Research Methodologies and Ethical Issues in Traditional Medicine

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Outline

- Research Methodologies
- Ethical Issues in Traditional Medicine
- Conclusions

Research Methodologies

Primary Objectives of Research on Therapeutic Methods and Medicinal Products:

To prove

- Safety
- Efficacy

Gold Standard: Methodology

Double – Blind Randomized Controlled Trial (RCT)

The 1st Randomized Controlled Trial

- Designed by Sir Austin Bradford Hill, a renown biostatistician
- Studied Streptomycin in TB patients in London
- Published in British Medical Journal in 1948
- It is the discovery of method for scientifically and impartially evaluate the treatment / product

	Male	Female	Total	Dead (after 4 m.)
Streptomycine	22	32	55	7%
No STM	21	31	52	27%

The Advantage of RCT

To reduce all biases:

- Recall Bias
- Allocation Bias → Randomization
- Treatment Bias → (Blinding)
- Evaluation Bias

Based on GCP Principles

Clinical research must be conducted in sequence:-

- Laboratory studies
- Animal studies
- Clinical Studies:
  - Phase I
  - Phase II
  - Phase III

Past Experiences in TM

- Research in Traditional Medicine can not STRICTLY follow GCP Guidelines.
- Require some modifications
- Often had substantial human use prior to Clinical Trial evaluation

Nature of Traditional Medicine

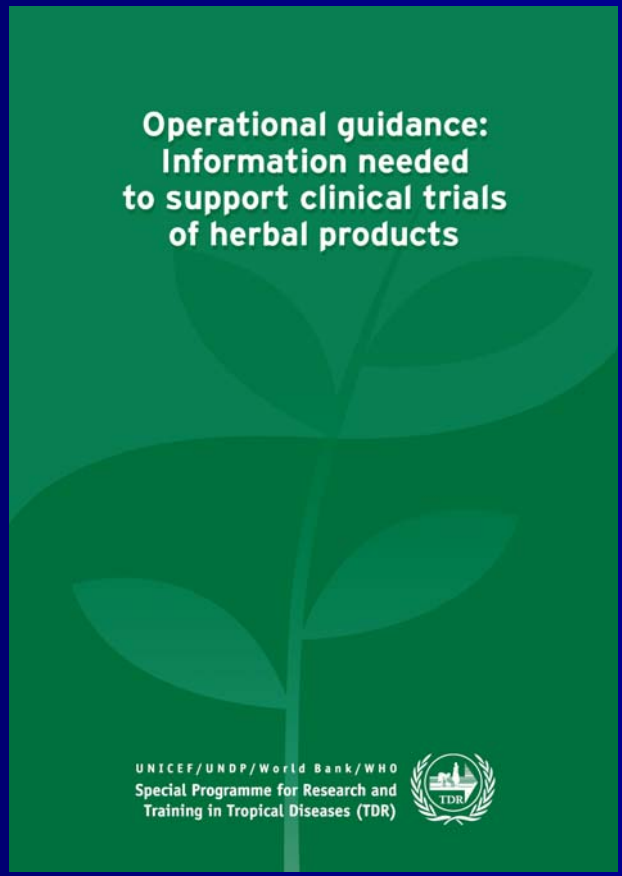
- Mixture of uncharacterized constituents
- Efficacy depends on combined actions of the mixture
- Very difficult to find active ingredient as a single molecule

The Declaration of Helsinki No 11

"Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of scientific literature, other relevant sources of information, and on adequately equipped laboratory and, when appropriate, animal experimentation."

Thus, it is not easy to comply with this requirement

TDR Operational Guidance 2005



- Phase I may take place without toxicology
  - Extensive used without known safety problem
  - Same preparation as used before
  - Documents in literatures of its safety in man

Design of the study

- It may not be easy to always apply RCT

Study Design

Apart from Randomized Controlled trial (RCT) whole spectrum of clinical research designs which are suitable for assessing traditional medicine is accepted :

- Observational design

Control groups

The control group may involve :

- Non-treatment
- Well-established treatment
- Different doses of same treatment
- Placebo treatment
- Full scale treatment
- Minimal treatment
- Alternative treatment

Study outcome measures

Appropriate outcomes may include :

- Quantitative and qualitative outcomes
- Primary and/or secondary outcomes
- Generic and/or highly specific outcomes

Basic Principle

Different study designs produce different levels of evidence

Levels of Evidence:

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization
IIb	Evidence obtained from at least one well-designed controlled study without randomization
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and / or clinical experience of respected authorities.

A Case Study : Qing hao

- Qing hao was traditional used for treatment of fever for thousand years
- It was good for treatment of malaria
- The active ingredient is Artemisinine
- The clinical study started at Phase II,III
- Phase I study conducted last

Ethical Issues

- Objectives
- Principles
- An Experience in Thailand

Objectives of Clinical Research in Traditional Medicine

- Same objectives as stated in ICH GCP Guidelines
  - Good protection of research participants
  - Data is credible

Ethical Principles

- Same as 1st stated in Belmont Report and stated again in CIOMS' Guidelines 1993
  - Respect for person
  - Beneficence and non-maleficence
  - Justice

An Experience in Thailand

Set up an " Ethics Committee for Research Involving Human Subject in Thai Traditional and Alternative Medicine"

Appointed by The Minister of Public Health

Modification of Guidelines

Only ONE article of ethical guideline of the Ethics Committee for Research in Human Subjects of the Ministry of Public Health

"2.7 SHOULD have adequate, convincing and qualified evidence to substantiate its safety based on PREVIOUS HISTORY OF USE, references OR TEXTBOOKS, animal experiment, or research papers"

On Safety issue

- Accept data and information from :
  - traditional knowledge
  - long experience in traditional use
- Toxicity study in small mammals, i.e. mice is accepted

On efficacy issue

- Accept traditional formula to be studied as a “single active ingredient”

Conclusions

- Ethics in practice for traditional medicine doctor is same as of modern medicine doctor
- Ethics in research on traditional medicine is the same as of modern medicine both in objectives and principles, but to make research on traditional medicine possible, some modifications of ICH GCP Guidelines are necessary.

- Any question???