



Considerations for continuing diet therapy in patients with epilepsy during the COVID-19 pandemic: A scoping review



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ABSTRACT

Diet therapy is an option for managing patients with drug-resistant epilepsy (DRE). Diet therapies used for patients with epilepsy include the classic ketogenic diet, the modified Atkins diet, the medium chain triglyceride diet, and the low glycemic index diet. The effectiveness of diet therapy is highly dependent on dietary adherence. Coronavirus disease (COVID-19), a novel infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has substantially impacted the lifestyles of people worldwide. Therefore, continuing a specific diet during the COVID-19 pandemic is expected to be difficult in some aspects. Here, based on the available literature, we summarize the perspectives for maintaining diet therapy during the COVID-19 pandemic, as a scoping review. Epileptologists and dietitians need to understand the difficulty of maintaining diet therapy during the COVID-19 pandemic. In addition, the education of patients and all stakeholders to continue diet therapy even during the current COVID-19 pandemic is crucial to control epileptic seizures. In conclusion, continuing diet therapy is not a matter only for patients during the COVID-19 pandemic, but medical staff should also help patients to overcome the problems associated with the pandemic by understanding their situations.

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1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel infectious virus that causes coronavirus disease (COVID-19). The outbreak first occurred in Wuhan, China, in late 2019, and has since continued to spread globally [1]. The World Health Organization (WHO) declared a pandemic situation in March 2020. Since then, the pandemic has substantially impacted the lives of people worldwide.

Epilepsy is a chronic neurological disorder characterized by the spontaneous recurrence of unprovoked seizures. Diet therapy is one of the treatment options for drug-resistant epilepsy (DRE) [2]. Diet therapy has a beneficial effect in patients with epilepsy, but the outcome is highly dependent on adherence to the diet [3]. Diet therapies for patients with epilepsy include the classic ketogenic diet, the modified Atkins diet, the medium chain triglyc-

eride diet, and the low glycemic index diet [2]. All of these diet therapies involve carbohydrate restriction and patience, which may prove to be an obstacle to adherence for some patients. Epileptologists and dietitians are required to create an environment that facilitates the continuation of diet therapy for patients with epilepsy.

The impact of COVID-19 on the society has been marked, and the pandemic has also affected the continuation of diet therapy for patients with epilepsy [4–6], especially for patients with DRE [7]. To remove the obstacles to continued diet therapy during the COVID-19 pandemic, we performed a systematic review to investigate and summarize the studies that researched the situation of patients with epilepsy who had undergone diet therapy. In addition, we suggest solutions to overcome these challenges based on an examination of the available literature.

2. Materials and methods

2.1. Search strategy

We conducted a search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide-

Abbreviations: COVID-19, Coronavirus disease; DRE, Drug-resistant epilepsy; KD, Ketogenic diet; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

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lines [8]. This review protocol has not been registered previously. The following databases were searched systematically from January 1, 2019, to March 20, 2021: MEDLINE (accessed from PubMed), CENTRAL (accessed from the Cochrane Library), and EMBASE. The following key words were searched in PubMed: (“Epilepsy” [MeSH Terms] OR “Epilepsy” [Title/Abstract] OR “seizure disorder” [Title/Abstract]) AND (“COVID-19” [MeSH Terms] OR “SARS-CoV-2” [MeSH Terms] OR “COVID-19” [Title/Abstract] OR “2019 ncov infection” [Title/Abstract] OR “SARS-CoV-2” [Title/Abstract] OR “2019 novelcoronavirus” [Title/Abstract]). The following keywords were searched in the Cochrane libraries: ([mh Epilepsy] OR Epilepsy:ti,ab OR “seizure disorder”:ti,ab) AND ([mh COVID-19] OR [mh SARS-CoV-2] OR COVID-19:ti,ab OR “2019 ncov infection”:ti,ab OR SARS-CoV-2:ti,ab OR “2019 novel coronavirus”:ti,ab). The following key words were searched in the EMBASE database: (“Epilepsy”/exp OR Epilepsy:ti,ab OR “seizure disorder”:ti,ab) AND (“COVID-19”/exp OR “SARS-CoV-2”/exp OR COVID-19:ti,ab OR “2019 ncov infection”:ti,ab OR SARS-CoV-2:ti,ab OR “2019 novel coronavirus”:ti,ab). We also searched ClinicalTrials.gov for unpublished, ongoing, terminated, or completed studies to avoid publication bias. We screened the reference lists of all relevant articles for additional data. We included all studies or articles written in English if they focused on continuing diet therapy for patients with epilepsy during the COVID-19 pandemic.

2.2. Inclusion and exclusion criteria

All studies that reported or described the difficulty in continuing diet therapy for patients with epilepsy during the COVID-19 pandemic were included. We defined diet therapy as ketogenic diet therapy, including the classic ketogenic diet, the modified Atkins diet, the medium chain triglyceride diet, or the low glycemic index diet [2]. We excluded (1) studies not yet recruiting, recruiting, or withdrawn on Clinical.Trials.gov; (2) studies that reported patients diagnosed with psychogenic non-epileptic seizures; and (3) studies written in languages other than English. We did not limit the article type or concomitant medication therapy. In addition, we did not limit the patient’s age as diet therapy can be applied to patients of any age.

To assess the quality of the included articles, we scored the level of risk of bias using the Joanna Briggs Institute checklist for cross-sectional studies and case series [9,10]. Any disagreements or discrepancies between the reviewers regarding outcomes were resolved through discussion.

2.3. Data extraction and outcome measurements

Two reviewers (NK and AF) independently screened the titles and abstracts and evaluated the full texts of the selected articles. Any disagreements were resolved through discussion between the reviewers (NK and AF). The following variables were extracted: author, publication year, article type, participants, country in which the study was conducted, research period, duration of diet therapy, difficulties in continuing the diet therapy, and the effectiveness of telemedicine/tele-follow-up.

3. Results

3.1. Summary of reviewed articles

The selection process is outlined in Fig. 1. A total of 802 studies were retrieved (217 papers from MEDLINE, 0 papers from CENTRAL, 583 papers from EMBASE, and 2 studies from ClinicalTrials.gov) up until March 20, 2021. After removing duplicates and screening the titles and abstracts, 22 studies were identified. The

full-text screening of these studies led to the exclusion of 17 studies that did not meet the inclusion criteria. We thereby identified a total of five articles from the PubMed search that were appropriate for discussing the continuation of diet therapy for patients with epilepsy during the COVID-19 pandemic [11–15].

3.2. COVID-19 affects numerous factors associated with adherence to diet therapy

Table 1 summarizes the findings of the included studies. Various factors are associated with the continuation of diet therapy, including finances, logistics of monitoring the progress of the diet, disrupted access to low-carbohydrate food, and motivation.

3.2.1. Costs

With regard to diet therapies, the cost of food, supplements, and additional laboratory testing should be considered [13]. In addition to those who have always had financial difficulties, there has been an increase in people facing financial difficulties due to the loss of work opportunities during the pandemic [13]. For patients who qualify for a diet therapy, financial support is recommended for their adherence to the diet. Moreover, society as a whole should be aware of the fact that some people may have to discontinue their diet during the pandemic, and should consider providing financial support to such patients.

3.2.2. Laboratory biomarkers of the classic ketogenic diet

One of the difficulties that arise when following diet therapy during the COVID-19 pandemic is the need for laboratory testing [14]. Monitoring physiological ketosis is helpful for classic ketogenic diet therapy and is performed by measuring daily ketone concentrations in urine or blood samples or by conducting a breath test for acetone.

3.2.3. Access to food

Patients who continue diet therapy during a pandemic face not only financial problems but also hampered access to food. This may occur when people of the general population stockpile items that they do not necessarily need, which can lead to a shortage of low-carbohydrate food required for diet therapy [16]. When the diet is not strictly adhered to, it increases the probability of seizures, which could cause low general status, impaired immune function, and several complications [17]. The increase in seizures and their consequences may also potentially lead to an increased exposure to COVID-19. Therefore, acquiring food that is compliant with diet therapy is a critical issue for such patients.

3.2.4. Maintaining motivation for diet therapy

A previous article described the possibility that patients with epilepsy or their caregivers may discontinue diet therapy due to the increased levels of anxiety or stress caused by the COVID-19 pandemic [13].

3.2.5. Initiation of diet therapy

In contrast to the results of follow-up, it has been suggested that the pandemic may have a high impact on the introduction of dietary therapy. Indeed, it has been reported that both outpatient and inpatient initiation of the diet have been considerably affected by the pandemic [12]. According to a study, less than 10% of facilities were able to implement diet therapy as planned, suggesting that many patients who would have benefited from the diet had their treatment postponed due to the pandemic.

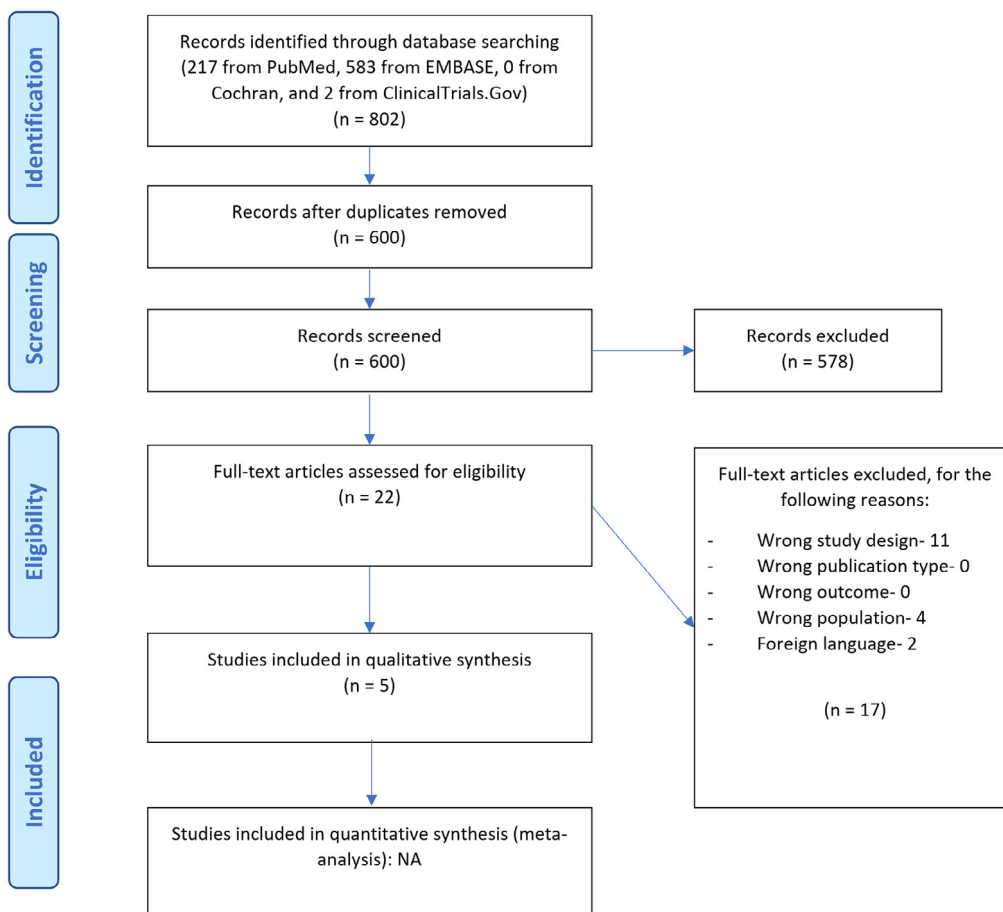


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of this research.

4. Discussion

As outlined above, patients with epilepsy who are on diet therapy are challenged with the maintenance of the diet during the COVID-19 pandemic. We have summarized suggestions to overcome these challenges and their efficacy/safety during the pandemic (Table 2).

4.1. Use of telemedicine

The possibility of diet therapy using telemedicine has been suggested even before the pandemic [18]. However, before the pandemic, telemedicine for diet therapy was generally intended for patients who were unable to visit hospitals due to residing in distant locations. It was also performed under the condition that the patient’s home had an adequate internet connection and was well prepared for telemedicine. However, during the unexpected pandemic, both medical professionals and patients have been forced to rely on telemedicine for diet therapy; thus, the effectiveness depends on the preparation and adaptability of both parties.

The reviewed articles reported mostly positive results for the continuation of diet therapy using telemedicine and tele-follow-up during the COVID-19 pandemic (Table 1). Most of the reviewed studies used WhatsApp® as a tool for telemedicine. According to Lima et al., other online communication tools, such as Zoom, Google meet, Polycom, Doximity, Facetime, Microsoft Teams, and

Skype, are useful; however, some patients have restricted access to the internet due to economic or housing issues [13].

A study from Argentina reported that 96.3% of 54 patient’s parents were satisfied with the management of diet therapy by telemedicine, and 72.2% of the patient’s parents recommended using telemedicine for diet therapy even after the pandemic [11]. Other studies from the USA and Italy supported the opinion that telemedicine allowed the continuation of diet therapies during the COVID-19 pandemic [11,12,14,15]. Another study reported the progress of patients on diet therapy during the COVID-19 pandemic through telemedicine and found that four out of seven patients discontinued the diet therapy during the pandemic [13].

Although telemedicine is a useful alternative, there are some concerns regarding its use. Some physicians and dieticians are skeptical regarding the use of telemedicine in their practice because of the lack of definite legislation permitting the use of telemedicine in their countries [19]. Another concern is that telemedicine could be inconvenient and cause participation difficulties for patients with hearing or visual impairments [20].

4.2. Consideration of the cost of diet therapy

According to a review article on diet therapy for patients with diabetes, lack of financial resources to maintain a balanced diet is a concern for poor patients, such as workers, during national lockdowns [19]. Epileptologists, dieticians, and researchers need to educate the society on the same through lectures, academic papers, newspapers, and magazines.

Table 1
Summary of articles demonstrating diet therapy for patients with epilepsy during the COVID-19 pandemic.

Author, year	Article type	Participants	Country	Quality	Research period	Duration of diet therapy	Described difficulties in continuing diet therapy	Effectiveness of telemedicine/tele-follow-up
Semprino et al., 2020 [11]	Survey study	54 families with DT (17 with cKD, 7 with modified cKD, 6 with MAD, 20 with MCT, and 4 with LGIT)	Argentina	2/8	March–May, 2020	-	Patients (4.3%) reported that it was difficult to understand how to prepare the meals by video call and that they need in-person instructions. Patients (7.6%) reported that it was difficult to understand how to perform ketonemia/ketonuria controls by telemedicine and that they need in-person instructions. 92.3% had some restriction in DT initiations in admission.	96.3% of parents were satisfied with the management of DT through telemedicine. 72.2% of families recommended using telemedicine for DT regardless of the pandemic. 97.4% of patients who received outpatient DT practice reported that they were able to manage with telemedicine.
Wirrell et al., 2020 [12]	Cross-sectional study	212 neurologists	U.S.A.	4/8	April, 2020	-		
Lima et al., 2020 [13]	Case series	7 patients with DT	Brazil	5/10	-	6 months; 24 months; 30 months; 14 months; 8 months; 30 months; 24 months	Four of seven patients discontinued DT during the COVID-19 crisis. Two patients discontinued due to financial problems. Two patients discontinued due to anxiety and stress due to the pandemic. One of four patients that discontinued experienced increased seizures.	
Kossoff et al., 2020 [14]	Letter	5 patients with DT (3 with cKD and 2 with MAD)	U.S.A.	6/10 (as a case series)	March–May, 2019	40 days; 4 weeks; 1 month; 4.5 years	Obtaining labs and other routine assessments may be more difficult. Management by telemedicine is difficult for young infants, children/adults with complications, those at high risk for hypoglycemia or metabolic issues, families without access to technology, and those unable to access emergent medical care if necessary.	Five patients were able to continue cKD in the following unique ways: Follow-up of cKD with video visits. Initiation of cKD by outpatient with telemedicine. Initiation of cKD by short admission and phone education. Initiation of MAD as a temporary alternative to cKD by telemedicine and e-mail. Follow-up of MAD with telemedicine.
Ferraris et al., 2020 [15]	Letter	- (Approximately 20 visits with cKD or MAD)	Italy	2/10 (As a case series)	March–May, 2020	-	One patient had more difficulty in continuing cKD, but this patient already had poor compliance history prior to the COVID-19 pandemic. A few patients reported some difficulties in finding supplements and DT products during lockdown.	Telemedicine was conducted without major problems.

-: Not stated in the manuscript, cKD: Classic ketogenic diet, DT: Diet therapy, LGIT: Low glycemic index diet, MAD: Modified Atkins diet, MCT: Medium-chain triglyceride.

4.3. Overcoming challenges in measuring biomarkers

Classic ketogenic diets need laboratory testing at regular intervals for the monitoring of ketosis, which may pose a challenge during the pandemic. Alternatively, a modified Atkins diet [12] requires monitoring of only blood glucose levels, which may be conducted at home, and also has the benefit of reducing potential negative health effects, such as nausea, caused by ketosis. These test kits may be mailed to the patients, and the results can be reported during a video conference or via e-mail as photographs [14].

4.4. Securing the food for the diet therapy

Although not limited to the pandemic period, the attitude and efforts of a patient and the patient’s family are important factors in maintaining the diet therapy. The efforts of patients and their

families are particularly important in terms of securing the necessary food to continue the diet.

Shopping online or using a delivery system is a good option to maintain diet therapy during the COVID-19 crisis [14]. As local grocery stores may be sold out of specific items, people can order food for their diet therapy online. Shopping online and use of a delivery system also allow access to food without risking exposure to the virus because the items are delivered to the doorstep. As another solution, some non-perishable foods such as canned fish can be stored for several months or years at room temperature [14]. These foods are generally easily available during crisis. Therefore, obtaining non-perishable goods is a good practice for people on diet therapy in general, not only during the COVID-19 crisis. The most basic and effective way to prevent food shortage is to consume all of the food in the house and avoid wastage wherever possible [14]. Therefore, keeping track of the expiration dates for food items is important. When cooking, people should use ingredients that are

Table 2
Suggested solutions to overcome the difficulties for patients receiving diet therapy during the COVID-19 pandemic.

Difficulties during the COVID-19 pandemic	Suggested solutions
Cost	Educate society
Laboratory biomarkers of a classic ketogenic diet	Change to modified Atkins diet [12] Mail kits to patients [14] Ask patients to report results via video conference or e-mail as photographs [14]
Access to foods	Online shopping [14] Delivery system [14] Store non-perishable foods [14] Consume all foods [14] Avoid wastage [14] Keep a track of the expiration dates [14] Organize the refrigerator, freezer, and pantry regularly [14]
Maintaining motivation	Careful follow-up E-mail patients with PDFs of dietary guidance materials [14] Photos of all food preparation stages [14] Suggest inexpensive brands to reduce costs [14]
Initiation of diet therapy	Lists of diet therapy-related food [14] Initiate modified Atkins diet or low glycemic index diet [12] Initiate classic ketogenic diet therapy in an outpatient setting with telemedicine [14]

close to their expiry date. Organizing the refrigerator, freezer, and pantry regularly will help people keep track of food items nearing their expiration dates.

4.5. Method to maintain patients' and their families' motivation for diet therapy

A previous article indicated that it is important to keep patients motivated for diet therapy through careful follow-up, even in telemedicine. Specifically, this includes e-mailing patients PDFs of dietary guidance materials, such as photos of all food preparation stages, suggestions for inexpensive brands to reduce costs, and lists of diet therapy-related food [14].

4.6. Method to initiate diet therapy during the COVID-19 pandemic

As admissions for the initiation of classic ketogenic therapy are restricted due to the COVID-19 pandemic, clinicians may consider initiating other diet therapies, such as the modified Atkins diet or low glycemic index diet [12]. However, clinicians must note that these diet therapies are known to be less effective than the classic ketogenic diet therapy [12]. Clinicians may also consider the initiation of the classic ketogenic diet therapy in an outpatient setting with telemedicine [14].

4.7. Efficacy and safety of diet therapy during the pandemic

The efficacy and safety were not investigated in two of the included cross-sectional studies [11,12]. This is because one focused on the satisfaction of patients or caregivers and the other was directed at physicians, and not patients or caregivers. Another case series from Brazil reported that three of seven patients were able to continue the diet therapy during the pandemic; among these three patients, one experienced seizure worsening, indicating relatively low efficacy [13]. Regarding the safety, this case series described that six of the seven patients experienced adverse effects of ketogenic diet or psychological complaints, indicating relatively low safety. However, one letter reporting on patients who underwent diet therapy with telemedicine found that almost

none of the patients experienced major problems [15]. This suggests that the use of telemedicine has high efficacy and safety. A letter from USA reported only five cases; in all of these, diet therapy was continued successfully and controlled seizures were reported; therefore, we could not determine the efficacy or safety of this diet therapy during the pandemic [14]. Thus, the efficacy and safety of the therapy have not yet been fully investigated, and further research will be necessary to clarify this issue.

4.8. Strengths and limitations of this study

The main strength of our study is that we elucidated the various difficulties in continuing diet therapy for patients with epilepsy during the COVID-19 pandemic via a systematic review of the existing literature. However, the findings of our study are limited because only five articles were included. The small number of included papers may be insufficient to describe all difficulties in continuing diet therapy during a pandemic.

5. Conclusion

In this article, we have summarized research studies and described the difficulties in maintaining diet therapy for patients with DRE using a systematic review approach. Even in cases where physical access to medical care providers is restricted due to the COVID-19 pandemic, patients can use the available technology to overcome such difficulties. Epileptologists need to promote such technologies and educate patients and caregivers on the strengths of the technologies, as well as how to use them.

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Ethical statement

Not applicable because of the systematic review.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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