

Clinician-reported outcomes in traditional Chinese medicine: A critical review

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Abstract

Introduction

Clinician-reported outcomes (CROs) are commonly used as an element of the evaluation of treatment. For traditional Chinese medicine (TCM), a skilled clinician must learn how to discern patterns, form a corresponding prescription and assess each patient throughout the treatment process. Because of the fundamentally important role of the clinician in monitoring the patient health status, this article reviews CROs used in TCM and provides recommendations for improving their quality in the future.

Discussion

Compared with that of western medicine, CROs in TCM are mainly the signs and symptoms induced by some

therapies, which is the reflection of pathological changes. Although the content of CROs in part overlaps with patient-reported outcomes (PROs) in TCM, they are distinct. Both CROs and PROs are subjective medical entities; the PRO research experiences in western medicine may be used to guide evaluation methods for CROs in TCM. CROs in TCM embody the spirit of pattern differentiation and individual treatments, which is an important part of curative effect evaluation. However, how to assess CROs in TCM is still an exploration. More attention should be given to the development of a conceptual framework of CROs in TCM for its further investigation.

Conclusion

CROs in TCM lay particular emphasis on the changing signs and symptoms of pathogenesis from the clinician's viewpoint. CROs in TCM provide complimentary information to PROs. Further development of the conceptual framework to support measurement clarity is underway.

Introduction

Outcomes are events, variables or experiences that are measured and potentially influenced by interventions¹. Clinician-reported outcomes (CROs) were included in a paper describing sources of data to evaluate the safety and efficacy of new drugs written by the Patient-Reported Outcomes (PROs) Harmonization Group at the U.S. Food and Drug Administration². CROs reflect the perspective of clinicians and serve as effectiveness endpoints for a wide range of diseases³⁻⁶. From 1997 through 2002, CROs appeared in 134 (62%) of 215 approved product labels reviewed of

new molecular entities in the United States⁷.

Traditional Chinese medicine (TCM) clinicians have relied on their understanding of the TCM theory, clinical experience and academic background to judge the patients' condition and evaluate treatment effectiveness. But the clinical judgment hidden in the course of treatment has not been specifically addressed in the literature. Most of the prior accounts of CROs are focused on western medicine. Increased attention given to CROs in TCM may help in better solving the problem of how to assess the effectiveness based on pattern differentiation and individual treatments.

In this article, we examine the potential use of CROs in TCM and provide guidance for future studies. First, we summarize the characteristics of CROs in TCM by reviewing the ancient TCM literature. Next, we illustrate the difference between CROs in TCM and western medicine. Then, we evaluate the relationship of CROs with PROs in TCM. Finally, we give some suggestions for future research.

Characteristics of CROs in TCM

We reviewed the TCM literature to evaluate the use of clinical effectiveness evaluations. We find representation in classic TCM books of the importance of evaluation, judging and collecting evidence⁸. A large number of clinical descriptions were noted such as 'induce slight perspiration', 'induce sweat', 'urine flow', 'bad blood purge', 'passing of flatus', 'draw poison out of the skin', 'spit pus', 'moistened mouth', 'floating pulse' and so on. These sorts of evaluations

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by clinicians have been documented for thousands of years, but they are implicit and fragmented. Applying these ideas from medical books to clinical evaluations in a systematic way is difficult⁹.

Our review of the literature indicates that clinicians use change in signs and symptoms as the primary indicators of whether the treatment is working or not. These signs and symptoms are obtained by clinicians by looking, listening and smelling, asking and touching. CROs are integrated into the TCM treatment process by virtue of adjustment to therapy based on clinician observations of pathological changes over time. Below we summarize three features of CROs in TCM.

CROs in TCM are closely related to pathological changes

Pattern differentiation is essential for ultimately achieving therapeutic effect. Discernment of the patterns within the signs and symptoms presented by the patient requires clinical expertise and skill. In particular, a 'pattern' is an abstract description of the pathological state and its changes to the sick body from a holistic and dynamic perspective, oriented around the theory of TCM¹⁰. 'TCM pathogenesis' means that the clinician grasps the relationship between external manifestation and internal essence, in order to summarize the patient's body functions in the occurrence and development of diseases¹¹. In order to pick an appropriate treatment, the clinician needs to collect the signs and symptoms to interpret how the human body may be in disharmony and discover patterns. On the subsequent visit, he can visualize an individual's particular pattern of disharmony, gauge improvement by symptom severity, tell what other subtle tendencies exist and implement other prescriptions based on the patient's status. Clinicians need to understand the ways in which the pathogenesis gets from one state

to another state and track this kind of state changes to make treatment decisions. Distinguishing changes of pathogenesis is the basis of CROs in TCM.

Signs and symptoms reflecting the pathological changes are monitored

Since TCM relies upon subjective signs and symptoms perceived by the clinicians, obtaining adequate information is a precondition for defining patterns. Because different clinicians may investigate the same patient from distinct points of view, different conclusions might be reached about the patterns reflecting the same patient's condition. Clinicians with varied practical experience and understanding of the TCM theory will vary in the particular prescriptions they implement to rebalance the disharmony in the patient's body. Moreover, TCM therapies are not fixed during the entire treatment course, but woven into each treatment session with emergent and contingent adjustments, according to ongoing clinical observations. Patterns recognized by clinicians are basically an immediate status of pathogenesis¹². Based on the pathological evolution and the different stages of diseases, clinicians grasp the key points in the pattern differentiation to predict the pathological development tendency and increase the treatment flexibility. In short, pattern discernment allows for a whole-person identification of disharmony manifesting in the individual, thereby guiding treatment at a particular point in time; therefore, integrity, dynamics and individualization of therapies need to be considered in TCM¹³.

CROs are associated with therapies conducted by clinicians

Pattern discernment is usually needed to decide upon appropriate treatment. TCM clinicians use their perception continuously to discern patterns and form a corresponding treatment to obtain harmony in the

patient. The classic book, 'YI XUE XIN WU', describes eight therapeutic methods: perspiration, vomit, purgation, harmonization, warming, disinhibiting, eliminating and nourishing activities¹⁴. No matter what kind of therapy is used, each is aimed at pointing the patterns in the direction of improvement and attempting to heal the disharmony of the body. When the patient goes through a treatment, changes in signs and symptoms occur in response to the therapies implemented by the clinicians. Examples previously discussed reflect a kind of harmony of pattern and treatment. The effect of perspiration is to 'induce slight perspiration' or 'induce sweat'; the appearance of 'urine flow' or 'bad blood purge' should be related to the method of purgation; and vomit is often the cause of 'draw poison out of the skin' or 'spit pus'. The expected exteriors should reflect pathological changes after the treatment. Patterns of disharmony are defined by the treatment prescribed for its rebalancing.

As noted above, we define CROs in TCM as the signs and symptoms induced by some therapies, which are followed by the pathological changes monitored by clinicians to help them evaluate the therapeutic effect. CROs in TCM embody the spirit of pattern differentiation and individual treatments and differ from those typically used in western medicine (as described in the sections below).

Comparison of CROs in TCM with Western Medicine

TCM and western medicine are two distinct medical systems. Western medicine pays attention to the diseases, whereas TCM pays more attention to the patients who suffer the diseases. The following example of a patient with a cold illustrates the difference. A western clinician uses laboratory tests to assess the patient's status, decide upon a treatment plan and monitor whether treatment is having the desired effect. When the

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FOR CITATION PURPOSES: Zhang YH, Liu BY, Li J, Zhang RS, Zhu WZ, He LY, et al. Clinician-reported outcomes in traditional Chinese medicine: A critical review. OA Alternative Medicine 2013 Jun 01;1(2):15.



patient visits a TCM clinician, signs and symptoms may lead to identification of a pattern of disharmony called 'wind cold', which yields a prescription under the principle of 'wind-removing' and 'cold-dispelling'. Chinese clinicians describe the patient's problem as different kinds of patterns of disharmony, whereas western clinicians typically perceive only one disease. Western medicine is concerned mainly with isolable disease categories and agents of disease, which it zeroes in on, isolates and tries to change, control, or destroy¹⁵. Because clinicians usually identify potential therapeutic targets to treat the disease, CROs in western medicine are closely correlated with the balance of physical morphology and body functions. Most CRO studies in the west include outcomes either observed by clinicians or requiring interpretation based on physiological outcomes^{3-7,16}. CROs can also be obtained using scales completed by health care clinicians based on information about the patients¹⁶⁻²². By analysing some typical cases, clinicians can summarize the general characteristics among diseases, therapies and outcomes. The same medical decision could be applied to groups who suffer similar diseases, with limited attention to individual variation.

However, under the direction of holism, TCM theory is formed on the basis of long-term accumulated experience, inheritance and innovation¹⁵. Clinicians probe into health status of human body from the whole perspective and emphasize the harmony between human body and outer environment, such as 'nature and humanity' and 'body and spirit'¹³. The content and form of CROs in TCM are distinct from western medicine. TCM treatments are highly individualized and lack redundancy. CRO measurement in TCM directly affects treatment of individual patients or treatment procedures. CROs in western medicine are often treated as endpoints, but in TCM, CROs are

intermediate outcomes. Considerable efforts have been made to study CROs in western medicine, but how to develop a methodology of CROs in TCM is still to be explored.

Comparison of CROs with PROs

A PRO is any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else²³. Research on the relationship of PROs and CROs reveal that there are large differences between them. For example, one study found that PROs and CROs were not consistent across chronic venous disease, irritable bowel syndrome and peripheral arterial occlusive disease²⁴. A meta-analysis of three randomized controlled clinical trials comparing treatment with anakinra and placebo in patients with active rheumatoid arthritis concluded that PROs yield more sensitive indicators of treatment effects than CROs²⁵.

Sole reliance on PROs is suboptimal, because patients may over-report their symptoms or disability to gain extra service, or under-report their symptoms if they have not accepted their condition or to please their clinicians. CROs may be less likely than PROs to be influenced by the patient's emotional state or personality patterns²¹. A study assessing community-dwelling people with metastatic breast cancer found that PROs strongly emphasized the difficulty patients experienced performing specific tasks while clinicians generally paid more attention to patients' stability and need for assistance while observing them perform these tasks²⁶. Thus, PROs and CROs may provide complementary information. Also, it is important to distinguish CROs requiring patient input from clinician-administered PROs, in that the former requires clinician judgment or interpretation when recording answers, while the latter involves recording precise, unmodified

patient responses to pre-specified questions⁷.

As mentioned earlier, signs and symptoms related to pathological changes are the main CRO elements in TCM. Signs are something that the clinicians look for but that the patients would not necessarily know or talk about, and symptoms are interpreted more as complaints, significant for decision making. The patients usually mention complaints about their sufferings. Since asking is one of the most important ways to gather clinical information, the earliest practitioners usually focused on the complaints reported by the patients as the criterion to adjust and evaluate the treatment; this is consistent with the use of PROs in TCM²⁷.

Good communication with a patient is essential for ensuring the quality and quantity of information, correctly depicting patient's status. The patient often takes the initiative in telling about what he is concerned about and anxious to improve; at the same time, the clinician pays attention to some signs and symptoms that commonly occur after the patient has taken Chinese herbs, acupuncture or other therapies, so as to estimate the prognosis and guide further treatment. During the communication process between the patient and the clinician, the patient's concerns might have been overlapped by what the clinician is concerned with. However, what the patient wants to say is sometimes not what the clinician wants to know, and the clinician needs to select and confirm some useful information to support his or her judgment and draw a conclusion. When some signs are difficult to perceive, such as facial colour, tongue picture and pulse manifestation, TCM clinicians have to estimate them by looking, smelling and touching methods, which are also components of CROs in TCM. Although the content of CROs in part overlaps with PROs in TCM, they are distinct⁸.

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Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

CROs are deeply entrenched in TCM. Although CROs in TCM have been adopted for thousands of years, they still remain at the experience level, and thorough, in-depth and systematic research is rare. In the past, clinicians may tend to neglect the subjective medical entities²⁸, and PROs are a backlash to clinicians being viewed as the all-knowing expert. We believe that CROs will also affect the comprehension and reflection of the treatment assessment in TCM. Some suggestions are offered here to provide guidance for future studies on CROs in TCM.

The PRO research experiences in western medicine may be used to guide evaluation methods for CROs in TCM. Similar to PROs²³, an important step in CRO research involves the articulation of a conceptual framework of subjective outcomes. The conceptual framework of CROs in TCM is a diagram of the expected relationships between specific outcome issues and the overall concepts, which provides the foundation for a future measurement development. Since clinician reports can yield abundant information including diagnosis, treatment and prognosis, it is essential to sort out the treatment effectiveness from other information. Concept clarification is the key point to develop the framework, including a general concept definition, classification of specific concepts hierarchically and translation of abstract concepts into concrete indications. Each clinician might have different way of

thinking, and the evaluation perspective is also in a very personal and individualized approach. The revision and compensation is necessary in the initial version to obtain correct measurement. The appraisal of CROs in TCM requires creative strategies but can be advanced by utilizing methods that build upon recent advances in the measurement of PROs.

Conclusion

CROs in TCM lay particular emphasis on the signs and symptoms that reflect the changing pathogenesis from the clinicians' viewpoint. CROs are an important indicator of the effectiveness of TCM treatment. CROs in TCM can be used to monitor pathological changes of the whole course and to identify differential patterns in evaluating TCM effectiveness. CROs in TCM provide complimentary information to PROs that can help reveal the spirit of pattern differentiation and individual treatments and can be used as an intermediate and dynamic variable to evaluate treatment effectiveness. A comprehensive look at CROs can yield new insights into assessing clinical outcomes and improve the quality of clinical trials of TCM.

Acknowledgements

Preparation of this manuscript was supported by the National Basic Research Program of China (973 Program) (nos. 2006CB504601) and the National Natural Science Foundation of China (NSFC) (nos. 81001583). Ron D. Hays was supported in part by grants from the NIA (P30-AG021684) and the NIMHD (P20MD000182).

Abbreviations list

CRO, clinician-reported outcome; PRO, patient-reported outcome; TCM, traditional Chinese medicine

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