

## KETOGENIC DIET AND ALZHEIMER'S DISEASE



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**Dementia can be described as a progressive syndrome caused by a variety of brain illnesses that affect memory, thinking, behaviour and the ability to perform everyday activities.<sup>1</sup>**

Diet is thought to have an effect on the progression of symptoms and function. In recent years, there has been growing interest in using the ketogenic diet for Alzheimer's disease. This article reports on recent research in this area and discusses the evidence for implementing the ketogenic diet in this patient group.

It is believed that one in six people over the age of 80 have dementia and is estimated that only 59% of people living with dementia in England have a formal diagnosis. Alzheimer's disease is the most common form and affects 62% of those with a diagnosis of dementia.<sup>2</sup> With an ageing population and increased awareness of dementia, more people are being diagnosed than in the past. It is important to try to obtain a diagnosis for dementia in order to rule out other possible causes of any symptoms. It allows an explanation for any changes to behaviour and is also important so that any possible treatment and support for individuals and their families or carers can be accessed.

Since 2010, the UK government has committed to increasing research funding into dementia.<sup>3</sup> However, a recent study concluded that even though this has improved, funding for research into dementia is still disproportionately low against disease burden compared to other diseases such as cancer and coronary heart disease (CHD). Dementia has the highest social care system cost of £10.2 billion per year compared to cancer and CHD. Despite this, in 2012, for every £10 in health and social care cost of disease, cancer received £1.08 in research funding, CHD received £0.65,

compared to dementia which received only £0.08.<sup>4</sup> Given disease burden, it is important for research to be carried out in this area. As a degenerative disease, if there are potential methods of reducing the rate of disease progression, then these should be investigated.

### WHAT IS A KETOGENIC DIET?

A ketogenic diet is a diet which results in ketone bodies being produced as a result of the body having to use fat as an energy source instead of carbohydrate. The exact composition of this diet can vary, but it is generally based on a high fat, low carbohydrate and adequate protein intake. The classical ketogenic diet uses a 4:1 ratio in calorie intake of fat to carbohydrate.<sup>5</sup> Variations, or less restrictive versions of this, include the modified Atkins diet, medium chain triglyceride diet and low glycaemic index treatment.<sup>6</sup>

In normal energy metabolism, the brain uses glucose as a primary energy source. However, a high fat and low carbohydrate intake results in fat being broken down in the liver to fatty acids and ketone bodies. This also happens during prolonged periods of starvation or fasting, when alternative energy sources are needed. The ketone bodies can then be used instead of glucose by the brain.<sup>7</sup> It has been found that once ketone bodies reach a concentration of 4.0mmol/L, they are used as an energy source by the central nervous system.<sup>8</sup>

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control, there are potential weaknesses; 30% of participants reported short-term gastrointestinal-related adverse effects and compliance with the diet was poor, with only 10% remaining on the diet for three to six years.<sup>5</sup>

#### EVIDENCE FOR KETOGENIC DIET IN ALZHEIMER'S DISEASE

Research into the use of the ketogenic diet for neurodegenerative conditions, including Parkinson's disease and motor neurone disease, is growing. Unfortunately, there is little evidence for the use of a ketogenic diet for Alzheimer's disease, particularly in human trials. Current evidence is based on animal studies, but this appears to be conflicting. Studies using Alzheimer's disease in mice that were fed a ketogenic diet have shown improvements in motor function<sup>9</sup> and a reduction in  $\beta$ -amyloid levels (which form the plaques associated with Alzheimer's disease).<sup>10</sup> In canines, however, effects were limited to the parietal lobe only.<sup>11</sup>

Although there is little evidence of the benefits of the classical ketogenic diet in humans, a less restrictive form of the ketogenic diet, such as the modified Atkins diet which would contain higher amounts of carbohydrate and protein intake compared to the classical ketogenic diet, could be a more realistic strategy to use and could improve compliance. Using the modified Atkins diet has been shown to be effective for children with epilepsy<sup>12</sup> and so it could be as equally effective as the classical ketogenic diet for Alzheimer's disease.

To minimise compliance issues, an alternative method of inducing ketosis, by using a ketone monoester alongside normal intake, has been investigated. It was shown to improve cognitive performance and reduce amyloid- $\beta$  and tau deposition in a mouse Alzheimer's disease model.<sup>13</sup>

A study which observed the effect of taking a ketone monoester supplement in one participant with Alzheimer's disease concluded that using this method is safe, convenient and can be taken regularly as a food supplement with no difficulty.

It resulted in the participant with early onset Alzheimer's disease improving from needing constant supervision to becoming more self-sufficient (within days) and carrying out more complex tasks, such as housework and gardening, by six weeks. He was also able to discuss events that had taken place the previous week.<sup>14</sup>

During this 20-month study, the participant's brain MRI was stable. Unfortunately, these effects were limited and he eventually deteriorated and also showed poor wound healing, respiratory infection and an outbreak of fever. Despite his poor outcome, this case study did show that not only did the ketone monoester slow down progression, but it also temporarily reversed some symptoms of Alzheimer's disease.

A stronger evidence base perhaps, including randomised controlled trials, is needed before these results can be generalised. ▶

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### MECHANISM OF ACTION

The mechanism through which a ketogenic diet improves symptoms of Alzheimer's disease is unclear; however, it is believed that it provides a neuroprotective effect. It has been shown in animal models (mice) that a ketogenic diet resulted in improved mitochondrial function and less oxidative stress and  $\beta$ -amyloid deposition compared to those fed a normal feed.<sup>10</sup> Cognition and alertness has been shown to improve with patients who are on a ketogenic diet for epilepsy<sup>15</sup>, which was thought to be due to improvements in seizure control, decreased medication, or a nonspecific effect of the diet.

Another study found that attention and social function improved in children with epilepsy.<sup>16</sup> Therefore, although there is a lack of evidence for the use of the diet in humans with Alzheimer's disease, there is evidence which demonstrates an improvement in cognitive function from following the ketogenic diet. The question that arises is whether it would result in a significant improvement in symptoms of Alzheimer's disease and at what stage of the disease would the diet need to be implemented in order to have a beneficial effect in slowing down the rate of progression of disease.

### PRACTICALITY OF IMPLEMENTING A KETOGENIC DIET IN THIS PATIENT GROUP

Although the evidence base for a ketogenic diet in this population is still building, the reality of being able to follow this diet in this patient group is another challenge altogether. Firstly, there is the issue of gaining informed consent to implement this diet, which may be difficult depending on what stage of dementia the individual is at. If an individual is confused, or if they are unlikely to remember or understand why their food choices have been restricted, then it may cause them unnecessary distress.

A further challenge is the actual implementation of the diet. This may vary depending on where the individual is living. For example, it may be easier to implement if the individual is within

a care setting and all meals are being catered for. However, it would require appropriate training for staff in care homes. If an individual is living in their own home and family members are caring for them, then they would require dietetic advice for a ketogenic diet. If an individual was still managing to prepare their own meals, it may be difficult to implement a change in their diet at a time when routine is key. If memory has been affected, then trying to remember new information will be difficult.

More importantly, we need to question the use of a restrictive diet in a group that may be facing existing nutritional issues. It is common for individuals with Alzheimer's disease to have a poor appetite, not recognise hunger or thirst, suffer from disease-related malnutrition, have difficulty chewing or swallowing, and, therefore, any restrictions to their food choices could have a further impact on their nutritional status. Maintaining nutritional status is usually a priority in this patient group. When considering malnutrition and the use of energy dense diets for people with dementia, the ketogenic diet would at least coincide with this, as both are based on a high fat intake. It would be important to assess people at an individual level to determine what the nutritional priority and the dietetic aim is and how appropriate the ketogenic diet would be for them.

Overall, there is limited evidence for the use of a ketogenic diet for Alzheimer's disease at present. More importantly, it is restrictive in a patient group that may already be facing nutritional issues. Familiar foods, nutritionally dense foods and maintaining nutritional status should remain the priority for people with Alzheimer's disease. However, we cannot ignore the potential for the diet to improve quality of life. It would be beneficial for the effects of the ketogenic diet to gain more research funding and it would be interesting to observe the potential future for its use in neurodegenerative disorders.

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