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Original Article

Aetiological Approach to Patient with Non- Specific Chronic Cough

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Abstract

Chronic cough is a problem commonly encountered by the practicing physicians. Definitive treatment depends upon identifying the cause of cough4.To develop an appropriate algorithm for diagnosis of non-specific chronic cough a Prospective case-control study was carried out in Asthma Centre,NIDCH, Mohakhali, Dhaka during the period of January,2000 to December,2001. Eighty two patients with history of cough for 3 weeks or more duration were taken in group A.The ages ranged from 11 to 68 years with mean age 35.5 ± 12.0 years. There were 43 males and 39 females. Equal number of subjects having no cough were taken as control (group B).The age of control subjects ranged from 11 to 68 years with mean age 35.6 ± 11.9 years. Diagnosis was made in all patients. PNDS was found in 41(50%), PNDS with cough variant asthma in 19(23.2%),cough variant asthma alone in 10(12.2%),GERD singly in 2(2.4%).In control group, only 5 (6.1%) persons were diagnosed as PNDS who had almost all features of PNDS except cough. In this studuy, PNDS alone and in combination with cough variant asthma were common causes of chronic cough.

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Introduction

Cough is the most important clinical symptom of respiratory disease. Patients with trivial viral respiratory tract infection to life threatening bronchial carcinoma may all present with simple cough. Sometimes cough is the only symptom of many respiratory diseases.

Non-specific chronic cough may be defined as a cough with duration of 3 weeks or more without any fever or systemic illness and where chest x-ray, sputum for AFB (3 samples) and spirometry are inconclusive[1].

Chronic cough is an important medical and economic problem. The prevalence of chronic cough in the United States among nonsmoking adults is reported to range from 14% to 23%[2]. Chronic cough is the fifth most common symptom seen by outpatient physicians[3] and estimated to be the primary reason for 30 million physician visits annually[3].

Major advances in the clinical approach to chronic cough have been made during the last 20 years. In 1977, Irwin and colleagues proposed an approach to chronic cough based on the anatomic locations of the receptors and afferent pathways involved in cough reflex[4]. Using such an approach, Irwin and colleagues reported in 1981 and again in 1990, that the cause of chronic cough could be determined 100% of the time and that subsequent cause-specific treatment was almost always successful[5].

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The aim of this study is to make an algorithmic approach to diagnose patients with non specific chronic cough.

Material and Methods

A prospective case control study was carried out in the Asthma Centre, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka. The study was conducted during the period of January 2000 to December 2001.A total number of 82 patients (group A) of chronic cough were taken as cases who fulfil the selection criteria and having no exclusion criteria and 82 healthy persons (group B) were taken as control.

After getting an informed consent detailed history and physical examination was done to establish initial diagnosis followed by collection of all data in a prescribed data sheet.

Study Procedure

STEP-I: A standard questionnaire was designed to identify the patients of chronic cough and was filled by the author himself.

STEP-II:The patients of chronic cough were identified by detail history taking, thorough physical examinations

STEP-I11; Investigation to rule out exclusion criteria:

(1)TC, DC, ESR, Hb%, (2) Sputum for AFB (3 consecutive samples) (3) Total circulating eosinophils count (TCEC) (4) CFT for filaria (5) X-ray chest P/A view (6) Spirometry (7) ECG

STEP-1V: Investigation to establish the causes of nonspecific chronic cough:

Methacholine challenge test – A 20% fall in FEV_1 with a concentration of Methacholine ranging from 0.4 mg/ml to 8 mg/ml was considered as a positive test[6]

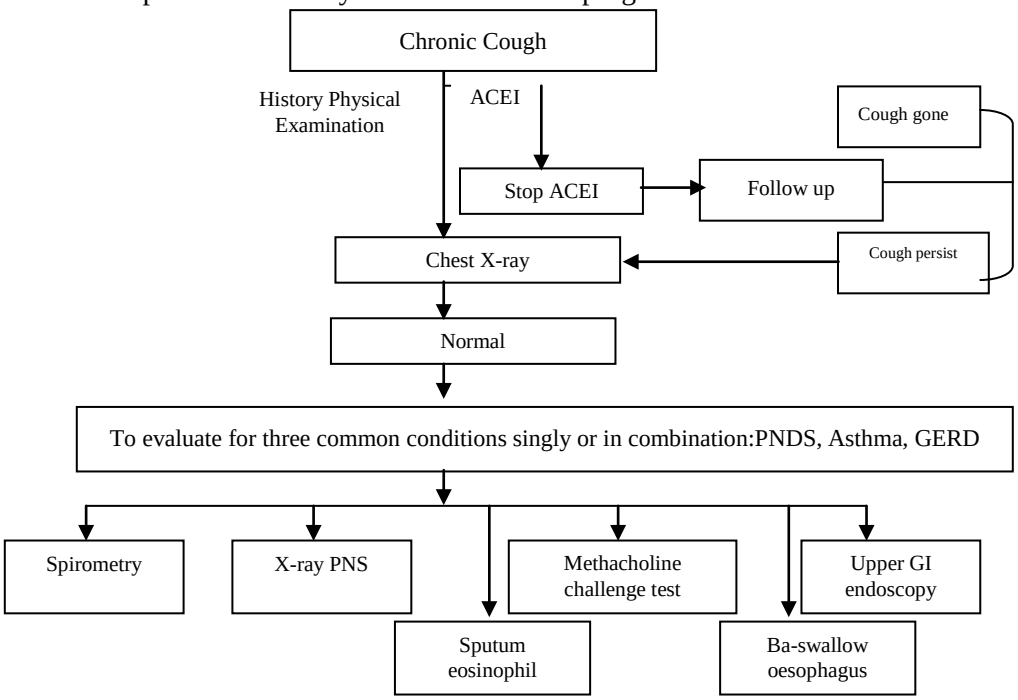
X-rayPNS – Mucosal thickening and/or haziness with air-fluid level was considered as abnormal**.**

Upper GI endoscopy – The earliest change reddening to multiple ulcers in the mucosa of lower oesophagus was considered as abnormal.

Barium swallow of oesophagus – Reflux during barium study in fluoroscope was taken as abnormal.

Sputum eosinophil count – Normally eosinophils should not be present in sputum. Presence of eosinophils in sputum was considered as significant.

STEP-V:Data compilation and analysis with SPSS 12.0 program.



Algorithm for diagnosis of chronic cough

Results

This prospective case-control study was carried out with a view to establish an algorithm for diagnosis of chronic cough. Eighty two patients with history of cough for 3 weeks or more duration were taken in group A. The ages ranged from 11 to 68 years with mean age 35.5 ± 12.0 years (table 1). There were 43 males and 39 females. Equal number of subjects having no cough were taken as control (group B).The age of control subjects ranged from 11 to 68 years with mean age 35.6 ± 11.9 years. Diagnosis was made in all patients. PNDS was found in 41(50%), PNDS with cough variant asthma in 19 (23.2%),cough variant asthma alone in 10(12.2%), GERD singly in 2 (2.4%).In control group, only 5 (6.1%) persons were diagnosed as PNDS who had almost all features of PNDS except cough. Results are displayed in following tables-

Table 1. Age and sex distribution of the study subjects

Age in years	Sex		Total	p-value
	Male	Female		
<25	17 (19.8)	11 (14.1)	28 (17.1)	0.281^{NS}
25-34	32 (37.2)	22 (28.2)	54 (32.9)	
35-44	20 (23.3)	27 (34.6)	47 (28.7)	
≥45	17 (19.8)	18 (23.1)	35 (21.3)	
Total	**86 (100.0)**	**78 (100.0)**	**164 (100.0)**	

Mean ±SD = 35.5±11.9 years, Male = 34.5±12.6 years, Female = 36.7±11.2 years
NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis
NS=Not significant (p>0.05)

Table 2 : Occupation of the study subjects

Occupation	Study subjects		Total	p-value
	Group A	Group B		
Service	32 (39.0)	44 (53.7)	76 (46.3)	0.237^{NS}
Labourer	14 (17.1)	8 (9.8)	22 (13.4)	
Student	15 (18.3)	14 (17.1)	29 (17.7)	
Housewife	21 (25.6)	16 (19.5)	37 (22.6)	
Total	**82 (100.0)**	**82 (100.0)**	**164 (100.0)**	

NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis NS=Not significant (p>0.05)

Table 3: Clinical presentation of the study subjects

Clinical presentation	Study subjects		Total (n=164)	p-value
	Group A (n=82)	Group B (n=82)		
Cough				
Duration of cough	53.3±7.6 m	0	53.3±7.6 m	NA
Relation with supine position	6 (7.3)	0 (0.0)	4 (2.4)	NA
Relation with food	6 (7.3)	0 (0.0)	2 (1.2)	NA
Haemoptysis	0 (0.0)	0 (0.0)	0 (0.0)	NA
Fever	0 (0.0)	0 (0.0)	0 (0.0)	NA
Breathlessness	15 (18.3)	0 (0.0)	15 (9.1)	NA
Chest tightness	18 (22.0)	0 (0.0)	18 (11.0)	NA
Chest pain	14 (17.1)	2 (2.4)	15 (9.8)	0.002^{S}
Nasal discharge	62 (75.6)	5 (6.1)	67 (40.9)	0.001^{S}
Sneezing	62 (75.6)	5 (6.1)	67 (40.9)	0.001^{S}
Recurrent throat irritation	62 (75.6)	5 (6.1)	67 (40.9)	0.001^{S}
History of heart burn	22 (26.8)	0 (0.0)	22 (13.4)	NA
History of taking ACEI	4 (4.8)	1 (1.2)	5 (3.0)	0.03^{S}
Family history of asthma	8 (9.7)	0 (0.0)	8 (4.9)	NA

NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis/fisher exact test
NA=Not applicable,NS=Not significant (p<0.05)

Table 4: Findings on physical examination of the study subjects

Physical examination	Study subjects		Total (n=164)	p-value
	Group A (n=82)	Group B (n=82)		
Chest auscultation				
Breath sound-vesicular	82 (100.0)	82 (100.0)	164 (100.0)	NA
Wheeze	0 (0.0)	0 (0.0)	0 (0.0)	NA
Crepitation	0 (0.0)	0 (0.0)	0 (0.0)	NA
Examination of nose				
Nasal congestion	55 (67.1)	5 (6.1)	60 (36.6)	0.001^S
Deviated nasal septum	50 (61.0)	5 (6.1)	55 (33.5)	0.001^S
Inferior turbinate hypertrophy	52 (63.4)	5 (6.1)	57 (34.8)	0.001^S
Examination of naso and oropharynx				
Mucoid secretion	62 (75.5)	5 (6.1)	67 (40.9)	0.001^S
Cobble stone appearance	37 (45.1)	0 (0.0)	37 (22.6)	0.001^S

NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis/fisher exact test
NA=Not applicable
NS=Not significant ($p<0.05$)

Table 5: Investigation of the study subjects

Investigations	Study subjects		Total (n=164)	p-value
	Group A (n=82)	Group B (n=82)		
Blood examination				
Leucocytosis	0 (0.0)	0 (0.0)	0 (0.0)	NA
Neutrophilia	0 (0.0)	0 (0.0)	0 (0.0)	NA
Sputum eosinophils	29 (35.4)	0 (0.0)	29 (17.7)	NA
Mean circulating eosinophils	350.4±116.3	282.6±84.7	316±106.9	0.001^S
Positive CFT for filaria	6 (7.3)	0 (0.0)	6 (3.7)	0.013^S
X-ray PNS-Abnormal	62 (75.6)	5 (6.1)	67 (40.9)	0.001^S
Barium swallow esophagus – Abnormal	6 (7.3)	0 (0.0)	6 (3.6)	NA
Upper GIT endoscopy –Abnormal	6 (7.3)	0 (0.0)	6 (3.6)	NA
Methacholine challenge test - Positive	29 (35.4)	0 (0.0)	29 (17.7)	NA

NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis/fisher exact test
NA=Not applicable, NS= Not significant ($p>0.05$),S=Significant ($p<0.05$)

Table 6: Diagnostic profile of the study subjects

Diagnosis	Study subjects		Total (n=164)	p-value
	Group A (n=82)	Group B (n=82)		
PNDS	41 (50.0)	5 (6.1)	46 (28.0)	0.001^S
PNDS-CVA	19 (23.2)	0 (0.0)	19 (11.6)	-
CVA	10 (12.2)	0 (0.0)	10 (6.1)	-
GERD	4 (4.9)	0 (0.0)	4 (2.4)	-
GERD-PNDS	2 (2.4)	0 (0.0)	2 (1.2)	-
ACEI	4 (4.9)	0 (0.0)	4 (2.4)	-
Psychogenic	2 (2.4)	0 (0.0)	2 (1.2)	-
Normal	0 (0.0)	77 (90.0)	77 (47.0)	-

NB. Figure in parenthesis indicate percentage
p-value reached from chi-square analysis with yates' correction
NS=Not significant ($p>0.05$)
S=Significant ($p<0.05$)

Table 7: Diagnostic criteria of PNDS (n=46)

Features	Group A (n=41)	Group B (n=5)
Nasal discharge	41 (100.0)	5 (100.0)
Sneezing	41 (100.0)	5 (100.0)
Recurrent throat irritation	41 (100.0)	5 (100.0)
Mucoid secretion	41 (100.0)	5 (100.0)
Abnormal X-ray PNS	41 (100.0)	5 (100.0)
Cough	41 (100.0)	0 (0.0)
Nose and pharyngeal findings		
Nasal congestion	36 (87.8)	5 (100.0)
Deviated nasal septum	33 (80.5)	5 (100.0)
Inferior turbinate hypertrophy	34 (82.9)	5 (100.0)
Cobble stone appearance	28 (68.3)	0 (0.0)

Table 8: Diagnostic criteria of Cough variant asthma (n=10)

Features	Frequency	%
Cough	10	100.0
Positive Methacholine test	10	100.0
Sputum eosinophils	10	100.0
Breathlessness	3	30.0
Chest tightness	3	30.0
Family history of asthma	2	20.0

Table 9: Diagnostic criteria of gastroesophageal reflux disease (n=4)

Features	%
Cough	4 (100.0)
Cough with supine position	4 (100.0)
Cough relation with foods	4 (100.0)
H/O heart burn	4 (100.0)
Barium swallow esophagus	4 (100.0)
Upper GI endoscopy	4 (100.0)

Table 10: Diagnostic criteria of ACEI induced cough (n-4)

Symptoms and signs	Group A (n=4)	Group B (n=0)
History of taking ACEI	4 (100.0)	1 (100.0)
Follow up remission of cough	4 (100.0)	0 (0.0)
Cough	4 (100.0)	0 (0.0)

Table 11: Diagnostic criteria of psychogenic cough (n=2)

Features	%
Cough	2 (100.0)
Exclusion of other causes of chronic cough	2 (100.0)

Discussion

Chronic cough is a problem commonly encountered by the practicing physician. Definitive treatment depends upon identifying the cause of cough[4]. A systematic manner of evaluating patients with chronic cough was presented for the first time in 1981[5]. Cough has been produced by multiplicity of diseases located in a variety of anatomic sites[4].

With a view to develop an appropriate algorithm for the diagnosis of non-specific chronic cough a case-control study comprising of 82 patients with history of cough and equal number of normal persons without cough was carried out in the Asthma Centre of the National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka.

All patients who came to Asthma Centre, NIDCH with chief complaint of cough for 3 weeks or more, nonsmoker, no known history of asthma, normal chest findings and no abnormality in X-ray chest and spirometry were considered for inclusion in the study. The patients were excluded from the study who had specific causes of chronic cough,

history of common cold in last 2 months and receiving immunosuppressive drugs.

The initial evaluation included a history, physical examination and questionnaire on the duration, frequency & severity of cough, postnasal drip symptoms, symptoms of gastroesophageal reflux and drug history. Relevant investigations then done.Diagnoses were made in all patients. The diagnostic profile in this study was PNDS in 41 (50.0%) followed by PNDS with cough variant asthma in 19 (23.2%), cough variant asthma singly in 10 (12.2%), GERD and ACEI induced cough each in 4 (4.9%) and GERD with PNDS and psychogenic cough each in 2 (2.4%) patients. Only 5 (6.1%) respondents were diagnosed as PNDS who had almost all features of PNDS except cough.

In this study, postnasal drip syndrome was the single most common cause of chronic cough. Similar findings were reported by Irwin RS, et al. 1981 (29%)[5], Irwin RS, et al. 1991 (41%)[7], Pratter MR, et al. 1993 (27%)[8] and Villanova CAC 1996 (33.3%). But Bruno Carlos Palombini, et al. 1999 and Poe RH, Israili RH, 1990 found postnasal drip syndrome as the second common cause of chronic cough (57.6% and 28.0% respectively)[9,10]. In their study, cough variant asthma was at the top of the list.

About one-fifth of the patients had PNDS in association with cough variant asthma and a few with gastroesophageal reflux disease. Similar combination was also found by others[5,7,8].

Ten of 82 (12.2%) patients were diagnosed as having cough caused by asthma alone. Nineteen had asthma in combination with postnasal drip syndrome. Twenty-nine of 82 (35.4%) patients had bronchial hyperresponsiveness on Methacholine bronchoprovocation challenge. The finding was consistent with others[8,11,12]. Only four of 82 (4.9%) patients labeled as having cough due to gastroesophageal reflux singly and other two in combination with postnasal drip syndrome. Similar combination also reported by many authors[8,9,11]. For the diagnosis of GERD, there are many oesophageal tests viz., acid infusion test, Oesophagoscopy, Barium swallow X-ray of oesophagus, Oesophageal biopsy, Oesophageal manometry, Oesophageal P^H monitoring. In this study only Oesophagoscopy and Barium swallow of the oesophagus were performed with a view to diagnose GERD. The other tests could not be done. In 1976, Behar J and Colleagues showed that the use of oesophageal tests in combinations had greater specificity than any test alone in patients with GERD[12]. But 24-hours monitoring of oesophageal P^H singularly useful in making the diagnosis of GERD even in the absence of gastrointestinal symptoms[8,9,11.] ACEI induced cough was diagnosed in another 4 (4.9%) patients of group A. The mean duration of cough was 17.5±10.5 months. Cough disappeared within four weeks of discontinuation of ACEI.

By the way of exclusion, only two patients were found to have chronic cough of psychogenic origin. Psychogenic aetiology of chronic cough also reported[8].

Conclusion

Nonspecific chronic cough is an important medical problem that commonly encountered by the physicians. The prevalence of chronic cough in our country is not yet known.In this study, the diagnosis of chronic cough is possible in 100% cases and Postnasal drip syndrome alone or in combination with cough variant asthma are common causes of chronic cough which is almost similar as different studies in other parts of the Globe.

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