Multimodal Clinical Management Approach to Patients with Moderate Alzheimer’s Disease

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Alzheimer’s Disease (AD) by the Numbers

5 Million
Americans living with AD

203 Billion
Direct costs of AD in billions (US)

Alzheimer’s disease is the most common form of dementia accounting for 70% of all dementia cases. There are currently no methods to prevent, cure, or meaningfully slow its progression.
AD: Identification of Modifiable Factors

- In 2015, Xu and colleagues conducted the first comprehensive systematic review and meta-analysis of risk and protective factors for AD that could be modified via personal, clinical and public strategy
  
  - Their findings suggested an effective diet, relevant medications, appropriate biochemical exposures, psychological condition, pre-existing disease and life-style changes may be promising options for preventative strategies in AD

- Healthy dietary pattern, high folate intake, cognitive activity, high Ab42/Ab40 ratio, fish consumption, high education, physical activity and high vitamin E and C intake were identified as protective factors in this disease

AD: A Comprehensive Therapeutic Approach

- Identification of protective factors in AD, especially those relevant to nutritional and life-style patterns, provides new opportunities for the development of novel therapeutic programs
  - To slow progression of this neurodegenerative disease
- In 2014, Bredesen reported the positive impact on cognitive decline in patients of moderate AD
  - Use of a novel, comprehensive, and personalized therapeutic program provided proof-of-concept evidence that modulation of protective factors in AD could have therapeutic value and potentially slow rate of decline

Multimodal Management of Patients with Moderate AD

Alzheimer’s disease diagnosis

**Biomarkers:**
- Goal
- Homocysteine > 7
- B12 > 500
- CRP <1.0; A/G >1.5
- Fasting insulin <7; HgbA1c <5.5
- Hormone balance
- GI health
- 25OH-D3 = 50 100ng/ml
- Optimize Zn:fCu ratio

**How to achieve goal**
- Me-B12, MTHF, P5P; TMG if necessary
- Me-B12
- Anti-inflammatory diet; curcumin; DHA/EPA; optimize hygiene
- Optimize diet
- Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol
- Repair if needed; prebiotics and probiotics
- Vitamin D3, K2
- Depends on values

**For all patients**

- **Optimize diet** (minimize inflammation and insulin resistance)
  - Low glycemic,
  - Low inflammatory, and
  - Low grain diets

- **Personalized life-style changes**
  - Reduce stress (yoga/meditation/music)
  - Optimize sleep (8hr/night, melatonin)
  - Exercise (30-60 min/day, 4-6 d/wk)

- **Enhance autophagy, ketogenesis** (reduce insulin levels and beta-amyloid)
  - Fast 12 hr/night including 3 hr prior to bedtime

- **Supplements**
  - **Optimize antioxidants and mitochondrial function**
    - Mixed tocopherols and tocotrienols, selenium, zinc, CoQ10, PQQ, ALCAR, reveratrol (SirT1 function), blueberries, N-acetyl cysteine, ascorbate, and alpha-lipoic acid
  - **Cognitive enhancement**
    - Curcumin, Ashwagandha, citicoline, DHA and pantothenic acid
  - **Reduction of beta-amyloid**
    - Bacopa monniera, magnesium threonate

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Summary

- A multimodal therapeutic approach as outlined by Bredesen is potentially more effective than unimodal approach for the treatment of cognitive decline due to AD.

- Preliminary clinical evidence for a recommended patient algorithm provides support to the concept that an appropriate diet with concurrent lifestyle and behavioral changes may be promising options for preventative strategies in AD.