

ICS and LABAs for the treatment of chronic asthma in adults and children aged 12 years and over

Personal statement:

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Personal standpoint

I have prepared this submission from my standpoint as a primary care clinician and researcher. I have extensive personal experience of treating asthma both in primary and secondary care clinical settings. I am in receipt of Asthma UK Senior Research Fellowship and have a programme of research aimed at understanding and improving the diagnosis and management of asthma in the community. This statement will be primarily directed to asthma management in a primary care setting.

Background

Asthma is a common clinical problem in General Practice and every GP will come across patients with asthma on a very regular basis. Most asthma is diagnosed and managed in the community, and the cases which reach secondary care are frequently severe, complicated and atypical. Much routine asthma care is now delivered by (hopefully suitable trained!) asthma nurses working to agreed protocols in dedicated clinics in the community. It is aimed to provide structured care for asthma by seeing and assessing patients on at least an annual basis, and proactive asthma care is encouraged in the 'performance related' Quality and Outcomes Framework' payments in the new GP contract. Acute asthma care will often however occur in emergency and out-of-hours settings, and decision making for maintenance treatment will not infrequently occur in this setting rather than in the planned clinic environment.

The BTS (now BTS/SIGN) guidelines for the management of asthma have been present for a number of years and have acted as the basis of GP asthma care for the last decade. They were the first disease specific guidelines that became available to GPs and although GPs have subsequently complained of guideline overload and 'fatigue', the asthma guidelines have generally been well received and have been most influential in determining treatment pathways and influencing prescribing decisions.

The message that there is an inflammatory basis to asthma so a need for anti-inflammatory treatment with inhaled corticosteroids has been well assimilated, and GPs and asthma nurses do understand that in all but the mildest cases, asthma needs treatment with inhaled corticosteroids. The 'flat' and individually variable dose-response relationship between ICS dose and clinical outcome has been less well assimilated and there is a tendency to think that if some is good more must be better, which is not necessarily the case with ICS. For most patients, clinical responses (measured in various ways) peak at low to moderate doses, and higher doses only increase the adverse risk profile. The arrival of long acting beta agonists and the research showing good outcomes associated with the use of this class of agent in patients uncontrolled on ICS alone has been a slightly difficult concept and message for GPs to take on board (in view of the inflammatory paradigm) but has been heavily marketed by the pharmaceutical industry and has been widely taken up. When to add in LABAs and in which patients has been less clear, with wide variations in practice between GPs. The process of care and outcomes of care have both shown evidence of improvement over the last 10 years (although with considerable local variations), and GPs probably diagnose and treat asthma better and more effectively now than in the past. There is however still a major burden of potentially avoidable morbidity related to asthma and it is possible that the improvements in outcome seen in the 1990s have reached a plateau and that there is a need to re-think asthma care provision to meet the still considerable un-met need. The model of nurse-run proactive asthma clinics and structured asthma care is very effective and suitable for many patients but does not meet the needs of all. Non-compliance with treatment and non-attendance for routine asthma care are common, and asthma outcomes are worse in disadvantaged populations and ethnic sub-groups. Teenagers and young adults and those with psycho-social problems have poor asthma outcomes, and often don't seem to find current management paradigms appealing; may high-risk patient receive much of there care in emergency and out-of hours settings.

There are now numerous different inhaled preparations for the treatment of asthma, with different drug classes, different molecules within a class and different delivery systems for the same medication. Fixed dose combination inhalers have arrived with a bang and have been heavily marketed in General Practice. The BTS/SIGN asthma guidelines do not specify which of the many therapeutic options is the best for the individual patient. Different preparations have different costs and health resource implications, with metered dose inhalers being generally the cheapest devices. However, poor co-ordination and poor inhaler technique are common in community practice, and poor delivery of active drug may be associated with treatment failure. Compliance is a major problem with regular prophylactic treatment, particularly with ICS, where patients may have excessive fears of steroid-related adverse events.

GPs come under pressure from several directions affecting treatment decisions for asthma; they are keen to earn QOF points, they are under pressure from prescribing advisor to limit prescribing costs, they are in receipt of marketing initiatives from the pharmaceutical industry, they may attend educational

initiatives and be aware of current research that may influence management decisions, and patient preference and patient fears and misunderstandings impact directly on them. They are keen to provide good quality care but may be confused as to what is the right thing to do with mixed messages coming to them from different sources.

ICS

ICS are absolutely fundamental to GP asthma management and there is a powerful body of evidence supporting the use of this class of agents in asthma. Overall use of ICS has improved, but patient fears remain a significant factor and many asthmatics harbor fears of side effects and loss of efficacy over time with long-term ICS use. The safety profile of ICS is very good in lower doses but there are concerns with the use of higher doses particularly over longer periods of time. There has in the past been a perception amongst some GPs that ICS are completely safe and it is possible that excessive doses have been used. Some patients undoubtedly do however benefit from higher doses (there is considerable individual heterogeneity of response to ICS amongst individuals and factors such as smoking may promote ICS resistance) but studies indicate that many patients can be 'stepped down' in ICS dose without any loss of control. It may be that GPs have been good at increasing doses to gain control but less assiduous about stepping down once control has been achieved. There are now a number of different steroid molecules available through a number of different delivery systems. There is a difference in potency between different molecules and indeed the same molecule may have differing potency with different delivery systems (eg beclomethasone via CFC containing and CFC free MDIs) and this may create confusion and inappropriate dosing. Some of the newer steroid molecules such as ciclesonide and mometasone have been claimed to be 'softer', i.e. to have lower systemic bioavailability and so to cause fewer local and systemic side effects, with some data to support these claims; the relevance of this to community practice remains to be established but these newer and generally more expensive agents may have a role in some patients, eg those needing higher doses for longer times.

LABA

A powerful body of research (mostly industry sponsored) has generally shown better outcomes in patients uncontrolled on standard doses of ICS who have a LABA added to those who have the dose of ICS increased, and this has led to a great increase in the use of this class of drugs, which have been heavily marketed. GPs have certainly found them to be very effective in asthma, and prescribe them widely as stand-alone or as combination inhalers. The LABA safety data from controlled trials has been good but more recently safety concerns have arisen from post-marketing studies (mainly in the USA). There is general agreement that LABAs should never be used without ICS in asthma, and their license specifies this; however, there is evidence that due to differential non-compliance with ICS treatment they are used alone by some patients in 'real life' settings. There may be some sub-groups (e.g. those with specific genotypes of

the B2 adrenoreceptor) who don't do well with LABAs, but at the moment there is a lack of clinical markers to detect such patients. The use of combination inhalers (ICS-LABA) gets around the problem of differential compliance and seems to be effective for many patients. Patients and GPs seem to like the simplicity and easily perceived effectiveness of combination inhalers and this has increased their popularity with both. There has been tendency for them to be used ever earlier in asthma care, and they are now not infrequently prescribed as the 'first-line' preventer inhaler by some GPs. This may however put some patients at risk of adverse outcomes, and it's likely that most patients can be controlled on ICS alone.

Cost Issues

GPs are under pressure to limit prescribing costs and the cheapest preventative treatment for asthma is currently beclomethasone via a metered dose inhaler. However the frequent changes in the cost of different inhalers, and the looming CFC transition issue also makes this an area in which cost changes are occurring constantly. There is a body of health economic data stressing that much of the costs of asthma relate to poor control, so cheaper inhalers that are either poorly used or not adhered to may result in higher overall costs if control is poor. Most GPs and nurses would feel that a variety of devices and preparations are needed and involving patients in decision making is good idea.

Conclusion

This is a complex area with many different factors involved. From the GP standpoint, issues such as patient education, patient and GP preference, adherence and inhaler technique are of crucial importance, and are often not addressed in classical RCTs and standard evidence based medicine approaches. There is a need for more pragmatic evidence form community based studies. Asthmatics are heterogeneous and it is unlikely that a 'one size fits all' approach will suit all patients. Perhaps the best we can do is advise on the order in which different therapeutic approaches should be attempted. As asthma is a chronic condition, safety is important and rare and long-term adverse events need to be considered. The economics of asthma are complex and costs of exacerbations need to be captured.