



COMPLETED GRANT SYNOPSIS

Use of fractional exhaled nitric oxide (FeNO) measurements in community pharmacy to improve asthma managementMara A. Kieser, MS, RPh¹; Marvin R. Moore, PharmD²; Angela Marsella, PharmD, MBA (resident)²¹University of Wisconsin School of Pharmacy | Madison, Wisconsin²The Medicine Shoppe | Two Rivers, Wisconsin**Background and Significance**

Pharmacists have played an integral role in asthma management for years. This project strives to enhance the pharmacist's assessment of a patient's asthma control and can easily be implemented in a community pharmacy setting.

Asthma management can be difficult due to complexity of the disease state. Asthma can differ between patients based on clinical, physiological, immunological, and histological presentation.¹ Wenzel defines asthma based on three major phenotypes: clinical and physiological, trigger-related, and inflammatory.² The ability to classify asthma based on phenotype can better target therapy and improve asthma management. Previous methods to measure inflammatory phenotypes include bronchoscopy and sputum analysis.¹ However, these methods are invasive and cumbersome, so they are not feasible in general practice. Another method to identify inflammatory processes in asthma was recently developed based on the molecule, nitric oxide (NO). NO is produced by numerous cells within the lungs.³ The endothelial cells produce lower quantities of NO while the airway epithelial cells produce significant quantities of NO. Epithelial cell production of NO is inducible by inflammatory mediators.³ The amount of NO produced in the lungs is directly related to the amount of NO in exhaled breath.³ Therefore, elevated levels of exhaled NO is an indicator of inflammatory processes in the airway.

Fractional exhaled NO measurements have been standardized for interpretation in asthma patients as outlined by the American Thoracic Society clinical guidelines.⁴ According to these guidelines, patients over 12 years old with FeNO below 25 ppb indicates no airway inflammation and FeNO above 50 ppb (or a 40% increase from previously stable levels) indicates uncontrolled airway inflammation. FeNO levels of 25 to 50 ppb indicate intermediate airway inflammation.⁴ Symptomatic patients with high levels of FeNO are likely responsive to inhaled corticosteroid therapy while symptomatic patients with low levels of FeNO are unlikely to respond to inhaled corticosteroids because they do not have the inflammatory phenotype of asthma. Smoking has been shown to reduce FeNO levels and these patients will be excluded from the study.⁴ The Wisconsin Pharmacy Quality Collaborative (WPQC) asthma-focused comprehensive medication reviews and assessments (CMR/As) will include assessment questions to determine if the patient has symptoms consistent with inflammatory asthma phenotype so the FeNO measurements can be interpreted accurately.

Community pharmacies are an ideal place to use FeNO measurements to assist in asthma management. Patients have greater access to pharmacy services versus physician services because pharmacies have night and weekend hours. Pharmacy services are usually being offered on a walk-in basis as well. Pharmacies have started demonstrating the advantages of their availability to patients with rapid antigen detection tests for diagnosing Group A streptococcal infections.⁵ While this diagnostic testing is not currently being billed to insurance, the availability of the service has value to the patient. This value comes from the accessibility of the pharmacies and the price of a visit to the pharmacy is lower than be seen at a physician's office. Similarly to streptococcal infection screenings, FeNO measurements in a community pharmacy can provide convenient access to a service that improves patient's health. It is anticipated that increased screenings, along with education of patients and communication with health care providers, will result in better asthma control and reductions in urgent care visits.

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FeNO measurements provide community pharmacists with an objective measurement of asthma control that can be included in the medication therapy recommendations to the health care provider. Aerocrine has developed the NIOX MINO[®] device which uses electrochemical technology to allow the direct measurement of the fractional exhaled NO (FeNO). This novel, handheld device reports FeNO measurements providing the clinician an immediate, objective measure of airway inflammation. Used in this way, FeNO is considered to be a surrogate marker of eosinophilic airway inflammation and a good predictor of corticosteroid response. Aerocrine’s NIOX MINO[®] is the only FDA approved device to measure FeNO. However, the major insurance plans at The Medicine Shoppe including Wisconsin Medicaid will not reimburse FeNO testing with a pharmacist’s NPI or with pharmacy as the place of service. This study will provide evidence of the benefit of community pharmacy FeNO testing which can be used to support the expansion of the billing rules to allow pharmacists to bill for FeNO measurements using the already established CPT code.

Needs assessment

Providing FeNO measurements as part of an asthma CMR/A is an asset to our patients and our community. Screenings conducted at the pharmacy point of care improves efficiency and accuracy of pharmacist recommendations and will increase the accessibility of asthma management services.

The pharmacist is able to obtain an objective measure of airway inflammation to assess a patient’s asthma condition within minutes. Current standard of care for WPQC asthma-focused CMR/As include subjective measures of symptoms using the Asthma Control Test[™], inhaler technique and objective measures of inhaler refill history. The asthma-focused CMR/A can be enhanced by including a FeNO measurement to quantify the extent of airway inflammation. FeNO measurements will support the pharmacist’s evaluation of the patient’s prescribed medication regimen, the pharmacist’s recommendations to health care providers, and demonstrate the importance of medication adherence to patients.

Objectives

1. Compare the change in ACT[™] scores from baseline in the standard of care group compared to the standard of care plus FeNO testing group.
2. Determine if pharmacist-initiated recommendations made during an initial WPQC asthma-focused CMR/A visit are concordant with the patient’s actual course of therapy at a three-month follow-up. The concordance rates will be compared between recommendations made to health care provider of patient’s receiving standard of care and patient’s receiving the addition of objective FeNO measures.

Methods

Design	<ul style="list-style-type: none"> • A randomized control trial with two treatment arms. Patients in the control arm (standard of care) will receive an initial WPQC asthma–focused CMR/A while patients in the intervention arm will receive an initial WPQC asthma-focused CMR/A with the addition of FeNO testing. Pertinent findings related to the patient’s asthma control, such as ACT[™] score, inhaler technique, adherence information based on refill data, and the FeNO measurement (for patients in the intervention arm) was collected and reported to the prescriber. A follow-up WPQC asthma-focused CMR/A was conducted three months post-initial CMR/A visit to re-assess parameters measured at the initial visit and review the patient’s prescription profile. The pharmacist will document changes in asthma therapy that occurred since the initial CMR/A visit. Finally, all patients will complete a survey regarding the WPQC asthma-focused CMR/A to assess patient satisfaction and those completing FeNO testing will complete additional questions regarding the FeNO monitoring. Patient satisfaction was measured utilizing an 11 question Likert scale questionnaire.* • <i>Inclusion characteristics include:</i> <ul style="list-style-type: none"> - Asthma diagnosis or symptoms consistent with asthma diagnosis for at least 3 months - Use of more than two reliever inhalers within a 90-day period in the past one year OR use of corticosteroid burst in the past one year OR urgent care visit for asthma in the past one year - Age ≥18 years old • <i>Exclusion characteristics include:</i> <ul style="list-style-type: none"> - Patients with only exercise induced asthma diagnosis
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	<ul style="list-style-type: none"> - Chronic Obstructive Pulmonary Disease - Current smoker
Study endpoints	<ul style="list-style-type: none"> • Comparison of the change in ACT™ scores from baseline in the standard of care group compared to the standard of care plus FeNO testing group • Comparison of concordance rate between recommendations made to health care provider of patient's receiving the standard of care and patient's receiving the addition of objective FeNO measures

Results

29 subjects met inclusion criteria. 24 subjects met with pharmacist and were randomized into the control arm (n=10) and the intervention arm (n=14). 6/10 (60%) subjects in the control arm completed the follow-up appointment. 11/14 (79%) subjects in the intervention group completed the follow-up appointment. The average change in ACT™ scores for the control arm and the intervention arm were +2 (-2 to +7) and +1.27 (-7 to +11), respectively. There was no significant difference in the average change in ACT™ scores between groups. The higher rate of change in ACT™ scores in the control arm is likely skewed due to lower percentage of patients who completed the follow-up appointments. Of the 4 recommendations (2 control arm; 2 intervention arm) for medication changes and/or initiation of a new medication sent to health care providers, 2 were accepted (1 control arm; 1 intervention); therefore, no conclusions can be drawn of the concordance rate between recommendations made to health care providers based on patient's receiving the standard of care compared patient's receiving the standard of care plus the addition of objective FeNO measures. The patient satisfaction survey consisted of 11 questions and were reported on a Likert scale from 1= poor to 5 = excellent. 16 surveys were completed. The results averaged and were as follow: Overall satisfaction: 4.625, Pharmacist's ability to prevent medication problems: 4.6875, Pharmacist's ability to provide medication information: 4.8125, Pharmacist's ability to provide health information: 4.6875, Pharmacist's knowledge: 4.75, Pharmacy's privacy: 4.6875, Pharmacist's ability to answer medication questions: 4.75, Pharmacist's ability to consider patient feelings and preferences in making recommendations: 4.875, Pharmacist's explanation clarity: 4.8125, Overall care: 4.875, and FeNO results discussion with pharmacist: 4.75.

Conclusion

The subjects were limited and limited conclusions can be drawn from these results. No significant change was seen in the ACT™ scores. The ACT™ scores average change was higher in the control arm; however, this is likely due to the smaller sample size. The rate of completed follow-up appointments was higher in the intervention group. No conclusion can be drawn based on the recommendations made to the health care providers since the same number of recommendations were accepted in both arms of the study. Overall patient satisfaction was high among both groups and both arms showed improvement, while not significant, in asthma control.

* FeNO Toolkit for Community Pharmacies, includes:

1. Appointment Materials
 - a. Fax Cover Sheet for CMR
 - b. FeNO SOAP Note
 - c. CMRA Outline for Initial Visit
 - d. CMRA Outline for Follow-up Visit
 - e. Patient Satisfaction Survey
2. Marketing Materials
 - a. Radio Advertisement Script
 - b. In-store Advertisement Poster
 - c. Off-site Advertisement Poster
 - d. Flyers for Provider Offices

References:

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4. Dweik RA et al. An Official ATS Clinical Practice Guideline: interpretation of exhaled nitric oxide levels (FeNO) for clinical applications. *Am J Respir Crit Care Med.* 2011;184:602-615.