Initiation of antiretroviral treatment for HIV infection. Studies in the general practice

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The situation with regard to the treatment of HIV-infected persons has changed dramatically between 1994, the year the HIV Intervention Study was designed, and 1997, the end of this study (general introduction; chapter I).

The first Dutch treatment recommendations, issued in 1991 by the AIDS specialists, were primarily based on the fact that AZT monotherapy could delay disease progression and prevent AIDS dementia complex. At that time, however, there were still many questions and uncertainties, and several large trials studying the efficacy of this form of treatment were still in progress.

In 1993, the results of one of these studies, the Concorde trial, demonstrated the ineffectiveness of AZT monotherapy on survival. These findings led to a general feeling of pessimism among doctors and patients and to a decline of AZT prescriptions. The transient benefit of treatment had to be weighed against its disadvantages.

The prevailing opinion in the Netherlands at that time was that it was justified to delay the initiation of therapy. This view was also reflected in the HIV-testing policy: as long as there was no effective treatment there was no real advantage of knowing one’s HIV status. The poor adherence to the Dutch treatment recommendations in 1994 (chapter II) and the rather negative attitude towards antiretroviral treatment of - in particular - the homosexual GPs at the start of our study in 1995 (chapter III) is understandable against this background. Our findings in primary care were consistent with data that were collected in 1993 and 1994 on 183 patients at the moment of their AIDS diagnosis in three Amsterdam hospitals. These data showed that at that time 38% of the patients did not know or did not want to know their serostatus, and that 61% of these AIDS patients had not used any form of pre-AIDS treatment.

At the end of our study the circumstances had changed completely. There was a better understanding of the HIV pathogenesis, and with the availability of protease inhibitors it had become possible to almost fully suppress viral replication. Although at first the clinical implications of undetectable viral load levels could only be anticipated, the virologic and immunologic results of triple-drug combinations including a protease
inhibitor were so overwhelming that they led to a revision of the treatment strategy in most countries, including the Netherlands, in the summer of 1996. Soon the positive effects of this new form of treatment became evident: since its introduction morbidity and mortality from AIDS have declined significantly.\textsuperscript{11,12}

In this thesis we have shown that, despite better treatment options, patients in 1997 generally still did not start treatment in accordance with the Dutch consensus recommendations of 1996\textsuperscript{13}, which advised to start therapy in the presence of a viral load > 10,000 copies/ml, a CD4+ cell count < 500 x 10\textsuperscript{6}/l, or HIV-related symptoms (chapters IV, VI & VII).

On the one hand, this poor adherence to the revised treatment recommendations may be considered to be a direct consequence of the restrictive HIV-testing policy in the Netherlands. Probably as a result of this policy, many patients were already in an advanced stage of the disease when they found out about their serostatus and presented at the HIV clinic (chapter VII). From a public health point of view, this is an important finding. The HIV-test should lose its taboo and become a routine diagnostic procedure for patients at risk now that an effective treatment is available for this infectious disease. A more active testing policy, which was ultimately recommended by the Dutch Health Council early in 1999, will hopefully result in a higher detection rate of HIV infection in an earlier disease stage.\textsuperscript{14}

On the other hand, it appears from this thesis that there was a delay in the initiation of antiretroviral therapy in a considerable proportion of patients diagnosed as HIV-positive once the criteria for treatment had been met (chapter IV). Although the GPs in this study did become much more positive about antiretroviral treatment over the years, largely as a result of the positive news about triple therapy, they still did not unanimously favour treatment of asymptomatic patients with CD4+ cell counts > 300 x 10\textsuperscript{6}/l in the beginning of 1997 (Chapter III). From this, one could conclude that they were somewhat lagging behind the AIDS specialists.\textsuperscript{15}

The GPs in our study were experienced in HIV care and could thus be expected to be knowledgeable about its treatment. The fact that their view on treatment differed from the view of the AIDS specialists should therefore probably be considered in light of the more commonly existing differences between generalist and specialty care. From a review paper on this subject by Donohoe appears an underuse of medication for a number of conditions by generalists.\textsuperscript{16}

In addition, GPs were found to adopt new treatments for HIV at a slower rate than AIDS specialists.\textsuperscript{15} Generalists, who provide more longitudinal care, may be more averse to prescribing medication that may possibly be harmful for the patient than specialists. This idea is supported by the fact that specialists were found to attach more importance to the beneficial aspects of hypertensives than generalists, who in turn showed greater concern for the possible adverse effects of these drugs.\textsuperscript{17}

Triple therapy for HIV infection indeed has several important drawbacks, and it is therefore not unlikely that GPs are more averse to recommending such treatment than
AIDS specialists. There have been some improvements, but initially dosing schedules of the prescribed drugs were so complex that adjustments to the routines of a patient’s daily life were frequently required. Strict adherence to the dosing instructions is necessary to prevent drug resistance. Side effects can be frequent and very serious and there is no certainty about the long-term effects of the drugs which, as it appears, will need to be taken for life.\textsuperscript{18-21} Although viral activity can be suppressed completely with the current potent therapy, HIV can still not be eradicated completely as virus has been found ‘hiding’ in the lymphoid tissue and central nervous tissue.\textsuperscript{22,23} It is therefore expected that, after an induction phase with triple therapy, ongoing treatment with a (possibly less intensive) maintenance therapy will be necessary in order to achieve a sustained effect. Last but not least: based on current knowledge of the HIV infection it is assumed that starting early is better than deferring treatment. There are still no clinical data supporting this assumption though; GPs may be inclined to await the clinical proof before they will comply with the treatment recommendations.

The fact that the GPs in our study were not explicitly positive about early treatment is likely to have played a role in our findings. It may be hard, for instance, to advise asymptomatic patients to initiate therapy when one is not convinced about the benefits of (early) treatment. From the seemingly contradictory observation that patients who had reported to have received sufficient information on HIV-related issues from their GP were less likely to start therapy than patients who had a desire for more information (chapter VI), one could deduce that the information the GPs had provided was biased. In any case, in the population that we studied decisions on treatment were seldom made by the GP alone.

Based on information provided by both the patients and their GPs, one of the conclusions that can be drawn from this thesis is that the patients actively participated in the decision-making (chapters IV & VI). Our study was performed in a sample of mainly homosexual, well-educated men with an average age of less than forty years, and confirms the results of several other studies in which younger age, higher education level, and worse prognosis have previously been identified as factors that are positively associated with patient participation in the decision-making on treatment of conditions other than the HIV infection.\textsuperscript{24-27}

The patient’s attitude towards therapy appeared to be a very important independent predictor of treatment initiation once qualifying for therapy. Patients who had a negative attitude before meeting the treatment criteria were less likely to start when qualifying for therapy as compared to patients with a neutral, or positive attitude (chapter V).

As has been described in the introduction of this thesis, the literature on the relation between disease stage (asymptomatic or symptomatic) and acceptance of treatment is scarce and inconsistent. In our study, we found that a generally more positive perception of their health prevented patients from starting with treatment, rather than the fact that they were asymptomatic when they met the criteria for therapy (chapter V).
The importance of patients' attitudes towards therapy and of their health beliefs for accepting HIV therapy and for adherence to treatment recommendations has previously been reported on in the literature (general introduction; chapter I). However, unlike those others we analysed data that were collected before patients met the criteria for treatment. Our findings suggest that patients' views on treatment are formed in an early stage of the illness, and therefore stress the importance of this stage for the decision-making on the initiation of therapy.

With regard to their reasons for rejecting or delaying treatment patients in this study did not differ from patients that have previously been described by others (general introduction; chapter I): a perceived lack of efficacy, a perceived lack of benefit at this stage of the disease, the risk of side effects, and uncertainty about the long-term effects of therapy prevented them from starting. However, within the group of patients who did finally start treatment we observed a high level of satisfaction with triple therapy after six months of treatment, despite initial reservations about therapy (chapter VI).

It may be that both the fact that these patients had actively participated in the decision to start, and the fact that by delaying treatment they had had plenty of time to consider and finally accept the possible disadvantages of therapy, has contributed to their positive attitude. Future research should be aimed at determining the relative importance of these factors. In view of the need for maximal adherence to triple therapy, it will be important to try and confirm the assumption that patient involvement in decision-making can be associated with a greater commitment to the agreed upon treatment.

In conclusion: current Highly Active Antiretroviral Treatment (HAART) has a positive effect on survival, but without doubt has several serious disadvantages as well which may prevent patients from taking it. Nevertheless, it seems not more than reasonable that every HIV-infected person will at least get the opportunity to make a well-considered decision whether or not to start (early) with HAART.

Given the fact that it takes time to make a well-considered decision on a complex issue like the initiation of antiretroviral therapy, it is important that physicians (GPs and specialists) explore the attitude and perceptions of their individual patients with regard to the disease and its treatment in an early stage. By providing more tailored information and support to (in particular) patients who have proven to be less likely to start with therapy, physicians may be able to influence the decision-making of these patients so that they also will make a well-considered start, in accordance with the treatment recommendations. If a patient decides not to want treatment, the physician should be assured that this decision was a well-considered one too.

This implies that patients will have to be tested early. Furthermore, it implies that GPs will have to know and acknowledge the current treatment recommendations. In case a GP does not approve of these recommendations, or feels he or she is lacking the skills or knowledge needed to guide the HIV-infected patient in the process of decision-making
on antiretroviral therapy, he or she should not hesitate to refer the patient to a GP who is
more experienced in HIV, or to consult an AIDS specialist.

Our recommendations with regard to the decision-making on antiretroviral treatment, finally, naturally follow from the current views on shared decision-making during the physician-patient encounter. In the shared decision-making model the exchange of information is two-way, and the content of the information is both medical and personal. The subsequent deliberation and deciding on the to be implemented treatment, furthermore, are processes in which both the physician and the patient take part.  

References


