MANAGEMENT OF ACUTE ASTHMA IN CHILDREN

D. K. Ng and K Chau, Department of Paediatrics, Kwong Wah Hospital, Hong Kong

The management of acute asthma should aim to prevent death, to relieve hypoxaemia, to normalise lung function as quickly as possible and to avoid future relapse. The basic principles of treatment therefore include early recognition and treatment preferably by working through a written action plan, with emphasis on symptoms and alterations in peak flow rate.

CLASSIFICATION OF SEVERITY

The therapy of childhood asthma should be geared to the severity of the attack at presentation. The severity of a childhood asthmatic episode can be classified as mild, moderate, severe and life-threatening.[1]

A *mild* attack includes cough and a wheeze *without any* of the following features: respiratory distress, cyanosis, tachypnoea, tachycardia, agitation and impaired speech. The peak expiratory flow rate (PEFR) is more than 80% of the predicted value or the best personal value if available for comparison. Pulse oximetry shows above 95% oxygen saturation in room air.

An asthma episode of *moderate* severity refers to evidence in the patient of the use of accessory muscles of respiration, tachypnoea, tachycardia, agitation and impaired speech in joined-up phrases. The PEFR is between 50-80% of the predicted value or of the personal best value. Pulse oximetry is between 91-95% oxygen saturation in room air.[2]

In a *severe* attack the patient is not able to speak through phrases, is not able to feed, and there is worsening of the clinical features listed as findings in a moderate attack. PEFR is less than 50% predicted or personal best.[3] Pulse oximetry is less than 91%. A post-bronchodilator oxygen saturation of less than 91% was found to be the *best indicator* for a severe attack.[4,5]

The presence of cyanosis, drowsiness, a 'silent' chest and bradycardia denote a *life-threatening* attack. There is no value or need to measure *pulsus paradoxus* as it adds nothing to the assessment of severity.[6]

Measurement of blood gases is rarely helpful in the initial management of asthma[1] but it is a good predictor of outcome in severe asthma.[7] In the presence of tachypnoea, a normal arterial carbon dioxide tension (P_aCO_2) indicates severe airflow obstruction; a raised P_aCO_2 level in spite of aggressive treatment should raise the need to consider assisted ventilation. A full blood count may be appropriate in patients with fever or purulent sputum, however a modest leucocytosis is common in an exacerbation of asthma as well as within one to two hours of systemic steroid administration. A chest radiograph should not be carried out as a 'routine' procedure except in those suspected to have an air leak, pneumonia and those who are presenting with the first wheeze.

Treatment

Appropriate treatment requires careful monitoring in addition to an understanding and a reasonable and efficient use of different drugs. Careful monitoring is mandatory to ensure timely intervention should the patient fail to respond to treatment. In this respect, the measurements and observations include respiratory rate, heart rate, PEFR, use of accessory muscles, colour, mental status, duration of the effect of a beta-agonist, pulse oximetry and arterial blood gases.

Heated humidified oxygen should be used either through a nasal cannula or a nasopharyngeal catheter or facial mask to keep a blood oxygen saturation of more than 90%.

The most promising regime is to use *Salbutamol* (5mg/ml) at a dose of 0.01ml/kg/dose (minimum 0.25ml, maximum 1ml)[8] which should be added to normal saline to make up a final volume of 3ml, and driven for three doses by oxygen flowing at 6-8L/min every 20 minutes. This is more effective than 0.03ml/kg/dose every hour.[9] Continuous nebulization of salbutamol (0.1ml/kg/hour) was also found to be beneficial. This drug can also be given by a metered-dose inhaler, with up to ten puffs through a spacer, with or without a mask, and at the rate of one puff every 15-30 seconds for those with asthma of mild or moderate severity. Large volume and small volume spacers are equally effective, and the choice depends on convenience, and patient or parental preference.

For the choice of inhalation system the nebulizer is simple to use and it has the additional benefit of concomitant oxygen delivery and is therefore still the system of choice in treatment of *acute severe* asthma in all age groups, even though several studies have demonstrated that the same end-results can be obtained with other inhalation systems.[10,11]

Other routes of administration include the subcutaneous and the intravenous routes. Evidence for a superior efficacy of subcutaneous terbutaline over the same drug administered by inhalation is lacking. However, intravenous infusion of salbutamol 15mcg/kg body weight over ten minutes in severe asthmatics on their admission to the emergency department was shown to have a shorter duration of the period of oxygen dependency and recovery time that were statistically significant, and without any difference in side-effects.[12]

Ipratropium bromide, an anti-cholinergic agent, was shown to have additional bronchodilator effect.[13] The recommended dosage is 0.5ml (0.25mg/ml) for infants, 1ml for toddlers and 2ml for children over five years. For children older than five years with acute severe asthma the addition of ipratropium, at a dose of 0.25mg every 20 minutes for one hour, was found to be safe; it also resulted in significantly lower hospitalisation rates and better improvement in FEV_1 when compared with the use of salbutamol alone.[13]

Nowadays *corticosteroids* play an important role in acute asthma management and their early use is recommended in moderate to severe asthmatic exacerbations. Corticosteroids do not have any immediate direct effect on pulmonary mechanics in acute asthma: a number of studies have noted a six-hour, or greater, delay from the time of administration

to the onset of a measurable effect on pulmonary function.[14,15] This delay is most likely attributable to the time necessary for the action of corticosteroids on the ß$_2$ –receptor including the synthesis of new receptors, and the reversal of desensitised and downregulated receptors.[16] Corticosteroids should be considered if there is an incomplete therapeutic response or a relapse of symptoms within four hours in the 'moderate' group, and in all those pertaining to 'severe' group.[17]

No difference was demonstrated in terms of efficacy between hydrocortisone, dexamethasone and beta-methasone.[18] Different doses of these steroids were also studied. Marquette *et al*. found no difference between 1mg/kg/day versus 6 mg/kg/day of methylprednisolone in 45 patients.[19] Barnett *et al.*[20] showed a similar admission rate for children with severe asthma that were randomised to receive either oral or intravenous methyl-prednisolone. Given the lesser mineralcorticoid effects of methylprednisolone as compared with hydrocortisone, the former is favoured. The dosage favoured is 1mg/kg every six hours for two days followed by 1-2 mg/kg/day, in two divided doses.[8]

The duration of steroid use depends on the severity and chronicity of underlying inflammation. Tapering is only needed if their use is deemed necessary for more than five to ten days.

No benefit was demonstrated in children admitted with severe asthma from *methylxanthines* and they were not recommended in the Second Expert Panel Report of 1997 in contrast to that of 1991.[8] However, an intravenous infusion of *aminophylline* at the rate of 5mg/kg over 20 minutes, followed by an infusion at 1mg/kg/hour was still recommended by the British Thoracic Society in 1997.[1] Yung *et al*.[21] had studied the use of intravenous aminophylline on severe acute asthma in 163 children who had been treated with salbutamol, steroid and ipratropium. The dosage used was 10mg/kg over one hour, followed by 1.1or 0.7mg/kg/hour for subjects younger than ten years of age, and they found significantly higher oxygen saturations, lower intubation rates, lower clinical scores, higher FEV_1, higher adverse effects of nausea and vomiting, and similar duration of Paediatric Intensive Care Unit stay. This group also found the use of aminophylline helpful in severe / life-threatening asthma attacks.

Magnesium competes with calcium uptake into smooth muscle cells. Thus the infusion of magnesium sulphate, at the rate of 25mg/kg over 20 minutes, was found to improve FEV_1 in adults. Dramatic results were reported in individual cases although Tiffany *et al.*[22] showed no substantial benefit in 48 patients with severe asthma treated. Meta-analysis of the published trials (five in adults, two in children) showed that a magnesium sulphate infusion was significantly better than placebo in producing an improvement of PEFR and a reduction in hospitalisation rate in those with severe asthma. This effect was not seen when all asthma subjects, irrespective of severity, were included in the study.

Chest physiotherapy and *mucolytic agents* are not recommended. The latter may actually worsen the cough and may result in airflow obstruction.[8]

Other treatment modalities

Some other largely unproven treatments are worth mentioning and should be used at the discretion of the attending doctors.

Nebulized *budesonide* was found to have additional benefits when compared to placebo in children with moderate to severe asthma when it was given in addition to oral steroid and nebulized salbutamol.[23]

Heliox is a gaseous mixture produced by the blending of oxygen and helium, and it has one-fourth of the density of air. Manthous *et al.*[24] reported on the use of an 80:20 mixture and demonstrated a reduction in *pulsus paradoxus* and an increased PEFR of 35%. Gluck *et al.*[25] found a significant decrease in peak airway pressure and P_aCO_2 in intubated patients treated with a 60:40 mixture. Sirgi[26] demonstrated a better peripheral deposition of salbutamol using heliox in 80/20 mixture. In spite of such reports its current role is mainly as an adjunct in decreasing muscle fatigue and allowing bronchodilators to work better.

Case reports cited the use of *ketamine* whose effects were thought to depend on a drug-induced increase in circulating catecholamines, direct smooth muscle relaxation, inhibition of vagal outflow and increased bronchial secretion. Howton *et al.*[27] reported a randomised controlled trial in adults of low-dose ketamine (0.1mg/kg bolus followed by an infusion over three hours at 0.5mg/kg). The only significant improvement detected was the patients' subjective scores. The low-dose is necessary to prevent dysphoria in adults although a higher dose might be more effective. As children are less prone to develop dysphoria, a higher dose may be tried in children.

Inhalational anaesthetic agents, including halothane and isoflurane possess bronchodilating properties[28] with isoflurane being the drug of choice as it has fewer side-effects.

Bronchoscopy and *bronchoalveolar lavage* using saline or acetylcysteine have been used in asthma for removal of mucus plugs. However, there is a concomitant increase in airway resistance during the procedure. Manipulation of the airways and the use of acetylcysteine may also result in significant bronchospasm which may further aggravate the clinical condition. This procedure should therefore be reserved for those that responded poorly to pharmacotherapy or those who have atelectasis demonstrable on a chest X-ray.[29]

Acupuncture of three sites, i.e. Dingchuan (neck), Taixi (ankle) and wrist (Kongzui), were found to decrease the exercise-induced fall in FEV_1, FVC and PEFR in a single randomised single-blind study of 19 children.[30] Another randomised, double-blind study[31] of acupuncture utilising a point located at the level of the mid-sternum on the line between nipples in 23 stable asthmatic adults showed no change in FEV_1 or PEFR, before and after acupuncture, although the patients experienced some improvement in quality-of-life measurement. Similar conflicting results were reported by other authors.[32,33,34] The NIH review of acupuncture showed that the evidence for its effectiveness was insufficient and hence this procedure can only be regarded as a possible adjunct treatment. Standardised acupuncture procedures, outcome measures and acupuncturists' qualification are keys to a further scientific assessment of the role of acupuncture in asthma.

Invasive ventilation

The exact moment for instituting intubation is a matter of clinical judgement, although respiratory arrest and circulatory collapse are absolute indications for intubation. Arterial blood gases alone are inadequate as indicators of the need for assisted ventilation. Indications for invasive ventilation include an absence of favourable response to optimal medical

treatment, exhaustion, an altered mental status with confusion, a falling blood pH and a PaO_2 <60 mm Hg.[17,29] Permissive hypercapnia up to 10kPa with pH down to 7.15 is well tolerated and thus controlled hypoventilation is recommended to avoid barotrauma. Most children can be extubated within 48 hours.

In patients with excessive air trapping, mechanical chest compression to assist expiration has been used to reduce hyperinflation while the patient is disconnected from the ventilator. The operator gives a sustained firm bilateral squeeze over the lateral lower rib cage at the end of inflation. The use of this technique should be applied as a last resort.[29]

Pre-discharge management plan

Recovery from an asthmatic attack is a joyful experience for the patients, their parents and the medical staff. It also provides a golden opportunity for appropriate and thorough asthma education for the whole family which should help to decrease unnecessary medical consultation, avoid hospital re-admissions and improve the overall quality of life of asthmatic children.

A pre-discharge home management training programme is advocated. In it the children and their parents are taught the symptoms and signs of asthma, the manner of recognition of a severe asthma attack, home treatment of acute asthma attack, the appropriate regular use of peak expiratory flow metres, the measurement and recording of personal best peak expiratory flow rate, indications for use of asthma reliever medications as well as indications for medical consultation. The programme is best delivered by nurses with specific training in asthma education.[35] Written materials and video recordings would help reinforce the message.

Bernard-Bonnin *et al.*[36] conducted a meta-analysis of published research about such home management training programmes and found no evidence that such programmes are effective in reducing morbidity. They suggested that a more specifically targeted audience with well-defined characteristics, such as disease severity, might be more likely to define benefits from such educational adjuncts. In a randomised single-blind controlled study, Madge *et al.*[35] found that a nurse-led home management training programme reduced the re-admission rate significantly.

CONCLUSION

Among the essential points for an effective management of acute asthma in children are an early recognition of an attack and regular monitoring of the response to treatment. Beta-agonists and a short course of systemic steroids are the cornerstones of the acute management. Other optional medications ipratropium, magnesium sulphate, aminophylline, heliox, ketamine and isoflurane should be reserved to the poor responders.

Recognition of a life-threatening attack is important, and judicious use of invasive ventilation and intensive care is often life-saving. Education about asthma after recovery is the most important step to ensure better control of asthma.

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