Agency for Healthcare Research and Quality

Evidence Report/Technology Assessment

Number 129

Diagnosis and Management of Work-Related Asthma

Summary

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Introduction

Occupational asthma (OA) is characterized by airway inflammation (partially or completely reversible), bronchoconstriction, and airway hyper-responsiveness in response to workplace airway asthmagens. More than 250 asthmagens have been implicated and identified as causative agents in the development of OA and new causes are identified each year. In developed countries, OA is among the most prevalent occupational lung diseases.[1] A review of 43 attributable risk estimates from 19 counties found the attributable risk of OA to be approximately 9 percent (interquartile range [IQR] 5 to 19 percent).[2]

OA can be broadly classified into two categories: OA with latency and OA without latency. Latency periods are observed in all instances of immunologically mediated asthma, even though the immunological mechanism may not yet have been clearly identified.[1] When a worker has OA with latency, specific inhalation testing with the causal agent will usually be positive and often an immunological response is achieved with specific skin prick tests (SPT) and/or IgE testing, particularly for high molecular weight (HMW) asthmagens. Many of the immunological responses associated with OA from low molecular weight (LMW) compounds have yet to be fully characterized. OA can also exist without a latency period and often occurs after exposure to irritant gases, fumes, or chemicals.[3] If the irritant occurs in a large, concentrated exposure, the worker can develop reactive airways dysfunction syndrome (RADS). Because there is no recognizable sensitization, the battery of diagnostic tests does not include specific inhalational challenge (SIC) or specific immunological tests. OA without latency is believed to represent only 5 to 15 percent of all OA cases.[4-6]

While a SIC test is considered to be the reference standard test, a definitive diagnostic test for OA does not exist. False negatives can occur when a worker with OA is challenged with the incorrect asthmagen.[1] Also, SIC is not widely available and testing is generally confined to academic centers in large metropolitan areas.[7]

There are several alternative techniques, used in isolation or in combination, which can be used to diagnose OA. Alternative diagnostic tests include: history and questionnaire, non-specific bronchial provocation (NSBP) challenge, serial lung function testing, specific immunological testing, exhaled nitrous oxide, and sputum induction. There are also several different approaches to managing OA. First, workers can be treated pharmacologically in a similar manner to patients with non-occupational asthma. Second, the worker's environment can be altered to reduce exposures to an "acceptable" level by making engineering changes to the workplace, by making administrative changes to work patterns, or by using personal protective equipment (PPE). Alternatively, the worker can be relocated to a different job or area of the workplace, or it may be possible to eliminate the agent or substitute a non-hazardous agent for the causative agent in use. Often, the final option is to remove the worker entirely from workplace; however, workers may not wish to be removed

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for a variety of financial or social reasons. Removal from exposure can have important economic implications for workers, industry, health care providers, and society.[8] Moreover, it has been reported that symptoms and impaired lung function persist, even after extended periods away from the causative agent[9] and this can result in permanent unemployment.

Objectives and Key Questions

The objectives of the University of Alberta Evidence-based Practice Center (EPC) were to systematically gather the existing evidence to determine which diagnostic techniques are effective at determining a case of OA and to evaluate the optimal treatment for such workers. The report was requested by the American College of Chest Physicians (ACCP).

Researchers attempted to answer the following questions:

1. What is the best diagnostic approach for a patient with suspected OA?
2. In what situations would SIC testing provide additional useful diagnostic information?
3. Which treatment is most effective for OA?
4. Must patients with OA be removed from the workplace environment to control symptoms and/or disease progression?

Methods

Literature Search

Appropriate search terms were adapted to search the following electronic resources: MEDLINE®, EMBASE®, Dissertation Abstracts®, Expanded Academic®, National Agricultural and Safety Database®, CINHAL®, Biological Abstracts®, Agricola®, Cochrane Airways Review Group registry, and trials registries (http://clinicaltrials.gov/; http://www.centerwatch.com/; http://www.cochrane.org/index0.htm; http://www.controlled-trials.com/; http://www.update-software.com/National/; http://www.trialscentral.org/). Web of Science® was searched by tracking the most sentinel articles forward.[10-15] The search was not limited by language or publication status and is considered current until February 2004.

Prominent authors were contacted regarding any missing studies and the reference lists of all included articles were reviewed. Relevant conference proceedings were hand searched for the years 2001–2003.

Study Selection

Each title, and when available, abstract was independently screened by two reviewers. The references identified as "potentially relevant" and "unclear" were then screened by an occupational medicine specialist with an interest in occupational asthma and an asthma researcher; the full text of those articles were retrieved.

Using pre-determined inclusion criteria, two reviewers independently assessed the full text of the articles. Disagreement among reviewers was resolved by discussion and consulting a third party as needed.

We excluded studies that assessed screening for workplace respiratory symptoms. In cases where multiple publications involving the same or a portion of the same workers were identified, the most recent article or the largest cohort was selected and any additional, unique information from previous publications was incorporated.

Quality Assessment

Assessment of the methodological quality was completed independently by two reviewers. The methodological quality of a diagnostic study was assessed using a quality tool based on Lijmer's empirical research examining biases in diagnostic studies.[16] The quality of each included cohort therapy study was independently assessed using Downs and Black's partially validated "Checklist of the assessment of methodological quality of both randomized and non-randomized studies of health care interventions".[17] Also, the funding source was recorded for each study. Controlled clinical trials were assessed using the validated Jadad scale and the Cochrane method.[18] Allocation concealment was assessed as "adequate," "inadequate," or "unclear."[19]

Data Extraction

Data were extracted by one reviewer using standardized forms and checked for completeness and accuracy by a second reviewer. For the diagnosis questions, data regarding the study population characteristics, diagnostic tests, and results (e.g., sensitivity, specificity, likelihood ratios, etc.) were collected. For each diagnostic test, the methodology, timing, inclusion/exclusion criteria, medication use, and definition of a positive test result were extracted. Additional outcomes included cost of diagnosis, time to complete diagnosis, and presence of adverse events. For the management questions, details concerning worker characteristics, interventions, tests used to measure outcomes, and outcomes were recorded. Interventions were described by change in exposure (continual, decreased, or removal from exposure), or the type, dosage, route, and timing of pharmaceutical treatment. Outcomes extracted included lung function, symptoms and medication scores, economic status, and adverse events. The length of followup was also recorded.

Data Analysis

For the diagnosis review, standard 2 x 2 tables (or 2 x 1 if only reference standard positive or reference standard negative

subjects were included) for each comparison test or combination of tests were generated. We pooled data from 2 x 1 tables separately from studies that presented data from which a 2 x 2 table could be generated. All results are presented with 95% confidence intervals (CI).

For studies pertaining to the management of OA, extreme heterogeneity prevented the use of meta-analytic techniques. Nonetheless, with some re-organization of the data we were able to sufficiently homogenize the information provided to include it within a descriptive summary.

For continuous outcomes, a mean was used as the measure of central tendency. In cases where the mean was not reported, the following substitutions were used: median and midpoint of the range or IQR. Similarly, standard deviation (SD) was used as the measure of variation and imputed if it was not available. When possible, a mean and SD were calculated from individual patient data. Data were grouped according to exposure status in followup as continued exposure, reduced exposure, or ceased exposure.

Results

Description of Diagnostic Studies

One hundred twenty-four unique cohorts were included in the diagnosis review. SIC was the most commonly cited reference standard; it was performed in 105 of the studies and most frequently, with di-isocyanates. The alternative reference standard was clinical diagnosis. Over half of the studies (67) included workers exposed to LMW agents. Not all studies had workers with a uniform exposure and/or type of OA: 24 studies included workers from several different occupations with various probable causes of OA. The most commonly reported diagnostic test was a single NSBP test. Only one study examined workers with RADS.

Workers were relatively infrequently selected consecutively or randomly and 37 studies failed to report the selection method; the remaining studies used alternative methods, such as choosing some workers in a factory or some clinic patients. All but 14 studies collected data prospectively; data collection was unclear in six studies. However, only three studies reported that both the reference standard and comparison test results were assessed blindly. The reference standard was adequately described in approximately 70 percent of the studies.

Differential bias is likely to have occurred in 26 of the studies and could not be assessed in 18 studies; the other studies did not have this bias. Partial verification bias was also present in 31 studies and it was unclear if it occurred in 18 studies. Partial verification bias did not occur in the remaining 75 studies.

Description of Management Studies

There were 67 publications referring to 52 cohorts. Two studies examined workers with RADS; in one study, the workers were exposed to sulfur dioxide in a pyrite mine explosion and, in the second, pipefitters were exposed to chlorine over three months.

The most common identified asthmagens in these studies were chemicals. The median sample size of the included studies was 26 workers (range 3–1011). Length of followup was variable within and between studies.

The most common intervention was removal from the workplace. Fourteen cohorts report results for subjects who continued exposure, and reduced exposure was assessed in 18 studies. Eight studies examined the effectiveness of PPE, while only two studies compared the use of medication. The most commonly reported outcomes were NSBP test and pulmonary function.

Thirteen trials were included. The most common asthmagen studied was isocyanates. Two trials assessed methods to reduce the level of asthmagen exposure, including the use of a respirator or hypoallergenic latex gloves. The remaining studies examined the efficacy of beclomethasone (with removal from exposure in two trials), indomethacin, atropine, nifedipine, verapamil, cromolyn, fenoterol, prednisone, and immunotherapy. All but one of the pharmacological trials was placebo controlled. The length of study intervention and followup varied; three studies followed patients for at least 6 months and the remaining studies were shorter. Response to SIC was a commonly assessed outcome and was measured in nine trials.

Among the cohort studies, the mean Downs and Black score of the 52 included studies was 16.4 (SD 4.0) from a total possible score of 29. Approximately half (27/52) of the studies provided some individual patient data. When reported, funding was most commonly provided by a government agency; 31 of the studies failed to disclose their funding source. Of the 13 clinical trials, the median Jadad score was 2 (IQR 2–3). Concealment of allocation was adequately reported in two of the trials, and inadequately in four trials; the remainder were unclear. Six trials did not report their source of funding and two trials were supported solely by government grants.

Diagnosis Results

Sixty-one studies compared the sensitivity and specificity (n=39), sensitivity alone (n=21) or specificity alone (n=1) of single NSBP test to SIC. Twenty-four of these studies reported both sensitivity and specificity among patients exposed to LMW agents. The pooled estimates for sensitivity was 66.7 percent (95% CI: 58.4 to 74.0 percent) and for

specificity was 63.9 percent (95% CI: 56.1 to 71.0 percent). Among the 10 studies examining HMW asthmagens, the pooled estimate for sensitivity was 79.3 percent (95% CI: 67.7 to 87.6 percent) and for specificity was 51.3 percent (95% CI: 35.2 to 67.2 percent). Five studies reported sensitivity and specificity results for various suspected agents of differing molecular weights. The pooled estimate of sensitivity was 83.7 percent (95% CI: 66.8 to 92.9 percent) and specificity was 48.4 percent (95% CI: 25.9 to 71.6 percent).

Forty-seven studies reported comparisons of specific SPT to SIC. Five studies reported both sensitivity and specificity of SPT of LMW agents and the pooled sensitivity was 72.9 percent (95% CI: 59.7 to 83.0 percent) while the pooled specificity was 86.2 percent (95% CI: 77.4 to 91.9 percent). Of the 16 studies that reported both sensitivity and specificity for patients exposed to HMW agents the pooled sensitivity was 80.6 percent (95% CI: 69.8 to 88.1 percent) while the pooled specificity was 59.6 percent (95% CI: 41.7 to 75.3 percent). Among the five studies that included patients exposed to various agents, the pooled estimates for sensitivity was 63.0 percent (95% CI: 41.5 to 80.3 percent) and the pooled estimate of specificity was 59.2 percent (95% CI: 45.4 to 71.7 percent).

Forty studies reported sensitivity and 19 reported specificity for serum specific IgE compared to SIC. Eleven studies reported both sensitivity and specificity for LMW agents; the pooled sensitivity was 31.2 percent (95% CI: 22.9 to 40.8 percent) and the pooled specificity was 88.9 percent (95% CI: 84.7 to 92.1 percent). Sensitivity was higher for the HMW agents studied; the pooled estimate of sensitivity was 73.3 percent (95% CI: 63.9 to 81.0 percent) and the pooled estimate of specificity was 79.0 percent (95% CI: 50.5 to 93.3 percent). Two studies examining a variety of agents reported both sensitivity and specificity. The pooled estimate of sensitivity was 85.1 percent (95% CI: 40.3 to 98.0 percent) and the pooled estimate or specificity was 61.2 percent (95% CI: 7.0 to 97.1 percent).

When possible, results were combined in union for the most frequently reported comparison tests. That is, all tests in combination had to be positive for the combined result to be considered positive; if any result was negative, the combination was considered negative. Four studies examined a single NSBP test and specific SPT in combination among HMW agents. The pooled estimate of sensitivity was 60.6 percent (95% CI: 21.0 to 89.9 percent) while the estimate of specificity was 82.5 percent (95% CI: 54.0 to 95.0 percent). Only one study investigated this combination of tests in LMW OA; the sensitivity was 100 percent (95% CI: 74.1 to 100 percent) and specificity was 80 percent (95% CI: 49.0 to 94.3 percent). Three studies of HMW agents yielded results for the combination of a single NSBP test, specific SPT, and serum specific IgE. The pooled estimate of sensitivity was 65.2 percent (95% CI: 6.7 to 98.0 percent) and for specificity was 74.3 percent (95% CI: 45.0 to 91.0 percent).

Management Results

We considered baseline (or diagnosis) lung function to ascertain whether there were differences in severity among subjects whose intervention may have included removal, reduced, or continued exposure to the workplace asthmagen. All but two studies reported an average baseline percent predicted FEV_1 above 80 percent, indicating reasonable lung function at the time of study entry, irrespective of their followup exposure status.

Less than half of the studies examining patients who were removed or reduced their exposure showed improved lung function over time as indicated by a positive difference between mean followup and mean baseline percent predicted FEV_1. Only one study of patients who remained exposed had a positive change in mean percent predicted FEV_1.

The ratio of non-specific airway hyper-responsiveness at followup compared with baseline concentration was calculated to assess change in hyper-responsiveness over time. All but one study of individuals who were removed had decreased hyper-responsiveness at followup. Less than half of the studies examining exposed patients displayed improved hyper-responsiveness. There were insufficient data to draw conclusions about change in hyper-responsiveness among patients with reduced exposure.

Medication needs were used as a proxy measure for disease severity and continued asthma symptoms. Among patients removed from exposure, the percentage of patients using medication at followup ranged from 17 to 100 percent and there was no indication that fewer patients were using medication as time from work removal increased. Only five studies reported medication use among patients who remained exposed or had reduced exposure; no clear pattern emerged.

Symptoms were measured by: mean symptom scores, categorical symptom scores, number of subjects who were asymptomatic or recovered, or were symptomatic, or had specific symptoms. Of the studies that reported results on removed patients, the majority demonstrated symptom improvement from time of removal for most of the patients. This was assessed by an improvement in symptom score or the majority of patients reported improved symptoms, or were considered asymptomatic. In nine studies describing symptoms among subjects whose exposure had been reduced by a workplace intervention or PPE, the same pattern emerged. Few studies reported that the bulk of patients were completely asymptomatic. Only two studies reported improved symptoms among those who remained exposed.

Seven studies examined socioeconomic outcomes among workers with OA. Four studies assessed change in financial situation after OA diagnosis and consistently found that removed workers suffered a loss in income. Two studies assessed the rate of worker's compensation claims and associated acceptance. In one study, a national Workers' Compensation Board more frequently approved claims among workers who were removed from the workplace than those who reduced their exposure. A different study concluded that the acceptance rate was similar, regardless of exposure status.

Two studies measured quality of life (QOL) and, in one, the results showed QOL did not significantly differ among those removed versus those who reduced their exposure. The second study concluded that workers with OA who had been removed from exposure and were receiving compensation had reduced QOL compared to workers with non-occupational asthma.

Thirteen clinical trials were identified: nine trials examined the effectiveness of pharmaceutical interventions (two of which treated patients who were also removed from exposure), two assessed workplace interventions, and the final study investigated immunotherapy. The following results were observed among the pharmaceutical trials: prednisone is more efficacious than indomethacin; inhaled beclomethasone is superior to placebo (including among patients removed from workplace exposure); and lung function did not change when using high-dose beclomethasone, but lung function was impaired when low-dose beclomethasone and placebo were used. Compared to placebo, salbutamol resulted in greater improvement in FEV_1. One study reported the results of four crossover trials where outcomes were measured after SIC, beclomethasone decreased airway responsiveness and improved FEV_1, and theophylline reduced the severity of asthma exacerbations but did not decrease airway responsiveness; verapamil, cromolyn, and placebo decreased FEV_1 and increased airway responsiveness. Another study comparing theophylline to placebo also concluded that theophylline had no effect on airway hyper-responsiveness, but did significantly reduce the severity of late asthmatic reactions. Finally, atropine was shown to have minimal effect on reducing asthmatic reactions after SIC, fenoterol significantly normalized airway resistance and improved expiratory thoracic gas volume, and nifedipine was shown to prevent immediate asthmatic reactions after SIC in three separate studies.

Compared to placebo, wheat flour immunotherapy resulted in a significant decrease in serum specific IgE, less skin prick sensitivity, non-specific bronchial reactivity, and subjective clinical improvement.

Two trials examined the effect of reducing exposure among workers with OA. In a crossover trial examining the efficacy of respiratory PPE, airway resistance and specific airway resistance were significantly improved when SIC was performed while wearing the respiratory PPE. The second study compared healthcare workers' asthmatic reactions to various latex gloves. Among the eight healthcare workers, hypoallergenic gloves reduced the risk of latex asthma exacerbations.

Discussion

Diagnosis

Prior to determining the accuracy of diagnostic tests, a reference standard must be available for comparison. The usual reference test for OA is SIC; however, it is of limited availability[7] and this test remains, to an extent, unstandardized .[20-21] It appears that there are no better alternatives in OA diagnosis at this time.

This review did not specifically examine the utility of symptom questionnaires in screening for OA. There appears little doubt about the utility of these approaches in screening patients for further evaluation and testing. In this review, all patients received referral to a clinic and/or symptom screening prior to further evaluation for diagnosis of OA.

Overall, it appears that a positive test result of a single comparison diagnostic test can assist clinicians in diagnosing OA in populations where the suspicion of OA is already reasonably high, but it cannot completely confirm the diagnosis. However, even within such selected populations, a single negative test result cannot exclude OA. For example, the data showed that a single NSBP test gave a reasonable sensitivity but somewhat lower specificity in predicting the outcome of SIC, usually from studies among workers identified in specialty clinics or workplace surveys where the pre-test probability of disease was high. Immunological testing also appears to be of use. Skin prick testing showed a higher sensitivity than serum IgE in comparison with SIC, whereas the converse was true for specificity. A clinical diagnosis (often comprised of many diagnostic tests) resulted in high sensitivities for HMW, LMW, and mixed asthmagens; however, the lower specificity suggested a negative clinical diagnosis was not sufficient to exclude OA. In addition, there were differences in how these tests performed in HMW and LMW agents.

Given the paucity of data available, further research is required to determine if any combination of tests may be a suitable alternative to SIC. The highest specificities arose from a combination of a single NSBP test and SPT, or a single NSBP test and specific IgE among HMW asthmagens. Given a high pre-test probability of disease, a positive combined test would largely confirm OA (post-test likelihood of ~80 percent). However, negative combined testing would not provide sufficient certainty that OA was absent. It should be noted that the data obtained precluded an evaluation of a sequential testing scheme as proposed by others.[1]

It is important, in interpreting these data, to recognize that these results are produced from a highly selected population that was pre-screened, usually by referral to a specialist clinic, a questionnaire, or a workplace study. However, in a clinical setting where patients are being investigated for OA, patients presumably would have undergone similar screening. Consequently, it seems reasonable to apply the pooled estimates of sensitivity and specificity derived from these analyses to those groups.

Management

Most reports indicate patients with OA have mild-moderate airflow limitation (>80 percent predicted FEV_1) at the initial assessment. We initially compared the different treatment groups using baseline percent predicted FEV_1 data as it related to exposure status (e.g., removed from exposure, reduced exposure, and remaining exposed). From these comparisons, it does not appear that a selection bias occurred with respect to subsequent work exposure based on baseline severity of illness (measured by FEV_1 status).

Workers who remain exposed (either partially or fully) experience continued deterioration in FEV_1 compared to baseline and this also appears to deteriorate over the time of exposure. In contrast, most of the groups who are removed from exposure appear to generally report improvement compared to baseline lung function. Despite removal, improvement appears to be neither dramatic nor progressive with time.

Improvement in non-specific bronchial hyper-responsiveness among the group who are completely removed from exposure did appear to be more impressive and progressive with time than FEV_1 results alone. Almost all of the groups who were removed from their workplace appear to improve compared to NSBP test results at diagnosis. Groups who remain exposed experience continued deterioration in NSBP test results compared to baseline and over time. This suggests that continued exposure is required for non-specific bronchial hyper-responsiveness to continue to decline.

Due to small study numbers, conclusions about medication and symptoms are difficult to draw. Overall, workers with OA, irrespective of subsequent exposure, often require asthma medications long after their initial diagnosis. Symptoms appear to persist and possibly worsen among workers who continue their exposure. There is mixed evidence that removal improves symptoms. Among workers who reduce their exposure, symptoms abate in some workers; however, the overall effect seems to be persistence of symptoms.

According to the studies cited, the economic consequences of developing OA are impressive. Among the workers included in the studies, those who left the workplace suffered economic repercussions of reduced income and/or unemployment. Workers who reduce their exposure or stay employed at the same workplace still appeared to lose some income over time, and their costs of medication increased.

One small clinical trial suggested spirometric, immunological, and symptomatic improvement when workers experiencing OA were treated with immunotherapy. A comprehensive Cochrane Review confirmed this therapeutic approach might be useful for asthma in general.[22] While this therapy may be as effective as inhaled corticosteroids, it is complicated by its long duration, limited availability, and not all immunotherapy compounds have been identified.

The evidence examining the effect of reducing exposure in the workplace is limited to two clinical trials. Evidence suggests that protective devices can reduce bronchial obstruction; however, they failed to provide complete protection and they require workers to be compliant with their use. In the special situation of latex allergy-induced OA, the use of non-latex gloves appeared to be a successful method of improving OA.

Finally, conclusions regarding OA medication are difficult to draw, as the trials suffered from limited duration of treatment and dissimilar comparisons; however, the effectiveness trends appear to be similar for OA and chronic asthma. In general, there was evidence that anti-inflammatory agents, such as systemic and inhaled corticosteroids, are effective in the treatment of OA. Theophylline reduced the severity of asthma exacerbations after SIC; however, airway responsiveness did not decrease. Other agents such as non-steroidal anti-inflammatories, calcium channel blockers, cromolyn, or placebo demonstrate limited or no benefit in the acute treatment of OA.

Potential Limitations

There is a possibility of publication bias in this systematic review. By missing unpublished unimpressive diagnostic or negative therapy studies, we may be over-estimating the diagnostic properties of OA tests and/or the effect of OA treatment, respectively. However, a comprehensive search was conducted, authors were contacted, and grey literature was extensively searched. Despite these efforts, we recognize that more unpublished studies may exist.

While SIC is considered the reference standard for diagnosing OA, some studies did not report this result for all patients. Some studies used a clinical "consensus" diagnosis to determine the presence of OA, which may have included SIC; it was usually not clear which patients had undergone SIC and why. Other studies only presented data from patients who were SIC positive. These situations could introduce two forms of bias: differential reference standard bias and partial verification bias.[16]

A further limitation was that not all studies presented data in a useful form to evaluate the diagnostic accuracy of a comparison test. It was not possible to use results presented as a difference between mean values of the comparison test when grouped by the reference test result. In other cases, individual patient data were available; however, the absence of an established cut-off value to define a "positive" test excluded these results. Consequently, fewer studies than identified could be pooled in some of the comparisons.

Finally, the studies included in the diagnosis review display considerable heterogeneity. This heterogeneity likely arises because many different asthmagens can cause OA and the diagnostic tests do not behave identically among the various asthmagens. In an effort to reduce heterogeneity, the results are presented by HMW and LMW and subgrouped by the specific asthmagen. Controversy exists with respect to pooling of heterogeneous data. Some would argue that the pooling in this setting is unhelpful and potentially misleading, while others believe this approach provides the best estimate of the test property. We recommend that the reader carefully examine and interpret the diagnostic results presented in this report.

One limitation of the management review is that the methodological quality of the included studies was relatively weak. The interventions were generally divided into removal, reduced exposure, or continued exposure; however, the definition of these approaches differed and allocation was not randomized. Also, the outcome assessments were often not comparable and tended to focus on physiological test results (e.g., pulmonary function tests, NSBP test, SIC, etc.) rather than quality of life. There was variability in length of followup within and between studies, making pooling problematic.

Conclusions

There is a lack of high-quality research to guide clinicians in the diagnosis and management of OA. Until better evidence exists, the findings from this systematic review may be unsatisfying to some. Based on the evidence, the following conclusions can be made about the diagnosis and namagement of OA:

Diagnosis

- Despite limited availability, SIC appears to be the main reference standard for the diagnosis of OA.
- In isolation, none of the diagnostic tests yielded a high combination of sensitivity and specificity that could replace SIC.
- In the absence of SIC, NSBP testing and SPT (although of limited availability) are the best available alternative tests in population with a relatively high pre-test probability of OA, yet their sensitivity and specificity alone are insufficiently discriminative to confirm or exclude OA.
- Adding SPT or specific IgE can enhance the specificity of NSBP testing and increase the likelihood that workers who test negative to both tests do not have OA. Many other combination tests have not been evaluated in sufficient detail to provide recommendations.

Management

- Within published research data the baseline FEV_1 does not predict subsequent exposure status.
- Workers who remain exposed will experience decreased FEV_1 over time, increased non-specific bronchial hyper-responsiveness, and continue to require medications.
- Most workers with OA who cease exposure will experience improved FEV_1 over time and less non-specific bronchial hyper-responsiveness; however, many workers will continue to have symptoms and require treatment.
- The evidence regarding outcomes for workers who reduce, rather than cease, their exposure is insufficient to draw firm conclusions.
- Anti-inflammatory agents appear to be effective short-term (<6 months) therapy for OA; however, limited high-quality research has been performed on patients with OA.

Future Research

- Clear comparisons between reference standards (preferably SIC) and alternative test approaches and report results using standardized diagnostic test methods.
- Conduct prospective, long-term outcome studies to understand the outcomes (physiological, social, economic, and quality of life) of OA using standardized reporting.
- Conduct longer term studies to determine optimal medication regimens and disease management for various OA populations, combined or not with continuous, reduced, or absent exposure.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the University of Alberta Evidence-based Practice Center, under Contract No. 290-02-0023. It is expected to be available in November 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295.

Requesters should ask for Evidence Report/Technology Assessment No. 129, *Diagnosis and Management of Work-Related Asthma*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

Suggested Citation

Beach J, Rowe BH, Blitz S, Crumley E, Hooton N, Russell K, Spooner C, Klassen T. Summary, Evidence Report/Technology Assessment No. 129. (Prepared by the University of Alberta Evidence-based Practice Center, under Contract No. 290-02-0023.) AHRQ Publication No. 06-E003-1. Rockville, MD: Agency for Healthcare Research and Quality. October 2005.

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AHRQ Pub. No. 06-E003-1
ISSN 1530-440X