oxidative damage of cells in this disease (Caccammo *et al.* 2013).

PATHOGENESIS

Apart from the clinical condition, it is complicated to follow the improvement or worsening of ALS. Damage and death of motor-neurons, in particular muscle motor-neurons, release certain substances into the blood, with creatine, creatinine, creatine kinase, and myoglobin being among them.

Survival time and blood test parameters were compared.

Serum creatine kinase levels increase in 43.3% of ALS patients, but the differences don't correlate with age, course of the disease, or clinical condition.

Creatine with coenzyme Q10 has even better neuroprotective effects and blocks the creation of alpha synuclein aggregates and prolongs survival time in ALS (Beal 2011).

The concentration of myoglobin as well as myoglobin synthesis is reduced in the muscle cells of ALS patients (Kawai *et al.* 1994).

ALS primarily affects motor-neurons, which means 5-hydroxytryptamine could be a key factor in the pathogenesis and therapy of ALS. The levels of tryptophan, i.e., the serotonin precursor molecule, are reduced in the cerebrospinal fluid in ALS.

THERAPY

Is was several times proved, that antioxidant therapy is very useful in the treatment of ALS. In ALS, it is important that antioxidants also be able to penetrate the hematoencephalic barrier of the brain.

The Earth has a huge number of electrons, therefore contact of human skin with the Earth causes a decrease in the number of free radicals.

Only riluzole (100 mg/day) is recommended as a therapy for ALS. However, it appears to only prolong life by approx. 2–3 months. Patients treated with riluzole have a slight decrease in SOD activity, riluzole improves bulbar and extremity mobility, but does not improve muscle strength. Arimoclomol, a derivate of hydroxylamine has been tested and shown to improve the expression of heat shock protein during cell stress. Its protective effects have been described in ALS, it improves neuromuscular function and prolongs life.

The inhibitor c-Abl (imatinib) prevents death of motor neurons. (Santa-Cruz and Tapia 2014). Also, melatonin is known to be very effective against oxidative stress and neurodegenerative damage in the nervous system of ALS patients.

ALS patients lose weight and strength. Defective energy metabolism and homeostasis contribute to selective vulnerability and degeneration of motor-neurons in ALS. An imbalance in energy metabolism is obviously an important factor both in the progression and possible treatment of ALS.

Quality nutrition greatly helps energy balance and lowers oxidative stress. Insufficient nutrition, cachexia, psychologic stress, and/or breathing disorders can increase oxidative stress in ALS (D´Amico *et al.* 2013).

Other food supplements that can have a positive effect on the course of ALS include virgin olive oil, (Oliván *et al.* 2014), carnitine, turmeric, ferulic acid, and curry. Other possible treatment is by using ursolic acid, lithium carbonate and valproate. Other therapy using cytokine IGF-1, vaccinotherapy, taurine + caffeine: improve the transfer of nerve stimuli, stabilize cellular membranes, maintain blood calcium ion concentrations, accelerates regeneration of tissues. The taurine dose is 1000–2000 mg/day. Daily doses of 5000 mg/day or higher can have side effects (diarrhoea, affecting of CNS, and disorders of short term memory); however, without taurine there is a danger of blindness during treatment. Caffeine strengthens its effects.

Edaravone increases uric acid in the plasma, which then acts as an effective peroxynitrite scavenger, however, it does not decrease the percentage of KoQ10. Edaravone with coenzyme Q10 might be suitable for lowering oxidative stress in ALS. Autologous bone marrow mononuclear cell transplantation, with Riluzole, has been shown to increase survival in ALS (Sharma *et al.* 2015).

CONCLUSION

Amyotrophic lateral sclerosis currently lacks a clear etiology as well as an effective treatment. The most probable explanation for ALS involves oxidative stress and substances that damage motor-neurons, such as aberrant pathologically conformed proteins, certain heavy metals, singlet oxygen, glutamate excitotoxicity, damaged glutamate transporters, and physically demanding work. Prevention seems to be successful (antioxidants, good nutrition) at slowing or delaying the onset of ALS. Regarding therapeutic options, good nutrition seems to be effective at preventing weight loss. Substances that help maintain serotonin levels (blockers of reverse serotonin resorption, i.e., antidepressant (mainly lithium compounds) can be useful. Additionally, other potentially effective and useful substances include: substances that slow motor-neuron death (Imatinib, trolox, and pyruvate (an antioxidant)), substances that protect against peroxides (atorvastatin, reduced glutathione, flavonoids), substances that protect against neurodegenerative diseases (melatonin, resveratrol, creatine, l-carnitine), and angiotensin converting enzyme inhibitors (captopril, ramipril).

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