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ALSUntangled No. 29: MitoQ

The ALSUntangled Group

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ALSUntangled reviews alternative therapies on behalf of patients with ALS (PALS). Here we review the use of MitoQ for ALS, for which we have had more than 1800 requests (1)

Overview

MitoQ (2) is an antioxidant. Its active ingredient is ubiquinone, as found in coenzyme Q10 and idebenone. However, the ubiquinone in MitoQ is attached to a positively charged, lipophilic molecule called TPP (triphenyl phosphonium), which allows it to selectively accumulate in mitochondria (3). This makes it more potent than untargeted ubiquinone analogs at protecting cells in culture from oxidative stress (3,4). It can be administered orally (5) and, at least in animals, can cross the blood-brain barrier and accumulate in brain mitochondria (6).

Mechanism(s)

Oxidative stress is believed to play a major role in ALS pathogenesis (7). Unfortunately, trials of antioxidants have thus far failed to show any benefits in patients with ALS (8,9). One explanation for these failures is that the antioxidants did not reach the optimal place. Since mitochondria are both the main producer and main target of oxidative stress, mitochondrial-focused antioxidant therapy might be more successful. Orally administered MitoQ can alter markers of both oxidative stress and mitochondrial dysfunction in cell culture (10) and animal model of ALS (11).

ALSUntangled assigns a TOE 'Mechanism' grade of B based on this information (Table I).

Pre-clinical data

MitoQ has been tested in two pre-clinical ALS models. In a cell culture model, treatment of G93A mutant SOD1 astrocytes with MitoQ was shown to protect their mitochondrial function, reduce their superoxide production, and ameliorate their ability to kill cocultured motor neurons (10). Problems with this study include lack of rater blinding. In a G93A mutant SOD1 mouse model, oral administration of MitoQ starting at symptom onset slowed the rate of mitochondrial loss in muscle and spinal cord, reduced markers of oxidative stress, improved hind limb strength and prolonged survival (11). There are multiple methodological problems with this study according to published guidelines (12), including incomplete sample characterization, small animal numbers, and failure to blind raters. These findings have not been independently confirmed.

ALSUntangled assigns a TOE 'Pre-clinical' grade of C based on this information (Table I).

Data in PALS

Within the online community PatientsLikeMe, three members report taking MitoQ for ALS (13); the only one of these with a publicly available treatment report notes no benefits from taking 10 mg daily for six months (14). E-mail and twitter queries allowed us to find two other PALS taking MitoQ. The first had been taking it at 10 mg daily for four months and reports "I believe that it's helping in general. Specifically, I feel like I have a little more strength and energy, and think more clearly/am more focused. I don't know if it is helping slow my progression" (15). He sent ALSFRS-R scores, which show very slow overall progression of 11 points over 34 months and no clear change in progression since starting MitoQ (15). A caregiver reported that her husband was taking 20 mg daily for 15 months, and when he stopped taking it he "felt especially tired" (15). No other benefits were noted. An e-mail from Greg Macpherson, CEO of MitoQ (the company that sell this product online) describes "one customer whose husband has ALS and they think he is getting benefit but it is quite difficult to determine given the challenging and changing nature of the condition" (16). Google search for 'MitoQ ALS treatment' identified no additional publicly available case data.

ALSUntangled assigns a TOE 'Cases' grade of D based on this information (Table I).

We were unable to find any trials of MitoQ in patients with ALS. ALSUntangled assigns a TOE 'Trials' grade of U based on this information (Table I).

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Table I. TOE grades for MitoQ as an ALS treatment.

	Grade	Explanation
Mechanism	B	MitoQ can alter markers of oxidative stress and mitochondrial dysfunction in an animal model of ALS
Pre-clinical	C	Multiple flawed peer-reviewed publications report benefits of MitoQ in ALS models
Cases	D	Subjective report(s) of benefit without validated diagnoses and/or benefits
Trials	U	There are no trials of MitoQ for ALS
Risks	C	At least 10% of exposed patients in human trials experienced adverse events (but no serious adverse events)

Risks and costs

MitoQ safety data were gathered systematically in two human trials (17,18): a year-long trial of 130 patients with Parkinson's disease (89 received MitoQ), and a 28-day trial of 30 patients with hepatitis C (20 received MitoQ). No MitoQ related serious adverse events were noted in the patients randomized to this treatment (17,18). Nausea and vomiting were the only adverse events that were more common in MitoQ treated patients than in placebo treated controls (17,18). Withdrawal due to nausea was more common in MitoQ treated patients than placebo treated patients (17,18).

It should be noted that these trials were using MitoQ at 40 mg or 80 mg daily (17,18). This is much higher than the 10 mg daily dosage recommended on the MitoQ website (19). None of the PALS whose data we received reported any side-effects. An e-mail from Greg Macpherson, CEO of MitoQ, stated that his company is aware of more than 50,000 patient months worth of use, with the percentage of side-effects being "virtually nil" (16). The problem with these data is that adverse events have not been systematically gathered during these exposures.

ALSUntangled assigns a TOE 'Risks' grade of C based on this information (Table I), with the qualifier that the grade may well be better using 10 mg daily.

The cost of MitoQ at 10 mg daily is $59.95 for a one-month supply (19).

Conclusions

MitoQ has a promising mechanism, positive pre-clinical data from two different ALS models, and appears reasonably safe and inexpensive, especially at doses of 10 mg daily. Available anecdotal data are insufficient to determine how helpful this might be in PALS. A small open-label pilot trial with validated ALS diagnoses and outcomes appears warranted.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. http://www.alsuntangled.com/open.php. Accessed April 12, 2015.
2. http://www.mitoq.com. Accessed April 20, 2015.
3. Kelso G, Porteous C, Coulter C, Hughes G, Porteous W, Ledgerwood E, et al. Selective targeting of a redox-active ubiquinone to mitochondria within cells. J Biol Chem. 2001;276:4588–96.
4. Jauslin M, Meier T, Smith R, Murphy M. Mitochondrial-targeted antioxidants protect Friedrich Ataxia fibroblasts from endogenous oxidative stress more effectively than untargeted antioxidants. FASEB J. 2003;17:1972–4.
5. Cocheme H, Kelso G, James A, Ross M, Trnka J, Mahendiran T, et al. Mitchondrial targeting of quinolones: therapeutic implications. Mitochondrion. 2007;7:S94–102.
6. Smith R, Porteous C, Gane A, Murphy M. Delivery of bioactive molecules to mitochondria in vivo. PNAS. 2003;100:5407–12.
7. Carri M, Valle C, Bozzo F, Cozzolino M. Oxidative stress and mitochondrial damage: importance in non-SOD1 ALS. Front Cell Neurosci. 2015;9:41.
8. Kaufmann P, Thompson J, Buchsbaum R, Shefner J, Krivickas L, Katz J, et al. Phase II trial of coq10 for ALS finds insufficient evidence to justify phase III. Ann Neurol. 2009;66:234–44.
9. Graf M, Ecker D, Horowski R, Kramer B, Riederer P, Gerlach M, et al. High dose vitamin E therapy in amyotrophic lateral sclerosis as add-on therapy to riluzole: results of a placebo controlled double-blind study. J Neural Transm. 2005;112:646–60.
10. Cassina P, Cassina A, Pehar M, Castellanos R, Gandelman M, de Leon A, et al. Journal Neurosci. 2008;16:4115–22.
11. Miquel E, Cassina A, Martinez-Palma L, Souza J, Bolatto C, Rodriquez-Botter S, et al. Neuroprotective effects of the mitochondria-targeted antioxidant MitoQ in a model of inherited amyotrophic lateral sclerosis. Free Radical Biology and Medicine. 2014;70:204–13.
12. Ludolph A, Bendotti C, Blaugrund E, Chio A , Greensmith L, Loeffler J, et al . Guidelines for preclinical animal research in ALS/MND: a consensus meeting. Amyotroph Lateral Scler. 2010;11:38–45.
13. http://www.patientslikeme.com/treatments/show/26368-mitoq-side-effects-and-efficacy#overview. Accessed April 26, 2015.
http://www.patientslikeme.com/treatment_evaluations/browse?condition_id = 9&id = 26368-mitoq-side-effects-and-efficacy. Accessed April 26, 2015.
14. Emails between patients and caregivers and ALSUntangled. April 2015.
15. Emails between Greg Macpherson and ALSUntangled. April 2015.
16. Snow B, Rolfe F, Lockhart M, Frampton C, O'Sullivan J, Fung V, et al. A double-blind, placebo controlled study to

assess the mitochondrial-targeted antioxidant MitoQ as a disease-modifying therapy in Parkinson's disease. Movement Dis. 2010;11:1670–4.
17. Gane E, Weilert F, Orr D, Keough G, Gibson M, Lockhart M, et al. The mitochondria-targeted antioxidant mitoquinone decreases liver damage in a phase II study of hepatitis C patients. Liver International. 2010; 30:1019–26.
18. http://www.mitoq.com/mitoq-5mg-capsules-60.html/. Accessed April 26, 2015.

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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.