



CLINICAL PRACTICE

Asthma – is survival good enough?

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Advances in asthma management, particularly the introduction of controller medication of which inhaled corticosteroids are the most important, has resulted in a steady decline in asthma mortality in most countries.^{1,2} This is usually accompanied by a decline in episodes of near-fatal asthma attacks and hospitalisations, and a reduction in other indicators of asthma morbidity.¹ These gains have led to a shift in thinking on the management of asthma, away from simply preventing death and hospitalisations, toward achieving and maintaining sustained control of all clinical features. This includes absence of daytime and night-time symptoms, no limitation of activities, no rescue β_2 -agonist use and normal lung function.³

Recent research has confirmed that this goal is achievable in a large proportion of patients with asthma of all severities,³ and new strategies have been devised to maintain these gains using the lowest effective treatment doses.^{4,7} Cost-benefit analyses have confirmed the efficacy of this approach in that a large proportion of asthma costs result from unscheduled visits and use of health care resources, such that it has recently been suggested that we cannot 'afford to not control asthma', even when initial maintenance therapy appears to be more costly.⁸

The so-called 'control-driven' approach to asthma management forms the theme of latest versions of international guidelines including the 2006 revision of the Global Initiative for Asthma (GINA).^{9,10} This approach sets as the goal of treatment, complete control of the clinical features of asthma. Both initial treatment and subsequent adjustments to treatment are directed towards achieving this goal. Following an approach identical in concept to that for other chronic diseases like diabetes and hypertension, the new asthma management and prevention programme recommends an initial assessment

of asthma control, treatment to achieve control and monitoring and adjustment of therapy to maintain control.

This approach differs from that in previous guidelines in that the latter tended to define degrees of asthma severity and to recommend treatment accordingly. The aim was to prevent serious morbidity and mortality rather than to offer a normal quality of life and activities free from the limitations of asthma. Treatment was therefore selected according to an arbitrary definition of severity, with the aim of improving rather than controlling disease, and because the consequences of uncontrolled asthma have not been perceived to be as important or dramatic as those of uncontrolled diabetes or hypertension, health care professionals and even patients were accepting of persistent limitation. This approach is no longer considered acceptable.

Assessment of control has been hampered by lack of a simple means of monitoring asthma. There is a need for regular, frequent assessments of control, using a simple validated instrument because health care professionals often underestimate the symptoms and limitations experienced by their patients, and patients themselves or caregivers of asthmatic children are often unaware of how their lives are limited and activities curtailed by their asthma. Objective measures of asthma control equivalent to a blood glucose or glycosylated haemoglobin in diabetes are needed. A number of asthma control measures have now been devised and validated and are being promoted both for self-assessment by patients with asthma, and for use by their caregivers and/or doctors.⁹ Assessment of control requires a composite measurement of clinical indicators. Such asthma control measures may also be useful as a guide to adjusting therapy to maintain maximal control with minimum doses of medicines. These include step-down routines, as once asthma is controlled, reductions may be safely carried out in the majority of patients.^{5,9}

Recently, a novel approach to making these adjustments to treatment has been proposed. Termed the single inhaler for maintenance and relief therapy (SMART) approach, this method only applies to those patients using a single combination inhaler containing the inhaled steroid budesonide and long-acting β_2 -agonist, formoterol, in a fixed combination.^{6,7} With this approach, patients take a regular daily dose of the combination as preventer (usually twice daily), but are able to take an additional dose or more at the first symptom of deterioration. This approach is possible as formoterol is a long-acting bronchodilator with a rapid onset of action. Several large studies^{6,7} of adult asthmatics have confirmed that

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early intervention in this way may prevent development of exacerbations and permit maintenance of control at remarkably low levels of controller treatment. Further studies of children and preschool children are needed as there is no separate published paediatric data on this strategy, and long-acting β_2 -agonists are not approved for use in preschool children.

How do these promising developments relate to South Africa? Firstly, current epidemiological data suggest that asthma is very common and increasing in prevalence. In recent surveys, utilising international methodology that permits comparisons with other countries (the International Study of Asthma and Allergies in Childhood (ISAAC) surveys)¹¹ the 12-month prevalence of asthma among 13 - 14-year-old South African adolescents was 20.3% higher than either the African (15.4%) or the global (13.7%) average. Moreover, an increase in asthma prevalence from 16.1% to 20.3% occurred over a 7-year period.¹¹⁻¹³ More alarming, however, was that in surveys of asthma mortality, South Africa ranked 4th or 5th highest in the world, whether expressed as deaths as a percentage of the total population or of the asthma population.¹³ Further analysis of the Cape Town ISAAC phase 1 data demonstrated that while asthma was more prevalent in affluent households, the burden of morbidity and mortality was greatest in households with low socio-economic status.¹⁴ Although many factors operating in impoverished communities contribute to the suboptimal care of children with chronic diseases like asthma, access to and the availability of controller medication remains one of the most important preventable factors.¹⁵

Although most South African asthma data relate to the Western Cape, some studies provide indicators of the situation in other parts of the country. Dating back to earliest observations by Wesley *et al.* on the differences of asthma admissions among black, Indian and white children in Durban, the rate of asthma events has been known to be lower among black children.¹⁶ However, in 1979, van Niekerk and colleagues demonstrated that this lower rate applied especially to black children from rural areas,¹⁷ their study showed that the prevalence of exercise-induced broncho-constriction in Xhosa children in Cape Town (3.17%) was 22 times higher than that of age-matched rural children in the Transkei (0.14%). Recent prevalence studies of asthma among school children in the harbour basin of Durban and in Thokoza, Gauteng, using different methodologies, have confirmed high levels of asthma, at least equal to those in Cape Town.^{18,19} Two additional studies of Xhosa children, similar to the original study by van Niekerk *et al.* have reported prevalences of 34% and 14.5% in one study, and 17% and 8.6% in urban and rural black children, respectively.^{20,21} Thus there is a rising asthma prevalence in both urban and rural children, with a reduction in the urban-rural gradient.

Under-recognition and under-treatment of a large proportion of both children and adults with asthma is a consistent feature

in local and international studies of the global burden of asthma. Large-scale surveys performed on several continents have confirmed unnecessary morbidity in the form of limitation of activities, absenteeism from work and school, nocturnal waking and hospitalisations resulting from inadequate recognition and treatment of asthma.²² In South Africa, even in patients with access to medication, the persistence of symptoms is unacceptably high. In a sample of 710 asthma patients surveyed in 1999 by Green and Rens,²³ although most were on inhaled corticosteroids, 46% described daily limitation of activity and an alarming 37% reported night-waking due to asthma on 4 or more occasions per week. Only 35% had not missed work or school in the preceding year and 16% reported a hospital admission during the previous year. There is an urgent requirement for increasing awareness of the diagnosis of asthma and of the use of effective controller regimens with long-term monitoring and follow-up. Although inhaled corticosteroids form part of the essential drug list and are available in most community health centres, under-prescribing, incorrect use or an erratic drug supply may be causes of preventable asthma-related morbidity and mortality. Furthermore there is a need to address cultural and language differences in defining asthma symptoms and a need to develop appropriate control measures and patient education for different patient populations.

Management of asthma in South Africa therefore appears to be suboptimal. How should the situation be addressed?

First must be the revision of the goals of asthma management toward controlling disease rather than simply avoiding hospitalisations or death. Erratic or partial treatment and improved access to emergency facilities for asthma exacerbations may have a modest effect on mortality, but will have little or no effect on the medical and societal burden of asthma.

What is required is a sustained co-ordinated emphasis on management of chronic respiratory diseases in which the diagnosis and management of asthma with effective controller drugs remains an important priority. The importance of chronic respiratory disease has recently attracted renewed interest and was identified in May 2000 as an important health priority particularly in developing countries by the World Health Assembly of the World Health Organization. This led to the creation and launch in March 2006 of the Global Alliance Against Respiratory Diseases (GARD). Among the GARD priorities are to propose a step-wise and integrated programme of prevention and control of preventable chronic respiratory allergies, with a special focus on developing countries, with asthma as one of the priority diseases. This development is timely in the light of the great strides that have been made in asthma management. For South Africa, the challenge is to ensure that asthma is not forgotten or eclipsed by the heavy burden of infectious respiratory diseases. Priorities are the



need for surveys on the morbidity and mortality of asthma in all provinces among both adults and children, the revision of guidelines in the light of the international trends mentioned above, patient and health care provider education and improved access to and use of controller therapy. In the public sector, an approach with some promise is the use of integrated guidelines in primary care that increase awareness and simplify asthma management and the incorporation of guidelines for management of childhood wheezing into the South African adaptation of the Integrated Management of Childhood Illness approach.²⁴ South Africa already has an infrastructure on which to build – existing guidelines for childhood and adult asthma, an essential drug list that includes inhaled corticosteroids, and a national asthma education programme. We have the tools to control asthma effectively – the challenge is to achieve widespread implementation and use of a control-driven strategy.

- Haatela T, Tuomisto LE, Pietinalho, *et al*. A 10-year asthma programme in Finland: major change for the better. *Thorax* 2006; 61: 663-670.
- Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59: 469-478.
- Bateman ED, Boushey HA, Bousquet J, *et al*. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control Study. *Am J Respir Crit Care Med* 2004; 170: 836-844.
- Bateman ED, Bousquet J, Busse WW, Clark TJH, Pedersen SE on behalf of the GOAL Investigators Group The correlation between asthma control and health status: the GOALstudy. *Eur Respir J* 2007 (in press)
- Bateman ED, Jacques L, Goldfrad C, Aienza T, Mihaescu T, Duggan M. Asthma control can be maintained when fluticasone propionate/salmeterol in a single inhaler is stepped down. *J Allergy Clin Immunol* 2006; 117: 563-570.
- O'Byrne PM, Bisgaard H, Godard PP, *et al*. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *Am J Respir Crit Care Med* 2005; 171: 129-136.
- Rabe KF, Atienza T, Magyar P, Larsson P, Jorup C, Lalloo UG. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study. *Lancet* 2006; 368: 744-753.
- Bateman ED. The economic burden of uncontrolled asthma across Europe and the Asia Pacific region: can we afford to not control asthma? *Eur Respir Rev* 2006; 15:1-3.
- Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. Workshop Report. *MCR Vision* 2006; 1: 1-92.
- Li JT, Oppenheimer J, Bernstein IL, Nicklas RA for the Joint Task Force Reviewer. Attaining optimal asthma control: A practice parameter. *J Allergy Clin Immunol* 2005; 116: S3-S22.
- Asher MI, Montefort S, Bjorksten B, *et al* and the ISAAC Phase Three Study Group. Worldwide trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368: 733-774.
- ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema. *ISAAC. Lancet* 1998; 351: 1225-1232.
- Zar HJ, Stickells D, Toerien A, Wilson D, Klein M, Bateman ED. Changes in fatal and near fatal asthma in an urban area of South Africa from 1980-1997. *Eur Respir J* 2001; 18:33-37.
- Beasley R. The Global Burden of Asthma Report, Global Initiative for Asthma (GINA). 2004. <http://www.ginasthma.org> (last accessed 7 February 2007).
- Poyser MA, Nelson H, Ehrlich RI, *et al*. Socioeconomic deprivation and asthma prevalence and severity in young adolescents. *Eur Respir J* 2002; 19: 892-898.
- Wesley AG, Clyde JH, Wallace HL. Asthma in Durban children of three racial groups. *S Afr Med J* 1969; 43: 87-89.
- van Niekerk CH, Weinberg EG, Shore SC, *et al*. Prevalence of asthma: a comparative study of urban and rural Xhosa children. *Clinical Allergy* 1979; 9: 319-324.
- Jack C, Naidoo R. Asthma in KwaZulu Natal. *South African Respiratory Journal* 2006; 12: 19-22.
- Mashalane MBN, Stewart A, Feldman C, Becker P, de Charmoy S. The prevalence of exercise-induced bronchospasm in nine and ten year old children at schools in Thokoza. MMed thesis report, University of the Witwatersrand, 2005.
- Steinman HA, Donson H, Kawalski M, Toerien A, Potter PC. Bronchial hyper-responsiveness and atopy in urban, peri-urban and rural South African Children. *Pediatr Allergy Immunol* 2003; 14: 383- 393.
- Calvert J, Burney PGJ. Increase in prevalence of exercise induced bronchospasm in a rural and urban population of African school children. *Current Allergy and Clinical Immunology* 2003; 16: 117.
- Rabe KF, Vermiere PA, Soriono JB, Maier WX. Clinical management of asthma in 1999: The Asthma Insights and Reality in Europe (AIRE) Study. *Eur Respir J* 2001; 16: 802-807.
- Green RJ, Rens H. The hidden cost of asthma. *South African Respiratory Journal* 2004; 10: 8-12.
- Fairall LR, Zwarenstein M, Bateman ED, *et al*. Effect of educational outreach to nurses on tuberculosis case detection and primary care of respiratory illness: pragmatic cluster randomised controlled trial. *BMJ* 2005; 331:770-754.