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ALSUntangled No. 18: Apoaequorin (Prevagen)

The ALSUntangled Group

Originally derived from jellyfish, now produced and sold as Prevagen by Quincy Bioscience, apoaequorin is a calcium binding protein similar in primary structure to endogenous human calcium binding proteins (1). Here, on behalf of patients who requested it, we review the evidence for using apoaequorin to treat ALS.

Rationale

Calcium dysregulation probably plays a key role in ALS pathophysiology. Elevated concentrations of extracellular glutamate may act through AMPA receptors to raise intraneuronal calcium levels. As a result, cells such as motor neurons that have low calcium buffering capacity to start with, may suffer damage to their mitochondria and endoplasmic reticulum (reviewed in (2)). If apoaequorin could help buffer calcium within motor neurons it could theoretically be neuroprotective in ALS.

Relevant animal data

ALSUntangled has been unable to find any published studies of apoaequorin or other exogenous calcium buffering proteins in animal models of ALS. Perhaps relevant are observations that motor neurons from transgenic mice overexpressing an endogenous calcium buffering protein (parvalbumin) are protected from an AMPA receptor agonist (3) or crush injury (4) compared to motor neurons from non-transgenic littermates. Also, intra-hippocampal infusion of the calcium binding protein aequorin can protect rat hippocampal cells from oxygen and glucose deprivation (5).

Relevant human data

ALSUntangled has been unable to find any controlled trials of apoaequorin or other exogenous calcium buffering proteins in patients with ALS. Small trials of calcium channel blockers were unable to show any benefit (6,7). There is a single published series of four patients with sporadic ALS who received apoaequorin along with CoQ10, Noni juice, turmeric extract, deprenyl, intravenous glutathione, lithium and a diet rich in medium chain triglycerides (8). All of these patients "experienced disease progression, however when compared to age and disease matched controls by the author the degree of progression is decidedly less" (8). ALSUntangled contacted the author of this publication, Anthony G. Payne, who provided additional details via e-mail. Diagnoses were confirmed by referring neurologists. Outcome measures included ALSFRS-R and spirometry, which were obtained every three months. Unfortunately, all these detailed data were lost and this is why only the above general comment can be made.

Costs and potential side-effects

The cost of Prevagen at doses used in the above-described case series (120 mg/day) is approximately $240 per month (9). No serious adverse events were noted by A G. Payne in this series. Within the PatientsLikeMe community, two persons taking Prevagen for multiple sclerosis reported serious adverse events; one described hypotension severe enough to cause coma, and the other described depression with suicidal thoughts. In terms of non-serious adverse events, Todd Olson at Quincy Biosciences reported the following via e-mail: "We track all that are reported to our company by any customer, health food store, or clinic. The incidence rate for any (adverse event) is 0.08%, a very low number… the breakdown looks like this: headache = 21%, nausea = 8%, constipation = 6%, edema = 6%, hypertension = 6%."

Other concerns

To our knowledge, oral apoaequorin has not yet been shown to survive digestion, cross the blood-brain

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barrier or enter the human central nervous system. If it does, it is not clear how it would be targeted to the cells specifically involved in ALS pathogenesis. Finally, even if it reached these cells and was endocytosed into them, it seems likely that it would be degraded by the endosome/lysosome system unless somehow further targeted for release from that system.

Conclusions

There is a rationale by which the calcium binding protein apoaequorin could work to slow ALS progression. Unfortunately, at this time there is insufficient information available to determine whether it does. The one small case series referred to above utilized a cocktail of therapies and is further weakened by the loss of its standardized outcome measurements. Information from the manufacturer suggests that apoaequorin is reasonably safe and well tolerated but there is no independent, systematic confirmation of this; two PatientsLikeMe members reported serious adverse events while taking it and it is fairly expensive.

At this time ALSUntangled does not recommend that patients with ALS take apoaequorin. Reasonable next steps would include controlled study of apoaequorin in an ALS animal model and/or a small series of well-characterized patients with ALS using validated outcome measures and including serum and CSF pharmacokinetics.

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Note: This paper represents a consensus of those weighing in. The opinions expressed in this paper are not necessarily shared by every investigator in this group.

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