BRIEFING PAPER No 6

HIV Infection
and
Traditional Chinese Medicine

The evidence for effectiveness

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The Evidence Series of Briefing Papers aims to provide a review of the key papers in the literature, which provide evidence of the effectiveness of acupuncture in the treatment of specific conditions. The sources of evidence will be clearly identified ranging from clinical trials, outcome studies and case studies. In particular this series of briefing papers will seek to present, discuss and critically evaluate the evidence.

HIV INFECTION AND TRADITIONAL CHINESE MEDICINE:
THE EVIDENCE FOR EFFECTIVENESS

Summary

Chinese medicine has been widely used over the past 15 years in the treatment of people living with HIV/AIDS. This paper reviews the available studies reporting on this intervention and concludes that, despite some promising indications of symptomatic relief, most of the reports are methodologically flawed and are also seriously limited in their value by pre-dating recent developments in Western medical diagnosis and treatment. There is a need for more controlled trials which are able to assess the impact of Chinese medicine on the biomedical markers of HIV infection (such as viral load and CD4 cell counts), for studies which focus on clearly targeted symptoms such as diarrhoea and neuropathy which are anecdotally reported as responsive to Chinese medicine, and for studies which explore the role of Chinese medicine in working alongside combination therapy to alleviate side effects and optimise effective intervention.

Introduction

Human immunodeficiency virus (HIV) infection targets and progressively destroys a type of white blood cell called a T4 Lymphocyte, eventually leading to the development of acquired immunodeficiency syndrome (AIDS). This presents with pathology either directly resulting from HIV infection, such as HIV induced neuropathy or encephalopathy, and/or with signs and symptoms that result from opportunistic infections, such as by bacterial, fungal, viral or protozoan pathogens and opportunistic malignancies such as Kaposi Sarcoma and Non-Hodgkins Lymphoma.

Since the early 1980's over 40 million individuals have contracted HIV worldwide and over 12 million have died. In the UK there had by 1998 been 11,073 deaths from AIDS since the first cases were reported in 1982; in addition 10,366 people were living with HIV and a further 3,616 individuals had developed AIDS defining illnesses (1). In the developed countries HIV infection is still predominantly a disease affecting gay men and intra-venous drug users. However more than 90% of HIV infected individuals live in developing countries where the medical, social and economic implications of HIV infection are devastating (2).

In recent years the introduction of regimes using several types of anti-retroviral drugs simultaneously - the so called combination therapy - has for the first time had a major impact

on the prognosis for people living with AIDS and in the USA in 1996, after a decade of relentless rises, the death rate from AIDS is finally declining. However, the cost of combination therapy is up to £10,000 per annum per patient, which is prohibitive for most sufferers in the developing countries, and there is increasing evidence of viral resistance and severe, potentially fatal side effects from the drugs leading to a renewed Western medical focus on the possibility of developing a preventive vaccine.

In the meantime there is a role for Chinese medical therapies to support individuals who are HIV+ and asymptomatic, to help to alleviate some of the side effects of the drug therapy, to improve well-being and to assist in the treatment of individuals who are either unwilling, unresponsive or resistant to combination therapy.

Literature Search

A search was made on the specialist database of the Acupuncture Research Resource Centre (composed largely of records from AMED and MEDLINE) using key words 'HIV' and 'AIDS'. After removing those concerned mainly with treatment rather than treatment evaluation, Chinese language papers and those that were duplicates or unobtainable, the original 90 were reduced to 16.

These articles can be divided into five categories:
1. Controlled trials
2. Reviews of controlled trials
3. Uncontrolled outcomes trials
4. Reviews of outcomes trials
5. Case histories

Controlled Trials

Only one controlled trial was identified, for HIV-related peripheral neuropathy. Shlay et al (1998) recruited 250 patients for a double-blind, placebo-controlled, multicentre study of acupuncture and amitriptyline. The design allowed comparisons to be made between any of the four groups: real acupuncture, sham acupuncture, amitriptyline, placebo medication. Patients in the acupuncture groups received 20 treatments, either a) SP9, 7 and 6 as standard plus KI3, 2 or Ba Feng points as indicated by symptoms, or b) superficial needles at three non-acupuncture points in the calves. Pain was assessed at six and 14 weeks (the end of the trial) using an appropriate rating scale (the Gracely scale). There were no significant changes in pain score to indicate that either acupuncture or amitriptyline were more effective than placebo.
This trial was large and well designed, and hence not subject to many of the usual criticisms of clinical trials of complementary therapies. However, the points chosen for the real acupuncture treatment have been criticised (Kaptchuk 1999) as being inappropriate and hence more suitable as a placebo. The points had been chosen by consensus among eight acupuncturists. This kind of debate will inevitably become more prominent if traditional Chinese protocols are used more frequently in research trials.

Reviews Of Controlled Trials

A recent review by Ozsoy and Ernst (1999) aimed to evaluate all randomised controlled trials of complementary therapies for HIV. As well as the one acupuncture study, they also located trials using herbs, supplements, stress management techniques and massage. After emphasising the paucity of good evidence, they suggest that these therapies may best be employed in a "caring" rather than "curing" mode, looking to increase quality of life.

Outcome Studies

Ten papers describe outcomes trials, which, having no control groups, may therefore be influenced by the placebo response, the self limiting nature of some conditions and by intervention from other forms of medical treatment.

There are three outcomes audits analysing treatment given in a Western setting (Smith 1988, Moffett et al 1994 and Flower 1998). Smith (1988) describes his experience at the Lincoln Hospital, New York, and two other metropolitan centres in the USA, in treating over 350 patients with AIDS or AIDS Related Complex (ARC) over a 5 year period using acupuncture and Chinese herbal medicine. He offers an evaluation of the response of these patients to this treatment through looking at changes to symptoms and survival times as measures of benefit. The exact methodology used is not described (what form of questionnaire was used etc.), nor are there details of the statistical analysis, but the conclusion to the study is that:

- there was a substantial reduction in symptoms such as fatigue, night sweats and diarrhoea;
- 30-40% of a small sample of 14 ARC patients seen between 1982-83 had a five year survival rate after receiving acupuncture frequently over a 2-6 month period of time;
- herbal intervention has improved results and has significantly reduced the drop out rate in the programme;
- two cases of early stage Kaposi Sarcoma showed apparent remission;
- there was a general report of fewer symptoms of infection and reduction in side effects from Western drugs.

This paper is not really a study but more a series of observations and a collection of case histories. It does not describe the methodology used, has no form of control, and reports on a very small sample of patients who **regularly** attended treatment. Whilst it is of some historical interest its clinical relevance is diminished by the fact that it precedes both viral load testing and other blood tests that could objectively correlate symptomatic changes, and also predates combination therapy, which would now almost certainly be prescribed to the majority of the cases described.

Moffett et al (1994) describe the underlying theory and practical structure of the HIV treatment programme at the American College of TCM in San Francisco. 67 patient outcomes were evaluated over a three-month period using a symptom checklist and a quality of life survey administered monthly, with "significant improvements" noted for fatigue, loss of appetite, lymphadenopathy and neuropathy. In general not only did the total number of symptoms diminish but also the severity. The shortcomings are similar to those for Smith's work, with no control, a small sample group reporting on a wide range of 28 possible symptoms and no objective measurement to correlate to this reported improvement.

Flower (1998) uses the Measure Your Own Medical Outcome Profile (MYMOP) questionnaire as part of an outcomes audit of 18 patients seen over a six-month period at London Lighthouse. 15 out of 18 patients reported relief in their presenting symptoms and improvement in well being. The shortcomings are the same as those mentioned above.

Su (1991), Xue (1993), Lu (1995) and Lu et al (1995) refer to the experience of a team of senior Chinese doctors invited to research the effect of Chinese herbal medicine on patients with AIDS in Tanzania. Differentiation was made according to traditional Chinese categories as well as a review of symptomatic changes and basic blood test results (Su 1991). The conclusion of Xue and Su is that Chinese herbal medicine did bring some symptomatic relief for AIDS patients.

Lu (1995) summarises the pharmacological rationale and the clinical experiences of the Chinese team in Tanzania after having treated a total of 158 individuals over a three-year period. The Karnofsky Score - a measure of the degree of disability caused by an illness - showed improvement in 82 patients, and symptomatic improvements were noted in lymphadenectasis, diarrhoea, anorexia, fever, weight loss, skin rashes and coughs. The methodology used to assess these changes is not given in the paper. The study also measured changes in T4 cells over time and T4/T8 ratios (3) and noted that 31% of patients showed at least temporary improvements in the former but the latter showed less response. Once again the details of these measurements have been omitted from the article and the amount or the duration of the T4 cell increase is not clear.

Lu et al (1995) report on eight cases of individuals converting from HIV+ to HIV- after taking Chinese herbal medicine, which at the time of writing had never before been reported in the medical literature and, if substantiated by future research under well-controlled conditions, is a potentially radical breakthrough. The subsequent absence of such research suggests these results have proved difficult to replicate and may have been due to an incorrect initial diagnosis of HIV status.

Guoqin et al (1996) used traditional Chinese medicine for treating AIDS-related respiratory tract infection in a group of 58 patients, finding a clinical cure in 31% and therapeutic effectiveness in a further 12%. A contemporary group of 22 patients treated by combined Chinese and Western medicine had a less positive response, but had started with more severe symptoms.

Both Tosches et al and Galantino et al (1999) have conducted pilot studies on the symptomatic treatment of HIV associated peripheral neuropathy with acupuncture. In the former study 39 patients were enrolled, and of the 26 who completed the first follow up there was improvement in seven cases, no change in 16 and deterioration in three. Galantino et al report on a small trial (complete data from only seven patients) where electro-acupuncture was administered daily for 30 days at points BL60, ST36, KI1 and LIV3. Assessment was by an HIV-specific questionnaire and nerve reflex measurement. All seven patients showed significant improvement on both counts. The results led both sets of researchers to conclude that there may be a role for acupuncture in the treatment of peripheral neuropathy. These studies combined subjective and objective data and focused on a specific condition, and in many ways act as models for future pilot studies to investigate the role of Chinese medicine in AIDS treatment.

Reviews Of Outcome Studies

Orman & Meargetis (1992) briefly review the effectiveness of acupuncture and Chinese herbal medicine as reported by several centres in the USA and consider some of the traditional theory and research into Chinese herbal medicine that underpins this work. Wu (1992) offers a more complete review of recent developments in the treatment of HIV & AIDS, including a variety of experiences gained by American practitioners, and also describing research conducted in Japan on Glycyrrhizin - an extract of Liquorice (Radix Glycyrrhhizae Uralensis). Wu also reviews the experimental research into Chinese herbs and describes the methodology by which several herbs and formulae were found to have anti-HIV actions in vitro. He also describes the inhibition of HIV replication in vitro but with no mention of an effect on clinical outcome.

Case Histories

Lei (1989) reports on two cases of AIDS treated with acupuncture, and describes the protocol used, which provided significant symptomatic relief. Haines (1994) concludes a useful article on the diagnosis and treatment of HIV & AIDS by acupuncture with a case history that accurately reflects the reality of working with people with advanced HIV infection. Smith (1988) and Xue (1993) both include several accounts of patients receiving treatment and Smith highlights the apparent remission of Kaposi Sarcoma in two patients.

Other Papers Of Interest

These four articles lack a direct clinical evidence content but are included here for general interest.

Cohen (1990) provides a theoretical analysis of the traditional pathology of HIV infection and considers HIV in the wider context of other diseases of chronic immune dysfunction such as systemic candidiasis and CIDS (Chronic Immune Deficiency Syndrome). She describes acupuncture and Chinese herbal medicine protocols, which she has found to be effective, but in this descriptive account there is no mention of any substantiating research.

Lu (1991) reviews the effects of Chinese herbs on regulating immune function, and on the inhibition of HIV, but does not give details of any clinical application of this work. Similarly Chen et al (1992) describe the impact of acupuncture treatment on the treatment of infectious diseases such as Hepatitis B, malignant diseases and on regulating immune dysfunction. The authors infer from the success of these interventions that acupuncture could have an important role to play in the treatment of AIDS, but once again fail to back up this hypothesis with any solid, clinically based evidence.

Anastasi (1997) describes the aetiology and Western treatment of HIV-related diarrhoea and then goes on to describe its TCM pathogenesis and treatment using acupuncture. The paper argues that Chinese approaches to diarrhoea may be relevant to people living with HIV/AIDS and that further research is needed to establish the veracity of this.

Discussion And Conclusions

In general the research into the efficacy of Chinese medicine as a treatment modality for people living with HIV/AIDS is at an early stage. There is, at the time of writing, only one randomised controlled trial into any aspect of the potential contribution of Chinese medicine to the treatment of HIV/AIDS, while the outcomes studies tend to be on a small scale, anecdotally or descriptively based on subjective responses, without any quantitative supportive evidence. There is a stark divide between some of the hard science being carried out in China and Japan and actual clinical research to test the theory in practical situations.
Changes also in the treatment of HIV/AIDS due to the introduction of combination therapy mean that whilst they are of some historical interest many of the studies have been rendered clinically redundant.
What is needed is a new generation of focused studies, combining qualitative and quantitative information and looking at specific aspects of living with HIV/AIDS to assess the real value of Chinese medicine in the treatment of this condition. The recent U.S. trials on neuropathy are indicative of a start in this direction.

Notes

(1) PHLS Communicable Disease Surveillance Centre (March 1998).

(2) J Mann, D Tarantola: **HIV 1998: The Global Picture**. *Scientific American, July 1998*, 62-63.

(3) The T4:T8 ratio is normally > 1 but in HIV infection this usually falls to <1 as the T4 Lymphocytes are destroyed by the HIV virus. The significance of this and all the other diagnostic procedures currently available are well described in the excellent "HIV & AIDS Treatments Directory" Pb. Nam publications - 16a Clapham Common Southside, London SW4 7AB. Tel 0171 627 3200.

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