

Pharmacovigilance

Effective pharmacovigilance of CAT medicines presents a difficult challenge to all stakeholders in their development, manufacture, prescription and utilisation. The current drive by the Department of Health to develop regulations for the control of the CAT medicine industry will go a long way to improving their safety, quality and efficacy. Although this legislation is desperately needed and would add considerable confidence to this area of medical practice, ongoing pharmacovigilance will remain an integral component in supporting the safe and effective use of CAT medicines, particularly within the context of HIV and AIDS management. Health care professionals need to engage more actively with traditional healers and allied health professionals who serve their communities. Most importantly, they also need to ask their patients, in a non-judgemental way, whether they use any CAT medicines. In addition, any adverse event or suspected drug interaction involving CAT medicines must be reported to the National Adverse Events Monitoring Centre (NADEMC) using the standard yellow report form. Contact NADEMC at tel. (021) 447-1618 or fax: (021) 448-6181.

References available on request.

THE ARV PROGRAMME IN THE WESTERN CAPE: BEST PRACTICE

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After 3 years of pilot projects with highly active antiretroviral therapy (HAART), the Western Cape was able to roll out antiretroviral treatment throughout the province during 2004. The HAART programme started in May 2001, in Khayelitsha, in a joint effort between the Department and *Médecins sans*

Frontières. The roll-out began in earnest at the beginning of 2004, following the National Cabinet decision to fund a national HAART intervention in all provinces. The experience of working with antiretrovirals, both in the MTCT programme and the pilot antiretroviral sites, gave the provincial team a working knowledge of the numerous issues that arise in the provision of this intervention.

More than 7 500 patients are already receiving treatment in the province and at least another 5 000 are expected to be on treatment during 2005, accounting for the vast majority of people who need treatment.

Programming HAART for the public sector

According to the Provincial ARV plan, HIV care is to be provided at all health facilities up to and including testing the CD4 count of the patient. These include clinics (run by nurses) or hospitals.

If the patient is considered to be a possible candidate for HAART, he/she is referred to one of 36 sites where HAART is provided. Patients referred to HAART sites are worked up and prepared for treatment, usually over a 4 - 6-week period, and started on treatment with 3TC, D4T and efavirenz/nevirapine.

There are trade-offs to be made with the selection of sites. From a patient's point of view it would be ideal to have HAART at every clinic, community health centre and hospital in the province. The expertise, however, does not exist at all facilities to provide HAART, which should only be started by a trained doctor. Follow-up visits may be shared with nurses. In a province such as the Western Cape, where there are almost 2 000 doctors in the public sector, it would seem appropriate to engage this level of expertise.

Limiting the number of sites allows pooling of expertise and the opportunity to focus management and training. Treatment at regional or tertiary hospitals, in particular, where patients travel great distances, is likely to show

lower adherence rates as the linkages to psychosocial support programmes in the communities are fewer than in district hospitals or community health centres.

Limiting the number of sites aids the effort to prevent drug resistance. This is premised on the notion that having too many clinicians prescribing antiretroviral treatment encourages liberal prescribing practice, especially where there is patient and family pressure to initiate treatment when patients are not ready and at risk of non-adherence. Once again, the correct balance needs to be found between reaching as many patients as possible in the shortest time, and getting treatment right first time around. Patients who develop drug resistance are at risk of spreading resistant virus, thereby disabling treatment potential among new entrants onto the programme. Public health benefits of treatment are placed at risk with the widespread development of resistance.

With this in mind, the protocol to be followed in the selection of patients for treatment initiation is crucial. This must, however, be balanced with the rights of patients to treatment. Psycho-social criteria such as geographic access to the site, disclosure, past history of adherence to treatment, and literacy levels become important in the decision to initiate a patient onto treatment. Other factors such as alcohol or drug dependency and mental state are also important in the selection of patients for treatment. None of these criteria are exclusive. A global assessment of the patient by the clinical team must be done before a decision is made.

Lessons and challenges of expanded access

The logistics of setting up a HAART programme are complex, related in large measure to the unpredictability of the demand for treatment. We were able to predict the total number of patients needing treatment from a demographic and epidemiological model developed by the Actuarial Society of South Africa. The model is able to predict the proportions of people infected with HIV by stage of

disease, allowing for global estimates of patients requiring treatment for each year of treatment over a number of years.

The task of converting these estimates into site-by-site estimates proved more difficult and required some guesswork. In the Western Cape, antenatal prevalence data were available for each health district following 3 years of district level prevalence studies, and this allowed for broad estimates of high, medium and low prevalence areas for AIDS.

A process of consultation with site-based clinicians gave an indication of both capacity to take on patients and waiting lists at each site. Estimates for each site were then converted into site budgets for drug and lab costs. Staff requirements for each site were built up, taking into consideration the existing capacity and requested additional capacity and adjusting this for broad norms for different categories of staff. Numbers of patients initiating treatment during each month were calculated to ensure that the expenditure generated fitted globally into the available budget.

Working with partners has been a major success factor in the antiretroviral roll-out. This has been particularly important in the early days of the roll-out when the Department's capacity and experience with implementing and managing antiretroviral treatment was limited.

The Department supported research projects, particularly at the 3 academic hospitals. All of these partnerships were framed as operational research projects aimed at working out best practices in the provision of antiretrovirals in the public sector.

Management model

The management model of the antiretroviral programme has been hailed as an important factor in its success, and while supporting this view, it is not easy to describe the model accurately. As the clinical and scientific information on the treatment of HIV/AIDS is constantly being updated it

was necessary to bring clinicians closer to the policy-making process. This was made possible by combining managers and clinicians into a common decision-making structure that meets regularly and develops the main policies of the programme. Site managers and clinicians joined as new sites were activated. Managers learned about the clinical and 'coal-face' issues and clinicians began to appreciate the managerial issues relating to the budget, human resources, supply chain, the need for building the health system infrastructure.

Psychosocial support

There are different models for psychosocial support and it is difficult to draw conclusions about which of these are the most effective. In the case of Khayelitsha, patients are required to select a treatment coach who becomes the main individual in the psychosocial support component. This is backed up by site-based counsellors and support groups. Drug literacy programmes are also conducted with the patients and their treatment coaches. Good adherence has been shown after 2 years.

In Gugulethu, the model is very different, with lay counsellors who are community-based looking after up to 40 patients, doing home visits and unannounced pill counts. These counsellors are the patient's first port of call with any problems. The counsellors spend part of their time at the site and are involved in the clinic-based management of the patient together with the doctor and nurse. The number of counsellors in this model is a lot higher than in the Khayelitsha model and is probably much more expensive. Two-year adherence is also good here.

At hospital sites, patients are counselled by site-based counsellors and then referred to home-based care organisations in the community. These models are being evaluated and decisions will be made in the combined clinician-management-partner forum as to the optimal model at the best cost. The model will be carried through each

site and financed in a way that allows for strong systems to be built at the community level.

How can everyone be reached?

The most important weaknesses relate to the time it takes to get patients onto treatment at most of the sites. Patients have their clinical workup fairly quickly and if the CD4 count is below 200, they fall into the group to be started on treatment. The actual initiation of treatment is a longer process; it takes between 4 and 6 weeks to prepare the patient. As a result, most sites have between 20% and 40% of their patients waiting to start treatment. This is compounded by the shortage of doctors and nurses at most sites. These backlogs are the most difficult part of a clinician's experience at an antiretroviral site. There is concern that a patient may develop a serious opportunistic infection in this period. Large backlogs lead to delays in starting treatment. The mean CD4 count for patients initiating treatment in Khayelitsha during the first 2 years of the programme was 50, which is too low. This generally leads to a situation where patients on treatment have a high degree of acuity of illness and more complications, a greater number of hospital admissions and a higher mortality rate on treatment.

The addition of 4 doctors to the service in Khayelitsha has led to an increase of 89 in the mean CD4 count of patients starting HAART. Doctors and nurses here report that the patients are generally easier to manage now that treatment is started earlier, and that less time is spent on patients who are already on treatment. This means that many more patients can be seen, leading to an overall improvement of care at these sites. The backlogs create other difficulties. Pregnant women with CD4 counts of less than 200 cannot wait 4 - 6 weeks to start treatment, but need to start immediately. When they are referred to antiretroviral sites with large backlogs, clinicians are placed in an ethical quandary about whether pregnant women should 'jump the queue' in place of patients already worked up and waiting for treatment.

This has led to a slow start to providing HAART in pregnancy. Fortunately, the backlog will be temporary, since in the case of the Western Cape the backlogs should be made up over the next 6 - 12 months, after which patients' treatment will be initiated earlier and those patients who need to be fast-tracked, such as pregnant women, will not have their treatment initiation delayed.

More complexities...

There are many more complexities that need to be understood and unravelled in the course of implementing an antiretroviral treatment programme. As many as 10 - 15% of patients requiring antiretrovirals will need referral to a specialist centre for specialised investigations before they start treatment, or for the management of immune reconstitution inflammatory syndrome (IRIS) or serious side-effects. Secondary and tertiary expertise is also crucial in providing clinical support,

outreach clinics and training to staff at the community health centre or district hospital level where the majority of patients should be on treatment.

The lack of infrastructural readiness of the facility has also been an issue at almost every site. This has mainly referred to the need for additional consulting rooms, counselling facilities and pharmacy infrastructure (additional space, systems, staff and equipment and fittings). As the public service is notorious for its slow response to building works, this is a problem most sites live with and it is generally 2 - 3 years before renovations are done or new facilities built.

CONCLUSION

After 3 years of pilot projects and another full year of rapid scale-up to the level of a province-wide HAART capability, the Western Cape has learnt many important lessons about the

challenges of such an addition to the package of care offered in the public health service.

We are certain that HAART is more effective at community health centres or district hospital levels where the synergies of providing treatment by skilled doctors and nurses can be combined with all-important community-based psychosocial support programmes aimed at enhancing adherence.

The most important lessons that have been learnt from the HAART roll-out in the Western Cape include the importance of flexibility, the importance of trust established through partnerships, communication with and involvement of clinicians and other health workers in the roll-out effort, and the impact that the availability of HAART has had on the morale of the clinicians throughout the public health sector.