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AIDS and Drug Rationing

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Abstract

Financial shortage in resource-limited and poor countries restricts treatment in HIV-infected patients especially in poor countries. Higher HIV prevalence in poorer countries makes drug rationing a real concern. Different countries solve the problem with different methods regarding WHO guidelines, but fairness and equity should be a major consideration in drug rationing. This paper is aimed at reviewing different strategic approaches to drug rationing in AIDS treatment and then discusses pharmacists' role. In conclusion, there is no fair and equitable strategy, and in each society, cultural, ethical and socioeconomic issues along with considering a critical role for pharmacists must be taken into account.

Keywords: *AIDS, ethics, rationing, pharmacist*

Introduction

Fairly distributing scanty and /or costly medications is considered a major challenge in health care. In a perfect world, providing all effective medicines for all human beings who need them shall be a routine. But financial shortfalls put every health care provider on a dilemma about providing the best medical interventions for the most deserving patients and at the real time. With continuously increasing numbers of human immunodeficiency virus (HIV)-infected patients, resource limitation plays a major role in community health. Financial shortages limit the number of patients who are eligible for anti-retroviral therapy (ART) even in the most conservative arena. Making decision in such situations is called rationing which was considered for scarce resources. The excess of demand versus supply, makes rationing inevitable. Developing countries are dealing with the availability of ART as a major public health concern. As long as financial shortfall is a major problem, drug rationing is a rational decision; however, some critic the uneven resource allocation (1). The aim of this paper is challenging ethical and practical issues of drug rationing in HIV positive patients and presenting the other ways which help us treating patients in the best way and at the proper time.

Epidemiology

According to the United Nations Joint Programme on HIV/AIDS (UNAIDS) report on global acquired immune deficiency syndrome (AIDS) epidemic, it was estimated that there were 33 million people living with HIV all over the world in 2007; and 2.0 million people died due to AIDS in 2007. South African countries have the highest incidence of HIV infections and the highest rate of death (35% of HIV infections and 38% of AIDS deaths in 2007) in the world. UNAIDS estimated the number of people receiving antiretroviral drugs in low and middle income countries in the end of 2007 to be 3 million individuals (2).

Regarding the high rate of HIV positive patients as well as the high rate of death in this population, especially in low-income countries, providing the most efficient treatment modalities is necessary. This led to establish the “3 by 5” Initiative of the World Health Organization (WHO) in order to put 3 million people on treatment by 2005 (3).

At the close of 2008, WHO estimated the number of AIDS patients in need of treatment about 9.5 million people, from whom only 42% had access to treatment (4). Considering the latest WHO reports in Sep 2009, scaling up priority HIV interventions, led to 36% increase in receiving ART in one year.

In Iran, according to the Ministry of Health and Medical Education's report in January 2008, the number of people with advanced HIV infection and the number of people receiving ART was 8730 and 829 individuals, respectively, while the percentage of HIV positive patients, who received antiretroviral therapy, was only 9.5%. Also the number of HIV-positive pregnant women in 2006 and the number of pregnant women who received ART for prevention of mother to child transmission was 220 and 22, respectively (5).

Treatment Modalities

Today we are passing 13 years since marketing potent ARTs which led to a significant decrease in AIDS and a change in the quality of life and survival of AIDS patients (6, 7). In this setting, resource shortage led to rationing medications; therefore, only the first line therapy can usually be ordered (8, 9). First line medications consist of a combination of a non-nucleoside reverse transcriptase inhibitor (NNRTI) and two nucleoside analogue reverse transcriptase inhibitors (NRTI). Second line treatment is often offered after treatment failure with first line medications and a proton pump inhibitor (PI) is recommended which is more expensive. Unfortunately, a high proportion of HIV infected patients develop treatment failure with first line treatment and need a PI (10). Therefore, it is tough to decide when to start second line treatment and how to provide it.

Regarding the WHO guidelines, ART can be used when the patients’ immune system is highly jeopardized (CD4 cell count of 200 cells per µL or showing constitutional symptoms) (11). Actually, there is a question under debate about the best outcome and the time of treatment initiation. Medical criteria alone are not useful in starting ART and socioeconomic contributory factors should be taken into account. In one study in South Africa, the researchers found that if the treatment begins at a less conservative CD4+ count (350 cells per µL as guided by US Department of Health and Human Services); the percent of eligible patients for therapy escalated from 9.5% to 56.3% (12). Abbas et al. found ART benefits for infected subjects as well as the uninfected individuals by decreasing mortality and disease transmission respectively (13). They reported larger individual and population advantage in early diagnosis and treatment which is in agreement with former findings (14).

The last WHO guideline considers treatment initiation at CD4+ count 200-350; however, the stage of the disease should be taken into account for decision-making (15). Taken these into consideration, the question is “How we can ration ART in the best possible way?”

How to Overcome the Complexities

Scientific facts and ethical judgment are needed for solving the problem. The nature of the disease in addition to the specific features of HIV positive patients (addiction, having dangerous sexual behaviors) and patients compliance are major points which have to be regarded for rationing medications. The scaling up priority includes HIV testing and counseling (free HIV testing is possible through public sector in some countries), preventive measures to limit mother-to-child transmission, and drug availability by lowering prices of the most first line regimens by 10-40% between 2006 and 2008, while the second line regimen is still expensive (16). Different methods of rationing drug therapy will have different socioeconomic consequences particularly in the high risk populations. Obviously, there is no unique method which can consider all contributory factors, so different approaches should be implicated in different situations and the mentioned methods may be regarded at the beginning. In continuation, some points should be considered a light shed to predict the pitfalls and prevent them. Therefore, the treatment efficacy should be defined at first as suppressing viral load or increasing CD4+ count in a continuous manner.

Adjusting Care Models

Making provisions for maintaining access to ART in developing countries needs adjustment of care models regarding the actual facts of these regions. Different countries manage the problem in different ways. While some are negotiating for receiving additional funds, others develop special policy in reprogramming patients' access to drugs. Limiting patients' access to medications such as protease inhibitors or other antiretroviral medications, and keeping patients in the waiting lists are some examples (17, 18).

Some countries compile policies and programs to determine the prior patients for treatment. The most known program is mother-to-child transmission (MTCT) MTCT-Plus, which prefers HIV-positive mothers of new infants in addition to skilled workers. The reasons behind this program are preventing mother to child transmission and preserving economic growth. Some governments prioritize health care workers while some others prefer treating poor patients (19, 20). Sometimes, programs and policies do not consider special socioeconomic group, but impede drug availability in the areas with high rate of HIV-infected patients, or oblige patients to make copayments (16). Targeting high risk group of patients impose some limitations because, mostly, their identification is not easily possible and this term in high prevalence populations like African countries does not make sense (21).

Some consider virological core groups who have a high viral load. These patients may belong to the late stage of the disease or early infected subjects. They suggest the advantages of this method as increasing treatment equity, the epidemiologic efficiency, and feasibility (21), but providing access to potent medications too late (patients at the stage III/IV, very low CD4 counts) may result in patients' death in the first 6 month after drug initiation (22, 23). However, the early mortality suggested as being multifactorial includes severe immune deficiency, new or undiagnosed opportunistic infections, nutritional deficiencies, etc (24).

Economical Solutions

In every threatening infectious disease, policy of healthcare system about distribution of scarce or expensive medications is highly critical because the system encounters two groups of people: patients and healthy people who are exposed to the danger. In the recent years, the increasing number of HIV positive patients has imposed additional economic burden on the low income governments.

Some governments consider AIDS treatment as a major priority which forces them in absorbing international funds to increase the number of treated patients. After 2002 on, fund mobilization into ART treatment by governments and international donor contributions were considered to be useful ways of treating HIV positive patients especially in African countries. However, this high amount of money paid in this way, confronted countries with lack of financial resources for treating other medical conditions (25).

Resource allocation can be viewed from different points. As it is a determinant factor in successful treatment and prevention of the disease in especially poor countries, it should be noted that many contributory factors can affect its efficacy. Zaric et al, defined the way of resource allocation and its proportion to HIV incidence and prevalence as a determinant in HIV preventive medicine (26). They designed a multilevel allocation in the following study by considering the role of decision-makers (27).

Practical obstacles

Providing ART at a late stage or using expensive medications after treatment failure create many practical difficulties which need special attention.

While scaling up treatment raised issues about drug resistance, detecting primary and secondary drug resistance seems to be a public health challenge (28, 29). Drug resistance has potential impact on the outcome and patients' compliance and their socioeconomic standing can affect it (30). Lack of budget for referring to the AIDS clinics for receiving medications, doing lab tests, and also the low patients compliance and adherence to treatment, raise the issue of resistance more seriously. There is a significant difference in patient's adherence to therapy between developing and developed countries (31) and it can play a crucial role in emerging resistance.

However, Walensky et al. studied the importance of resistance surveillance as a guide in treatment plans, but they found drug costs and efficacy as a major influencing factor on treatment policy rather than resistance (32).

In this field, the type of medication seems to be crucial. It is noteworthy that failure of PI-based regimens causes slower disease progression than NNRTI regimens (33, 34). This phenomenon may be due to the differences in basic immunologic response of the patients to these two classes of drugs (35, 36). In addition lateness treatment modification after failure of NNRTI regimens increase risk of immunologic failure and mortality (37).

Ethical Issues

The most critical issue in the HIV drug rationing and also medical interventions is observing ethical issues which give legitimacy to the act. Along with the four ethical principles: beneficence, non-maleficence, justice, and autonomy; patients' dignity and patients' right should be regarded as the most significant ethical issues in health care.

Scaling up HIV treatment, equity, justice and fairness enjoys special importance while human rights and its international norms, standards and instructions are taken into account more specifically.

Regarding the WHO and UNAIDS recommendations, efficiency and fairness are two main fundamental issues in treatment initiation in resource- limited settings (38). No doubt, drug therapy in HIV-infected patients have great profits for both patients and the society, while the time of initiating drug therapy more complicates the balance between beneficence and non-maleficence. But as discussed before, and according to the WHO criteria, in rich regions, the medical treatment does not delay until CD4+ count of ≤200 or late stage of the disease. Starting treatment at these conditions not only renders difficulties in patients' improvement, rather brings resistance and opportunistic infections into account. Therefore, the principles of beneficence and non-maleficence more affirm the necessity of starting treatment as soon as the disease is diagnosed. Also treating HIV-positive pregnant women at the right time and by proper medications more emphasizes patients beneficence. But we should be aware of the best approach for drug rationing in order to minimize harms.

As far as delayed or restricted availability of HIV treatment demolish patients' survival in all age groups, children are notably sensitive. In adults, the transit time from HIV infection to AIDS is about 8-10 years, while, without effective treatment, more than half of all HIV positive infants pass away before their second birthday (39, 40).

Early HIV diagnosis and treatment was confirmed by researchers (41, 42) while some of the studies could not find any higher survival with highly active antiretroviral therapy (HAART) initiation at CD4 counts of above 350 cells/µL (43). Also the probability of recovering CD4 counts to high levels increased when HAART starts during primary HIV infection (PHI) in comparison to chronic infection (44). Therefore, the need for further evaluation and possible revision of WHO guidelines is fairly advisable.

Also the term of justice might be considered in patients' selection. Justice in patients care is defined as making provisions for providing identical patient care facilities when there is insufficient supply. In resource-limited settings, patients do not have the right to take all their health care needs, however, there is a limitation. Morally, health care providers' duty is to provide the health services as much as possible in order to preserve patients' health and function. Therefore each limited chance for living should be respected. In this setting, patients prioritizing are an important issue and should be done based on the disease severity, prognosis, etc, as well as preventive measures which more complicates the dilemma. Daniels et al. presented the justice framework of accountability for rationality. He defined special situations in which the equitable decision is made; therefore, the decision will be accepted by the majority. Instead of discussing about disagreements on decision making, he verifies the bases of it (45). Taken together, justice should be considered in the center of moral judgment.

In terms of autonomy and limited resources, time shortage for diagnosis more confirms the negligence of patient's autonomy (46).

Other than the above-mentioned criteria, feasibility, economic efficiency, equity, rationing potential on disease transmission, ethical issues and sustainability should be respected in each rationing system (25).

Supporters of scaling up ART treatment believe that there should be no charge on ART. In some poor areas, the patients cannot pay the cost of even transfer to a doctor's or they have to stay waiting for physicians/ pharmacists visit. Therefore, there are controversial views about the balance between equity and sustainability.

Clinical Pharmacist's Role

The critical role of pharmacists in health care system has to be considered as a unique duty which is mixed with ethical concerns.

A pharmacist who dispenses medications can modify the drug rationing in the best way which helps both patient and the health care system. Although lowering drug costs is one of their responsibilities in the world, the propagatory role of pharmacists in protecting pharmaceuticals profits weakened their crucial duty (47). This type of conflict of interest is always questionable and yet has not been resolved. Instead, it can be expected that pharmacists always play their primary role as patients' supporter which necessitate their active contribution in promoting health interests. Using combination products is a useful method in reducing drug costs and increasing patients' adherence to therapy.

Reviewing drug regimens thoroughly, and regularly by a pharmacist may assist in choosing the best candidate for drug therapy according to the patients status, compliance and adherence; determining treatment failure, side effects, and making sure about the right medication. By reviewing drug regimens, drug resistance and side effects will be diagnosed earlier which prevents money wasting or imposing more economical burden on patient or community. The complexity of HIV-treatment because of existence of the other opportunistic infections in AIDS such as tuberculosis, pneumonia, etc makes drug interactions a serious matter of concern. Evaluating patients profile will help determine any drug interactions especially with

HIV medications which are a potent drug class influencing enzymatic metabolism of drugs.

Reducing the dose of ART and/or particularly PI is another method which reduces the costs of ART. Several studies and clinical trials have been conducted all over the world, which show promising results even in patient's tolerance, but it needs more evaluation (48-50).

Conclusion

Finally the important things that has to be figured out in treating HIV-infected patients successfully, are providing medications accessibility with low cost, reducing the long-term effects of HIV on socioeconomic development, and putting all eligible patients under treatment. Patient's eligibility should be evaluated by scientific facts and moral judgment. Thus, the importance of ethical issues in HIV drug rationing should not be ignored or underestimated.

Taken together, drug rationing must be considered as a rational way for treating HIV-infected patients in resource-limited settings; however, many criteria should be considered and/or revised for rationing and no method is completely fair and multilateral. Putting all principles (scientific and ethical) together increases the intricacy and debates around the matter. While regarding ethical judgment seems necessary in finding the best way of scaling up ART with the least harm, illuminating, and assessing health care systems output deem advisable.

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