Cholinergics, Airway Eosinophils and Asthma Exacerbation in the Elderly

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ABSTRACT

Cholinomimetic agents have a number of potential indications in an ageing population. This case series emphasises the need to exercise caution while prescribing cholinergic drugs in elderly patients with asthma, particularly in patients with a history of virus-induced exacerbations and airway eosinophilia. [Indian J Chest Dis Allied Sci 2011;53:59-61]

Key words: Asthma, Elderly, Cholinergics, Sputum eosinophils.

INTRODUCTION

There is a steady increase in the prevalence of asthma from adolescence to old age.1 However, in the elderly patients, asthma is often under-recognised and under-treated.2 Asthma control in the elderly is further complicated by numerous co-morbidities. Coexisting conditions may exacerbate asthma, hinder effective therapy and reduce asthma control. We highlight the risks of the use of drugs with cholinergic activity in asthmatic patients using the following examples.

CASE REPORTS

Case-1

A 65-year-old male with chronic airflow limitation due to asthma and smoker’s bronchitis was admitted to the intensive care unit (ICU) for ventilatory support and intercostal drainage of pneumothorax and mediastinal emphysema. At the time of admission, he was on 10mg daily of prednisone and a combination of inhaled fluticasone (500μg) and salmeterol (50μg) twice daily. A paracardiac mass was detected and resected that turned out to be a lymphocyte-rich thymoma. At the time of discharge from the hospital, the values for forced expiratory volume in one second (FEV₁) and vital capacity (VC) were 1.4L (64%) and 2.2L (66%), respectively. He had further three episodes of bacterial bronchitis associated with sputum neutrophilia and normal eosinophils (total cell count greater than 25 million cells/gm, neutrophil >85%).³ These did not result in asthma exacerbation. However, an episode of respiratory syncytial virus bronchitis that was associated with sputum neutrophils and eosinophils (total cell count 11 million/gm, neutrophil 88%, eosinophil 4%) resulted in another admission with an FEV₁ of 0.6L. He recovered within 14 days, with FEV₁ improving to 1.3L. The patient was discharged on 30mg daily prednisone. Subsequently, prednisone was tapered off without any further decline in the FEV₁, by regular monitoring of the sputum cell counts that did not show any eosinophils as the prednisone dose was stopped. Four months after discontinuing prednisone, he started complaining of increased fatigue and exertional breathlessness. The FEV₁ and VC had declined to 1.0L and 1.6L, respectively and the inspiratory mouth pressure was 30% of the predicted. Sputum cell counts were normal. A clinical diagnosis of Myasthenia gravis was confirmed by demonstrating anti-cholinesterase receptor antibodies. However, treatment with pyridostigmine resulted in increasing chest tightness and wheezing and the FEV₁ dropped to 0.7L that improved to 1.2L upon discontinuing the drug. He is now on 7.5mg daily of prednisone for his Myasthenia gravis.

Case-2

An 82-year-old female was evaluated for cough and exertional breathlessness. The FEV₁ and VC were 1.0L and 1.8L, respectively. Sputum showed 5%
eosinophils. Symptoms and lung function improved significantly (FEV₁=1.4L) and remained stable for almost three years after she was treated with fluticasone (250μg) and salmeterol (25μg). In August 2008, her family doctor prescribed donepezil (Aricept®) 10mg daily for slight cognitive decline and memory loss. Within two weeks of starting therapy, she had six episodes of central chest heaviness and shortness of breath, all occurring between 2 AM and 3 AM. She was seen at the emergency room during four of these episodes and was documented to have wheezing with mild hypoxaemia (SpO₂=91%), low peak expiratory flow (PEF=100 L/min), and normal electrocardiogram (ECG) and serial cardiac enzymes. On each occasion symptoms improved with inhaled salbutamol and oxygen. The emergency room physician also recommended ipratropium bromide (4 puffs four times a day). Post-bronchodilator FEV₁ improved by 70%, and sputum, for the first time, showed 3% eosinophils. Since discontinuing donepezil, she has had no recurrence of these symptoms during 12 weeks of follow-up. Currently, FEV₁ is 1.3L and sputum does not show eosinophils.

Case-3

A 79-year-old female with chronic open angle glaucoma and frequent winter bronchitis presented with new onset wheezing shortly after she had been prescribed timolol maleate (Timoptic XE ©) 0.5% eye drops by her family physician. PC₂₀ methacholine was 1.2mg/mL. Sputum cell counts were normal indicating that she did not have bronchitis. Timolol was discontinued. Four weeks later, PC₂₀ methacholine was 5.6mg/mL and wheezing had improved without any further need for daily salbutamol inhaler. Treatment was substituted with pilocarpine 0.5% eye drops three times a day. After seven days, she presented again with daily and nocturnal wheezing. Sputum showed 2% eosinophils and the PC₂₀ methacholine had dropped to 2.4 mg/mL and FEV₁ had decreased by 400mL. Pilocarpine was discontinued and substituted with latanoprost (prostaglandin F2 alpha analogue) 0.005% by the ophthalmologist. She has not since required salbutamol inhalation.

DISCUSSION

These cases highlight three clinically relevant aspects of asthma management in the elderly. First, caution needs to be exercised in prescribing cholinergic agents for beneficial effects in diseases that particularly affect an ageing population. These include Parkinson’s disease, Alzheimer’s disease and glaucoma. Second, this phenomenon may be particularly problematic in patients who have a history of virus-induced bronchoconstriction. Thirdly, cholinergic stimulation may increase airway responsiveness and airway eosinophilia resulting in asthma exacerbations.

Acetylcholine is the primary para-sympathetic neurotransmitter in the airways and is thought to induce airway smooth muscle contraction by acting on the M3 receptors on the smooth muscle. Viral infections cause a marked increase in vagally-mediated bronchoconstriction. This is likely due to increased acetylcholine release as a result of loss of inhibitory M2 muscarinic receptors in the cholinergic nerve fibers resulting from the increased bronchial hyperreactivity associated with inflammation. Possible mechanisms are illustrated in the figure below. As illustrated in the first case history, presence of airway eosinophilia, not neutrophilia, at the time of viral bronchitis, may exacerbate muscarinic receptor dysfunction. It is also likely that cholinergic stimulation can increase eosinophil recruitment to the airway by indirect mechanisms. This needs further investigation. Examination of sputum cell counts enables the recognition of the type of bronchitis, and thus, initiate appropriate treatment.
Cholinomimetic agents have a number of potential indications in an ageing population. They are used for diseases of the eye (glaucoma), the gastrointestinal and urinary tract (post-operative atony and neurogenic bladder), the neuromuscular junction (*Myasthenia gravis*), central nervous system (Alzheimer’s), and the cardiovascular system (hypertension, myocardial infarction). This case series emphasises the need to exercise caution while prescribing cholinergic drugs in patients with asthma particularly in those with history of virus-induced exacerbations and airway eosinophilia.

**REFERENCES**


Free the Mother Earth from Tobacco Sacrilege

Burnt out lips nail tips cheek palate ruminate
Inflamed mucosa cancer in wait knocking at gate
Stained mutilated teeth putrid gum in dire state
Tell tale signs of smoke and lurking death fate!

Coarse wrinkles and salt pepper define hair line
Signs of getting old and grey at young age shine
Ravages of tobacco indelible entire body line
Foolishly embracing the killer on dotted line!

Air passage filled with fumes tar coal most time
Tiny air sacs rendered useless bloated all time
Hacking cough and difficult breathing every night-time
Phthisis and cancer cutting lifeline giving no time!

Poisonous carbon monoxide well stealth in smoke
Nicotine arecoline clogging coronaries to broke
Numerous insults, attacks after attacks and stroke
Heart stops suddenly slaps of tobacco and smoke!

Why don’t we wipe the tobacco gutka and gul?
Protect all our siblings’ kids’ kith kin and ‘kul’
Curse of deadly poisonous substances and bull
Going hell and gruesome ringing of tobacco death bell!

Let us take this pledge with all our grit and might
Not to cultivate sell share deal chew or alight
Say no more tobacco good bye gutka, bidi and smoke
Never to touch pipe spice or snuff even in joke!

Big no to surti spitting smoking around the ground
Our mother earth free from tobacco sacrilege abound
Dawn shining fragrant filled with breeze and sound
Making this planet a heaven to lounge around!

Dr Shridhar Dwivedi