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Awareness of Nutrition's Impact on Mental Health and Ketogenic Diet's Therapeutic Potential for Mental Illness and Other Chronic Disorders

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ABSTRACT

Mental health affects millions of people worldwide, and current pharmaceutical treatment approaches often lead to worse outcomes, weight gain, and increased cardiovascular risk. The ketogenic diet offers hope in the treatment of schizophrenia and other neurological and psychiatric disorders. The aim of this project is to explore public awareness of nutritional psychiatry and the ketogenic diet's clinical utility for various conditions including schizophrenia, mood disorders, Parkinson's, and multiple sclerosis. Study participants (n=108) completed a 12-question survey about individual nutritional habits and current knowledge of KD. Responses were obtained from medical students, practicing healthcare professionals, college undergraduate students, and members of the general public. It was found that 74.5% of participants consciously utilize nutrition to improve their wellbeing. 84.9% of participants reported negative mental wellbeing when eating unhealthy foods. Similarly, results showed that 63.2% of individuals noted improved mental health when eating healthier food options. While 85.4% of participants agree with the statement that KD has a role in weight management, there was no significant difference in the perceived role of KD in depression and psychosis. The perceived role of KD for relieving symptoms was observed for chronic seizures, Parkinson's and MS. The findings of this study highlight the need for future research on KD's clinical utility in chronic disease. With greater public awareness in both the medical and non-medical communities, healthcare teams can reduce the alarming rate of metabolic syndrome that is comorbid with many chronic conditions and prevent premature deaths in severe mental illness.

KEY WORDS: ketogenic diet (KD), alternative and adjunct therapy, nutritional therapy, drug-resistant mental illness, chronic disease, gut microbiome, metabolic syndrome

INTRODUCTION

Although schizophrenia affects less than 1% of the total population in the United States, it is associated with an increased risk of morbidity for patients and their caregivers. It remains among the top leading causes of disability worldwide, and it is estimated that nearly 28.5 years of life are lost in individuals with schizophrenia. Treatment that includes psychotherapy in combination with antipsychotic medications has been shown to be the most effective approach; however, many neuroleptic medications increase the risk for metabolic syndrome, muscular rigidity, cardiovascular, and neurological symptoms. While this is the mainstay of treatment, a subset of patients is treatment-resistant and shows no signs of improvement in symptoms, social, or occupational functioning despite multiple medical treatments and approaches. Factors such as resistance and the risk of harm with continued long-term use in treatment-resistant patients require adjunct and complementary approaches as traditional approaches fail to reduce symptoms. It is important to state that clinicians and researchers attribute higher rates of metabolic syndrome, poor diet and inactivity, and undiagnosed heart conditions to premature and sudden unexpected deaths commonly seen in this patient population.

Early intervention and measures aimed at reducing the risks of cardiovascular disease ought to be more emphasized and integrated into clinical practice. Premature death from cardiovascular disease is preventable, and current treatment regimens and healthcare systems are failing to address the issue that is so prevalent in the mental health space. Historically, the ketogenic diet has been utilized in the treatment of childhood seizure disorders; however, today the KD is more commonly recognized as a weight loss tool by the general public. While brain chemistry changes associated with the KD continue to be studied, it is clear that altering the brain's fuel source from glucose to ketones produces profound effects that may be further influenced by the gut

microbiota. Palmer et al.⁵ found that after the induction of a KD in treatment-resistant patients, symptoms improved over the course of several months and went into total remission without the use of any antipsychotic medications. In this report, the effects of KD on mental health, mood, and behavior will be explored in addition to public awareness of the diet's therapeutic potential.

BACKGROUND

While the concepts of metabolic syndrome and KD are not new, an in-depth analysis might be helpful before exploring the effects of KD on brain metabolism. The leading cause of premature death in patients with severe mental disorders remains cardiovascular disease, and risk factors include hyperglycemia, hypertension, elevated triglycerides, low HDL, and central obesity. These are classically termed modifiable as simple lifestyle changes such as nutrition and exercise, if implemented early, can greatly reduce the risk of a heart episode. Kahl et al in their comparative study of pericardial adipose tissue and metabolic syndrome in patients with MDD and controls, show the direct implications of metabolic syndrome in patients with severe psychiatric disease. In their study, pericardial adipose tissue volumes were significantly increased in patients with chronic MDD compared to acute MDD and control samples. These findings were consistent with autopsy findings in schizophrenic patients with sudden deaths in which cardiovascular disease was found to be the leading cause of death.

When it comes to addressing the risks of metabolic syndrome, the DASH (Dietary Approach to Stop Hypertension) diet has been recommended by the American Heart Association for the treatment of hypertension, but perhaps it's time to consider the KD. The DASH diet is a heart-healthy diet that limits the consumption of sodium to under 2.4 grams/day in addition to lowering the overall intake of sweetened beverages, sugar, sweets, fatty meats, and full-fat dairy.⁸ In a comparative study, the low-carbohydrate diet resulted in greater improvements in mean

systolic blood pressure, blood glucose, and weight loss over a 4-month span. There is limited data on cardiovascular outcomes between diets; while past research has demonstrated the positive effects of the DASH diet on blood pressure, blood glucose, and weight, the KD showed statistically significant improvement in outcomes when compared to DASH. Limitations of the study included no standardized method for diet adherence and non-representative samples. Nonetheless, the findings call for future research comparing the effectiveness of these two dietary approaches.

The KD, as mentioned above, consists of transitioning the body's fuel supply to fatty acids and ketones instead of carbohydrates and has been historically utilized for the treatment of childhood seizure disorders. The complex physiologic effects of ketosis on the brain continue to be a topic of research, but current evidence has shown ketosis may help reduce microinflammation, increase select neurotransmitters, and promote neuroprotective mechanisms in neurons, processes that become dysregulated in many nervous system disorders. The KD has been utilized clinically in treatment-resistant epilepsy since the early 1920s. Neal et al. 10 conducted a randomized controlled study including over 73 children with failed anticonvulsant therapy to test the efficacy of the KD and reported that following 3 months of initiating the diet, the average number of baseline seizures reduced to 62% compared to an increase of 137% for controls. While treatment facilities are limited for adult patients, an observational study conducted at the Johns Hopkins Adult Epilepsy Diet Center concluded that the KD may be a safe and effective tool in the management of chronic epilepsy, although more rigorous studies are needed to determine the efficacy in adult patients ¹¹ While the underlying pathway and mechanism for depression are multifactorial, early rat models indicate the KD may have clinical utility.

The KD has also been implicated in major depressive disorder. Guan et al. 12 conducted mouse models for depression and reported the KD improved depressive-like behaviors and social interactions. The authors attribute the improved outcomes to enhanced neuronal signaling via decreased excitability of microglia. Rats fed a KD following the injection of neurotoxin had significantly decreased microglial cell volumes and increased axonal processes compared to controls. KD-fed rats were also found to have significantly lower levels of proinflammatory cytokines and chemicals in specific brain regions believed to play a role in depression. There is increasing scientific literature that points to the KD as a potential nutritional therapy for a variety of neurological disorders including schizophrenia, mood disorders, Parkinson's, Alzheimer's, multiple sclerosis, cancer, migraines, and autism spectrum through mechanisms that restore mitochondrial dysfunction, improve neuroprotection and cell signaling, and reduce oxidative stress. Research on human mitochondrial and neuronal tissue is limited, but rat models serve as a proxy in understanding the underlying mechanisms that may lead to adaptive changes in human cells. 13-16 Another area of research that has been implicated in many neurological psychiatric disorders involves what scientists have termed the gut-brain axis.

The proliferation of the microbiota, which occurs during infancy, is influenced heavily by childbirth, breastfeeding, antibiotics, infections, and nutrition. The gut microbiome has been implicated in several chronic diseases and neurological disorders including IBS, psychological disorders, multiple sclerosis, and other neurological disorders. Containing over an estimated 10^13 microbiota, the human gut is composed of bacteria, viruses, and yeasts involved in many cellular functions of immunity, metabolism, and nutrient absorption. Bacteria compose the largest organisms found in the gut with Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria being the most abundant. Other species are included in lesser abundance, with

fungi and viruses found in lesser quantities.^{17,18} Several mechanisms have been proposed for the gut-brain axis, which include stimulation of autonomic vagal fibers, endocrine, metabolic, and immune signaling.

Cell signaling between peripheral 5-HT/SERT and its binding site for 5-HT in the GI and CNS via 5-HT3/5-HT4 is altered in IBS leading to chronic and recurrent symptoms. Scientists theorized the KD could be used to restore the altered signaling and using animal models, Orlando et al. 19 reported improved levels of neuroprotective peptides (BDNF) and its regulation of altered 5-HT signaling. Comparatively, Schneider et al. 20 conducted a randomized controlled trial including 60 patients with major depressive disorder and brain changes were analyzed before and following the administration of probiotic supplements. They reported improved verbal learning memory and improved working memory tasks with an associated decrease in hippocampal hyperactivity in probiotic supplement groups compared to placebo. The gut microbiome is thought to be involved in the development of neurological disorders, including multiple sclerosis, although the mechanisms underlying the autoimmune process remain largely unknown.

Researchers from Germany sought to find the association between the gut microbiota, multiple sclerosis, and the KD. The composition of colon flora was analyzed in patients diagnosed with MS and healthy controls before and during 6 months of KD. It was found that the diversity and concentration of colon flora were reduced in MS patients compared to healthy controls. During the KD, total bacterial concentrations in MS patients initially decreased before rising to levels typical for healthy controls and significantly higher concentrations measured before diet implementation.²¹ Although the improved bacterial concentrations indicate alterations in metabolism following ketosis and implicate gut bacteria in nervous system disorders, it remains unclear the exact role bacteria play in the progression and treatment of neurologic disorders.

One of the most promising therapeutic potentials of the KD is the treatment of drug-resistant psychosis. Large randomized controlled studies have yet to be conducted but anecdotal case studies serve as a model for future research. The first patient, an 82-year-old female, was diagnosed with schizophrenia when she was just 17 years old. Prior to initiating the KD for weight loss, the patient's chronic psychosis and suicide attempts were treated with antipsychotic and mood-stabilizing drugs which offered no relief. Within weeks of starting the diet, there was a marked reduction in psychotic symptoms in addition to weight loss with complete remission of hallucinations and paranoia after several months. The patient no longer takes antipsychotic or mood-stabilizing drugs and has remained symptom-free with improved social and personal functioning. The second patient is a 39-year-old female with a history of depression, anxiety, and psychosis who throughout life experienced bouts of hospitalizations and suicide attempts. Similar to the other patient described in the study, she had been unsuccessfully treated with antipsychotics and antidepressants. She began the KD for chronic IBS and after discontinuing her medications, experienced weight loss and complete remission of her psychotic symptoms. For 5 years, the patient remains free of psychotic symptoms and completely off her antipsychotic medications.3

The importance of nutrition cannot be disputed and while underlying mechanisms remain to be completely elucidated, it seems the KD may serve as a beneficial alternative or adjunct therapy to many conditions. Many challenges exist in implementing dietary practices including adherence, access, misperceptions, and dominant standard practices, but a better understanding of public attitudes towards nutrition and health may help in the design of easily adaptable lifestyle changes and programming aimed at improving health outcomes.

METHODS

A formal questionnaire created through Google Forms was electronically shared via email and social media. Parameters for inclusion included anyone 18+, friends, Augsburg, and AAPA community members. To maximize survey participation, an incentive was offered for a free ketogenic diet recipe and a chance to win \$10. The survey was made available for one week, and descriptive statistics using Excel spreadsheets were used to analyze the data. A formal student classroom project IRB application was submitted for review to the course chair, outlining the research question, purpose of the study, survey contents, method of survey and data collection, subjects and confidentiality, and informed consents. The survey and methods satisfied IRB requirements for research ethics and prior to conducting research, obtained exempt status.

RESULTS

Enlisted participants completed a 12 question survey and obtained results are as follows. Excel spreadsheets were utilized to calculate p-values, confidence intervals and other statistical data. The null hypothesis for each condition set was p=0.5 and the critical value=0.05 for 95% CI.

1. I use nutrition as a tool in my life for my mental health:

There was an observed statistical difference for the intentional use of nutrition to improve mental wellbeing as 74.5% of participants reported conscious nutritional habits (n=106, P=0, CI=0.6623,0.8282, SD=0.0423). In contrast, 4.7% of participants reported eating what is most convenient while 20.8% of participants eat foods according to pleasure and taste.

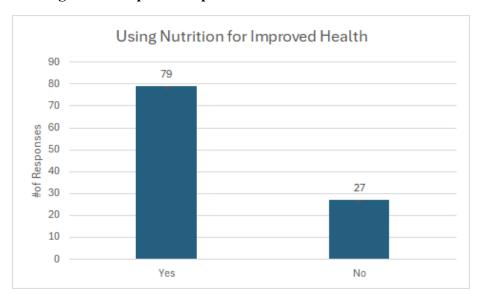


Figure 1. Graphical Representation of Intentional Nutrition

Eating Habits as Reported by Study Samples 60 50 40 30 23 22 20 10 0 Fast Follow Strict Diet Homemade Meals Tastefully Pleasing Food/Convience 56 5 ■Series3 23 22

Figure 2. Graphical Representation of Eating Habits

2. I have noticed my mental health is affected when I eat certain foods:

There was an observed statistical difference in subjects' mental health when eating unhealthy foods with 84.9% of participants noticing negative wellbeing (n=106, P=0, CI=0.7809,0.9172,

SD=0.0348). 24.5% admitted to sometimes noticing these changes, while 15.1% of participants reported very little or no change in their wellbeing. Similarly, it was found that 63.2% of individuals noted improved mental health when eating healthier options (P=0.0065, CI=0.5404,0.7238, SD=0.0468) while 17% reported little to no improvement.

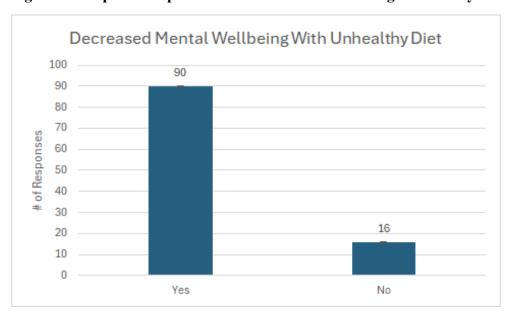


Figure 3. Graphical Representation of Mental Wellbeing: Unhealthy Diet

3. Is there a role for ketogenic diet in symptom relief for the following health conditions? (Seizures, Severe Depression, Parkisons, Multiple Sclerosis, Schizophrenia)

Finally, when assessing public awareness of the KD, 85.4% of participants agreed with the statement that KD has a role in weight management (n=103, P=0,CI=0.7864,0.9224, SD=0.0348). The role of Ketogenic Diet in the management of childhood seizure disorder was recognized by 60.8% of individuals (n=102, P=0.0294, CI= 0.5131,0.7025, SD=0.0483). 59.6% of participants believed the KD has a role in managing Parkinson's (n=104) with statistically

significant P-value of 0.0498, CI=0.5019,0.6905, SD=0.0481. 72.5% of participants believed the KD may have a role in relieving symptoms of MS (n=102, P=0, CI=0.6389,0.8121, SD=0.0442). Additionally, the role of KD in severe depression was not statistically significant as 50% of individuals believed the KD may be implicated in relieving symptoms (n=104, P=1, CI=0.4039,0.5961 SD=0.0490). For the treatment of psychosis in Schizophrenia, 57% of participants believed the KD may have a role; however, the observed data was not statistically significant (n=100, P=0.1615, CI=0.4732,0.6668, SD=0.0495). When participants were asked if they would consider utilizing the KD for any of the conditions: seizures, major depression, Parkinson's, multiple sclerosis, and schizophrenia, 82.5% reported yes (n=103, P=0, CI=0.7519,0.8985, SD=0.0374) while 56.3% would consider utilizing the KD for weight loss; however, the data was not statically significant for weight loss (P=0.2002, CI=0.4673,0.6589, SD=0.0489). Other recognized diets for managing medical conditions as reported by survey participants included mediterranean, plant based, low FODMAP, low sodium gluten free, carnivore, pescatarian, dairy free, intermittent fasting, low oxalate, paleo, Pritikin, and Atkins.

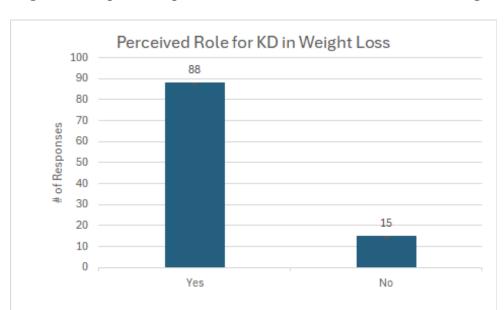


Figure 4. Graphical Representation of Perceived Role of KD in Weight Loss

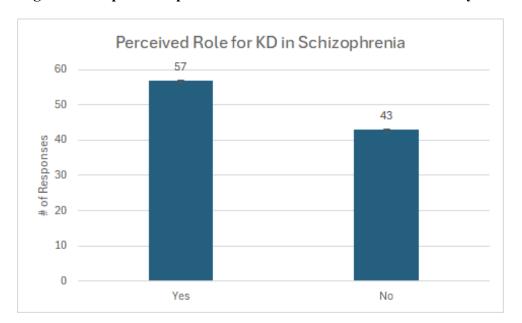


Figure 5. Graphical Representation of Perceived Role of KD in Psychosis

DISCUSSION

While previous research has demonstrated the potential benefits of the ketogenic diet in managing chronic conditions, the primary focus in this study was on public knowledge and attitudes towards nutritional psychiatry. The main findings are in agreement with current understanding concerning the relationship between food and health as evidenced by participants' positive wellbeing when eating healthy foods and decreased mental wellbeing when consuming a diet high in excessive fats. While stress and other mental health conditions impact appetite and food cravings, certain foods have a powerful effect on levels of stress and wellbeing. Potential areas for future research include identifying which individuals gravitate towards unhealthy diets during stress or when suffering from an underlying mental illness and which individuals are susceptible to increased stress and mental illness as a result of unhealthy food choices.

Furthermore, assessing duration of conscious eating as well as quality of foods is an important

area to explore to better understand nutrition's impact on mental health. 74.5% of participants reported consciously utilizing nutrition to improve their wellbeing and more research aimed at studying long term outcomes with diets is needed, especially the KD. It's worth highlighting that many chronic diseases are preventable and negative effects can be dampened or avoided by healthy changes in lifestyle. As described earlier in the report, patients with severe mental health often experience premature deaths as a result of genetics, environment and unhealthy lifestyles despite frequent contact with healthcare professionals. Patients who seek guidance for their chronic conditions remain unseen and unheard by professionals with good intentions to help. Empowering and encouraging individuals to take ownership and responsibility for their wellbeing through nutritional education should be part of the solution in addressing health and disease. As hypothesized, participants were more familiar with the ketogenic diet as a weight management tool versus a tool for managing chronic conditions; however, the number of people who would consider the KD for chronic seizures, major depression, Parkinson's, multiple sclerosis, and schizophrenia was statistically significant. The number of individuals who believed in the potential of the KD diet to reduce symptoms in seizures, Parkinson's, and MS was statistically significant, but that was not true for depression or psychosis. Although not surprising, the data highlights the lack of public awareness for all the potential benefits of KD outside of weight loss. This study was particularly interested in public attitudes of the diet's clinical use for chronic psychosis and awareness among study participants was not statistically significant. This is an important finding as the study included medical students and practicing Physician Assistants. Given the chronic nature of severe psychosis and other brain disorders, more research is needed to better understand the impacts of altered energy metabolism associated with many of these conditions. Palmer et al.⁵ have provided a model for future research and their

case studies serve as examples for the millions of people who may benefit from a ketogenic diet. Collaboration with nutritionists, social workers, psychiatrists, and other members of the healthcare team will be necessary to effectively implement change and lasting outcomes. The dietary plan requires routine blood work to assess ketone levels, cholesterol and other biomarkers for potential disease, in addition to strict intake levels of protein, carbs, and fats. Some limitations of this study include small sample size, biased or unclear survey choices, and unrepresentative samples. Data regarding public knowledge of the ketogenic diet's clinical utility may have been skewed by input from individuals with medical backgrounds and therefore not representative of the overall general population.

CONCLUSION

This study aimed to investigate public attitudes on nutritional psychiatry as an emerging adjunct therapy to many chronic health conditions such as depression, multiple sclerosis, Parkinson's, and schizophrenia. The findings revealed that while a majority of study subjects are aware of the ketogenic diet's potential as a weight loss tool, more education and public awareness in the medical community and general public is needed to highlight nutrition's clinical utility as an adjunct tool for chronic conditions. Another key aim of the study was to assess the subject's relationship with food and how it impacts their mental wellbeing. There was an observed difference in outcomes when people report consuming healthy and unhealthy foods; however, it's unclear how an individual's underlying mental illness or mood affect cravings for certain foods. This report highlights the importance of future research to expand on the existing work that has shown that KD can successfully be used in treatment of epilepsy, depression, psychosis, and other drug-resistant conditions. To better meet the needs of patients and prevent premature deaths

caused by metabolic imbalance, an assessment of DASH vs KD as well as exploring other dietary plans ought to be carried out to assess the risks, benefits, short and long term outcomes based on individual needs, accessibility, and adaptability into patient's everyday lives.

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