Drug Resistance ← Pt / policy / system / buy.

NTI BULLETIN 1993, 29/3&4, 45-47

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MULTIDRUG RESISTANCE OF TUBERCLE BACILLI*
Facts and Implications for National Programmes

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Several recent publications, especially from the US, indicate a rising number of tuberculosis cases caused by multidrug resistant strains in hospitals, AIDS treatment centres and prisons and among alcoholics, drug addicts and the homeless who are very often infected with HIV[1-18].

In many instances there is acquired resistance resulting from treatment failures or relapses due to disorganized treatment programmes which do not respect the universally accepted principles of chemotherapy, which involve taking a correct combination of medications for a sufficient period of time: these principles are not followed by high risk groups which contribute the majority of tuberculosis cases in industrialized countries. This poor compliance explains the rise in prevalence of acquired resistance.

These strains (whose multidrug resistance is ignored or has only been lately recognized) will cause transmission of infection, facilitated by the crowded conditions in which these patients live. In addition these multidrug resistant cases remain contagious for prolonged periods due to inefficient chemotherapy and failure to isolate them[19]. The rate of transition from infection to disease increases, especially among patients with immunodeficiency associated with HIV infection: multidrug resistant bacilli will be isolated from these patients who have not previously been treated with chemotherapy. This explains the rising initial resistance to one or several drugs, mainly observed in New York for example, where it rose from 10% in 1982-1984 to 23% in 1991[18], though it had steadily decreased in the US between 1975 and 1982[20]. An increased rate of initial resistance had already been observed in children in Brooklyn in 1981-1984[21].

With an overall level of resistance (initial and acquired) of 33%, case fatality of tuberculosis is alarming, reaching 27% after 9 months' follow-up in patients in New York City[18]. For the US as a whole, nearly 90% of resistance appears in HIV positive patients with a case fatality rate of 70-90% four to sixteen weeks after diagnosis[19].

This disaster is not surprising considering that resistance to isoniazid and rifampicin has reached 19% of the isolates in New York[18], and that 42.6% of the tuberculosis cases aged 30 to 44 are HIV positive. It is well known that dual resistance to isoniazid and rifampicin compromises the results of chemotherapy, and how disappointing the lack of compliance among high risk groups is: those leaving hospital in an improved condition often stop taking the drugs and will be rehospitalized when their condition worsens again.

Data from well organized national programmes in Algeria[22], Korea[23] and South Africa[24] provide the direction as to how to address this problem: in these programmes, there has been a decrease in initial and acquired drug resistance in recent years.

In Korea rates of initial resistance to any single drug have declined from 30.6% in 1980 to 15% in 1990; acquired resistance has declined in the same period from 75.4% to 46.8%, multidrug resistance (≥ 3 drugs) was found only in 4.7% of newly found cases and 12.9% in old cases. These results were achieved when the National Programme recognized the problem, placed high priority on achieving good results of chemotherapy in the initial treatment of cases and provided the means to carry it out. A similar concentration on good results of initial treatment has achieved the same results in Algeria: the rate of acquired resistance fell from 81.9% in 1965-67 to 35.7% in 1981-85, and primary resistance from 15.0% to 6.3% in the same period[22].

The best policy in regard to drug resistance is to prevent its development in the first place. This approach has been clearly demonstrated in Tanzania, where initial resistance to isoniazid has been stable between 1968, 1978 and 1988, at between 5 and 8%. Acquired resistance was 41% in treatment failures and 59% in relapses[25].

* From the IUATLD Newsletter - June 1993

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The relation between HIV infection and drug susceptibility has been studied in Zaire. In Kinshasa, the rate of initial resistance to H was 19.5%, to H and R 0.9%, to one drug 22%, to 2 drugs 1.8%, and to 3 drugs 0.9% in 349 samples of consecutive cases[26]. In this study there was no significant difference in resistance between the 218 seronegative and the 131 seropositive patients: these results indicate that the development of drug resistance in the United States is unlikely to be directly related to HIV. These still relatively low rates of initial resistance in Africa promise excellent treatment results, given that resistance to H, S and even SH induces only few failures when an initial four drug regimen, HRSZ or HRSE, is used[27]. The success of such programmes is built upon ensuring strict control of the use of rifampicin and the provision of an adequate and complementary retreatment regimen.

In IUATLD programmes, the use of rifampicin is restricted to the initial phase where drugs are given strictly supervised; this eliminates the risk of development of resistance to rifampicin in the continuation phase (often less well supervised) due to bad compliance.

In future, the highest priority must be to avoid the development of resistance within National Tuberculosis Programmes. This can only be achieved by a regular supply of all the essential drugs[28], strict control of the use of rifampicin, strict observation of its administration and use in combination tablets and the prohibition of sales of the drug in the private sector in conjunction with the use of an adequate retreatment regimen. The very high cure rates which can be achieved in initial chemotherapy[26,29] are essential to the prevention and reduction of resistance. In this regard, the strengthening of National Programmes and the application of the principles of the IUATLD model in tuberculosis programmes is of the utmost importance.

An improvement of the situation in the US and its prevention in other industrialized countries required a better awareness of the tuberculosis problem in the general public and among health professionals. Attention to the basic principles of tuberculosis control and the provision of adequate material support is needed.

The solution to the tuberculosis problem must be tackled internationally, given the level of migration from the south to the north and the need for economic assistance from the north to the south.

The global interdependence that has already been demonstrated in the clinical trials which resulted in modern chemotherapy is again put to the test with the problem of multidrug resistance.

Acknowledgement

I would like to thank Dr. Y.P. Hong, from Korea, for his pertinent comments which have been integrated into this article.

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