傳統醫學研究指引

General guidelines for methodologies o research and evaluation of traditional medicine, WHO, 2000

台北榮民總醫院

郭英調

「傳統醫學研究指引」內容

1. Methodologies for research and evaluation of herbal medicines
2. Methodologies for Research and Evaluatio of Traditional Procedure-Based Therapies
3. Clinical Research
4. Other Issues and Considerations

Annex I-X

1. Methodologies for research and evaluation of herbal medicines

1.1 Definitions

- *Herbs*
- *Herbal materials*
- *Herbal preparations*
- *Finished herbal products*
- *Traditional use of herbal medicines*
- *Therapeutic activity*
- *Active ingredients*

1.2 Botanical verification and quality considerations

- Botanical verification is **necessary**.

1.3 Research and evaluation of safety and efficacy

Literature review

- ..... the first step involves the evaluation of literature reports.
- .....cite primary references that can be consulted for in-depth analysis.
- For both safety and efficacy, a pharmacological effect observed in vitro or in animal models is **n necessarily applicable to humans**.

1.3 Research and evaluation of safety and efficacy

Safety

- The absence of any reported or documented side-effects is **not** an absolute assurance of safety for herbal medicines.
- However, a full range of toxicological tests **may not be necessary.**

1.3 Research and evaluation of safety and efficacy

Safety

- Only when there is **no documentation** of long historical use of a herbal medicine, or when **doubts exist** about its safety, should additional toxicity studies be performed.
- Where possible, such studies should be carried out ***in vitro*.**
- If *in vivo* studies are needed, they are to be conducted **humanely**.

1.3 Research and evaluation of safety and efficacy

Efficacy

- .....the requirements for proof of efficacy, ..., should depend on the **nature and level of the indications**.
- For the treatment of minor disorders, for nonspecific indications, or for prophylactic uses, less stringent requirements (e.g. observational studies) may be adequate to prove efficacy.

1.3 Research and evaluation of safety and efficacy

Efficacy

- The level of the evidence and the grading of recommendations must correspond to the nature of the illness to be treated or the nature of the physical or mental function to be influenced and regulated.

1.3 Research and evaluation of safety and efficacy

- *Clinical trials*
  - In the case of a new herbal medicine, a **new indication** for an existing herbal medicine, or a **significantly different dosage** form or **route of administration**, the general principles and requirements for a clinical trial should be very similar to those which apply to conventional drugs.

1.3 Research and evaluation of safety and efficacy

Clinical trials

- Well-established, randomized controlled clinical trials provide the highest level of evidence for efficacy.
- However, methods such as randomization and use of a placebo may **not always be possible** as they may involve ethical issues as well as technical problems.

1.3 Research and evaluation of safety and efficacy

Clinical trials

- In the case of herbal medicines with a strong flavour, placebo substances with the same flavour may have a similar function.
- In such cases, it may be advisable to use a **low dosage** of the same herbal medicine as a control.

2. Methodologies for research and evaluation of traditional procedure-based therapies

2.1 Types of traditional procedure-based therapies Clinical trials

- .....without the use of medication,....., for example, acupuncture and related techniques, chiropractic, osteopathy, manual therapies, qigong, tai ji, yoga, naturopathy, thermal medicine, and other physical, mental, spiritual and mind – body therapies.

2.2 Evaluation of safety and efficacy

Theories and concepts

- The theories and concepts of the various systems of traditional medicine are **very Important**.

2.2 Evaluation of safety and efficacy

Safety

- In general, traditional procedure-based therapies are **relatively safe**, if they are performed properly by **well-trained practitioners**.

2.2 Evaluation of safety and efficacy

Safety

- The most effective safety measures, therefore, are to ensure that the **equipment used is of good quality**, as well as ensuring that the practitioners who use it have had sound and well supervised theoretical and **practical training**.

2.2 Evaluation of safety and efficacy

Efficacy

- The efficacy of most forms of traditional procedure-based therapies depends heavily upon the **proficiency of the practitioners**, including their skills and experience.

3. Clinical Research

1 General considerations

Evaluate traditional medicine in **its own theoretical** framework.

Evaluate traditional medicine in the theoretical **framework of conventional medicine.**

Compare the efficacy of different systems of traditional medicine and/or **conventional medicine**

Compare the efficacy of **different traditional practices** within a system of traditional medicine.

3.2 Literature review

- The starting point in the design of a research protocol is **a complete literature review**, including the traditional use of the proposed practice and existing scientific research in the field.

3.2 Literature review

- A review of the literature should identify the **current level of evidence** of efficacy and safety for the proposed intervention.
- ....the efficacy of a particular treatment
- may also **vary** according to the **skill and experience** of the practitioner.

3.3 Selection of study design

Study design

- Clinical research aimed at evaluating traditional medicine should incorporate the conventional concepts of research design, such as **randomized controlled trials** or other types of clinical studies, such as **observational studies**.

3.3 Selection of study design

Single-case design

- In a single-case design, the patient is his or her own control.
- Treatment can be randomized for a patient, rather than the patient being randomized for a treatment.
- Such designs are appropriate for the **development of research hypotheses**, **testing those hypotheses** in daily clinical practice and **refining clinical techniques.**

3.3 Selection of study design

black-box design

- This means that the treatment and **all of its components are delivered** as they would be in the usual clinical situation.
- This allows the **effectiveness** of traditional medicine to be determined either within its own theoretical framework or within that of conventional medicine.

3.3 Selection of study design

Ethnographic design

- These and other qualitative studies can **provide baseline information** from which hypotheses may be generated, and can lead to further research.

3.3 Selection of study design

bservational design

Observational studies have specific advantages in studying aspects of clinical **safety**.

The use of such studies to prove **efficacy** is **limited** because bias in patient selection may occur.

3.3 Selection of study design

Observational design

- Cross-sectional study.
- Cohort study.
- Case-control study.

3.3 Selection of study design

udy outcome measures

It is essential that the outcome measures chose
be **appropriate** to the research question.
Appropriate outcomes may include
quantitative and qualitative outcomes;
primary and/or secondary outcomes; and
generic and/or highly specific outcomes.

3.3 Selection of study design

Selection of patients

- Publication of the study requires a clear **description** of the patients using both **traditional and conventional terms**.
- The **reliability** of the categorization/diagnostic criteria used in the study should be considered and stated.

3.3 Selection of study design

Selection of patients

- The source of the patients under study should be comprehensively described along with **details of the recruitment process**.
- The **inclusion and exclusion criteria** should be completely described and rationalized.

3.3 Selection of study design

Sample size

- The number of patients in a study needs to be **adequate**, in order to be able to determine any **clinically important differences** between the study groups.

3.3 Selection of study design

Control groups

- well established treatment
- non-treatment
- different doses of the same treatment
- sham or placebo treatment
- full-scale treatment
- minimal treatment
- alternative treatment..

3.3 Selection of study design

Control groups

- Randomized controlled trials **require one or more control** groups for purposes of comparison
- Placebo-controlled trials are intended to establish **whether treatment is valuable over and above** what might be achieved by a control treatment.

3.3 Selection of study design

Control groups

- The use of a **placebo**, when possible, is desirable alternative treatment.
- It is preferable to compare **a herbal medicine** with both **a well-established treatment** and **another control** group

3.3 Selection of study design

Randomization

- Randomization is essential to **control** various known, and even unknown, **biases**.
- .. randomization can be **impossible or unethical**.
- .. solve ..by the proper **selection of control treatments.**

3.3 Selection of study design

Blind assessment

- Blind assessment is a **critical** component of conventional evaluation of therapeutic interventions
- Treatment blinding is **difficult to implement** in most types of traditional procedure-based therapies.

3.3 Selection of study design

Blind assessment

- It is important, however, to reduce any bias introduced by non-blinded treatment by carrying out a **blinded assessment of the primary outcomes** of the study.

3.3 Selection of study design

Evaluation of quality of life

- The WHO *QOL user manual*,

3.3 Selection of study design

Other issues related to therapeutic interventions

- the therapeutic intervention;
- reasons for selection the intervention
- rationale for the choice of the study outcomes;
- description of the outcome measurements, including validity and reliability
- a comprehensive protocol measurements
- expected outcomes the statistical method was based

3.3 Selection of study design

Other issues related to therapeutic interventions

- The type of intervention
- The training, skills and experience of the traditiona medical practitioner (intra-practitioner variability and inter-practitioner variability)
- The dose, frequency and duration of a treatment.
- The duration of follow-up.
- Temporal considerations (seasonal variations)

4. Other issues and considerations

4.1 Pragmatic research issues

- The infrastructure for research in traditional medicine is significantly less developed than that for conventional medicine.

4.2 Ethics

- The international ethical guidelines for biomedical researc involving human subjects **should be implemented** in each clinical trial.
- Rescue treatment may be provided to patients involved in clinical trial involving the use of a placebo or unproven treatment.

赫爾辛基宣言之精神

- 自主：受試驗者，是在被充分告知相關訊息後，自由決定要參加的。
- 有益：參加試驗的風險相對於可能有的好處，是可以接受的。受試驗者參加試驗後，並不會犧牲其權益，仍會受到已證明有效的最佳照顧。

評估臨床試驗最常問的倫理問題(1/3)

EMEA

- 這個臨床試驗是不是有必要？

  Was there really a need for this clinical trial?
- 對照組該給予有效治療或是安慰劑？

  Best active control treatment or placebo group?
- 這個臨床試驗是不是沒有明顯的偏差或缺失

  Has the clinical trial eliminated obvious bias and deception?

評估臨床試驗最常問的倫理問題(2/3)

EMEA

- 若有效的話，這個臨床試驗的樣本數和統計檢定力是否足以呈現其效果？

  Are sample size and statistical power adequate to show an effect if present?

- 病患接受有效治療的機率是否能夠接受?

  Were patient's chances of receiving an active medicine acceptable?

評估臨床試驗最常問的倫理問題(3/3)

EMEA

- 參與此臨床試驗之病患的安全性如何？

  What was the safety of patients entering the clinical trial?

- 參與此臨床試驗的病患是否恰當？

  What type of patients should have been entered?


Thank you!