinics were spread out over several days when necessary to account for extra time needed to educate patients and caregivers about use of telemedicine services prior to the visit. Dietitians joined the televisit, scheduled a separate telephone call at a later time, or answered questions via the electronic medical record secure messaging system as appropriate per licensing requirements and depending on the needs of the patient.

In total, 9 new patients were started on the MAD, and 28 follow-up patients have been seen to date in this manner. Patient feedback has been overall positive regarding receiving KDT training and follow-up via telemedicine visit although there were a number of technical challenges related to poor internet connections, inability to connect to the virtual platform, or poorly functioning audio or video capabilities. This workflow improved with the addition of a medical assistant prior to the start of the visit, who contacted patients and families and instructed them on the steps to connect to the telemedicine visit 15 min prior to the start of the visit.

Like with pediatric patients, adults reported that major barriers to following MAD included lack of availability of meat and fresh produce at local grocery stores, particularly shortly after the stay-at-home order was issued. Several relied heavily on eating out and found it difficult to cook at home. Some patients found success in utilizing food delivery services to minimize exposure to COVID-19 from going to the grocery store in person. Several companies providing ketogenic products have offered to donate these to patients free-of-charge during the pandemic.

### 2.2.2. Case 5

A 31-year-old right-handed woman with glucose transporter type 1 deficiency disorder (a rare genetic disorder which prevents glucose to be adequately utilized in the brain and for which KDT is standard therapy) was started on a strict MAD 4.5 years ago, after being diagnosed as having this disorder as an adult. On the diet, seizures resolved, and there was a marked improvement in her cognition (full-scale intelligence quotient [IQ] increase from 37 to 52) although she continued to have sporadic paroxysmal exercise-induced dyskinesias. She lived with her parents who prepared meals at home at nights, and on weekends, she attended a day program where she ate a MAD lunch. During her follow-up teleneurology visit, her parents noted a marked reduction in dyskinesias while at home (her day program was closed during the pandemic). The only change to her diet was that they had incorporated a new high-fat shake into her morning routine, which she had not received while participating in the day program. Since then, other adults with intellectual disability being cared for exclusively by their parents with strict adherence to MAD have also been reported to have a significant seizure reduction during this time period in contrast to their daily arrangements outside of the home prior to the pandemic.

### 2.3. Lessons learned from other KDT centers

In April 2020, Dr. Kossoff contacted members of the International KDT pediatric consensus group, along with other experts such as MC, SB (authors), Emma Williams, Elizabeth Neal, PhD, RD, Susan Wood, RD, and Marisa Armeno, MD. Questions were asked regarding particular issues seen in their KD centers during the COVID–19 pandemic. Most had not seen problems maintaining ketosis or seizure control in those affected by the COVID-19 virus. Many have also started to utilize telemedicine for starting and maintaining KDT as well. Other advice is listed in Table 2.

### 3. Discussion

Our centers’ experiences would suggest that KDT can be successfully initiated with creativity, an individualized approach, and advanced planning during this pandemic. There are various options for starting KDT, and all are potentially appropriate. One option (Cases 1 and 3) is to continue to admit children to the hospital for the classic KD but with a shortened admission (e.g., 1–2 days) through the use of focused education, no fasting, quick titration in ratio or calories over 24 h, and providing a DVD or video of classes and written materials to enhance learning. Afterwards, provide close contact by phone, text, email, and/or telehealth for questions and confirmation of the educational experience. A second method (Case 2) is to start the classic KD by outpatient gradual induction with telehealth visits and education. We suggest this approach for patients that are reliable and well-established in follow-up, providing scales and other materials in advance, having the parents shop for foods several days before starting, giving precise recipes to use and not fasting, and creating a formal virtual schedule for educational classes. Although we did not attempt this method of starting the KDT, we believe that it is possible to do group sessions of 3–4 families, recognizing the need for patient privacy agreements beforehand. Third, the MAD is a theoretically excellent option (Case 4) as there is no requirement for using food scales, there is less risk for hypoglycemia and overketosis, it is already widely published as safe and effective starting as an outpatient, with no need for fasting, and there are many materials and recipes online [3]. In Case 4, plans were made to start the MAD and switch to the classic KD if necessary. Lastly, patients with gastrostomy tubes can have their formula switched easily as long as there is guaranteed insurance approval or financial coverage for and home delivery of the ketogenic formula.

Maintenance of patients on KDT is also possible in a pandemic. In fact, our experience suggests that telemedicine has several advantages

| Table 2 | Advice for families and patients on KDT in a pandemic. |
| --- | --- |
| Ensure there is a home scale for obtaining weight of the patient. Test and use telemedicine software (e.g., Zoom™, FaceTime™, Microsoft Teams™, hospital-based, Polycom™, Doximity™, etc.) in order to stay connected with your KDT team. Gather adequate supplies of high-fat foods, especially those with long shelf-lives. Consider obtaining a letter from your KDT team to be provided to grocers if there are limits on food purchases. Also, consider food delivery services including premade ketogenic meals. Obtain 90-day supplies of antiseizure medications but also KDT supplements, vitamins, calcium, and urine ketone strips. Recognizing some children may try to cheat, and are home (not in school), lock or secure away high-carbohydrate foods the child could obtain. Laboratory monitoring of patients on KDT is important but could be delayed several months in most cases. However, remember to obtain the labs and elective studies when safe. |
over the prior state of KDT care [6–10]. In our video visit follow-up appointments, the pediatric or adult epileptologist and dietitian can interact with the patient and family at the same time. Without traffic, waiting rooms, registration, and triage, visits can be shorter and more time-efficient which allows for more patients to be seen in a day potentially. Telemedicine allows the team to see the patient in their own house (and kitchen) and even see their foods prepared when appropriate. Multiple family members and caregivers can join the educational sessions, even from different homes, and these sessions can be recorded for future viewing. Additionally, patients who live a far distance from the KDT center, those with autism, intellectual disability, mobility issues, adults unable to drive, patients with nursing needs such as suction or mechanical ventilation, and/or behavioral disorders, and their caregivers may find this method of medical care preferable.

However, there are potential disadvantages to KDT follow-up care by telemedicine. Obtaining labs and other routine assessments can be more difficult; measuring the patient’s height and weight may be more imprecise, and significant technological limitations remain. A comprehensive neurologic exam is more challenging to conduct in patients with fluctuating neurologic symptoms via telemedicine, and the physician and medical staff cannot assist if the patient has a seizure during the visit. For starting KDT by telemedicine, there is certainly more work involved in advance to ensure everything is ready for the first day of the initiation. In-depth, detailed discussions (e.g., for KDT failure, stopping KDT) may be less personal when done by video. Ketogenic diet therapy by telemedicine both in terms of initiation as well as maintenance may not be appropriate for young infants, very complicated children, adults, those at high risk for hypoglycemia or metabolic issues, families without access to technology, and those unable to access emergent medical care if necessary.

In many ways, providing KDT care in a pandemic has led our centers to reexamine ideal aspects of providing this service and what is truly necessary. An early study of the MAD in the management of adults with drug-resistant epilepsy showed that initiation and maintenance using email was feasible [11]. In 2015, the International League Against Epilepsy Task Force for Ketogenic Diet Therapies created a guideline for KDT in developing countries with limited resources [4]. This guideline has many similarities to our current situation with the recognition that outpatient KDT, with limited need for laboratory monitoring, serial studies, and access to advice from nearby larger centers, is relevant. Even though the 2018 KDT consensus guideline for pediatrics recommended starting the classic KD in the hospital according to 80% of the panelists, 92% believed that this was optional and in this pandemic, that is a reasonable approach [3].

4. Conclusions

In conclusion, both starting and maintaining KDT can continue successfully in a pandemic crisis. It is a very viable nonpharmacologic option for drug-resistant epilepsy in children and adults and should not be discouraged or stopped. In fact, some advantages to telemedicine in KDT provision do exist and are worth continuing when this crisis resolves.

Declaration of competing interest

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