Current Research and Clinical Applications

Blinding in Clinical Trials

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In randomised controlled trials (RCTs) blinding is an important design feature to control for bias. Studies that have not been blinded have been shown to produce exaggerated treatment estimates. Blinding of trial participants, researchers and outcome assessors can be difficult to establish and maintain. Recently a number of reviews have asserted that some 'assurance of blinding' (statistically evaluating whether trial participants, researchers and outcome assessors are unaware of which intervention or treatment group they have been allocated to) should be reported in published studies. Several recent journal articles have reviewed the assessment of blinding in biomedicine RCTs as well as some herbal medicine studies.

Montori and colleagues[1] evaluated 200 biomedical RCTs for evidence of blinding assurance. They reported that explicit reporting of blinding status for the trial participants only occurred in 15% of the studies, while blinding of the researcher/health care provider was reported in only 5% of studies. They also found that blinding of the data collectors' occurred in only 12% of trials and data analysts were reported as blinded in only 2.5% of cases.

Fergusson and colleagues[2] evaluated a random sample of 191 trials from leading general medicine and psychiatry journals. They reported that only seven of the 97 general medicine trials provided evidence on the success of blinding, with five of the seven reporting the success of blinding was imperfect. For the psychiatric journals the success of blinding was reported in only eight of the 94 trials (9%) with four reporting the blinding was imperfect.

A more recent study by Boutron[3] reviewed 90 biomedicine studies and found that 58 of the studies did assess blinding. However, there was variance in consistency in timing of assessment and mode of answering. They further stated that only 57% of the trials used statistical analysis whereby the proportion of correct guesses was compared to those produced by chance. A year later a systematic review of the methods of blinding of 472 trials by the same group[4] concluded that more than half of the studies (n = 472; 58%) described the blinding but 236 papers (29%) gave no details and only 111 gave some data on blinding.

Finally, Machado[5] reviewed 126 trials using 25 different placebo interventions. They reported that the adequacy of blinding was assessed in only 13% of trials. They also noted that in 20% of the studies the placebo intervention was a potentially genuine treatment. To overcome this problem Brinkhaus et al[6] has proposed a placebo quality checklist for pharmacological trials to help investigators select an appropriate placebo and help readers interpret the study findings with more care.

Few studies have looked at the issues that face herbal medicine researchers when designing and conducting a placebo controlled trial. The placebo in some clinical trials may be difficult to formulate because Chinese medicine preparations have special macroscopic (appearance, weight, size of the particles) and sensory characteristics (colour, smell and taste) making a perfectly matching placebo nearly impossible.

Zick[7] assessed whether trial participants could distinguish between ginger and placebo capsules. They found that of the eighty people in the trial, 42 correctly identified the capsule they received. Of those that received the placebo capsule, 82% correctly identified their allocation status. Of those subjects who received the ginger, 22.5% correctly identified their capsule. With the increasing evaluation of Chinese herbal substances in RCTs the issue of blinding evaluation is being scrutinised.[8] Herbal substances tend to have a strong odour and powders may be highly coloured due to the colour of the base herbs used in the formulation. More recently Qi and colleagues[9] evaluated the validity of placebos used in blinded RCTs of Chinese herbal medicine. They reported that of the 77 full length articles they evaluated nearly half did not pay any attention to the physical quality of the testing drug and placebo. Only two articles specifically validated the comparability of the placebo herbal substance and the testing herb or drug. They concluded that

'quality specifications and evaluation of the placebo should deserve attention to reduce the bias in randomised controlled studies of Chinese herbal medicine'.

In summary, placebos that are improperly formulated or implemented may introduce bias into a trial. Even though blinding is important in RCTs, and thousands of trials are conducted every year, the reporting of blinding and success of blinding are often inadequate. Many researchers and a number of reviews of blinding and its evaluation have concluded that there is minimal assessment of blinding and when there has been it has been poorly reported. Future Chinese herbal medicine studies that incorporate a placebo control need to evaluate carefully their choice of placebo material and to establish if they are successful in blinding the researchers, trial participants, outcome assessors and data analysts.

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Smoking Cessation

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The application of acupuncture for substance withdrawal in general was identified early in the history of acupuncture in the West. The link between substance abuse and acupuncture may be understood as a reflection of the desire of proponents of acupuncture in the West to demonstrate that an ancient, traditional medicine could be used for 'modern diseases'. Much of the work in this area was stimulated by reports of Smith's pioneering work with substance abusers, mainly heroin, in the late 1970s.[2,3] In Australia, Smith's work captured the attention of a number of traditionally trained acupuncture practitioners. The intention was to apply naturalistic therapies to a local and intractable public and social health concern. Indeed, a peculiarly Western inspired approach to needling was applied and known as the National Acupuncture Detoxification Association (NADA) protocols. It is also worthy to note that, in Australia, this approach helping substance abusers through the acute detox phase has been used for over twenty-five years. The central point to this introduction is that not only could acupuncture help in general medical conditions, it could also help where there was a significant social and psychic dimension to health care.

Much has already been written suggesting the view that acupuncture may indeed retain a strong neuro-physiological basis that helps us understand acupuncture mechanisms. The assumption was that such processes could also help us understand addictive, self-harming behaviours, locating the problem as residing within the individual.

Contrary to anecdotal clinical reports, the application of acupuncture and related interventions to smoking cessation in particular, however, does not seem to bear out the initial promise with most reviewers suggesting that further methodological problems need to be overcome. It seems that there is no consistent evidence that acupuncture is effective for smoking cessation.

Adrian White in collaboration with a number of other colleagues has written extensively on the subject especially from the point of view of reviewing acupuncture trials on quit smoking.[5] We need to bear in mind that the inclusion criteria, was that trials must be of the randomised controlled trial (RCT) type. Taking heed of White's earlier reviews, Bier et al[1] implemented a trial taking into account concerns raised by White et al regarding design flaws, randomization and other factors. Published in 2002, their conclusions were positive. They found that the combination of acupuncture and a smoking cessation educational program demonstrated rates of 40% cessation and 53% post treatment reduction in total cigarettes smoked. Completing another review of the literature in 2006, White et al[4] rejected Bier et al findings because of 'inconsistencies in data presented which could not be clarified by contacting the authors'. No further discussion ensues in their report detailing with what the inconsistencies were.

Where does this leave practitioners working in the field? What does seem to be somewhat bewildering to this writer is the preponderant attitude of researchers to the notion of 'one size fits all' in relation to acupuncture points used in trials. In some instances the reader is not told which points were used at all other than being offered a statement such as, points used for 'good for the lungs'. In many trials, auricular points are used which appear to be NADA protocol points or variations of it and as stated earlier, tend to be used in the acute detox phase of heroin withdrawal. Sometimes auricular points are combined with a body point(s). Interestingly, the assumption behind using NADA points is that their actions are transferable to tobacco smoking cessation. Again, the assumption of one-size fits all re-appears.

In addition, minimal attention is given to for instance the rationale for point selection. From a simple content analysis approach, it is unusual to read more than a short paragraph on point selection. The lack of intent to discuss these matters is conspicuous by its absence. In contrast, there is often substantial discussion on the minutiae of research design.

Traditionally trained acupuncturists are aware of the axiom '*tong bing yi zhi - yi bing tong zhi* - different treatment for the same disease and same treatment for different diseases' which is another way of saying one size does not fit all. Acknowledging the notion, it is rather strange that researchers, presumably cognisant of this fundamental treatment principle persist in the attitude of minimising, indeed, discounting the importance of traditional acupuncture point selection. If acupuncture points are taken to be the 'bread and butter' of acupuncture why then do researchers give them so little attention? From a traditional acupuncturist's perspective, such research trials are flawed from the outset.

We are still left with our first question – how useful is acupuncture in helping smokers quit? Perhaps the RCT is not the only or best way to explore addictive, self-harming behavior of tobacco smoking.

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