INTRODUCTION

No standardized methods exist to measure patient-reported outcomes (PRO) related to Hospital-Acquired Bacterial Pneumonia (HABP). The purpose of this literature review was to identify signs, symptoms, and measurement tools associated with patients' experience of HABP. The results will be used to inform the development of a valid PRO tool for HABP that is consistent with the FDA PRO Guidance.

METHODS

To identify relevant literature, MEDLINE (1946 to 2014) and EMBASE (1988 to 2014) databases were searched individually and in combination using terms related to Hospital-Acquired Pneumonia (HAP), HABP, signs and symptoms, and patient reported outcomes.

RESULTS

The search identified 1384 abstracts, 225 were excluded as duplicates or for lack of relevant content. 1145 abstracts were excluded based on pre-specified criteria. The remaining articles were scrutinized for eligibility and focus on outcomes assessment, resulting in six that met the inclusion criteria (Figure 1). The six studies that were identified addressed a range of signs and symptoms for HABP. Study designs included 3 randomized clinical trials, 2 reviews, and 1 prospective observational study (Table 1).

Evidentiary Gaps and PRO Development

To date, there is a significant gap in the literature concerning the effect of HABP treatment on symptoms and health-related quality of life and the utilization of PROs to measure treatment effects in HABP.

A review of the literature by the Foundation for the National Institutes of Health Biomarkers Consortium (FNIH BC) HABP/VABP Project Team (2013), and subsequently by ICON Clinical Research, confirmed that no PRO instruments assessing HABP symptoms have been developed.

Very few articles have focused exclusively on HABP as compared with HAP and VAP. Only a few studies have assessed the effect of HABP on patient outcomes, quality of life, and the utilization of PROs to measure treatment effects in HABP.

Current HABP clinical trials have not included endpoints that directly measure how a patient feels and functions. The most frequently cited signs and symptoms of HABP were fever, cough, purulent sputum, dyspnea, rales, chest pain, elevated respiratory and heart rate and elevated white blood cell count. Other symptoms reported less frequently in studies included altered mental status, chills, depression of consciousness, and headache (Table 2).

The conceptual framework will be expanded, evaluated and modified throughout the PRO qualitative development process.

FIGURE 1: INCLUSION OF SIGNS AND SYMPTOMS and PRO ABSTRACTS / ARTICLES

FIGURE 2. HABP CONCEPTUAL FRAMEWORK

TABLE 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Citation</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talbot, George H.4; Howard, Kellee</td>
<td>Fever, cough, purulent sputum, dyspnea, rales, chest pain, elevated respiratory and heart rate and elevated white blood cell count. Other symptoms reported less frequently in studies included altered mental status, chills, depression of consciousness, and headache.</td>
<td></td>
</tr>
</tbody>
</table>

The concept of the framework is expanded, evaluated, and modified throughout the PRO qualitative development process.

Sigs and Symptoms

- The most frequently cited signs and symptoms of HABP were fever, cough, purulent sputum, dyspnea, rales, chest pain, elevated respiratory and heart rate and elevated white blood cell count. Other symptoms reported less frequently in studies included altered mental status, chills, depression of consciousness, and headache (Table 2).

- Current HABP clinical trials have not included endpoints that directly measure how a patient feels and functions.

CONCLUSIONS

The HABP literature has historically focused on clinical global impressions of change to evaluate treatment efficacy and there is currently limited evidence assessing the impact of antibiotic therapies on patient-reported symptoms in HABP patients. Endpoints, such as clinical response, clinical cure, and time to event, are only indirect measures of treatment benefit. It is essential to develop reliable, well-defined and clinically relevant endpoints that measure tangible benefits for patients in clinical trials of antibiotic drugs in accordance with the FDA Guidance for PRO measures and HABP. This literature review is the first step in identifying concepts that will be explored further in qualitative interviews with HABP patients.

AFFILIATIONS AND ACKNOWLEDGEMENTS

1ICON Clinical Research, LLC, San Francisco, CA, USA, 2Biomarkers Consortium, Foundation for the National Institutes of Health, Bethesda, MD, USA, 3George Washington University School of Medicine, Washington, DC, USA, 4Talbot Advisors LLC, Anna Maria, FL.

The data described within this document represents the work of ICON and is supported through the kind support of FDA BAA-13-00119 - Development of a Patient Reported Outcome (PRO) Instrument in Hospital-Acquired Bacterial Pneumonia.

Additional expertise and support is provided through collaboration with the FNIH Biomarkers Consortium Project "Developing Endpoints for Clinical Trials of Drugs for Treatment of Hospital-Acquired Bacterial Pneumonia (HABP) and Ventilator-Associated Bacterial Pneumonia (VABP)." This project was submitted to the Biomarkers Consortium for execution and is managed by a Biomarkers Consortium Project Team. In addition to the NIH and FDA, participating and funding organizations include Achaogen, Actelion, Basilea, Bayer, Cubist, The Medicines Company, Merck, Merica, Novartis, Roche and Telesphere. Clinical trial data is also contributed to the project by Piller, Shionogi and Theravance.

REFERENCES

