UNIT NO. 2

ZERO TOLERANCE TOWARDS ASTHMA DEATHS IN SINGAPORE: ROLE OF THE FAMILY DOCTOR

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ABSTRACT

Asthma is a common chronic respiratory disease in Singapore and it is the primary cause of chronic respiratory disease burden in childhood and early adulthood. Despite having one of the best healthcare systems in the world, our asthma mortality rates are several folds higher than other first world countries. Most asthma deaths are preventable. We illustrate a case of fatal asthma and highlight some learning points from this case.

Keywords: Asthma; Mortality; Prevention; Primary care;

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INTRODUCTION

Asthma is a chronic respiratory disease characterised by variable respiratory symptoms such as wheeze, breathlessness, chest tightness and cough. In Singapore, 4.9% of the population has asthma[1] and it is the primary cause of chronic respiratory disease burden in childhood and early adulthood[2]. Despite 81-95% of our population having access to asthma medications, our asthma mortality rate remains at a high of 16 per 100000, which is three times that of other developed nations such as the United States and New Zealand[1]. This prompted an audit of fatal and near-fatal (FA/NFA) asthma in 4 restructured hospitals in Singapore. Between 2011-2015, there were 340 patients which accounted for 384 FA/NFA events, 17.1% had no regular asthma follow-up, and 32.1% were not on inhaled corticosteroid (ICS) i.e. Step 1 of GINA[3]. Lack of prior treatment with ICS and follow-up were associated with greater risk of death and hypoxic encephalopathy. The importance of a timely and accurate diagnosis of asthma, initiation of treatment with ICS and regular follow-up and assessment of asthma control is therefore a matter of paramount importance. Here, we present a patient with fatal asthma to illustrate some of the factors which could have prevented his demise.

CASE ILLUSTRATION

Mr K was a 44-year-old Chinese man who had a history of asthma since childhood. He was married with no children and worked as a sales manager. His asthma control was poor with symptoms 3-4 times a week. He doctor-hopped and saw different General Practitioners (GPs) for exacerbation about 2-3 times yearly and was given a course of prednisolone and bronchodilator nebulisations each time. Two months prior to his presentation to hospital, he was prescribed combination of ICS and Long-acting Beta agonist (LABA) by a GP but he was not taking it regularly, relying instead on a Salbutamol inhaler almost daily. Two days prior to admission, he had upper respiratory tract infection symptoms and was using his Salbutamol inhaler up to 4 times each day. He developed worsening breathlessness and chest tightness on the morning of his admission to hospital which was not relieved by his Salbutamol inhaler. His wife called for an ambulance after noticing that he was getting increasingly breathless. The ambulance paramedics initiated nebulisation of bronchodilators and supplemental oxygen but he went into cardiac arrest while still en-route to hospital. CPR was commenced immediately and he was intubated at the Emergency Department. He eventually had return of spontaneous circulation after 30 minutes of resuscitation and was transferred to the Medical Intensive Care Unit (MICU). Intravenous corticosteroids and regular bronchodilators were given.

On Day 2 of admission, the patient showed no brainstem reflexes on neurological testing and an MRI brain showed changes consistent with hypoxic-ischaemic encephalopathy. The patient's condition continued to deteriorate and he eventually passed away one week later.

Mr K's death could have been prevented by:

1. Early diagnosis, assessment of severity and appropriate treatment of asthma
2. Regular follow up for asthma and adjustment of treatment according to response
3. Early detection of worsening asthma control, self-management and use of a Written Asthma Action Plan (WAAP)

PRINCIPLES OF ASTHMA DIAGNOSIS AND MANAGEMENT

(A) DIAGNOSIS

A diagnosis of asthma is made when the patient has a history of variable respiratory symptoms (e.g. wheeze, chest tightness and cough) and confirmed variable expiratory airflow limitation on lung function testing. It is important to note that airflow limitation may be seen in many other chronic respiratory diseases such as chronic obstructive pulmonary disease and bronchiectasis, but what distinguishes asthma from these conditions is the presence of variable expiratory airflow limitation. In asthmatics, the lung function may vary between completely normal and severely obstructed in the same patient. Similarly, patients with conditions such as eosinophilic

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bronchitis or chronic cough from upper airway cough syndrome may be wrongly labelled as having cough-variant asthma but these patients have normal spirometry and airway responsiveness[4]. Due to the presence of many asthma mimics (anxiety, vocal cord dysfunction, gastro-oesophageal reflux disease, etc), use of objective tests to confirm variable expiratory airflow limitation is highly recommended.

TABLE 1: DIAGNOSTIC CRITERIA FOR ASTHMA IN ADULTS, ADOLESCENTS AND CHILDREN 6-11 YEARS[5]

DIAGNOSTIC FEATURE	CRITERIA FOR MAKING DIAGNOSIS OF ASTHMA
1. History of variable respiratory symptoms	
Wheeze, shortness of breath, chest tightness and cough	• Generally, more than one type of respiratory symptom (in adults, isolated cough is seldom due to asthma) • Symptoms occur variably over time and vary in intensity • Symptoms are often worse at night or on waking • Symptoms are often triggered by exercise, laughter, allergens, cold air • Symptoms often appear or worsen with viral infections
2. Confirmed variable expiratory airflow limitation	
Documented excessive variability in lung function (one or more of the tests below) **AND** documented airflow limitation	The greater the variations, or the more occasions excess variation is seen, the more confident the diagnosis At least once during the diagnostic process when the FEV_1 is low, confirm that FEV_1/FVC is reduced
Positive bronchodilator reversibility test	*Adults*: increase in FEV_1 of >12% and 200mL from baseline, 10-15 minutes after 200-400mcg salbutamol *Children*: increase in FEV_1 of >12% predicted
***Excessive variability in twice-daily peak expiratory flow (PEF) over 2 weeks**	***Adults*: average daily diurnal PEF variability >10%** ***Children*: average daily diurnal PEF variability >13%**
***Significant increase in lung function after 4 weeks of anti-inflammatory treatment**	***Adults*: increase in FEV_1 of >12% and 200mL (or PEF by >20%) from baseline after 4 weeks of treatment, outside of respiratory infections**
Positive exercise challenge test	*Adults*: fall in FEV_1 of >10% and 200mL from baseline *Children*: fall in FEV_1 of >12% predicted, or PEF >15%
Positive bronchial challenge test (usually only performed in adults)	Fall in FEV_1 from baseline of ≥20% with standard doses of methacholine or histamine, or ≥15% with standardised hyperventilation, hypertonic saline or mannitol challenge
*Excessive variation in lung function between visits (less reliable)	*Adults*: variation in FEV_1 of >12% and 200mL between visits, outside of respiratory infections *Children*: variation in FEV_1 of >12% or >15% in PEF between visits (may include respiratory infections)

***These tests can be performed in primary care clinics if spirometry is not available**

Fractioned exhaled nitric oxide (FeNO) is a non-invasive marker of eosinophilic airway inflammation. It has recently been shown to predict response to ICS in patients presenting with non-specific respiratory symptoms (cough, breathlessness or wheeze for > 6 weeks) to primary care clinics[6]. The test is easy to perform and can be considered for clinical use especially in the primary care setting.

(B) ASSESSMENT OF ASTHMA SEVERITY

Asthma severity is assessed retrospectively during the healthcare visit based on the level of treatment needed in order to control asthma symptoms and prevent exacerbations[7,8]. Asthma severity does not remain constant for a patient and frequent reassessment is needed.

(C) TREATMENT

The goal of asthma treatment is to achieve **good symptom control** and to **minimize the risk of future exacerbations**. Effective asthma management involves optimal pharmacological therapy and shared decision-making between the patient and his/her healthcare provider[9].

The pharmacological options for the long-term treatment of asthma fall into 3 main categories:

1. Controllers (Inhaled corticosteroids, ICS or Inhaled Corticosteroids/Long-acting beta agonist, ICS/LABA combination inhaler): These are used daily to prevent symptoms of asthma and reduce likelihood of exacerbations. They work by reducing airway inflammation and also help reduce bronchial hyperreactivity. ICS is the cornerstone of asthma therapy.
2. Relievers (Short-acting beta agonist, SABA): These are used only as-needed for relief of worsening symptoms during an exacerbation. Ideally, the patient should not require any reliever therapy at all if their asthma is well-controlled.
3. Add-on therapies: These may be considered when the patient has persistent symptoms and/or frequent exacerbations despite optimising their controller medications.

The use of regular ICS as the maintenance treatment to achieve control of asthma symptoms is recommended for most patients. Despite having "mild asthma", this group of patients still have airway inflammation[10] and they remain at risk of severe life-threatening exacerbations[11]. The SYGMA 1 trial published this year compared the use of 1) regular budesonide-formoterol to 2) 'as-needed' budesonide-formoterol and 3) twice-daily placebo plus 'as-needed' SABA (current GINA Step 1) in patients with mild asthma[12]. Regular use of ICS provided the best degree of asthma control; ICS used 'as needed' was non-inferior to regular ICS in terms of preventing severe asthma exacerbations and most importantly, ICS used 'as needed' was superior to 'as needed' salbutamol for asthma control and prevention of exacerbations (64% lower rate of severe exacerbations). It is also important to realise that while short-acting bronchodilators provide fast and effective symptom relief, they do not treat the underlying pathology – which is airway inflammation[13] – and regular use of short-acting bronchodilators is also associated with a higher risk of exacerbations[14].

In summary, ICS is the most effective treatment for asthma[15,16]. Use of ICS in asthma:
1. Reduces mortality
2. Reduces exacerbations
3. Reduces healthcare costs
4. Improves lung function
5. Improves asthma symptoms and control
6. Reduces missed days at work or school

Given the evidence presented above, we recommend the use of regular inhaled corticosteroids in all patients and to avoid monotherapy short-acting bronchodilators where possible as part of best clinical practice.

(D) REGULAR FOLLOW-UP FOR ASTHMA AND ADJUSTMENT OF TREATMENT ACCORDING TO RESPONSE

Asthma is a chronic disease and hence requires regular review by their healthcare practitioners. In control-based asthma

management, asthma therapy is adjusted in a continuous cycle of 1) Treat, 2) Assess control and 3) Adjust treatment and this has been shown to improve asthma outcomes[17].

Assess Control

At each follow-up visit, the healthcare practitioner should assess the patient's asthma control by taking history and using standardised tools such as the Asthma Control Test or Asthma Control Questionnaire. Patients who are current smokers should be advised to quit smoking, inhaler techniques should be checked at every visit and adherence to medications assessed.

Regular review is also important as there is often a mismatch between patients' perception of asthma control and actual outcomes (exacerbations, severe life-threatening asthma exacerbations etc.)[18]. In an online survey of 2467 patients with asthma from 8 Asian countries which included Singapore, 89% of patients felt that their asthma was well-controlled but in that same group of patients, 73% had experienced 1 or more exacerbations in the past year[19]. As patients tend to view good asthma control as being able to relieve symptoms from exacerbations instead of preventing them, healthcare practitioners are in the best position to educate patients on their condition, address the mismatch between patients' perception and reality of outcomes, and influence their attitudes toward treatment.

Adjust Treatment

Depending on the assessment of asthma control during the visit, the patient's asthma medications are then adjusted accordingly. If a patient's asthma control remains poor despite optimisation of controller medications, first confirm the diagnosis of asthma and exclude other conditions that may mimic asthma (e.g. congestive cardiac failure). Ensure that the patient has been adherent to usage of inhalers and that the inhaler technique is correct. Assess for the presence of modifiable risk factors that may worsen asthma control and treat those accordingly. If all these have been thoroughly evaluated and asthma control still remains suboptimal, we suggest for an early referral to a Respiratory specialist for further evaluation.

(E) SELF MANAGEMENT AND USE OF WRITTEN ASTHMA ACTION PLANS

A written asthma action plan (WAAP) helps to guide patient self-management by providing written instructions on how patients can make small adjustments to their asthma medications based on changes in their level of symptoms. Figure 1 shows a sample of a WAAP. All asthma patients (or their caregivers) should be given one with clear instructions on how to use it.

Figure 1. Written Asthma Action Plan

Symptoms	Medication
WHEN WELL • No asthma symptoms • Before exercise	Regular Controller Treatment **EVERYDAY**: 1. 2. 3. Reliever ____ puffs **ONLY** when necessary
CAUTION If you • Wake at night due to asthma symptoms • Have day time asthma symptoms more than 2 times • Used reliever more then 2 times • Have limited activity or exercise • Have flu like symptoms	**STEP UP** TREATMENT 1. ____ puffs ____ times/day for next 7-14 days. If improved go back to regular treatment. 2. Reliever ____ puffs 4-6 hourly x 3 days **If on Symbicort®** 2-4 puffs at a time Do not exceed 12 puffs/day If improved go back to regular treatment.
EXTRA CAUTION • If **NO** improvement at anytime with the above treatment then add …	Prednisolone 30 mg per day x **5-7** days. **(for Adults)** *(Children should consult Dr. first)*
DANGER **GET HELP WHEN** • Severe shortness of breath • Reliever medicine is not helping • Can only speak in short sentence • Feeling frightened	**SEE YOUR DOCTOR** **DO NOT WAIT** **CALL 995 FOR AN AMBULANCE** Reliever ___ puffs at 10 minutes interval till you get to the nearest Dr. or hospital. Prednisolone 30 mg immediately.
Affix Patient Stickers	Reinforced by: Date:

CONCLUSION

Asthma is a chronic respiratory disease that is often under-recognised and under-treated. Untreated asthma can be fatal and even relatively asymptomatic patients can develop severe life-threatening asthma exacerbations. Morbidity and mortality from asthma are mostly preventable and we should aim to achieve good symptom control and to minimize the risk of future exacerbations for our patients. Most importantly, we need to develop a mindset of "**Zero Tolerance Towards Asthma Deaths in Singapore**."

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LEARNING POINTS

- **Most asthma deaths are preventable**
- **Asthma deaths can be prevented by:**
  - **Early diagnosis of asthma**
  - **Early treatment with inhaled corticosteroids. Avoid monotherapy with short-acting bronchodilators**
  - **Treating asthma as a chronic disease with control-based asthma management, adjusting asthma therapy in the continuous cycle of 1) Treat, 2) Assess control and 3) Adjust treatment**
  - **Early detection of loss of control and treatment of exacerbations.**
- **Asthma fatality can occur in patients with "mild" asthma as patients often over-estimate their asthma control**