Efficacy of Adjunctive Extra Virgin Coconut Oil Use in Moderate to Severe Alzheimer’s Disease

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Abstract

Background: Ketogenic compounds derived from medium chain triglyceride (MCT) oils have been claimed to have beneficial health effects in the Alzheimer’s disease (AD) mainly attributed to its medium chain triglycerides. AD is known to have been characterized by early and region specific decline in cerebral glucose metabolism. It is hypothesized that Alzheimer brain tends to preferentially utilize ketones generated from medium chain triglycerides in light of decreased glucose metabolism to improve cognition. Extra virgin coconut oil with predominance of MCT content was used in subjects with moderate to severe AD to examine its efficacy in improving cognitive performance.

Methods: Daily oral administration of extra virgin coconut oil (20 gm) was evaluated in 31 subjects with predominantly moderate to severe AD diagnosed as per DSM IV TR criteria for AD in a 6 week trial using quasi experimental non randomized pre-post intervention design. Subjects were on a normal diet and continued taking approved AD medications. Primary cognitive end points were mean change from baseline in the AD Assessment Scale-Cognitive subscale [ADAS-Cog], and Clinicians Interview based Impression of Change Plus Caregivers input [CIBIC-Plus]. Active oil administration continued for 4 weeks from baseline with successive ratings on measures of cognitive change at 2, 4 and 6 weeks respectively.

Results: There was a significant difference between the ADAS-Cog scores from baseline over repeated ratings at 2, 4 and 6 weeks (Mauchly’s Chi Square X2 = 81.1, χ2=0.4, F =14, p=0.00, η2=0.31). Post hoc comparisons of ADAS-Cog scores from baseline at 4 and 6 weeks were similar [At 4 weeks, Mean difference=4.1, P=0.00, C.I= (1.4-6.7); at 6 weeks, Mean difference=4.1, p=0.00, C.I= (1.0-7.2)]. The response rate of CIBIC-Plus defined as improved or no change was significantly improved over successive ratings from 2 weeks to 6 weeks (Cochran’s Q=22.5, df=2, P=.00). No statistically significant difference could be noted for the total cholesterol, Triglycerides and LDL fractions over the study trial except for the HDL fraction over repeated measures at 4 and 6 weeks over baseline (Mauchly's Chi Square X2 (df=2)=6.5, c=0.8, F (df 1.6, 49.9)=6.4, p=0.005, η2=0.17).

Conclusions: Addition of adjunctive coconut oil is likely to have beneficial effects in cognitive performance for those suffering from moderate to severe AD and the effects were sustained for at least 2 weeks after the oil administration stopped. No deleterious effects on the overall lipid profile could be elicited.

Keywords: Alzheimer’s Disease; Extra virgin coconut oil; Medium Chain Triglycerides (MCT)

Abbreviations

AD: Alzheimer’s Disease; VCO: Virgin Coconut Oil; MCT: Medium Chian Triglycerides; ADAS-Cog: AD Assessment Scale-Cognitive Subscale; CIBIC-Plus: Clinician Interview Based Impression of Change plus Caregiver Input; BHB: β-hydroxybutyrate; MMSE: Mini Mental Status Exam; GM0: Genetically Modified Organisms; BMI: Body Mass Index; TSH: Thyroid Stimulating Hormone; HbA1c: Hemoglobin A1 C; DSM IV TR: Diagnostic and Statistical Manual IV Text Revision; TG: Triglycerides; HDL: High Density Lipoproteins; LDL: Low Density Lipoproteins; APOE: Apo Lipoprotein E; ANOVA: Analysis of Variance

Background

Lately there has been significant attention focused on the use of coconut oil in the management of AD which is a common age associated, progressive neurodegenerative disease [1]. The available data ranges from anecdotal reports to critical debates in media on the pros and cons of using coconut oil as a supplement in AD subjects. The scientific data in this direction is sparse and conflicting.

It has been known that AD is characterized with regional low cerebral glucose metabolism mostly affecting posterior cingulate, parietal, temporal and prefrontal regions. [2-4]. Furthermore, these deficits can be detected in presymptomatic, at risk individuals well before widespread neuronal loss or plaque deposition takes place suggesting that glucose hypometabolism is an early feature of the disease [5]. Various hypotheses have been put forward for the observed glucose hypometabolism in AD brain. Some implicate loss of...
neuronal or dendritic fields [6]; some implicate mitochondrial dysfunction due to fragmentation of amyloid beta A and Apo E4 protein [7], while others indicate changes in insulin signaling [8-12]. Interventions targeting the cellular metabolism deficit in AD subjects might be beneficial in improving outcomes in these patients.

The finding of glucose hypometabolism in AD brain becomes interesting since it opens avenues for a possibility of utilizing alternate sources of energy for neurons and one such promising fuel for cells is ketones [13-15]. Ketogenic diets find extensive use in children with refractive epilepsy [16] and other neurological conditions such as amyotrophic lateral sclerosis [17], traumatic brain injury [18] and ischemia [19].

The scientific data indicating benefits of induction of ketosis in AD comes from animal studies and neuronal culture studies [20,21]. In a pilot study of mild to moderate AD patients, induction of ketosis by AC-1202, an oral ketogenic compound rapidly improved cognitive performance in subjects lacking the APOE4 allele [22]. Only one RCT [23] was available to indicate that induction of mild ketosis by administering oral AC-1202 compound in subjects with mild to moderate AD resulted in significant improvement in ADAS-cog scores from baseline on day 45 and day 90 of intervention.

Virgin Coconut Oil (VCO) with its predominance of medium chain fatty acids are preferentially transported through the portal venous system into the liver and are more readily available for oxidation to ketones to provide a rapid source of energy, thereby providing a relatively inexpensive source of alternate fuel to compromised neurons in subjects with AD [24]. VCO has been shown to have anti-inflammatory, analgesic, and antipyretic properties [25,26], decrease lipid levels in serum and tissue as well as LDL lipid peroxidation [27], enhance antithrombotic effects related to inhibition of platelet coagulation and low cholesterol level [28] and increase antioxidant activity and inhibit lipid peroxidation in rats [29].

The main aim of the present study was to assess whether daily dosing of VCO in subjects with predominant moderate to severe AD would improve cognitive performance as measured by change from baseline in the AD Assessment Scale-Cognitive subscale (ADAS-Cog) coupled with Clinicians Interview based Impression of Change-Plus Caregivers input (CIBIC-Plus) ratings over active oral VCO administration over 4 weeks and if the effects would be sustained for additional 2 weeks after cessation of VCO administration. Additional outcome measure was to assess the effects of oral VCO on the lipid profile of the subjects during the study trial.

Materials and Methods

Participants

The study sample was recruited from the White and Yellow Cross (WYC) Foundation for care for the elderly on the Island country of St Martin in the Dutch Caribbean. The participants included were from the residential facility, St Maarten Home, the dementia day care facility and from the district nursing, a community service of the White and Yellow Cross Foundation.

The diagnosis of dementia of Alzheimer’s type in the eligible subjects was made on the basis of DSM IV TR criteria and MMSE [30] was used to categorize the severity of AD into mild (21-24 points), moderate (10-20 points) or severe (≤9 points) [31]. Diagnosis was performed by qualified psychiatrists. Subjects were required to have a Modified Hachinski Ischemia Scale score of less than 4 [23]. Key exclusion criteria at Screen were: major depression as determined by a Cornell Scale for Depression in Dementia [32] score of >13, clinically-significant hypothyroidism as determined by thyroid function assessment, clinically-significant B12 deficiency, clinically-significant renal disease or insufficiency, clinically-significant hepatic disease or insufficiency, and any type of diabetes (HbA1C assessment). Detailed physical examination was carried out for all eligible subjects by a qualified physician. Other exclusion criteria were any significant neurological disease, current history of alcohol abuse or other substance abuse within 24 months prior to baseline, known HIV infection and use of any investigational compound within 30 days prior to screening, prior or current use of medium-chain triglycerides (MCTs) for medical purposes and known allergies to coconut oil.

Subjects receiving currently approved AD medications were included and required to remain on stable dosing throughout the duration of the study.

The study was approved by the ethics committee of the WYC Foundation. Subjects and their caregivers provided written informed consent for participation in the study. All clinical site monitoring and data management procedures were carried out in accordance with Good Clinical Practice Guidelines.

A total of 50 subjects were approached for eligibility out of which 18 refused to participate or did not meet the inclusion requirements. Therefore 32 subjects were screened and 1 subject dropped out due to inability to monitor virgin coconut oil administration. The final sample size was 31 subjects which completed the duration of the study.

Investigational product

Extra virgin coconut oil (VCO): The Nutivac brand of extra virgin coconut oil was used which is non-hydrogenated, non-refined, and non-deodorized and non-bleached coconut oil. It is organic being free from pesticides, GMO or hexane. The product does not require refrigeration; is solid at room temperature and melts at 76 F. Traditionally, virgin coconut oil is produced by fermentation method, where coconut milk expelled from freshly harvested coconuts is fermented for 24-36 hours, and during this period, the oil phase gets separated from aqueous phase. Further, the resulting wet oil is slightly heated for a short time to remove the moisture and finally filtered [33]. Coconut oil has a long shelf life and is used in baking industries, processed foods, infant formulas, pharmaceuticals, cosmetics and as hair oil. The oil contains 92% of saturates consisting of medium chain fatty acids in the form of triglycerides, and about 8% of unsaturates consisting of oleic and linoleic acids as triglycerides. The oil has a small amount of unsaponifiable matter (<0.5%), and is colorless [33]. Roughly 45 to 50% of fatty acids of coconut oil form lauric acid. Lauric acid is known to kill viruses and bacteria that are enveloped in a phospholipid membrane [33]. Daily administration of 20gm of virgin coconut oil was used as a supplement mixed with (pudding, oatmeal, yogurt, or drunk as such). The oil was blended in the food product. If the subject was unable to consume the entire product in one time, it could be consumed slowly and the blended food product could be stored in a refrigerator for a maximum period of 24 hrs. The administration was done under supervision of a nurse who ensured that adequate amount was consumed by the subject. The administration was done shortly after a major meal (breakfast) to avoid any adverse events. Adverse events expected and noted were diarrhea, nausea, flatulence, stomach discomfort, hyperactivity or derangements in lipid parameters. The subjects who presented with...
mild GI side effects were found to tolerate the recommended dose in divided doses. In case of intolerable adverse events the subject were excluded from the study.

**Study visits**

Participants were scheduled for five study visits: Screening, Baseline, and post-baseline at 2 weeks, 4 weeks and 6 weeks. The oral VCO administration lasted for 4 weeks after baseline assessment and for the last two weeks assessments were carried out in absence of oil administration. Screening assessments included: demographics, medical/surgical history, DSM-IV criteria for dementia, prior and concomitant medications, physical examination, height, weight, BMI, vital signs, TSH, B12, lipid profile, and HbA1C assessments. At baseline, ADAS-Cog, MMSE and Cornell Scale for Depression in Dementia were applied. After baseline parameters VCO administration started under supervision of the nursing staff. At 2, 4 and 6 weeks ADAS-cog, MMSE was repeated and CIBIC-plus was applied. Lipid profile was repeated at 4 and 6 weeks. The adverse events were charted throughout the study trial after administration of the coconut oil.

**Outcome measures**

As required by the protocol, all cognitive testing was carried out by trained psychiatrists.

The Alzheimer's Disease Assessment Scale-Cognitive scale (ADAS-Cog) [34] generally requires 30 to 45 minutes to complete, is one of the most widely used cognitive tests for anti-dementia drugs and is frequently considered the "gold standard" in evaluating cognitive outcomes. The ADAS-Cog subscale consists of 11 tasks measuring cognitive abilities in memory, language, orientation, and praxis. The test includes seven performance items and four clinician-rated items, with a total score ranging from 0 (no impairment) to 70 (severe impairment). The memory items includes two performance items (word recall and word recognition), and one clinician rated item (remembering test instructions). In word recall, the subject is shown ten words on flash cards and then asked to recall the words in any order. In word recognition, the subject is read aloud 12 words from flash cards. The cards containing the 12 words read to the patient are then mixed with 12 new word containing cards, and all 24 cards shown to the subject. The subject is then asked to distinguish the new words from the words that were read aloud. Language items include two performance items (naming objects and following commands) and three clinician rated items (spoken language ability, word finding difficulty, and comprehension of spoken language). In naming objects, the subject is presented with real objects (such as pencil, wallet, or comb) and asked to name them. In the clinician rated language items, the clinician evaluates the subjects' overall ability to understand and communicate spoken language during the course of the test. The orientation item consists of one performance test, in which the subject is asked a series of questions related to where the subject physically is located and time and date. Praxis items include two performance items [constructional and ideational]. In constructional praxis, the subject is asked to draw several specific geometric shapes. In ideational praxis, the subject is asked to perform a task, such as mailing a letter, and is scored on the ability to complete the task. The higher the ADAS-Cog score, the more impaired the subject. Lowering of the ADAS-Cog score is a measure of cognitive improvement.

The Mini Mental Status Examination (MMSE) is a simple test used primarily for screening for dementia. It was used to measure the severity of dementia. Higher scores on MMSE indicate less impairment. The MMSE is much less sensitive than the ADAS-Cog to change, yet is advantageous in that it can be easily administered [30].

Clinician Interview Based Impression of Change plus Caregiver Input (CIBIC-Plus) is a comprehensive global measure of detectable change in cognition, function and behavior, based on separate interviews with patients and care-givers. It was introduced to add observations from the care givers. It uses a seven point scale, from 1 (markedly worse) to 7 (markedly better). For CIBIC plus a dichotomized analysis was predefined as no change (likert points 1-4) and improved (likert points 5-7) [35].

**Statistical Analysis**

The descriptive statistics were used to delineate the socio demographic and clinical variables. Repeated measures ANOVA with post hoc comparisons were used to compare ADAS-cog scores from baseline over 2, 4 and 6 weeks. Lipid fractions of total cholesterol, LDL, Triglycerides and HDL were also analyzed with repeated measures ANOVA from baseline over 2, 4 and 6 weeks. Cochran’s Q test was used to analyze the CIBIC-Plus ratings over 2, 4 and 6 weeks from baseline.

### Results

| Characteristic | Mean + SD  |
|---------------|-----------|
| Age (Years)   | 81.9 + 9.63 |
| Height (cm)   | 57-100    |
| Mean + SD     | 162.3 + 10.3 |
| Range         | 143-181   |
| Weight (Kg)   | 65.9 + 12.1 |
| Mean + SD     | 45-100    |
| Range         | 24.8 + 3.5 |
| Sex           | 20-34     |
| Male n (%)    | 10 (32.3) |
| Female n (%)  | 21 (67.7) |
| Education     | 27 (87.1) |
| Grade School n (%) | 3 (9.7) |
| High School n (%) | 1 (3.2) |

Table 1: Socio demographic characteristics.
The mean age of the sample was 81.9 ± 9.63 years with higher representation of females (67.7%) and majority (87.1%) being educated up to the grade school (Table 1).

The mean BMI of the sample was 24.8 ± 3.5 kg/m². The relative proportion of subjects categorized as having moderate and severe dementia based on MMSE scores at baseline were 54.8% and 49.1% respectively. 83.9% of subjects were on approved anti-dementia medications and were allowed to continue as such. The mean ADAS-cog scores were 51.3 ± 14.8. The data including the baseline lipid profile is detailed in Table 2.

| Characteristic                      | Use of Anti dementia medications |
|------------------------------------|----------------------------------|
| Present n (%)                      | 26 (83.9)                        |
| Absent n (%)                       | 5 (16.1)                         |
| MMSE Scores                         |                                  |
| Mild (MMSE:21-24) n (%)            | 1 (3.2)                          |
| Moderate (MMSE:10-20) n (%)        | 17 (54.8)                        |
| Severe (MMSE:< 9) n (%)            | 13 (41.9)                        |
| Baseline MMSE Score                |                                  |
| Mean + SD                          | 10.4+ 7.2                        |
| Range                              | 0-21                             |
| Baseline ADAS Cog Scores           |                                  |
| Mean + SD                          | 51.3+ 14.8                       |
| Range                              | 20-70                            |
| Baseline Total Cholesterol (mg/dl) |                                  |
| Mean + SD                          | 209+ 50.9                        |
| Baseline HDL cholesterol (mg/dl)   |                                  |
| Mean + SD                          | 53.6+ 15.2                       |
| Baseline Triglycerides (mg/dl)     |                                  |
| Mean + SD                          | 112.6+ 52                        |
| Baseline LDL cholesterol (mg/dl)   |                                  |
| Mean + SD                          | 132.7+ 42.5                      |
| Presence of Adverse Effects        |                                  |
| Diarrhea n (%)                     | 2 (6.5)                          |
| Flatulence n (%)                   | 0                                |
| Nausea n (%)                       | 2 (6.5)                          |
| Stomach Dyscomft n (%)             | 2 (6.5)                          |
| Hyperactivity n (%)                | 3 (9.7)                          |

Table 2: Clinical Characteristics and baseline measurements

The adverse events of diarrhea, nausea and stomach discomfort were observed in 6.5% of the sample whereas hyperactivity was seen in 9.7% of the subjects. However, none of the subjects had to be excluded due to the adverse effects as dividing the dose of the VCO eliminated the adverse events.

Primary outcome defined by the protocol were change from baseline in ADAS-Cog at 2, 4 and 6 weeks post baseline. Table 3 represents the comparison of ADAS-cog scores from baseline over repeated measures at 2, 4 and 6 weeks using repeated measures ANOVA. The comparison was significant at p=.00 indicating that with the daily administration of VCO cognitive performance of the subjects
showed a consistent improvement over 4 weeks of active coconut oil administration. The intervention yielded a modest effect size of 0.3. On further post hoc comparisons all comparisons from baseline over 2, 4 and 6 weeks were significant at p=.00, with improvement more pronounced at 4 weeks (Mean difference=4.1, P=0.00, C.I= (1.4-6.7) than at 2 weeks [Mean difference=2.6, p=.00, C.I=(0.6-4.5) from the baseline. The effects seem to stabilize from the end of 4 weeks to 6 weeks post baseline with post hoc comparisons being similar [At 4 weeks, Mean difference=4.1, P=0.00, C.I= (1.4-6.7); At 6 weeks, Mean difference=4.1, p=0.00, C.I=(1.0-7.2)].

Since higher ADAS-Cog scores represent increased impairment, a negative score in change from Baseline represents an improvement in cognitive performance. Figure 1 illustrates the inverse relationship between improvement and ADAS-Cog scores. Figure 2 and Figure 3 represents the plot of mean ADAS-cog scores over repeated measures from baseline at 2, 4 and 6 weeks showing a consistent decrease of the mean ADAS-cog scores up to 4 weeks of VCO administration and then plateauing off from 4 to 6 weeks in absence of VCO administration.

| Characteristic                  | Mauchly’s Chi Square | ε   | F     | P     | Effect Size η² | Confidence Interval |
|--------------------------------|----------------------|-----|-------|-------|----------------|---------------------|
| ADAS Cog Scores                |                      |     |       |       |                |                     |
| Baseline (Mean + SD)           | 51.3+ 14.8           |     |       |       |                |                     |
| At 2 weeks (Mean + SD)         | 48.7+ 15.4           | 0.4 | 14.0  | .00** | .31            |                     |
| At 4 weeks (Mean + SD)         | 47.2+ 16.3           |     |       |       |                |                     |
| At 6 weeks (Mean + SD)         | 47.2+ 16.3           |     |       |       |                |                     |
| Post hoc comparison            |                      |     |       |       |                |                     |
| ADAS Cog (baseline) vs         |                      |     |       |       |                |                     |
| ADAS cog at 2weeks             | 2.6                  |     |       | .00** | (0.6-4.5)      |                     |
| ADAS cog at 4 weeks            | 4.1                  |     |       | .00** | (1.4-6.7)      |                     |
| ADAS cog at 6 weeks            | 4.1                  |     |       | .00** | (1.0-7.2)      |                     |

Table 3: Comparison of ADAS-cog scores at 2, 4 and 6 weeks over baseline using repeated measures ANOVA (n=31). p<0.001** Green House Geisser ε.

| Characteristic   | df | Cochran’s Q | p     |
|------------------|----|-------------|-------|
| CIBIC-Plus       |    |             |       |
| 2 weeks          |    |             |       |
| Improved n (%)   | 13 (41.9) |             |       |
| No change n (%)  | 18 (58.1) |             |       |
| 4 weeks          |    |             |       |
| Improved n (%)   | 26 (83.9) |             |       |
| No Change n (%)  | 5 (16.1) |             |       |
| 6 weeks          |    |             |       |
| Improved n (%)   | 26 (83.9) |             |       |
| No Change n (%)  | 5 (16.1) |             |       |

Table 4: Comparison of CIBIC-Plus ratings over successive ratings at 2weeks, 4 weeks and 6 weeks using Cochran’s Q test. (n=31).
Figure 1: Mean Change in ADAS-cog from baseline over 2, 4 and 6 weeks. Y Axis is change in ADAS-cog scores from baseline. X Axis represents time in weeks. Subjects were administered VCO up to the end of 4 weeks. The subjects demonstrated significant difference in ADAS-cog scores over baseline over repeated measures at 2, 4 and 6 weeks. The results were more pronounced 4 and 6 weeks. For number of subjects, confidence intervals, and p-values, see Table 3.

Figure 2: Mean ADAS-cog scores at each point of assessment from baseline over 6 weeks. The mean ADAS-cog scores registered a decline at 2 weeks post intervention and the effects were pronounced at 4 and 6 weeks indicating improvement in cognitive performance. The effects stabilized from the end of 4 weeks to 6 weeks when the administration of VCO had stopped. For p values see Table 4.

Figure 3: Representation of subjects rated on CIBIC-Plus ratings at 2 weeks, 4 weeks and 6 weeks. The subjects were rated as a dichotomous variable as improved or no change. Post intervention with VCO at 2 weeks [13] 41.9% of subjects were rated as improved and by 4 and 6 weeks the number of subjects showing improvement doubled to 83.9% [26]. The improvement was consistent within 4 to 6 weeks of study duration when the administration of VCO had stopped. For p values see Table 4.

CIBIC-Plus scale was used to see the clinical cumulative effect of small improvements in several domains (e.g., cognition, behaviour, function). The results of the analysis revealed that there was a significant difference (Cochran’s Q=22.5, df=2, p=.00) over successive ratings at 2, 4 and 6 weeks (Table 4). Compared to 41.9% of subjects showing improvement at 2 weeks, the subjects registering improvement doubled to 83.9% at the end of 4 weeks when the oil administration stopped with effects sustained at 6 weeks with cessation of coconut oil administration. The mental/cognitive and the behavioral domains were observed to show the most pronounced and no perceptible changes were observed in the functioning domain. The caregivers and the nurses observed more alertness, ease of expression of language and improvement in overall activity. Appreciable changes were observed in the affect with the subjects showing emotional expression and cooperativeness in their overall demeanour. No significant statistical difference could be elicited for the total cholesterol, Triglycerides, and LDL fraction from the baseline over subsequent ratings at 4 weeks on oil administration and after 6 weeks without coconut oil administration from baseline. The comparisons for different lipid fractions as yielded on repeated measures ANOVA was: Total cholesterol: Mauchly’s Chi Square X²(df=2)=2.8, ε=0.9, F(df 1.8, 54.8)=0.2, p=0.7, η²=0.009; Triglycerides (TG): Mauchly’s Chi Square X²(df=2)=2.9, ε=0.9, F(df 1.8, 54.7)=1.36, p=0.2, η²=0.04; Low density lipoproteins (LDL): Mauchly’s Chi Square X²(df=2)=8.2, ε=0.8, F(df 1.6, 48.1)= 0.5, p=0.5, η²=0.01. High Density Lipoproteins (HDL) cholesterol was the only one that showed statistical significance over repeated measures. (Mauchly’s Chi Square X²(df=2)=6.5, ε=0.8, F(df 1.6, 49.9)=6.4, p=0.005, η²=0.17).

In general, no significant differences between groups were observed for changes in serum chemistry and hematology values, or vital signs over the study duration.
Discussion

The results of the index study indicated that administration of oral virgin coconut oil in subjects with moderate with severe AD brought about significant improvement in cognitive performance as measured on the outcome measures of ADAS-cog and CIBIC-plus ratings. The intervention was seen to have a modest effect size of 0.3. The improvement was elicited over a short duration of 2 weeks and was more pronounced by the end of 4 weeks till the oil administration lasted and the improvement was sustained for the next two weeks in absence of coconut oil administration.

There is significant literature available on the beneficial effects of coconut oil on many different maladies mainly attributed to the medium chain fatty acid content of the coconut oil [33]. It has shown to be effective in various malabsorption syndromes [36], HIV [37], has antibacterial and antifungal properties [38], anti-inflammatory and anti-cancer properties [39,40]. Besides these it has also been shown to have beneficial antithrombotic [25], lowering cholesterol and antioxidant effects [41,42]. The effects on improving cognition in subjects with AD have only recently gained attention. A case study [43] suggests cognitive improvement in subjects with early onset AD after dietary intervention with coconut oil.

We observed improvement in ADAS-cog scores early in the study duration at 2 weeks and they were more pronounced by 4 weeks, the effects being sustained for additional two weeks after cessation of the intervention. The data is comparable to other studies showing rapid response rates after intervention. In the study by Henderson et al. [23] the subjects with AD on oral ketogenic compound AC-1202 showed significant improvement in ADAS-cog scores at days 45 and days 90 compared to a placebo. Similar rapid results were also seen in another study [22] where 20 subjects with mild to moderate AD given single dose tricaprylic acid [40 gm] vs. placebo on another occasion showed improved Paragraph Recall scores 90 minutes after just one dose and in nine ApoE4+ persons ADAS-Cog improved by average of 6 points. The rapid response rates observed might indicate that the intervention might be acting more at the level of cellular metabolism rather than the disease process by addressing more typical targets, such as amyloid or tau which would be expected to take much longer to bring about any change if any.

Our study indicated statistically significant difference on ADAS-cog scores over repeated measures at 2, 4 and 6 weeks over baseline, we were interested in capturing clinically larger differences whether the caregivers felt improvement of the intervention. This was achieved by successive ratings on CIBIC-Plus. An individual on CIBIC-Plus may be rated as improved because of the cumulative effect of small improvements in several domains e.g., cognition, behaviour, function. We found significant improvement from 2 weeks to 4 weeks and it was further sustained for additional two weeks with cessation of coconut oil administration. It was further observed that most of the caregivers observed improvements in the mental/cognitive domains of alertness, expression of language and overall activity. There were also pronounced improvements noted in the affect, however no perceptible changes were noted in the functioning domain of the CIBIC-Plus. Similar effects have been reported in the case reports on the use of coconut oil in subjects with AD. Newport [44] reported improvements in characteristics such as alertness, ability to initiate and maintain conversation, improved recognition, not looking lost and normalization of gait and vision on 2months of daily coconut oil administration. The administration of coconut oil was fairly tolerated by the subjects without alteration of their regular diet and none of the subjects was excluded due to presence of adverse effects. Placebo response might be indicated especially due to the lack of strong efficacy in MMSE and CIBIC-Plus due to relative insensitivity of these tests, the small number of subjects, and/or the short duration of the trial, the observed results seem to be in line with the direction of improvement recorded on ADAS-cog scores, and limited data supports this finding [44] we submit caution in over-interpretation of these results. It does however indicate the positive overall beneficial effects of coconut oil in different domains of AD perceptible to the caregivers.

Most of the studies [22,23] have focused on the subjects with mild severity of AD or mild cognitive impairment. Our sample had a predominance of subjects with moderate (54.8%) and severe (41.9%) degree of AD. Our study reveals improvement in cognitive performance for subjects with fairly advanced disease process. The beneficial effects of virgin coconut oil might not be limited in the early disease process but clinical gains are likely to be appreciated later during the disease stage.

Though the index study did not aim to investigate the cause for the observed cognitive improvement in subjects with AD after administration of virgin coconut oil, the literature reported postulates induction of ketosis from the Medium Chain Triglycerides (MCT) as a potential mechanism for cognitive improvement in subjects with AD. A pilot study to assess the effects of beta hydroxyl butyrate (BHB) on cognition in memory impaired subjects yielded beneficial effects on cognition after a single dose of 40 gm of tricaprylic acid [22]. Perhaps in one of the more systematic efforts on the issue [23] on 152 patients with mild to moderate AD received AC-1202 (containing 20 g MCT) or placebo for 90 days in a double-blind, randomized design the results revealed a mean change from baseline in ADAS-Cog score on Day 45: 1.9 point difference, p=0.0235 in ITT; 2.53 point difference, p=0.0324 in per protocol; 2.6 point difference, p=0.0215 in dosage compliant. Furthermore, ApoE4+ patients taking AC-1202 differed from placebo by 5.73 points at Day 45 (p=0.0027) and by 4.39 points at Day 90 and even more significant in dosage compliant patients. The data from the preclinical studies with induction of ketosis in aged dogs [45], neuronal culture studies [20] provide further leads into hypothetical mechanisms by which ketosis might bring about a desirable improvement in subjects with AD, however the precise mechanism by which induction of ketosis brings about cognitive improvement is yet to be understood [23].

Most of the studies have concentrated on the induction of ketosis from specific medium chain triglycerides such as AC 1202 with primarily 8 carbon atoms (C8) in the study by Henderson et al. [23] and tricaprylic acid in the one by Reger et al. [22] and the results are argued based on the observed correlations between cognitive performance and circulating Beta Hydroxy Butyric acid [BHB] levels. It might be argued that use of coconut oil with its more variable composition [MCT with 8-12 carbon atoms [33] and unique character of healing properties might be contributing to improvement by factors beyond induction of ketosis. Suggestion towards this comes from several reports implicating MCTs in increasing fatty acid oxidation with possible roles in weight loss [41]. However, in general, very little MCTS with C8 reaches the blood stream after ingestion of an MCT and with complete hydrolysis in the gut lumen and obligate oxidation in the portal vein [46-48]. In studies on humans dosed with C8 containing MCTs, very little free C8 is found in arterial blood [49]. Furthermore, in the study by Henderson et al. [23] AC-1202 induced transient increases of ketosis that reached average levels of 0.3 to 0.4
mM in the 2 hour postdose sample on Days 45 and 90. It has been seen
that oral ingestion of coconut oil yields comparable serum ketone
levels of 0.3-0.5 mM [43] which is further comparable to the one
produced during exercise [43]. In studies of low carbohydrate diets,
average levels of BHBB after 2 weeks range from 0.4 mM to 0.65 mM,
and these levels frequently decrease over time and may return to
Baseline after 10 to 12 weeks [50-53]. Ketogenic diets yield more
sustained levels of BHBB above 1 mM [54,55]. As a comparison, much
higher levels of serum BHBB are found during 5–6 weeks of starvation
(4–8 mM) [56] and in cases of diabetic ketoacidosis (9–10 mM) [57]. It
is unclear if the proposed induction of mild ketosis as suggested in
earlier studies [1] is the sole underlying cause of observed beneficial
effects since similar levels of ketosis are observed in other states and
further the levels are observed to decline after a time period. It might
therefore be suggested that coconut oil by virtue of its variable
composition, with similar beneficial effects and limited sustained
effects (at least two weeks of the study duration) might be acting by its
unique properties beyond the induction of ketosis. These unique
properties should be a focus of further investigation especially
considering that VCO offers a relatively inexpensive and yet clinically
relevant avenue for cognitive improvement in AD.

As secondary outcome measure our study points to the improved
outcomes on the lipid profile of the subjects over repeated measures of
the study duration with significant difference observed in the HDL
profile while the other fractions of total cholesterol, LDL and TG
fractions did not reveal any significant change over the baseline. We
submit that this finding may be considered with caution especially in
light of the minimal effect size of 0.1 observed for this association. The
available literatures on the effects of coconut oil on the lipid profile
have been conflicting [24]. Some studies have failed to find any
association of coconut oil with adverse lipid profile changes [58] and
some have showed that coconut oil consumption has beneficial effects
compared to other dietary fats [59]. The effectiveness of polyunsaturated fatty acids in reducing serum cholesterol and LDL
cholesterol has been well documented [60]. It has been hypothesized
that the consumption of coconut oil, as a part of routine diet, may not
contribute to the risk for coronary artery disease directly by affecting
the lipid profile or indirectly by aggravating oxidative stress [24].

The index study was a preliminary effort to document the effects of
virgin coconut oil on cognitive performance in subjects with moderate
to severe dementia triggered by limited evidence in this area of AD
research. The study had limitations in terms of small sample size and
short study trial with limited ability to address the safety and efficacy
of longer periods of administration. The future efforts should be
directed in investigating the effects of virgin coconut oil in a larger
sample with a randomized placebo controlled design over extended
periods of follow up. In line with the approach of Hendersen et al. [23]
possibilities of incorporating serum ketone analysis and genetic
analysis for the carriagge status of the epsilon 4 (E4) variant of the
apolipoprotein E gene (APOE) might offer more clarity in the
direction and mechanisms coconut oil yields benefits in the subjects
with AD.

Conclusions

Index study suggests that adjunctive use of virgin coconut oil in
subjects with moderate to severe AD offers significant improvement in
cognitive performance as measured by not only on significant
statistical gains measured on ADAS-cog scores but also more
perceptible clinical gains as captured on the CIBIC-Plus ratings over
the study duration. Previous studies have focused on the use of oral
ketogenic compounds from MCT oils as showing benefits in cognition
in subjects with mild to moderate AD, we submit that similar
improvement may occur using an equivalent amount of virgin coconut
oil, more widely available to world populations and relatively
inexpensive. Though induction of ketosis seems promising as the
underlying mechanism but further investigations are warranted
considering the unique properties of virgin coconut oil and its
widespread clinical applications. The study indicated beneficial effects
on the HDL profile over the study duration however; we submit that
more research is indicated in this area with more rigorous designs
implicating use of coconut oil as a useful adjunct without interfering
with the diet, other medications or comorbidities in subjects with AD.

Competing Interests

The authors may benefit from the publication. The White and
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