Axona and Dementia

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Mary Ann Forciea MD
I have heard of axona

1. Yes
2. No
I am aware of Axona from the following:

1. JAGS cover June 2013
2. NY Times article
3. Patient calls
4. Medical literature
5. Web (blogs, alerts)
6. Other
Ketosis is a good thing for my patients

1. Yes
2. No
Axona = Caprylic Acid

• Formulation: medium chain triglyceride with glycerin and caprylic acid
  – Metabolized in the liver to B-hydroxybutarate (BHB)
• BHB crosses the blood-brain barrier
  – Utilized in neuronal mitochondria
  – Enters citric acid cycle and generates ATP, NAD
• Supplied as a powder, mixed with water/food for immediate, once daily consumption
Background

• On fluorodeoxyglucose PET, decreased cerebral metabolism, esp in AD
  – Temporal-parietal region most affected
• Suboptimal delivery of glucose substrates
  – Neurotransmission failure
• Ketones can serve as alternate energy sources for neurons
• Small (23) human trial of MCI patients on ketogenic diets for 6 weeks
  – Improvement in verbal memory which correlated with ketone levels
RCT

- Funding source: Accera, Inc (manufacturer)
  - Published in 2009

- Method:
  - 152 subjects with mild-mod AD; APOE-4 status
  - 90 day (5 visits: pre, 0, 45 days, 90, 104 days)
  - Randomized, double-blind, placebo-controlled
  - Subjects continued other meds
  - Outcomes: ADAS-cog and ADCS-CGIC scores
Flow sheet of study

• Fig 1

• Enrollment: blinding broken by an “independent monitor’ to ensure 50 completers
  – Overpopulation into treatment due to high adverse effects

• “Intention to treat”
  – Selection at end of patients who took at least one dose and had one follow up visit
Demographics - Table 2

• No major breaks, but no analysis
Does the medication enter the bloodstream?

- Figure 3
- Yes.
  - Possible accumulation
Does Memory improve?

• Figure 2 ASAS-Cog
• Small but clinically insignificant change
• More impressive in Apo E positive patients

• No graphs of GCIC results
  – Tables, text admit no change
Harms?

• GI
  – Diarrhea 24%/13%
    • Withdrawal for adverse event: 23%/6%

• Renal
  – “None exceeded 2.5 times upper limit of normal”
    • 7 in treatment group - ? None in placebo?
Authors’ conclusion

• Ketogenic diets have been used in other neurological conditions
• Dementia patients won’t adhere to diet manipulation
• Axona produces low level ketonuria
• They did show statistical change in one measure of cognitive performance
• LICENSURE AS A MEDICAL FOOD
My conclusion

• Interesting hypothesis
• Low quality data
  – High bias risk
  – Odd counting
  – Partial reporting of outcomes
• Very small benefit
• Unpleasant but probably not dangerous harms
• Is this worse than donepazil?
My practice

• Probably not offer as a recommendation
  – Very small subset of very determined MCI patients
  – ? Low carb diet instead?
JAGS advertisement was appropriate

1. Yes
2. No
3. I don’t care – I skip the ads