Medium Chain Triglycerides (MCT’s)

An alternative approach to the treatment of Alzheimer’s disease

If one takes a realistic view, modern medicine appears to have little of real significant to offer patients with Alzheimer’s disease. Treatments are symptomatic and do not significantly decelerate or prevent progression. Behavioural and psychiatric challenges of great concern to caregivers are attacked with powerful drugs not approved for these indications, and have serious and sometimes permanent adverse effects. A new approach appears desperately needed. While it has been known for decades that Alzheimer’s disease is associated with impaired cerebral glucose metabolism, only recently has this observation begun to attract serious attention and now some even call Alzheimer’s disease Type 3 diabetes. This article addresses therapeutic approaches to cerebral hypoglycemia which directly or indirectly involve providing an alternative brain fuel to counteract decreased glucose metabolism. The alternative fuel consists of ketone bodies produced by ketogenesis in the liver. Clinical studies and limited randomized controlled trials have provided evidence for both the biological plausibility of this alternative approach and its efficacy and safety in the treatment of mild cognitive impairment and Alzheimer’s disease. In addition, what appear to be highly satisfactory oral precursors of the required ketone bodies are natural products readily available in many health food stores. This has generated considerable anecdotal evidence recently reviewed in a book by a respected physician that makes an important contribution to this field.
Introduction

Mainstream medicine treats early to moderate stages of Alzheimer’s disease (AD) with cholinesterase inhibitors (Aricept, Exelon, Razadyne and rarely Cognex). For moderate to severe stages, memantine (Ebixa), a drug that regulates the activity of glutamate, a chemical involved in learning and memory, is frequently employed. While aggressive combination therapies can produce small decreases in the frequently relentless increase of dementia or deterioration in daily living scores, progression remains (Atri 2008).

“Currently available treatments for AD are symptomatic and do not decelerate or prevent the progression of the disease” (Herrmann 2011). There is considerable support for this view (Farrimond 2012, Galvin 2012, Lanctot 2009, Popp 2011).

In the US there are no drugs approved for dealing with behavior and psychiatric challenges associated with AD which cause significant problems for caregivers. However, the whole arsenal of antidepressants, anxiolytics and antipsychotics are widely used off-label. The problems and side effects associated with these drugs, both transient and permanent, can be significant (Breggin 2008). While these drugs modify symptoms, their adverse effect profile casts doubt on their true utility. Conventional therapies and the small changes they can affect provide little of real significant to offer patients with Alzheimer’s disease.”

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Ketone Bodies--A Replacement Brain Fuel

The three so-called ketone bodies are water soluble compounds (acetone, acetoacetate and beta-hydroxybutyrate) produced in the liver from fatty acids (ketogenesis). Ketone bodies bypass insulin controlled cellular entry and can serve as energy sources in the mitochondria of tissues including the brain. It was once accepted that upon weaning, the brain was limited solely to glucose for metabolic energy. This view has changed as the neuroprotective potential of ketone body administration has been shown for neurodegenerative conditions, epilepsy, hypoxia/ischemia and traumatic brain injury,
and that there is an age-related therapeutic potential for ketone bodies as an alternative substrate (Prins 2008, White 2011). Also dietary ketosis has been shown to enhance memory in mild cognitive impairment, and there is evidence of protection against neuronal insults, an increase in metabolic efficiency relative to glucose, and in general such diets appear to some extent to mitigate neurodegenerative mechanisms (Krikorian 2012, Veech 2004). Perspective regarding the role of ketones in brain metabolism can be gained by considering that during starvation or very low carbohydrate intake, the liver turns to making ketones (Owen 1967). This defence mechanism evolved eons ago and was likely necessary for human survival.

Starvation is obviously not a practical therapeutic intervention. Neither is a severely ketogenic diet for many patients. Adherence to a classical ketogenic diet is a serious problem since about 90% of energy must come from fat. An obvious solution is an oral supplement or “medicinal food” that provides a source of the needed ketone bodies. Either natural or synthetic medium chain triglycerides (MCT) are obvious sources.

**Oral Medium-Chain Triglycerides To Treat Alzheimer’s Disease**

One of the prominent researchers in the field of brain hypometabolism, Samuel Henderson, was instrumental in the development of a MCT-based product to treat AD called AC-1202, which contained one MCT and could be taken as a dissolved powder. It was patented and tested in several trials and recently a multicenter randomized controlled trial reported (Costantini 2008, Henderson 2009). The compound rapidly elevated serum ketone bodies in patients with AD and resulted in significant improvement in cognitive scores in those with mild to moderate AD when compared to a placebo. MCT oil ingestion has also been found in a placebo controlled study to preserve brain function during hypoglycaemia in intensively treated patients with Type 1 diabetes (Page 2009). Some would consider these results convincing evidence concerning the biological plausibility of the hypometabolic hypothesis.

AC-1202 is available only by prescription and approved by the FDA as a “medicinal food” called Axona. It contains only one ketone generating MCT. Coconut oil and MCT oil are natural sources generating several ketone bodies and offering flexible dosing throughout the day.

The leading advocate of MCT oil and coconut oil is Dr. Mary Newport, M.D., a paediatrician and director of a neonatal ICU at a Florida hospital. In 2008 her husband had moderately advanced AD that was progressing significantly. She first heard of the use of MCTs for AD in 2008 when she came across reference to Henderson’s patent, found AC-1202 contained a MCT and ascertained that MCTs were present in coconut oil which was available at natural food and health food stores. She decided there was nothing to lose by trying coconut oil. This was a turning point in her husband’s life as well as hers. Results were remarkably rapid, AD progression apparently stopped, and over the following three to four years many cognitive and behavioural deficits were significantly reduced and many lost functions recovered. In her words, she “got her husband back.” This is detailed in Dr. Newport’s recent book (Newport 2011).

One of the most fascinating aspects of Dr. Newport’s husband’s change was that initially he was totally unable to draw a clock, a standard test in mental assessment, and a few weeks after starting coconut oil his clock, while not perfect, was significantly improved. This is illustrated in Dr. Newport’s book and in the article on the internet (Newport 2008). In addition, sequential MRI studies revealed that the progression of brain atrophy had been totally halted. It appears that conventional, approved treatments have never produced such a result, or in a significantly sustained manner, any of the above results, especially when the patient has fairly severe AD. Today, most of the interest in this intervention is among lay persons who become aware of MCT oil and coconut oil while doing an internet search for natural AD treatments, through the social media, by word-of-mouth or from Dr. Newport’s book (Newport 2011).

In this book, Dr. Newport provides details and a summary of anecdotal caregiver reports (60 cases) she received after the do-it-yourself treatment became popular. Unfortunately, there is uncertainty as to dose, source of MCTs, adherence, severity of the disease and the quality of reportage from caregivers concerning changes. Nevertheless, 90% of those who tried MCTs were observed to be improved, as indicated by better scores on tests, improved clock drawing, better cognition, more alertness, brighter outlook, improved awareness, less foggy or hazy behaviour, being able again to recognize people or places, being less distractible, and having a better sense of direction.

MCT oil yields higher serum ketone body levels than coconut oil, but the decline over time is more rapid.
than seen with coconut oil. Thus coconut oil taken with MCT oil helps smooth out daily fluctuations with higher average levels and coconut oil may have some other benefits not provided by the commercial MCT oils since it contains other fatty acids (Newport 2011). This influenced Newport’s final protocol which involved using an approximately 1:1 mixture of coconut oil and MCT oil at a dose of three tablespoons with each meal and two at bedtime. To avoid diarrhea, the only known adverse effect of MCTs reported, dose escalation is sometimes needed. It is important to note that while attention was paid to a healthy diet, the macronutrient intake of Dr. Newport’s husband was not drastically altered. In fact, the use of MCTs has the advantage of not requiring significant diet changes and can even be used along with conventional treatments.

Ketogenic Diets

An alternative to ingesting MCTs is to use a ketogenic diet. Newport claims that the ketogenic diet is capable of producing up to 10 times or more ketone bodies than possible with the doses of MCTs commonly being used, and this becomes an attractive next step for those who do not respond to MCT therapy (Newport 2011). The ketogenic diet has been used to treat epilepsy and especially patients who failed to respond to antiepileptic drug therapy. The initial interest occurred in the early 1920s and then there was a long hiatus followed by recent renewed interest. There is now considerable evidence of efficacy in epileptic adults and children (Auvin 2012, Lambrechts 2012, Nam 2011). There has also been recent interest in ketogenic diets to treat Alzheimer's disease (Kossoff 2012, McPherson 2012, Yao 2011). It has also been found that dietary ketosis enhances memory in mild cognitive impairment (Krikorian 2012). In addition, improvement in memory impaired adults has been correlated with orally induced increases in the serum level of the ketone body beta-hydroxybutyrate (Reger 2004).

There are four recognized major ketogenic diets, the classical diet with 90% of calories from fat, the MCT diet, the modified Atkins diet and the low glycemic index diet. The MCT diet has been used since the 1970s and involves using coconut oil while limiting carbohydrates. The modified Atkins diet uses a very low carbohydrate induction diet (70% calories from fat, 24% from protein) as the permanent intervention, whereas the low glycemic diet has 45% from fat and 28% from protein with emphasis on carbohydrates selected for low glycemic index (Kossoff 2012).

Conclusions

What might be called the alternative fuel approach to treating AD has strong biological plausibility. Limited results from clinical and randomized controlled trials provide evidence of efficacy and safety. Treating hypometabolism with a prescription MCT (Axona) has FDA approval for the indication of cognitive impairment. When trial data is combined with a large body of anecdotal evidence, the picture emerges suggesting AD patients appear to obtain much more benefit from this alternative approach than from conventional medical therapy.

Individuals with AD frequently have a mixture of vascular and AD-type abnormalities and some have dementia associated with Lewy bodies. Hypothyroidism, micronutrient deficiencies, heavy metal overload, etc., may also contribute to the symptomatic presentation and the alternative fuel approach would not be expected to impact some of these abnormalities. There is also an issue with genetics. In the AC-1202 clinical studies patients not carrying the E4 variant of the apolipoprotein gene (about half of those with AD) showed the highest response (Costantini 2008, Henderson 2009). However, Dr Newport's husband is ApoE4+ and showed remarkable response (Costantini 2008, Henderson 2009). However, Dr Newport's husband is ApoE4+ and showed remarkable regression (Newport 2011).

It is disappointing that there is not more clinical trial evidence, but therapies involving natural MCT oil and coconut oil are of no interest to pharmaceutical companies, and the very nature of this therapy invites the criticism of not being adequately evidence based and in fact simply another quack treatment. Those who believe in the future of alternative treatments must recognize the necessity of tolerating these hostile views because meeting the demands of so-called evidence-based medicine will be a slow and frustrating adventure, and individuals with AD and their caregivers may be actively discouraged from trying a therapy with the potential for greater benefit than appears attainable by any other means. Judging by what Dr. Newport reports, many AD caregivers will not settle for what mainstream medicine has to offer and seek to circumvent the hostile attitude of modern medicine. They simply adopt the approach that “What is there to loose? We can do this at home...”, a view directly applicable to MCT therapy. Everything needed is available online or at the local health food store, including a mixture of MCT and coconut oil in the proportions used by Dr. Newport (sold as a salad dressing). Finally, the use of MCTs in primary prevention as one ages remains to be studied but intuitively would appear to have merit.
The website of the company making Axona mentions caution when patients have a history of gastrointestinal problems, metabolic syndrome, uncontrolled diabetes and/or kidney disease. The extent to which these warnings apply to mixed MCT oil and coconut oil is unknown, but Dr. Newport reports only diarrhea.

Guidance and monitoring by a physician is always highly desirable.