

ALS-UNTANGLED

ALSUntangled No. 28: Acupuncture

The ALSUntangled Group

ALSUntangled reviews alternative therapies on behalf of patients with ALS (PALS). Here we review the use of acupuncture for ALS, for which we have had more than 200 requests (1).

Overview

Acupuncture is a technique from ancient China in which thin needles are inserted into specific locations along the skin to produce a therapeutic effect (2). Variations have arisen, including the additions of pressure, heat, laser light, shock waves, electricity or medications (2,3); for the purposes of this review we consider all these variations under the term ‘acupuncture’. Acupuncture has been advertised to improve pain, spasticity, cramps and anxiety in patients with ALS, and to slow, stop, and sometimes even reverse their muscle weakness (4–6). In Shanghai China, more than 50% of PALS use it to treat their illness (7). This review does not address symptomatic benefits, but focuses on purported effects on ALS disease progression.

Mechanism(s)

There are at least two mechanisms by which acupuncture has been suggested to exert its therapeutic effects.

Traditional Chinese Medicine (TCM) holds that body functions are regulated by an energy called ‘qi’ which flows along specific paths or meridians (2,3). Disruptions or blockages in the flow of this energy are thought to be responsible for disease, and insertion of needles into specific locations (acupoints) restores energy flow and ameliorates disease (2,3). No convincing scientific evidence for qi, meridians or acupoints has yet been found (3,8,9).

More modern concepts start with needle insertions activating the endogenous opioid neuropeptides enkephalin, beta-endorphin, and dynorphin (3,10). These in turn are purported to have downstream effects on brain areas involved in pain perception. Opioids can also modulate the immune system

(11–13); in so doing, they could theoretically alter the progression of diseases where the immune system plays a pathogenic role, including ALS (14,15). Some studies find elevated beta-endorphin levels (10), altered functional MRI patterns (16–20), and even altered inflammatory markers (21,22) including in ALS animal models (23,24), following acupuncture. Some studies find that opioid antagonists such as naloxone or genetic down-regulation of opioid receptors can block the beneficial effects of acupuncture (10). ALSUntangled assigns a TOE ‘Mechanism’ grade of B based on this information (Table I).

However, there are some problems with these modern theories. They do not explain acupoints; in some studies, ‘sham’ acupuncture utilizing telescoping needles that do not break the skin works as well as ‘real’ acupuncture, raising the possibility that acupuncture works via a placebo effect (3). The data are not consistent across investigators (3,25). Many of the ‘positive’ studies on acupuncture mechanisms originate in China (3,8), and the percentage of ‘negative’ studies published by Chinese investigators has been found to be unusually low (3,26), meaning there may exist a publication bias.

Pre-clinical data

Two papers by the same group have examined the effects of acupuncture in the SOD1 mutant mouse model of ALS (23,24). Both papers showed that acupuncture was associated with reduced inflammatory markers compared to mice not receiving acupuncture (23,24). One paper showed that acupuncture was associated with improved motor neuron survival and delayed loss of motor performance compared to mice not receiving acupuncture (23). There are multiple methodological flaws in these papers according to published guidelines (27), including incomplete sample characterizations, 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).

Table I. TOE Grades (2) for acupuncture as an ALS treatment.

	Grade	Explanation
Mechanism	B	Acupuncture can alter inflammatory markers in an animal model of ALS
Pre-Clinical	C	Multiple flawed peer-reviewed publications report benefits of acupuncture in ALS models
Cases	A	One or more peer reviewed publications report benefits of acupuncture in PALS
Trials	D	One peer reviewed publication reports benefits from acupuncture in a flawed ALS trial
Risks	D	More than 0% but less than 5% of patients treated with acupuncture experienced death or hospitalizations

Data in PALS

There is one small pilot trial of acupuncture in PALS (28). Eighteen patients were treated twice daily for five days, with before and after measurements of oxygen saturation, end-tidal carbon dioxide, respiratory rate, pulse rate and ALSFRS-R. Statistically significant improvements were seen only in oxygen saturation and pulse rate after acupuncture. There are several problems with this study including small numbers, short duration, lack of a control group, and lack of blinding. The findings have never been replicated. The sizes of the observed improvements in mean oxygen saturation (from 95.42% to 95.58%) and in mean pulse rate (82.49 to 80.08) are of dubious clinical significance. ALSUntangled assigns a TOE 'Trials' grade of D based on this information (Table I).

Two groups have published case series describing the effects of acupuncture in PALS (29–32). The first group published in Chinese (29,30); we reviewed an available translation (31). Between 1980 and 1996 this group reportedly treated 46 PALS for six to 24 months. In addition to acupuncture, treatment included Chinese herbs and exercises (31). Six of the patients were said to have achieved 'clinical remission, where atrophic muscles were largely restored, the patient then being able to survive with the disease more than 10 years after the diagnosis' (31). In 11 of the patients, the treatments were said to be 'markedly effective, where the ability of managing daily activities was enhanced somewhat, or being able to survive more than five years after diagnosis' (31). For 24 patients, treatments were said to be 'fairly effective, muscular atrophy slows down, with survival over three years' (31). In the remainder, treatments were 'ineffective, symptoms do not improve significantly, with survival less than three years' (31). Criticisms of this work include a lack of detail regarding the ALS diagnoses, lack of a control group, lack of blinding and failure to use validated ALS outcome measures.

The second group reported on two PALS treated with acupuncture five days per week for four weeks and a 'detoxification' supplement regimen (32). From the information provided, patient 1 would have been classified as 'clinically probable ALS'

(EEC). Patient 2 had no documented upper motor neuron findings and thus may have had 'progressive muscular atrophy' (33) or 'lower motor neuron predominant ALS' (34,35). Subjective measurement of speech intelligibility and manual muscle testing improved in both patients over the study period. Problems with this study include an incomplete work-up for ALS mimic syndromes in patient 2 (testing to exclude atypical myasthenia gravis or multi-focal motor neuropathy should have been performed (36)). Also, outcome measures were subjective with no apparent blinding of the raters, the concomitant 'detoxification' regimen is not well described, and the follow-up duration was short.

Within the online community PatientsLikeMe, 72 members reported trying acupuncture for ALS and 19 of these completed evaluations of it. In terms of effectiveness, three reported it to be 'moderate', seven 'slight', six 'none' and three 'unknown' (37). Google search identified no additional case reports. ALSUntangled assigns a TOE 'Cases' grade of A based on this information (Table I).

Risks and costs

Large series suggest that acupuncture is generally safe but not entirely without risk (3). Mild adverse events such as pain or bleeding occur in 7–11% of patients (3,38–40), and serious adverse events have occasionally occurred including cardiac tamponade (3,41), pneumothorax (3,42), and transmission of infections (3,43). ALSUntangled assigns a TOE 'Risks' grade of D based on this information (Table I).

Costs of acupuncture vary greatly depending on the specific type and frequency. PALS on Patients-LikeMe report a range of costs from less than \$25 to more than \$200 per month.

Conclusions

Acupuncture is reasonably safe, and has potential mechanisms of action, pre-clinical studies and case reports suggesting that it could be a useful treatment for ALS. However, before it can be endorsed even as a candidate for a phase II trial, the studies described above need to be independently replicated using more clearly verified diagnoses and more rigorous

designs, including appropriate controls and validated ALS outcome measures.

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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.