Ensuring Quality Use of Medicines – Engaging with PBMs and PMBs

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INTRODUCTION

This postscript to the Quality Use of Medicines series of reviews will look back at the principles put forward in the first article, while considering how these should be deployed by the family practitioner in the current practice milieu.[1] The articles in the series have tried to convey how the application of evidence can promote the "therapeutically sound and cost-effective use of drugs" – what the World Health Organization (WHO) calls the "rational use of medicines".[2] The approach suggested in that first paper was the WHO "P-drug" process – a systematic way to select and apply medicines, taking into account the efficacy, safety, suitability and cost of different options.[3] Can this process help the individual practitioner to ensure the quality use of medicines in the face of changing circumstances? ***(SA Fam Pract 2004;46(1): 43-46)***

Changing circumstances

The implementation of a number of health policy choices is beginning to impact upon individual family practitioners. Apart from the rapidly changing evidence base for family practice itself, the development of new medicines, new diagnostic tests and new guidelines from a wide variety of "authoritative" sources, the practitioner must also keep abreast of changes in the marketplace.

Two acronyms should by now be familiar – PBMs and PMBs. Both have been brought into sharper focus by the extension, in January 2004, of the "prescribed minimum benefits" (PMBs) to include 25 chronic conditions, treated predominantly in the ambulatory care setting. The full list can be obtained from the Council for Medical Schemes web site.[4] The idea behind the PMBs is explained by the Council – they "were introduced into the Medical Schemes Act to ensure that members of medical schemes would not run out of benefits for certain conditions and find themselves forced to go to state hospitals for treatment". Critically, the law expects the medical scheme to cover the "diagnosis, treatment and care" of these conditions, including the supply of medicines, "in full, without co-payment or the use of deductibles" from the general risk pool and not from any form of medical savings account. The Council views this as positive: "The inclusion of the 25 chronic conditions in the list of PMBs is a major step towards helping people who have struggled to pay for their treatment of chronic diseases, and have increasingly had to dip into their own pockets for this treatment". However, it does recognise the potential danger of this move: "In order to contain the costs of providing such cover to you, certain measures have been put in place to ensure that schemes can cover those members who need it, without putting the scheme at financial risk".

Apart from the use of "designated service providers", the Council has indicated which other measures may be used to limit the financial risk to the scheme, particularly in terms of the cost of the medicines to treat these 25 chronic conditions, and which may not be used: here is how they explain this to the public:

- "The minimum standards of treatment for all prescribed minimum benefit conditions have been published in the Government Gazette, and are known as treatment algorithms (benchmarks for treatment). Your scheme may decide what treatment it will pay for for each chronic condition, but the treatment may not be below the standards published in the treatment protocols".
- "Your scheme may draw up what is known as a formulary - a list of

safe and effective medicines that can be prescribed to treat certain conditions. The scheme may state in its rules that it will only cover you if your doctor prescribes a drug on that formulary. Often the medicines on the list will be generics - cheaper copies of the original brand name drug. If you want to use a brand name medicine which is not on the list, your scheme may refuse to pay for that medicine, or it may foot only part of the bill and you will have to pay the difference between the price of the medication you use and the one on the formulary. If you suffer from specific side effects from drugs on the formulary, or if a substituting drug on the formulary with one you are currently taking affects your health detrimentally, you will be able to put your case to your medical scheme and ask the scheme to pay for your medicine. Generally, however, it is likely that the scheme will expect you to stick to the medication on the formulary".

- "Some schemes, especially those that have appointed state hospitals as their designated service provider, are suggesting that members who do not want to use the designated service provider, or members who want to take medication not included on the scheme's formulary, can use their savings accounts to pay for this medication. The Council for Medical Schemes regards this as a contravention of the law".

To some this may sound the death knell of independent practice, devoted solely to the care of the individual. In contrast, those with a more "public health" bent may recognise positive spin-offs, for example improving quality by removing unwarranted variation in treatment, improving the application of evidence-based guidelines. One thing is certain though – a degree of power has shifted from the individual practitioner to persons and mechanisms collectively known as "managed care". One of these is the mechanism of "pharmaceutical benefit management" (PBM). PBMs in South Africa are generally part of medical aid administrators' pack of services to the individual medical schemes. Unlike in the United States, they have not been as closely allied to pharmaceutical manufacturers, and therefore presumably not as prone to perverse behaviour.[5] US commentators have characterised them as having to take "the tough decisions that no one wants to take".[6] The activities of PBMs, and managed care in general, have been strictly constrained in the Regulations to the Medical Schemes Act, published on 4 November 2002.[7] A policy document on Managed Care was issued by the Council in 2003.[8] Two definitions, from the Regulations and repeated in the policy document, are important: "**'evidence-based medicine'** means the conscientious, explicit and judicious use of current best evidence in making decisions about the care of beneficiaries whereby individual clinical experience is integrated with the best available external clinical evidence from systematic research" and "**'managed health care'** means clinical and financial risk assessment and management of health care, with a view to facilitating appropriateness and cost-effectiveness of relevant health services within the constraints of what is affordable, through the use of rules-based and clinical management-based programmes".

The interaction between practitioners and managed care organizations has also been covered by the Health Professionals Council's "Policy Document on Undesirable Business Practices".[9] Some of the principles espoused may not be attainable – that "[P]rofessional independence should be inviolate" seems unrealistic. While medical involvement in guideline development is certainly important ("The medical protocols, clinical guidelines and review criteria used by medical schemes and managed care organisations must be developed by doctors according to scientific criteria"), it is probably unrealistic to expect that cost will not be an issue at some point ("These guidelines should not be dictated or influenced by managers of HMO organisations whose primary objective is cost-saving"). However they were arrived at, the basic treatment protocols (algorithms) have been published already.[10] Are they overly prescriptive? Will they make it impossible for a family practitioner to practise good quality medicine?

Engaging – an example

As an example, I have used some of the data presented by students in the Master of Clinical Pharmacology programme at the University of Natal. In the June 2003 examinations for a second year module, the following question was posed: "You have been contracted by a medical scheme to help it develop a rational, legal and cost-effective approach to the provision of medicines to cover one of the Chronic Diseases now listed as a Prescribed Minimum Benefit – ulcerative colitis. Your first task is to help decide which of the competing medicines available on the South African market should be made available for the initial (i.e. in the face of "active" disease) and continued (i.e. in remission) management of proctosigmoiditis. For active disease the Council for Medical Schemes' algorithm lists "oral 5-ASA's or 5-ASA suppositories/enemas and/or corticosteroid enemas". For maintenance of remission it lists "oral 5-ASA's or 5-ASA suppositories". The medical scheme staff have noted that Salazopyrin® is apparently a lot cheaper than the newer 5-ASAs, such as Asacol® and Dipentum®, and want to make only the older version available. By reference to the available evidence, advise your clients on whether the newer 5-ASAs (mesalazine or olsalazine) are any better than the original

sulphasalazine – take into account issues of efficacy, safety, suitability and cost (in the private sector only)". This formed the bulk of the 5-hour open-book examination. Students were given access to the Internet and any available standard texts and literature.

Suppose this was reversed – a family practitioner might be confronted by a managed care protocol that specified sulphasalazine (SASP – a pro-drug, with 5-aminosalicylic acid bound to sulfapyridine) as the only product available for the management of this condition. Suppose the patient has been treated for some years by the same family practitioner and has used both SASP and the newer 5-aminosalicylic acid (5-ASA) products. While she tolerates maintenance doses of SASP, she claims not to be able to tolerate the higher doses used for induction of remission. How could evidence be used to back up an alternative choice?

The relevant part of the algorithm is shown in Box 1, starting from the diagnosis of the condition and differentiating this from extensive colitis.

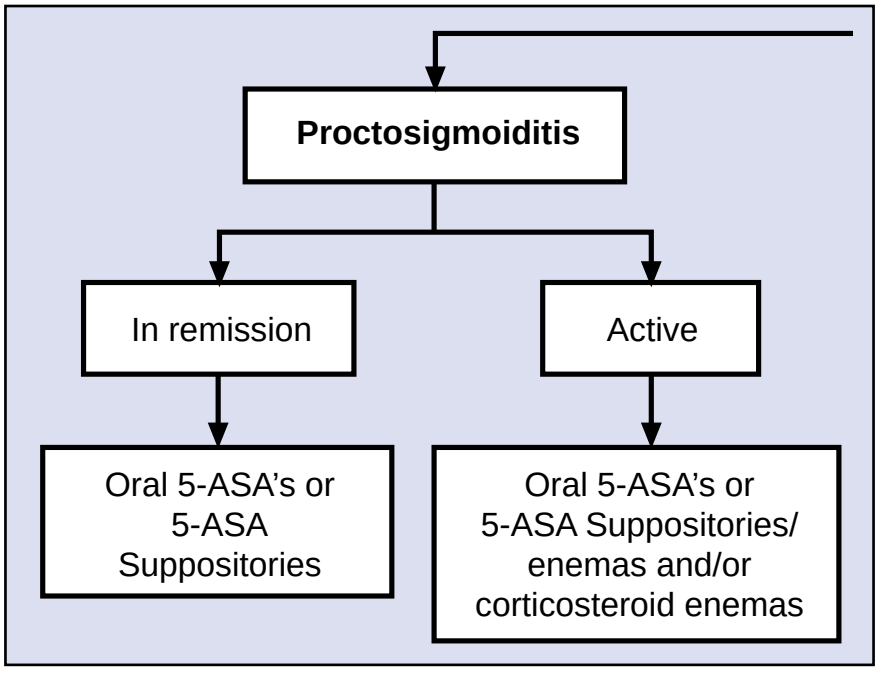
The evidence

In a managed care system that relies on scientific evidence, motivating on the basis of past usage would not generally be well received. Engaging with the PBM over this PMB would need a higher grade of evidence. In the examination, the students all quickly tracked down two relevant Cochrane Reviews.

In the first, Sutherland *et al* looked at the oral 5-ASAs for maintenance of remission.[11] Eleven studies, involving a total of 1 598 patients, had examined SASP and the newer agents. In 8 studies the dose of SASP was limited to 2g/day, and in one trial it was set at 4g/day. When the endpoint was defined as the failure to maintain endoscopic or clinical remission, SASP was superior to the newer forms of 5-ASA (odds ratio 1.29, 95% confidence interval 1.05 to 1.57). When 3 studies of lower quality were removed, the result was similar. However, when only those studies that assessed outcome at 12 months were included, there was no statistical difference (OR 1.15, 95%CI 0.89 to 1.50). When only the 5 trials with olsalazine (marketed in South Africa as Dipentum®) were considered, SASP was significantly better (OR 1.40, 95% CI 1.07 to 1.84). Looked at in isolation, this seems to back the hypothetical formulary choice. Adding to this view, the review could find no significant difference in side effect profiles between SASP and the newer 5-ASA delivery systems (such as mesalazine, marketed here as Asacol®). In contrast, olsalazine was associated with a greater number of treatment withdrawals, mostly due to diarrhoea.

The second Cochrane Review, by Sutherland and MacDonald, looked at the same agents used for induction of remission in ulcerative colitis.[12] When measured by the ability to achieve complete global or clinical remission, data from 6 studies comparing SASP and 5-ASAs showed no significant differences (OR 0.84, 95%CI 0.57 to 1.24). This was also not sensitive to the inclusion of poorer quality studies. The same held true when global or clinical improvement was reported. However, there was a significantly higher withdrawal rate associated with SASP in 7 studies (OR 0.34, 95% CI 0.25 to 0.57). Two of these were olsalazine trials, in which the difference was not statistically significant (OR 0.61, 95% CI 0.17 to 2.20). So, although efficacy seems to be comparable, it is possible to point to evidence of greater tolerability at higher doses, at least for mesalazine if not olsalazine.

Finding a meta-analysis is important, as smaller studies have sometimes shown quite different results, favouring one or other of these competing agents. Over-emphasis on the "sulpha" moiety in SASP has also diverted attention from the very real side effects of the newer 5-ASAs. However, if a full motivation for alternative choices were to be made, a number of other options might be explored, such as topical (rectal) preparations and corticosteroid enemas. Quality assessments of other reviews than those contained in the Cochrane Library can also be illuminating – for



Box 1: Excerpt from the ulcerative colitis algorithm (Council for Medical Schemes)

example, an NHS Centre for Reviews and Dissemination assessment of a meta-analysis that concluded that rectal 5-ASA is superior to rectal corticosteroids was criticized on methodological grounds, and the reviewers concluded that the original authors' conclusion could not be supported and that the review should be repeated.[13] A number of recent review articles can also provide good pointers.[14,15]

No motivation would be complete without mention of the costs involved. The results can be surprising. Enetric-coated sulphasalazine 500mg retails at R436.63 for 100 tablets. At the maximum dose of 2g given 6 times a day, a three-week intensive course would cost R2 200.62. By contrast, a maximal dose of mesalazine (4g/day) would cost R1 274.09 for a 3-week course. Mesalazine is sold in 400mg tablets, with 90 tablets retailing at R546.04, with VAT. Mesalazine is also available in suppository and enema forms. Steroid enemas are expensive, ranging from R88 each for budesonide to R101 each for prednisolone, the latter being given as often as twice a day.

Conclusion

While it is clear that family practitioners' independence cannot forever remain "inviolate", this should not mean that they have to abandon the medicines selection terrain entirely. Engaging with the new actors in this arena can be rewarding and can provide an opportunity to exercise new skills in critical appraisal, in evidence-based medicine, and in the careful consideration of efficacy, safety, suitability and cost. If all else fails, there are always clinical pharmacologists to call upon.

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