ORIGINAL ARTICLE

Methacholine Challenge Test as an Adjunctive Investigative Tool in Patients with Asthma-Like Symptoms: The Sabah Experience

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SUMMARY

Introduction: Patients with asthma-like symptoms pose a diagnostic dilemma when physical examination is normal. The usual practice in Malaysia would be to give empirical asthma treatment. Bronchial challenge test (BCT) is widely used in many countries to diagnose asthma objectively but it is not widely available in Malaysia.

Objective: To describe our experience with BCT using methacholine at Queen Elizabeth Hospital as a supporting tool in the investigation of patients with asthma-like symptoms.

Methodology: Review of case notes of patients who underwent BCT from July 2008 till April 2009. BCT was performed via dosimeter technique. Results were classified as high hyper responsiveness if the provocative dose of methacholine required to achieve 20% fall in FEV_1 (PD_{20}) was less than or equal to 0.125 µmol, moderate hyper responsiveness if PD_{20} was between 0.125 to 1.99 µmol or mild hyper responsiveness if PD_{20} was between 2.00 to 6.6 µmol. PD_{20} of more than 6.6 µmol constitutes a negative MCT.

Results: 29 patients had BCT during the study period. 19 cases were included in this review. The age ranged from 13 to 70 years old. There were 12 males and 7 females. Duration of symptoms ranged from 2 weeks to 23 years. BCT was positive (mild or moderate hyper responsiveness) in 10 out of 19 patients. No patient had high bronchial hyper responsiveness.

Conclusions: BCT is a useful adjunctive tool in the investigation of patients presenting with asthma-like symptoms. This test obviates empirical asthma treatment. BCT should be made available in all major hospitals in Malaysia.

INTRODUCTION

Patients presenting with asthma like symptoms like intermittent cough or dypsnoea can be challenging to physicians as there is a wide range of differential diagnosis. A Bronchial Challenge Test (BCT) has been used in this group of patients in many countries. However, in Malaysia, we are currently the only center providing this service. Our center has been performing this test since July 2008 and we aim to share our experience with the medical community in Malaysia.

Empirical asthma treatment is still widely practised in Malaysia. A study[1] demonstrated that up to 34% of patients treated as asthma based on symptoms alone actually did not have asthma. Therefore it is crucial to utilize all diagnostic means to secure an objective diagnosis before embarking on life-long treatment.

Many agents are used for BCT such as methacholine, histamine, hypertonic saline, exercise and mannitol. In our center, we use methacholine. Methacholine choride (acetyl-β-methycholine) is a parasympathomimetic synthetic analog of acetylcholine. It stimulates muscarinic, postganglionic parasympathetic receptors, causing bronchial smooth muscle constriction[2]. Guidelines for its use in clinical practice had been clearly established in the literatures[3, 4]. It is commonly used to confirm the diagnosis of asthma in a patient with asthma-like symptoms and normal or near normal FEV_1.

MATERIALS AND METHODS

Subjects

A total of 29 BCTs were performed from July 2008 to April 2009. Only patients with asthma-like symptoms were included in this review. Patients' case notes were retrieved and relevant information obtained from the medical record. 7 case notes could not be retrieved. One patient was excluded because he was a known asthmatic before BCT was done. One patient had poor spirometry technique. Another patient was excluded since he presented with spontaneous pneumothorax. Therefore, only 19 patients were included in this review.

All patients underwent BCT after routine history, clinical examination and investigations. Verbal consent was taken before BCT. Patients who had an FEV1 of less than 80% predicted were not eligible for BCT. All patients were given an information sheet listing a number of drugs, food and beverages that must be avoided for certain hours before BCT. All patients had negative TB screening by induced sputum for AFB and chest radiograph. Since this is a descriptive study, no statistical test was employed.

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Table I: zation of degree of bronchial hyperresponsiveness

Increase responsiveness	Less than or equal to 0.125 µmol
Moderate responsiveness	Between 0.125 and 1.99 µmol
Mild responsiveness	Between 2.00 and 6.6 µmol

Table II: Patients who had positive MCT

No	Age (Year)	Smoking status	Presenting symptoms	Chest imaging done	Co-morbidities	Result of MCT
1	56	Non-smoker	Cough for 2 weeks	CXR and HRCT normal	Gastritis, HT, BPH	Positive at 4.03 µmol
2	23	Non-smoker	Cough for 5 months	CXR normal	Nil	Positive at 4.03 µmol
3	58	Non-smoker	Cough for 2 years	CXR and HRCT normal	Allergic rhinitis	Positive at 0.13 µmol
4	18	Non-smoker	cough and dyspnea for 4 years, associated with wheezing	CXR and HRCT normal	Allergic rhinitis	Positive at 0.52 µmol
5	63	Smoker	Intermittent dyspnea for 23 years	CXR and HRCT normal, CTPA normal.	HT, hyperlipidemia, CAD with CABG done 2006.	Positive at 0.26 µmol
6	70	Non-smoker	Cough for 5 years	CXR and HRCT normal.	HT, hyperlipidemia	Positive at 1.03 µmol
7	33	Smoker	Dyspnea for 3 months	CXR normal	HT, Gout, PUD	Positive at 2.03 µmol
8	69	Non-smoker	Cough for 10 years	CXR normal	CAD, HT, hyperlipidemia, Lymphocytic colitis	Positive at 0.26 µmol
9	13	Non-smoker	Cough for 3 months,	CXR normal	Nil	Positive at 2.03 µmol
10	35	Non-smoker	Dyspnea and rhinitis for 8 years	CXR normal	Nil	Positive at 4.03 µmol
11	56	Smoker	Cough for 10 years	CXR and CT Thorax normal	HT, DM, Hyerthyroidism, Gout	Positive at 0.52 µmol

CXR: Chest-X-Ray
HRCT: High Resolution Computer Tomography
HT: Hypertension
BPH: Benign Prostatic Hyperplasia
CAD: Coronary Artery Disease
CABG: Coronary Artery Bypass Grafting
CTPA: Computer Tomography of Pulmonary Artery
PUD: Peptic Ulcer Disease
DM: Diabetes Mellitus
CT: Computer Tomography

Fig. 1: DeVilbiss 646 nebulizer.

Fig. 2: KoKo Dosimeter.

Methacholine Challenge Test (MCT)
Methacholine solution was prepared from a commercial powder (Provocholine; Methpharm, ON, Canada) using standard aseptic technique. Methacholine concentration of 1.25, 10 and 40mg/ml were prepared with dilution with 0.9% sodium chloride solution with contain 0.4% phenol. These solutions were delivered to subjects through a mouthpiece attached to a DeVilbiss 646 nebulizer (Sunrise Medical, Somerset, Pennsylvania, USA) driven by the KoKo Digidoser system (Pulmonary Data Service; Louisville, CO). The KoKo Digidoser/nubulizer was calibrated to produce an output of 0.009mL (±10%) per 0.6s actuation. After normal tidal expiration to functional residual capacity, the technologist triggered the dosimeter at the onset of inspiration, and the subject was asked to inhale slowly and deeply over 5 seconds to total lung capacity. Subjects held their breath for 5 seconds, followed by a slow exhalation for 5 seconds. A minimum of three but not more than four FEV_1 measurements were performed at 30 and 90 seconds after each challenge. All subjects wore a nose clip.

Each challenge began with a diluent followed by the lowest concentration of methacholine, and this was increased until either a 20% decline in FEV_1 was achieved or the maximum methacholine concentration was administered without at least a 20% change in FEV_1.

The test results were expressed by the cumulative dose that caused a 20% decrease in FEV_1 (PD_{20}). The cutoff dose was 6.6µmol [5]

RESULTS
19 patients who had MCT with complete data were included in this review.

The age ranged from 13 to 70 years old (mean=47.5 years). 12 were male, 7 were female. Duration of presenting symptoms ranged from 2 weeks to 23 years. 11 patients (53%) had positive MCT. Of note, patient number 7 was diagnosed after 23 years of symptoms.

DISCUSSION
Management of patients with chronic cough or dyspnoea depends on its cause. In a patient with chronic cough, asthma should always be considered as a potential aetiology because asthma is common and cough may be the only symptom. Other cardinal symptoms of asthma (wheezing, chest tightness and dyspnoea) can be difficult to elicit in among Malaysian polyglot patients. In one study[1], after re-examining the diagnosis of all patients by history, spirometry, trial of corticosteroid and methacholine challenge test, 34% of patients actually did not have asthma and another 7% of patients had COPD associated with asthma.

Reversibility testing using bronchodilator is commonly used in Malaysia to diagnose asthma. However, this practice may not demonstrate the improvement (12% and 200mls) if the initial spirometry is normal. Furthermore, a negative reversibility testing cannot confidently exclude asthma.

In patients with high pretest probability of asthma, i.e. patients with asthma-like symptoms, positive BCT test at low PC_{20}, bronchial asthma can be diagnosed with high degree of certainty[6,7,8]. A negative test can effectively rule out asthma4.

BCT is relatively easy to perform in a Pulmonary Physiology Laboratory which is already familiar with spirometry. In our experience, we didn't encounter major side-effects such as severe bronchospasm needing immediate medical attention. This is consistent with other reports[9].

The underutilization of BCT in Malaysia is partly due to unfamiliarity of the test, perceived technical complexity and complication of the test. These concerns are unjustified as it is used widely in many countries.

The limitation of this study is it was retrospective in nature and a small number of patients. However, this review has given us the confidence to continue using BCT as an adjunctive tool to diagnose airway hyper-responsiveness.

CONCLUSION
BCT is an excellent adjunctive diagnostic tool in patients with asthma-like symptoms. We strongly recommend that BCT be made available in all major respiratory centers in Malaysia to reduce empirical asthma treatment. Future study using a larger sample size from all three major ethnic groups as well as a prospective study is recommended.

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