Corticosteroid therapy in acute paediatric asthma exacerbations: systemic or inhaled therapy?

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Acute exacerbations are an important cause of morbidity in young children with asthma and may result in recovery shortened, thereby reducing the need for hospital admission.4 Children with severe disease and with an initial suboptimal response to β2-agonist therapy, benefit the most. The beneficial effect is seen within 4 hours of administration of OCS. Early introduction of OCS is most helpful in preschool children with viral-induced exacerbations as the number of wheezy days, emergency room visits and hospital admissions are reduced significantly.5

OCS (prednisone or prednisolone) have excellent bioavailability and are preferred to parenteral therapy because of similar effectiveness at a fraction of the cost.6 Tablets are prescribed for older children. Younger children can also take tablets crushed and mixed with soft food like chocolate syrup or apple sauce.7 Parents often prefer liquid preparations; however, they are bitter and have an unpleasant aftertaste. Effective doses often translate into large volumes which young children may find difficult to retain. The more concentrated solutions could be prescribed to overcome this problem. In the event of vomiting the dose should be re-administered. Palatable liquid preparations will not become available in the foreseeable future.

The optimal dosage of OCS for asthma exacerbations has not been established.1 A prednisone dose of 1 mg/kg/day (as a single daily dose) has been used with good effect in the early intervention of viral-induced exacerbations in preschool children.6 A higher dose of 2 mg/kg/day is indicated in children with an incomplete response to bronchodilator therapy in an emergency care setting.8

The suggested duration of therapy with OCS during exacerbations ranges between 3 and 14 days. The South African Childhood Asthma Working Group (SACAWG) supports a 7-14 day course not exceeding 60 mg/day.5 Tapering of short-course OCS is not necessary.

Intravenous corticosteroids

Only in those patients in whom orally administered steroids are not tolerated or retained should intravenous administration be considered.6

Intramuscular corticosteroids

Methylprednisolone acetate as a single intramuscular injection has been used as an alternative to a 5-day course of OCS. The acetate facilitates slow absorption into the systemic circulation with a longer duration of action. The disadvantages are more frequent systemic side-effects than with a short course of OCS,7 complications at the site of injection and the aversion that children have to intramuscular injections. This option should only be considered when intolerance to oral therapy occurs or when adherence to oral therapy is a real concern.

Inhaled corticosteroids (ICS)

Children, and in particular those under 5 years, suffer from frequent acute exacerbations. The frequent use of short courses of OCS may result in systemic side-effects. The long-term effect of regular short courses of OCS is also not known. Clinicians are therefore reluctant to prescribe short courses of OCS on a regular basis and opt for therapy consisting of a regular bronchodilator and increased doses of ICS or nebulised budesonide. The question that is paramount is whether a higher dose of ICS or nebulised budesonide is as effective as a short course of OCS in acute exacerbations.

Doubling of maintenance ICS doses

The doubling of maintenance doses of ICS, at the onset of an acute exacerbation, is ineffective for the management of asthma exacerbations in children and should not be included in self-management plans.10

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**High doses of ICS**

Gonnet and Lenney\(^\text{11}\) compared the efficacy of placebo to very high doses of inhaled budesonide (1,600 µg/day via spacer with mouthpiece or 3,200 µg/day via spacer with mask) during viral-induced acute exacerbations in pre-school children. Treatment was continued until symptoms resolved or for 7 days. A reduction in night-time wheeze was demonstrated during the first week but no modification in cough, bronchodilator use or duration of symptoms was noted. Another study\(^\text{12}\) in preschool children, but this time not specifically during viral-induced exacerbations, using beclometasone 2,250 µg/day showed similar results. Neither of these studies demonstrated a reduction in the need for OCS or hospital admission rates.

Volovitz \textit{et al.}\(^\text{13}\) on the other hand showed a reduction in the need for OCS and hospital admission rates when very high doses of ICS (starting at up to 1,600 µg/day of budesonide and tapered over 8 days) were used during acute exacerbations in children 1-14 years of age. These patients were predominantly older well-controlled asthmatics with mild to moderate persistent disease, compared with the young asthmatic patients studied by Gonnet \textit{et al.}\(^\text{11}\) who had repeated viral-induced acute exacerbations. Their exacerbations did not seem severe as none of them needed hospital admission.

**HIGH DOSES OF ICS COMPARED WITH OCS**

There are very few studies comparing high doses of ICS with short courses of OCS therapy during exacerbations in young children. Inhaled budesonide (delivered via turbuhaler with a starting dose of 1,600 µg/day and reduced by 25% on alternate days) was compared with oral prednisone (starting dose of 2 mg/kg/day and reduced by 25% on alternate days) in 6-16-year-old children with moderately severe acute exacerbations.\(^\text{14}\) ICS were as effective as OCS. Studies in adults,\(^\text{15,16}\) again using 4-5-fold higher doses of ICS than for maintenance therapy, also demonstrated ICS to be as effective as OCS. Findings to the contrary were reported in 5-17-year-old children suffering from severe exacerbations, treated with fluticasone (2,000 µg/day) or OCS.\(^\text{17}\)

High doses (4-5-fold higher than maintenance treatment) of ICS seem to be as effective as OCS in controlling moderate to severe exacerbations, but not for very severe exacerbations.\(^\text{18}\) The use of high-dose ICS during acute exacerbations remains controversial. While the Global Initiative for Asthma (GINA), in an international review of the asthma literature published in 2002, alludes to the possibility of high-dose ICS therapy,\(^\text{19}\) a more recent review\(^\text{20}\) concludes that OCS should be the treatment of choice for exacerbations in young children and high doses of ICS should only be considered for mild exacerbations. Young children with viral-induced exacerbations should receive OCS rather than ICS.

**Pitfalls of therapy with ICS during acute asthma exacerbations**

Insufficient lung delivery of inhaled therapy is common in children. This is a problem during acute exacerbations especially in the very young, because of the smaller calibre of the airways and the presence of copious airway secretions. Ineffective use of the delivery device may compound the problem.

The medication itself and the delivery system may also contribute to deficient lung delivery. ICS for nebuliser use come in a suspension formulation, which requires specific nebuliser properties. Delivery to the small airways is therefore less reliable than for the water-based bronchodilator solutions. OCS should be administered if ICS lung delivery cannot be guaranteed.

**PRINCIPLES FOR CORTICOSTEROID THERAPY DURING ACUTE EXACERBATIONS**

**Initiate therapy early**

Children who do not respond to an initial dose of a rapidly acting β\(_2\)-agonist or with a response that is not sustained or with a history of severe exacerbations should receive corticosteroid therapy as soon as possible, preferably administered at home.

This practice reduces the number of wheezy days, acute exacerbations, emergency room visits and hospital admissions in preschool asthmatics known to develop repeated and severe viral-induced exacerbations.\(^\text{4}\) OCS should be administered at the onset of upper respiratory symptoms (even before the onset of wheezing).\(^\text{5}\) The inflammation of viral-induced exacerbations can progress substantially from the onset of infection to arrival at the emergency room. This subgroup of asthmatics should be identified and equipped with the necessary education on how to effectively deliver a bronchodilator and be in possession of a prescription for OCS in order to initiate early, preventative treatment.\(^\text{1}\) Clinical assessment by their medical practitioner should follow to monitor disease progression/resolution and to keep track of OCS use.

**Select the most appropriate route of corticosteroid delivery at the correct dose**

OCS therapy is more convenient to use and is usually more successful than ICS. Furthermore OCS will benefit all children with acute asthma exacerbations.

The treatment of exacerbations should however be determined by the most effective option for the individual patient. In patients with less severe exacerbations ICS may be more beneficial and safer than OCS, provided that the child is capable of using the prescribed inhalation system effectively. ICS should also be considered if repeated courses of OCS have been used in the past and the development of systemic complications becomes a concern. The unavailability of OCS at the onset of an exacerbation, previous important adverse events related to OCS (e.g. psychiatric reaction), and brittle diabetes are additional indications for ICS. Importantly, ICS should be started early at 4-5 times the dose used for maintenance therapy.

OCS are indicated for more severe exacerbations, in children where effective lung delivery of ICS cannot be guaranteed and in young children with acute viral-induced exacerbations. Prednisone or prednisolone can be used at 1-2 mg/kg once daily.

**Introduce maintenance ICS during acute exacerbations**

It is mandatory that children with acute exacerbations who are treated with OCS receive maintenance therapy in the form of ICS as well. A higher dose of ICS should be prescribed at this time and tapered according to the SACAWG guidelines.\(^\text{9}\) This practice effects a substantial reduction in the relapse rate of asthmatics discharged from an emergency department.\(^\text{21}\)

**CONCLUSIONS**

The most important modality of treatment for acute exacerbations is prevention. Educating caregivers and afflicted children, and adhering to published guidelines for the management of chronic childhood asthma, should optimise the quality of ambulatory care.

Acute asthma exacerbations will however still occur. An individualised written management strategy, to be implemented at the onset of exacerbations, should therefore be in place for every child. Optimal strategies
involving early onset of treatment with correct doses of OCS (and, in selected cases, ICS) will reduce the morbidity, mortality and total cost of asthma care.

REFERENCES


CHAIRMAN’S REPORT

This issue of the journal has been published to coincide with the Dare to Care Congress, a joint congress of ALLSA, SATS, and the Critical Care Society of Southern Africa. ALLSA has always endeavoured to work with societies that share a common interest. This joint congress is an attempt to work collaboratively and to bring together healthcare professionals with common interests.

The ALLSA programme consists of a comprehensive overview of allergology. There are many sessions on asthma with specific emphasis on the wheezy infant. Included in the programme are sessions on upper airway allergy and its impact on the lower airways. We have sessions on food allergy, anaphylaxis, atopic eczema and immunomodulation of allergic diseases.

Our local and international guest speakers are experts in their fields. Prof. Hugh Sampson has worked extensively on food allergy and has undertaken cutting edge research in this field. Dr Le Souef has published extensively on the epidemiology of allergic disease and Dr Lars Jacobsen has done groundbreaking work on immunomodulation of allergic diseases using immunotherapy. We welcome our overseas guest to our country and look forward to their presentations.

Dr Heather Zar and Dr Alan Puterman have worked tirelessly organising this meeting on behalf of ALLSA. I would like to thank Heather and Alan for their hard work and sacrifice.

The elections for the ALLSA Excom have been held. The following candidates were elected: Prof. Cas Motala, Prof. Matt Haus, Dr. Heather Zar, Dr Sharon Kline, Dr Elvis Iruen and Dr Adrian Morris. I will remain on Excom as past-Chairman. Three more members will be co-opted onto the Excom and will be announced at the ALLSA AGM to be held at the congress.

My term as chairman has been a challenging but enjoyable one and I thank all the ALLSA members for their support.

Dr Ahmed Manjra