Is Your Cough Getting Better?

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Undoubtedly, cough is one of the most common symptoms that make people visit physicians for its treatment. It is also apparent that management of chronic cough is not so simple. Underlying causative diseases are diverse, pathogenic mechanism is not clear, and patients' complaints from personal subjective feelings often make physicians even more frustrated. Furthermore, some patients fail to comprehensively explain their symptoms, and they do not score the severity of their symptoms exactly on a standardized scale. Indeed, precise assessment of the severity and characteristics of cough would be helpful in evaluating the effectiveness of certain therapeutic approaches.

Unfortunately, physicians do not have perfectly reliable tools to objectively measure treatment outcomes of cough patients. In clinical practice, physicians, who eagerly want to know about cough severity in patients with chronic cough, frequently ask the patients "Is your cough getting better?" In addition, physicians modify the management plan based on patients' description of symptom changes. This is a usual pattern in clinical practice for cough patients. It may be alright for physicians seeing patients in their clinics to simply ask the patients about changes in cough severity to 1 or 2 weeks after prescribing cough medications. However, in clinical studies or trials of new antitussive drugs, it is of no value in obtaining clinical information to simply ask "Is your cough getting better?" A validated way to objectively measure cough in quantity and quality is necessary.

An excellent review article about tools to assess outcomes in clinical studies on cough has recently been published by the CHEST Expert Cough Panel.¹ Originally, tools to assess the magnitude of cough were developed to evaluate the efficacy of new antitussive medications because valid tools should be used to measure outcomes of administration of antitussive agents in clinical trials. This panel suggests that assessment of cough consider various aspects of cough, such as severity, cough-specific quality of life (QoL), frequency, and sensitivity. It is recommended that validated and reliable cough-specific health-related QoL questionnaires be used to assess cough se-

verity of patients, and it is specifically suggested that Cough-Specific Quality-of-Life Questionnaire (CQLQ) and Leicester Cough Questionnaire (LCQ) be used because they are most extensively studied and found to be valid and reliable.^{2,3}

Although QoL surpasses other measures in assessing cough, questionnaires are usually developed solely based on patients' input, and the methodology is somewhat subjective. Thus, tools to objectively assess cough in quantity could at least compensate for imperfect measures only based on personal assessment. Acoustic cough counting is a relatively well-known tool to measure cough frequency, which is recommended for the assessment of cough in clinical studies as an ancillary measure in the newest Expert Report. Inhalation challenges with tussigenic agents, such as capsaicin, may be another reasonable method to objectively measure cough responses of patients. However, introduction of this method into clinical practice is not recommended at this moment, and the method should be used only for research purposes. Other simple measures for patients' global assessment include visual analog and numeric rating scales. However, only limited data exists on the justification of the introduction of those methods into clinical use.

Considering that the development of new and effective anti-tussive agents, which can specifically reduce increased cough sensitivity, has become an important unmet need, standardization of assessment tools to assess cough is necessary to enhance the reliability of clinical trials. Furthermore, globally acceptable standardized tools are certainly prerequisite for improvement in values and efficiencies of clinical studies recruiting a large number of patients with cough from different countries. In order to encourage the use of such standardized questionnaire tools, validated versions in various languages should

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Received: March 26, 2015; Accepted: March 27, 2015

• There are no financial or other issues that might lead to conflict of interest.

be prepared for clinical use. An existing accepted questionnaire should be translated into another language through established methodology, including backward and forward translation steps to preserve content validity.⁴

In the article by Kwon *et al.*,⁵ the Korean version of the LCQ was evaluated in terms of reliability and validity as a tool to assess cough in the Korean population using Korean language. In that article, the Korean version has been proved to be a valid assessment tool. Strict rules should be applied to the use of health-related questionnaire in clinical studies. Since any minor modification of the QoL questionnaires has the potential to result in different outcomes, no questionnaire item should be changed. If there is a need to modify even small part of the previously well-validated questionnaire, the changed version should be re-evaluated for its validity and reliability.⁶ Thereafter, physicians can be confident in using cough-specific questionnaires while conducting cough studies and measuring outcomes of the studies. Apparently, questionnaire is the only reliable and validated tool to measure outcomes of cough patients after application of any clinical intervention because there are no valid biomarkers that can be measured in biological samples from patients. Thus, a well-validated and globally acceptable questionnaire is particularly critical for cough research and clinical studies.

In clinical practice, a validated questionnaire is actually good enough for assessing cough. Precise measurement of responses to certain therapeutics will have additional value in facilitating clinical practice. A short modified version may be even more helpful in clinical practice. Cough severity can be measured more easily by using the visual analog or numeric rating scale; however, they should be standardized prior to use.

What we need to keep in mind is that all validated and reliable questionnaires are not perfect tools to measure outcomes in cough studies, although they are the best way to cough study as mentioned above. In order to compensate for the disadvantages of QoL's subjectivity, additional objective measures may be

needed. Of course, standardization and development of new tools is always justified. Given that cough hypersensitivity primarily induced by neuropathy is believed to be a pivotal pathogenetic mechanism underlying chronic cough, it is reasonable that novel objective measures for assessing cough should reflect the magnitude of cough sensitivity and the degree of neuropathic abnormalities. These approaches would greatly help not only improve clinical practice but also conduct basic research into pathogenic mechanisms. Finally, another issue we need to consider is that an adequate assessment tool to assess cough is also urgently needed in children. The article in this issue of the *AAIR* mainly focuses on adult patients with cough. Therefore, this version cannot be extended to pediatric patients with cough, but we can anticipate that ideal tools to assess cough in children will be available in the near future.

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