Setting up a clinical trial

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All clinical research projects have their pitfalls, but acupuncture trials may present more problems that most, as I have discovered myself. I was going to write about the trial into the use of acupuncture in migraine, which I have set up at Southampton University. However, there have been so many problems with the protocol, that the trial is still in its infancy. So I shall concentrate instead on the difficulties of setting up a trial, so that others may learn from my experiences.

Anyone thinking of setting up a research project must take into account the following factors:

1. Definite diagnosis of condition to be studied
2. Homogeneity of grouping
3. Adequate randomisation
4. Nature of control treatment: real placebo or mock acupuncture
5. Status of operator and assessor: blind or non-blind
6. Continuity of follow-up and clear end points
7. Size of the trial groups

Dependent on knowledge of natural history of the disease

Diagnosis: some projects have concentrated on groups of patients with very non-specific diagnosis. For example, musculo-skeletal pain was treated in one well-publicised trial. In such cases, the natural history of the condition is extremely variable and therefore the trial produces inconsistent results which are not statistically significant. In drawing up the protocol for the migraine trial, we decided on a precise diagnosis of migraine as a recurrent headache, occurring at least twice a month and with two out of three associated features — vomiting, visual disturbance and unilateral distribution. Any patient whose condition did not fit these criteria was excluded from the trial.

Homogeneity: it is essential to study a homogenous group, since the disease process may vary according to such factors as age and sex. Because the natural history of migraine varies according to sex, we randomised male and female patients in separate groups. Naturally, such randomisation must be carried out blind.

Controls: mock acupuncture probably has some beneficial effects and, therefore, cannot be regarded as a true placebo. From the evidence of numerous trials, it appears that a true placebo is 30 per cent effective, mock acupuncture 50 per cent effective and true acupuncture about 70 per cent effective. Consequently, it is difficult to obtain statistically significant results by comparing mock acupuncture with true acupuncture and it is far preferable to introduce a true placebo.

In our own migraine trial, we are using mock TNS. We attach our patients, by means of skin electrodes, to a small, battery-powered stimulator. The stimulator is switched on but, unknown to the patients, no current runs through the system because one of the leads is disconnected. We gave considerable thought to the nature of the placebo and, in our opinion, this is the best option, since it cannot possibly be regarded as therapeutic and yet it is readily acceptable to the patient.

Blindness: in my opinion, true double blind acupuncture trials are impossible, as are trials involving a blind operator. The only option, therefore, is to use a blind assessor. We decided to use the patients as assessors. Each patient completes a daily chart of his headaches, with notes about associated features and medication. This daily assessment will continue for six months after treatment ends.

Follow-up: it is important that all patients should be followed up — including those who fail to attend — and there should be specific points for assessment during the follow-up period.

Numbers: the size of the trial group depends upon whether one is comparing true acupuncture with the mock variety or a real placebo. In order to obtain a 98 per cent power to detect a significant difference in a trial of placebo versus acupuncture, only about 40 patients are needed in each arm of the trial (see figure 1). However, more than a hundred patients are needed for each arm when comparing true acupuncture with mock acupuncture. It was for this reason that we decided to use a true placebo in our migraine trial.